


Relative associations of abdominal and thigh compositions with cardiometabolic diseases in African Caribbean men

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Abstract

Background: Regional body compositions are differentially associated with cardiometabolic risk factors. Simultaneous inclusion of both upper and lower body composition predictors in models is not often done, and studies which do include both measures (1) tend to exclude some tissue(s) of potential metabolic relevance, and (2) have used study populations with underrepresentation of individuals with African ancestries. Further, most body composition analyses do not employ compositional data analytic approaches, which may result in spurious associations.

Objective: The objective of this analysis was to assess associations of abdominal and thigh adipose (AT) and muscle tissues with hypertension and type 2 diabetes using compositional data analytic methods.

Research Design and Methods: This cross-sectional analysis included 610 African Caribbean men (median age: 62 years; mean BMI: 27.8 kg/m²). Abdominal (three components: subcutaneous [ASAT] and visceral [VAT] AT, 'other' abdominal tissue) and mid-thigh (four components: subcutaneous and intermuscular AT, muscle, bone) compositions were measured by computed tomography; additive log ratio transformations were applied to each composition. Regression models were used to simultaneously assess associations of abdominal and thigh component ratios with continuous risk factors (blood pressures, fasting glucose and insulin, HOMA-IR) and disease categories.

Results: A two-fold increase in ASAT:'Other' ratio was associated with higher continuous risk factors and with odds of being in a higher hypertension (OR: 1.77, 95%CI: 1.10–2.84) or diabetes (OR: 1.81, 95%CI: 1.06–3.10) category. A two-fold increased VAT ratio was only associated with higher log-insulin and log-HOMA-IR ($\beta = 0.10$, $p < 0.05$ for both), while a two-fold increased thigh muscle:bone ratio was associated with a lower diabetes category (OR: 0.37, 95%CI: 0.14–1.01).

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Conclusions: These findings support ASAT as a significant driver of cardiometabolic disease in African Ancestry populations, independent of other abdominal and thigh tissues.

KEYWORDS

body composition, hypertension, type 2 diabetes

1 | INTRODUCTION

The regional growth of adipose tissue (AT) is a major risk factor for cardiometabolic diseases such as hypertension and type 2 diabetes. Simultaneous comparisons of the effects of upper- and lower-body compartments with type 2 diabetes indicate harmful effects of upper-body AT accumulation and protective effects of lower-body AT accumulation.¹ Imaging methods such as computed tomography (CT) can identify different ATs and muscle groups within scanned regions, allowing for assessment of tissue-specific associations with cardiometabolic disease. Upper body abdominal subcutaneous (ASAT) and visceral (VAT) ATs are both associated with increased risk of hypertension and diabetes, with VAT associations tending to be stronger.²⁻⁶ Within the thigh, results are more mixed. High subcutaneous AT (TSAT) is not significantly associated with hypertension,^{5,6} while TSAT and muscle appear to be mostly protective against type 2 diabetes and related biomarkers.⁷⁻¹² The impact of thigh muscle may even have opposing associations seemingly due to effect modification by obesity status.^{9,13} Lower body intermuscular AT (IMAT) is generally positively associated with type 2 diabetes status^{7,8,10,14-17} and with hypertension.⁵

It is important to note that the above studies may have lacked CT scans of either the abdomen or the thigh, or if both were present, that final models may not include all measured abdominal and thigh tissues. The exclusion of metabolically relevant tissues can lead to an incomplete picture of the associations of regional tissue accumulation with health. Additionally, individuals with African ancestry are underrepresented in studies including both abdominal and thigh CT scans. African ancestry individuals have different AT distributions (greater ASAT¹⁸⁻²⁰ and IMAT,²¹ lower VAT¹⁸⁻²⁰) when compared to European ancestry counterparts. There are also racial/ethnic differences in the contributions of specific tissues to cardiometabolic health, with ASAT having greater importance compared to VAT in African ancestry populations.^{22,23}

A further limitation of previous studies is in the analytic treatment of body imaging data. Compositional data are defined as components which sum to a whole, and as such, they have an inherent correlation structure so that in order to hold size constant, an increase in one component must come at the expense of at least one other component.²⁴ Therefore, ignoring this inherent correlational structure can result in biased and misleading estimates. Compositional data are more appropriately modeled after application of a compositional data analysis (CoDA) transformation, which effectively removes this correlation structure.²⁴

Body composition CT data are compositional data, as they investigate components (various tissues) which sum up to a whole (the total scanned area). However, while health sciences fields such as high-throughput sequencing,²⁵ physical activity,²⁶ and diet²⁷ are applying compositional approaches to their data, few studies^{28,29} have applied compositional methods to body composition data. This analysis uses a cohort of African Caribbean men that has both abdominal and thigh CT scans. A CoDA approach was used to compare the simultaneous associations of abdominal (ASAT and VAT) and thigh (TSAT, thigh IMAT, and thigh muscle) body tissues with hypertension and type 2 diabetes. The hypothesis was that ASAT, VAT, and thigh IMAT would be positively associated, while TSAT and thigh muscle would be negatively associated, with hypertension and type 2 diabetes.

2 | METHODS

2.1 | Study population

All men in this analysis were from the Tobago Health Study, which has been previously described.³⁰ Briefly, the Tobago Health Study is a population-based, prospective cohort study of community-dwelling men aged 40 years and older, residing on the Caribbean island of Tobago, Trinidad and Tobago. Men from Tobago are of homogeneous African ancestry with low European admixture (<6%).³¹ Participants in the Tobago Health Study were recruited without regard to health status and men were eligible if they were ambulatory and not terminally ill. The baseline visit occurred from 2004 to 2007 and recruited 2482 men; of these, a random subset ($N = 1725$) attended the first follow-up visit from 2010 to 2014. Men used in the current analysis attended an ancillary study visit from 2014 to 2018, when a convenience sub-sample of $N = 768$ participants from the prior visit had CT scans of the abdomen and mid-thigh for ectopic AT assessment. Exclusion from the current analysis included non-African Caribbean ethnicity by self-report ($N = 67$), missing CT scans in the abdomen or in one or both thighs ($N = 31$), missing covariate data ($N = 53$), being underweight ($N = 4$), and non-fasting serum samples ($N = 1$). Two individuals were also excluded for improper serum handling that led to glucose degradation. The final analytical sample included 610 individuals. Written informed consent was obtained from each participant using forms and procedures approved by the University of Pittsburgh Institutional Review Board, the U.S. Surgeon General's Human Use Review Board, and the Tobago Division of

Health and Social Services Institutional Review Board. This study was completed in accordance with the Declaration of Helsinki.

2.2 | Computed tomography scans

CT scans were performed at the Calder Hall Medical Clinic, Tobago. Abdominal and thigh volumes were assessed on 3 mm thick slices and 500 mm display field of view from scans acquired using a GE dual slice, high-speed NX/I CT scanner (GE Medical Systems) with 120 KVp, 250 mA, 0.7 s gantry speed, and pitch of 1.5:1. For participants with body weight greater than 200 lbs, the mA was increased to 300. CT contrast was not used. Only one CT scanner was used, and a single individual collected the scans for all participants. Scans were electronically transmitted to the central CT reading center at Vanderbilt University Medical Center (VUMC) where image analysis and quality control were performed.

Image analysis was performed using a semi-automated method. Briefly, images were analyzed using a dedicated imaging processing workstation with custom-programmed subroutines (OsiriX, Pixmeo) and a dedicated pen computing display (Cintiq, Wacom Technology Corporation). A radiologist-trained analyst manually traced anatomical boundaries (skin, muscular fascia, muscle, bone, and peritoneum) in CT scans. Tissue attenuation thresholds of -190 to -30 Hounsfield Units (HU) were used to distinguish AT voxels in these defined regions and tissue attenuations of -29 to 160 HU were used to distinguish lean muscle voxels. For each tissue, the volume (mm^3) was calculated.

Abdominal VAT and ASAT were measured from CT scans of three contiguous slices of 3 mm thickness centered at L4-L5. A lateral scout image was used to determine the z-axis location of the L4-L5 intervertebral space and that location and the slice immediately above and the slice immediately below were used to reconstruct a 9-mm-thick single block of images. VAT was defined as AT located within the peritoneal cavity; ASAT was defined as AT located beneath the skin and superficial to the abdominal muscular fascia. The remaining non-VAT and non-ASAT tissues (e.g., organs, bone, abdominal muscle, abdominal IMAT) were not separately measured at the L4-L5 intervertebral space, and so these remaining tissues were combined to form a third "Other abdominal tissue" group.

TSAT, thigh IMAT, thigh muscle, and thigh bone volumes were measured from CT scans of 10 contiguous slices of 3 mm thickness at the mid-thigh level in both legs. An anterior-posterior scout scan of the entire femur was used to localize the mid-thigh position, and that location and the four slices immediately above and five slices immediately below were used to reconstruct a 30-mm-thick single block of images. Hand-drawn boundaries were traced at the medulla, cortex, thigh muscles, fascia, and skin in three of the 10 slices; boundaries were imputed over the remaining slices and verified for accuracy by the trained analyst. Bone volume was identified as the cortical volume. Lean muscle volume was defined as the sum of the adductors, hamstrings, and quadriceps muscles across both thighs. TSAT was defined as AT located between the skin and the muscle fascia, and IMAT was defined as AT located within thigh muscle groups.

2.3 | Generation of compositions and additive log ratio transformation

Two separate compositions were created: abdominal and thigh. The abdominal composition was comprised of VAT, ASAT, and the 'Other' remaining abdominal tissues. Similarly, thigh composition was comprised of TSAT, IMAT, muscle, and bone.

The additive log ratio (ALR) transformation is described in greater detail elsewhere.²⁴ Briefly, for a composition made up of D components (x_1, x_2, \dots, x_D), the ALR transformation generates $D-1$ terms where each term is the log of the ratio of each component to a referent component, for example, $\log(x_1/x_D), \log(x_2/x_D), \dots, \log(x_{D-1}/x_D)$. For the abdominal composition, the 'Other' tissue component was used as the referent; for the thigh composition, the bone component was used as a referent. A \log_2 transformation was applied to these ratios such that interpretation of coefficients is for a two-fold increase in the ratio of the numerator tissue compared to its respective referent component.

2.4 | Outcome definitions: Hypertension and type 2 diabetes categories

Systolic (SBP) and diastolic (DBP) blood pressures were measured 3 times in a seated position with 10 min of rest in between readings using an automated sphygmomanometer (Omron); the average of the last two readings was used for this analysis. Hypertension was defined using ACC/AHA 2017 criteria,³² and individuals who were on an antihypertensive medication were assigned Stage 2 Hypertension regardless of SBP or DBP.

Fasting serum glucose and insulin measures were measured at the Advanced Research and Diagnostics Laboratory (ARDL), University of Minnesota. Fasting serum glucose was measured using an enzymatic procedure (interassay CV: 1.3%–1.8%), and fasting serum insulin was measured using a Sandwich immunoassay procedure (interassay coefficient of variation: 3.1%) (assays manufacturer: Roche Diagnostics). Insulin resistance was estimated using the HOMA-IR equation.³³ Diabetes categories were defined based on American Diabetes Association (ADA) fasting glucose criteria.³⁴ Individuals taking antidiabetic medications were classified as "Type 2 Diabetes" regardless of measured fasting glucose.

2.5 | Other measures

Standing height was measured to the nearest 0.1 cm using a wall-mounted stadiometer. Body weight was recorded to the nearest 0.1 kg without shoes on a balance beam scale. BMI was calculated from body weight and standing height (kg/m^2); obesity status was defined as normal weight (18.5 – $24.9 \text{ kg}/\text{m}^2$), overweight (25 – $30 \text{ kg}/\text{m}^2$), or obese ($>30 \text{ kg}/\text{m}^2$). Information on current smoking [yes/no], number of hours walked per week, watching 14 or more hours of television (TV) per week [yes/no], current intake of alcohol of more than four drinks

per week [yes/no], family history of hypertension or diabetes [yes/no] and medication use were assessed using standardized interviewer-administered questionnaires. Lipid-modifying medications were defined as the use of a statin, ezetimibe, or a combination of the two. Self-reported information on walking was recorded as walking is the predominant form of physical activity on the island of Tobago. Men were asked to bring all prescription medications taken in the past 30 days to their clinic visit.

2.6 | Statistical analyses

Population characteristics were reported overall and stratified by obesity status; *p*-values for linear trend were reported, with linear contrasts used for continuous variables and Cochran-Armitage trend test used for categorical variables. Ternary plots for abdominal and thigh compositions were generated using the package 'compositions'³⁵ in R version 3.5.2,³⁶ and the mean compositions for each hypertension and diabetes category was plotted over the population distribution. Age-adjusted Pearson correlations were reported between the ALR-transformed components, BMI, and continuous risk factors. Linear regressions were performed for continuous risk factor outcomes (SBP, DBP, glucose, insulin, and HOMA-IR); log transformations were applied to non-normal distributions. Ordinal logistic regression models were performed for hypertension and diabetes categories; a partial proportional odds models with unequal slopes for lipid-modifying medications was chosen for the diabetes category model after rejection of the score test and empirical cumulative logit plots indicated that this variable was the only one violating the proportional odds assumption. All models were adjusted for age, BMI, family histories of diabetes, drinking 4+ alcoholic drinks per week, current smoking, watching TV ≥ 14 h per week, hours walked per week for exercise, taking lipid-modifying medications, total measured abdominal and thigh volumes, and the ALR-transformed abdominal and thigh compositions; the continuous biomarker models were additionally adjusted for antihypertensive or antidiabetic medication use. Interactions of abdominal or thigh tissues with BMI were assessed and visualized using the PROCESS macro³⁷; interaction models with hypertension and type 2 diabetes outcomes used a dichotomized version of these outcomes. Statistical significance was based on $\alpha = 0.05$, and analyses were performed using SAS 9.4 software (SAS Institute, Inc.).

2.7 | Sensitivity analyses

Three sets of sensitivity analyses were performed. In the first sensitivity analysis, models only included either the abdominal composition or the thigh composition, but not adjusting simultaneously for both regions.

In the second set of sensitivity analyses, HU-based estimates to generate abdominal muscle and IMAT components, as there were no direct measures of abdominal muscle/IMAT at the L4-L5 intervertebral space. Abdominal muscle and IMAT were estimated without manual

tissue tracing in the area between the peritoneal cavity and the muscular fascia using attenuation tissue thresholds defining AT (−190 to −30 HU) and lean muscle (−29 to 160 HU). Two individuals had missing data, leading to a sample size of 608 individuals for this sensitivity analysis. Abdominal compositions in the sensitivity analyses now consisted of ASAT, VAT, abdominal IMAT, abdominal muscle, and remaining 'Other', such that two new log ratio terms (IMAT:Other and Muscle:Other) were included in models. Models were otherwise constructed as indicated in the main analyses.

In the third sensitivity analysis, thigh muscle attenuation was included as a surrogate measure for intramuscular fat accumulation.³⁸ Thigh muscle attenuation was defined as the average HU across measured thigh muscle volumes; a lower average HU reflects greater fatty infiltration.

3 | RESULTS

3.1 | General baseline characteristics

Overall population characteristics and characteristics stratified by obesity status are displayed in Table 1. Men had a median age of 62 and mean BMI of 27.7 kg/m². About 75.5% of the men had stage 1 or stage 2 hypertension, while 23% of the men had type 2 diabetes; more than half of individuals with hypertension or diabetes were on a medication for that disease.

Ternary plots (Figures 1 and 2) were constructed to show overall abdominal and thigh composition distributions in the population, as well as the mean compositions for each of the cardiometabolic disease categories. Ternary plots are read such that the closer an individual is plotted towards a particular corner, the greater that individual's composition is comprised of that component (with a corner being completely 100% that composition). In the abdominal compositions (Figures 1 and 2, left panels), individuals in higher cardiometabolic disease categories appeared to have a greater % ASAT, and a slight shift to having a greater %VAT. In the thigh compositions (Figures 1 and 2, right panels), individuals in higher cardiometabolic disease categories appeared to have greater %TSAT and a slight shift towards having a greater %IMAT.

3.2 | Association of tissue depots with anthropometric measures and diabetes categories

Age-adjusted Pearson correlations (Table 2) were performed to investigate associations between ALR-transformed abdominal and thigh components, BMI, and continuous risk factor measures. BMI was most strongly correlated with ASAT and TSAT ($r = 0.69$ and 0.70 , respectively; all $p < 0.001$), and moderately correlated with VAT and IMAT components ($r = 0.58$ and 0.61 , respectively; all $p < 0.001$); similar correlations were also observed between tissue components and their respective total measured region (abdomen or thigh). Interrelationships among all AT components were high, with some of

TABLE 1 Population characteristics, overall, and by BMI category

Variable	Mean (SD), Median (IQR), or N(%)				p-value
	Overall (N = 610)	Normal weight (N = 177)	Overweight (N = 266)	Obese (N = 167)	
Demographic and lifestyle factors					
Age (years)	62.0 (57.0, 68.0)	63.0 (58.0, 71.0)	62.0 (57.0, 69.0)	60.0 (56.0, 65.0)	0.0003
Weight (kg)	85.5 (15.4)	70.6 (7.0)	84.2 (7.9)	103.4 (12.3)	<0.0001
Height (cm)	175.5 (6.7)	176.0 (6.6)	175.4 (6.9)	174.9 (6.3)	0.1186
BMI (kg/m ²)	27.8 (4.7)	23.2 (21.7, 24.2)	27.4 (26.2, 28.3)	32.9 (30.9, 35.4)	<0.0001
Current smoker [N(%)]	44 (7.2%)	16 (9.0%)	19 (7.1%)	9 (5.4%)	0.1906
Drinks 4+ alcoholic beverages per week [N(%)]	75 (12.3%)	20 (11.3%)	36 (13.5%)	19 (11.4%)	0.9699
Watches TV ≥ 14 h per week [N(%)]	294 (48.2%)	84 (47.5%)	128 (48.1%)	82 (49.1%)	0.7609
Walking for exercise (hours per week)	1.9 (0.0, 5.0)	1.5 (0.0, 4.5)	2.1 (0.0, 5.0)	1.5 (0.0, 5.0)	0.5095
On lipid-modifying medications [N(%)]	79 (13.0%)	18 (10.2%)	33 (12.4%)	28 (16.8%)	0.0696
Has family history of type 2 diabetes [N(%)]	340 (55.7%)	90 (50.8%)	148 (55.6%)	102 (61.1%)	0.0564
Has family history of hypertension [N(%)]	331 (54.3%)	79 (44.6%)	145 (54.5%)	107 (64.1%)	0.0003
Cardiometabolic disease measures					
Fasting glucose (mg/dL)	89.0 (81.0, 102.0)	87.0 (79.0, 97.0)	89.0 (82.0, 102.0)	93.0 (83.0, 115.0)	0.0008
Fasting insulin (μU/mL)	9.0 (5.8, 14.0)	5.7 (4.0, 7.7)	9.0 (6.3, 13.2)	15.0 (11.5, 19.8)	<0.0001
HOMA-IR	2.2 (1.3, 3.5)	1.3 (0.9, 1.8)	2.1 (1.4, 3.1)	3.7 (2.5, 5.5)	<0.0001
Type 2 diabetes categories [N(%)]					<0.0001
Normal glucose	401 (65.7%)	136 (76.8%)	176 (66.2%)	89 (53.3%)	
Impaired fasting glucose	70 (11.5%)	13 (7.3%)	31 (11.7%)	26 (15.6%)	
Type 2 diabetes	139 (22.8%)	28 (15.8%)	59 (22.2%)	52 (31.1%)	
Antidiabetic medication use [N(%)]	106 (17.4%)	23 (13.0%)	46 (17.3%)	37 (22.2%)	0.0251
SBP (mmHg)	142.0 (21.8)	134.0 (120.5, 152.0)	139.5 (126.5, 156.0)	145.0 (19.4)	0.0013
DBP (mmHg)	79.7 (12.2)	74.5 (68.0, 82.5)	79.9 (11.6)	83.5 (12.0)	<0.0001
Hypertension categories [N(%)]					<0.0001
Normal	68 (11.2%)	33 (18.6%)	28 (10.5%)	7 (4.2%)	
Elevated	82 (13.4%)	35 (19.8%)	36 (13.5%)	11 (6.6%)	
Stage 1	76 (12.5%)	21 (11.9%)	34 (12.8%)	21 (12.6%)	
Stage 2	384 (63.0%)	88 (49.7%)	168 (63.2%)	128 (76.7%)	
Antihypertensive medication use [N(%)]	244 (40.0%)	43 (24.3%)	110 (41.4%)	91 (54.5%)	<0.0001
Body composition tissue measures					
ASAT volume (cm ³)	181.8 (129.2, 245.7)	101.8 (49.3)	188.2 (50.9)	308.3 (100.3)	<0.0001
VAT volume (cm ³)	86.1 (52.3, 125.0)	44.6 (26.7, 68.4)	92.4 (39.6)	138.6 (56.6)	<0.0001
Other abdominal volume (cm ³)	312.8 (46.6)	288.9 (37.8)	308.5 (40.6)	345.2 (46.3)	<0.0001
Total abdominal volume (cm ³)	581.5 (485.6, 690.6)	442.8 (69.8)	590.0 (79.4)	792.0 (139.7)	<0.0001
TSAT volume (cm ³)	341.2 (229.9, 485.0)	204.0 (111.9)	361.6 (133.7)	587.1 (228.3)	<0.0001
Thigh IMAT volume (cm ³)	118.4 (50.5)	80.3 (36.8)	120.4 (37.4)	143.6 (118.5, 187.7)	<0.0001
Thigh muscle volume (cm ³)	1068.4 (172.8)	951.1 (139.6)	1079.3 (144.0)	1175.2 (171.4)	<0.0001
Thigh bone volume (cm ³)	44.3 (41.6, 47.9)	42.8 (40.5, 45.4)	44.6 (5.1)	46.3 (4.8)	<0.0001

TABLE 1 (Continued)

Variable	Mean (SD), Median (IQR), or N(%)				p-value
	Overall (N = 610)	Normal weight (N = 177)	Overweight (N = 266)	Obese (N = 167)	
Demographic and lifestyle factors					
Total thigh volume (cm ³)	1608.9 (326.0)	1278.2 (176.0)	1605.9 (174.8)	1964.2 (254.4)	<0.0001

Note: Continuous p-values: linear regression predicting the characteristic (for parametric), or Joncheere-Terpstra Test (for nonparametric). Categorical p-values: Cochran-Armitage trend test for binary variables, or Mantel-Haenszel Chi-square test for ordinal variables.

Abbreviations: ASAT, abdominal subcutaneous adipose tissue; BMI, body mass index; DBP, diastolic blood pressure; IMAT, intermuscular adipose tissue; SBP, systolic blood pressure; TSAT, thigh subcutaneous adipose tissue; TV, television; VAT, visceral adipose tissue.

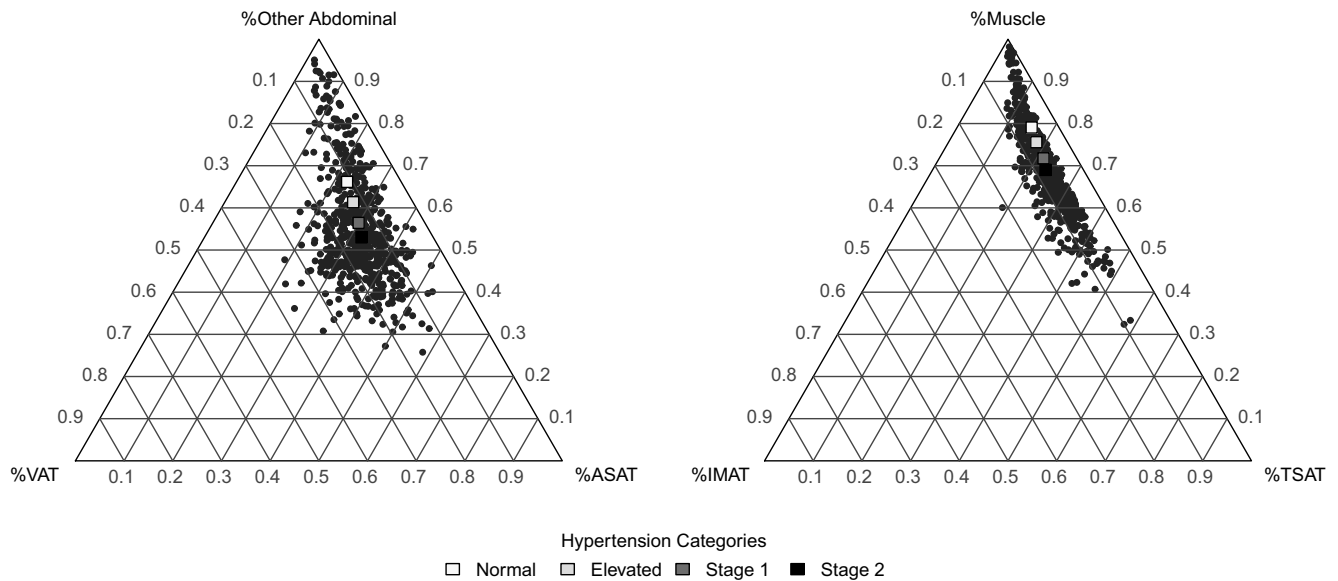


FIGURE 1 Ternary plots of abdominal (left) and thigh (right) compositions, with average composition by hypertension category overlaid. VAT, visceral adipose tissue; ASAT, abdominal subcutaneous adipose tissue; IMAT, (thigh) intermuscular adipose tissue; TSAT, thigh subcutaneous adipose tissue

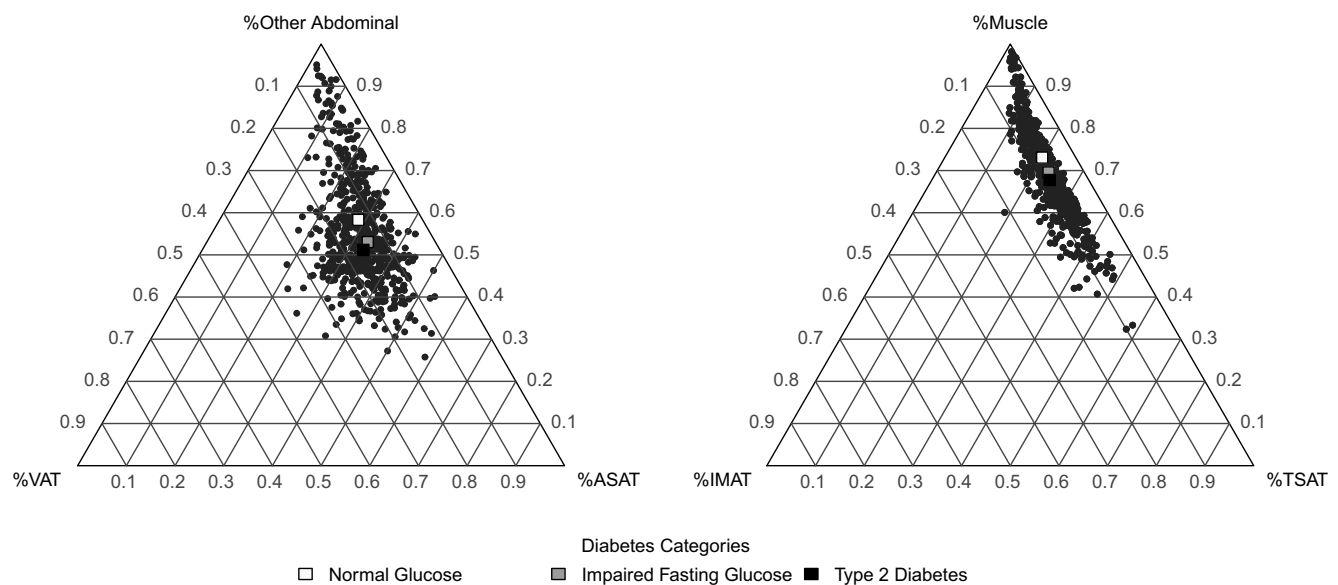


FIGURE 2 Ternary plots of abdominal (left) and thigh (right) compositions, with average composition by diabetes category overlaid. VAT, visceral adipose tissue; ASAT, abdominal subcutaneous adipose tissue; IMAT, (thigh) intermuscular adipose tissue; TSAT, thigh subcutaneous adipose tissue

TABLE 2 Age-adjusted Pearson partial correlation coefficients for ALR-transformed components, BMI, and continuous risk factors

	ASAT ^a	VAT ^a	TSAT ^a	Thigh IMAT ^a	Thigh muscle ^a	BMI (kg/m ²)	Abdominal volume (cm ³)	Thigh volume (cm ³)
ASAT ^a	1	0.73**	0.89**	0.80**	0.14*	0.69**	0.72**	0.70**
VAT ^a	0.73**	1	0.64**	0.61**	0.13*	0.58**	0.68**	0.53**
TSAT ^a	0.89**	0.64**	1	0.82**	0.20**	0.70**	0.71**	0.77**
Thigh IMAT ^a	0.80**	0.61**	0.82**	1	0.29**	0.61**	0.64**	0.69**
Thigh muscle ^a	0.14*	0.13*	0.20**	0.29**	1	0.27**	0.19**	0.35**
BMI (kg/m ²)	0.69**	0.58**	0.70**	0.61**	0.27**	1	0.91**	0.87**
SBP (mmHg)	0.21**	0.19**	0.16**	0.14*	0.04	0.18**	0.18**	0.14*
DBP (mmHg)	0.24**	0.22**	0.18**	0.16**	0.04	0.24**	0.24**	0.20**
Log glucose	0.16**	0.16*	0.09*	0.06	-0.04	0.18**	0.13*	0.005
Log insulin	0.60**	0.54**	0.55**	0.46**	0.22**	0.66**	0.62**	0.58**
Log HOMA-IR	0.58**	0.53**	0.52**	0.42**	0.15*	0.64**	0.60**	0.51**

Abbreviations: ASAT, abdominal subcutaneous adipose tissue; BMI, body mass index; DBP, diastolic blood pressure; IMAT, intermuscular adipose tissue; SBP, systolic blood pressure; TSAT, thigh subcutaneous adipose tissue; VAT, visceral adipose tissue.

^aLog₂ ratio transformed AT depot.

* $p < 0.05$, ** $p < 0.0001$.

TABLE 3 Multivariable-adjusted regressions for body composition tissues with continuous risk factors (top) and ordinal risk factors (bottom)

Risk Factor	VAT	ASAT	TSAT	Thigh IMAT	Thigh muscle
SBP ^a	1.04 (-1.92, 4.00)	4.14 (-0.99, 9.27)	-0.36 (-4.38, 3.65)	-2.05 (-6.18, 2.08)	4.82 (-4.24, 13.87)
DBP ^a	0.51 (-1.02, 2.03)	3.28 (0.77, 5.78)	-2.04 (-4.44, 0.37)	-0.90 (-3.24, 1.44)	1.25 (-3.58, 6.08)
Log glucose ^a	0.001 (-0.03, 0.03)	0.06 (0.02, 0.11)	-0.03 (-0.07, 0.02)	-0.002 (-0.05, 0.04)	-0.07 (-0.16, 0.03)
Log insulin ^a	0.10 (0.04, 0.17)	0.09 (-0.02, 0.19)	0.06 (-0.04, 0.16)	-0.07 (-0.17, 0.03)	0.15 (-0.06, 0.36)
Log HOMA-IR ^a	0.10 (0.02, 0.19)	0.15 (0.04, 0.27)	0.03 (-0.08, 0.15)	-0.07 (-0.18, 0.04)	0.08 (-0.19, 0.35)
Hypertension categories	0.92 (0.68, 1.23)	1.77 (1.10, 2.84)	0.80 (0.51, 1.27)	1.21 (0.76, 1.93)	1.10 (0.43, 2.80)
Type 2 diabetes categories ^b	0.95 (0.70, 1.28)	1.81 (1.06, 3.10)	0.71 (0.43, 1.18)	1.07 (0.67, 1.71)	0.37 (0.14, 1.01)

Note: Data are reported as the multivariable adjusted β (95% CI) for continuous risk factor data and OR (95% CI) for Ordinal categorical data. All models adjusted for age, BMI, drinking 4+ drinks per week, current smoker, watching television ≥ 14 h/week, hours walked per week for exercise, lipid-modifying medication, family history of diabetes, log ratios of abdominal tissues (with "Other" tissue as referent component), log ratios of thigh tissues (with bone volume as referent component), and total measured abdominal and thigh volumes.

Abbreviations: ASAT, abdominal subcutaneous adipose tissue; BMI, body mass index; DBP, diastolic blood pressure; IMAT, intermuscular adipose tissue; SBP, systolic blood pressure; TSAT, thigh subcutaneous adipose tissue; VAT, visceral adipose tissue.

^aAdditionally adjusted for antihypertensive or antidiabetic medication use, respectively.

^bPartial proportional odds for lipid-modifying medication.

the highest correlation coefficients being between ASAT, TSAT, and IMAT ($r = 0.80$ – 0.89 ; all $p < 0.0001$). Despite these higher correlations, multicollinearity was not identified when investigating condition indices and variance proportions in regression models.

Continuous risk factor outcomes were analyzed using linear regression models, and cardiometabolic disease categories using ordinal logistic regression models (Table 3). For the abdominal composition, after adjustment for confounders, medication use, and other abdominal and thigh tissues, a two-fold higher ASAT:"Other" abdominal tissue ratio was significantly and positively associated with higher DBP ($\beta = 3.28$, 95% CI: 0.77–5.78), log-glucose ($\beta = 0.06$, 95% CI: 0.02–0.11), and log-HOMA-IR ($\beta = 0.15$, 95% CI: 0.04–0.27),

and borderline associated with higher SBP ($\beta = 4.14$, 95% CI: -0.99–9.27) and log-insulin ($\beta = 0.09$, 95% CI: -0.02–0.19); meanwhile, higher VAT:"Other" was only significantly associated with higher log-insulin ($\beta = 0.10$, 95% CI: 0.04–0.17) and log-HOMA-IR ($\beta = 0.10$, 95% CI: 0.02–0.19). For the thigh composition, no component was statistically significantly associated with continuous risk factor outcomes; however, two-fold higher TSAT:bone and muscle:bone ratios were inversely associated with log-glucose (TSAT: $\beta = -0.03$, 95% CI: -0.07–0.02; muscle: $\beta = -0.07$, 95% CI: -0.16–0.03) and positively associated with log-insulin (TSAT: $\beta = 0.06$, 95% CI: -0.04–0.16; muscle: $\beta = 0.15$, 95% CI: -0.06–0.36), while a two-fold higher IMAT: bone ratio was inversely associated with both log-insulin ($\beta = -0.07$,

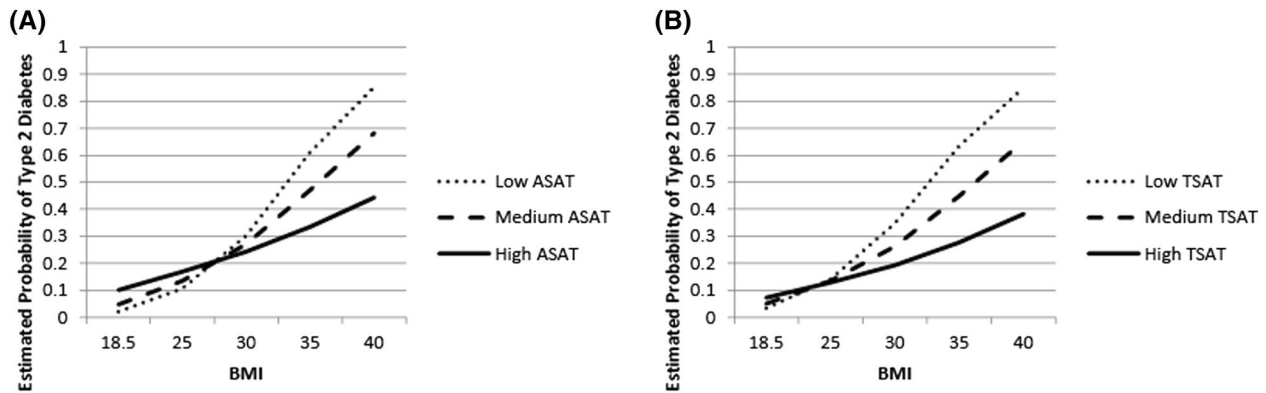


FIGURE 3 Estimated probabilities of type 2 diabetes at specific BMIs and levels of ASAT (left) and TSAT (right) in fully adjusted models. “Medium” levels of ASAT and TSAT are the mean values of each ALR-transformed tissue, with “High” and “Low” representing the values at one standard deviation above and below the mean for each tissue type, respectively. ALR, additive log ratio; VAT, visceral adipose tissue; TSAT, thigh subcutaneous adipose tissue

95% CI: $-0.17, 0.03$) and log-HOMA-IR ($\beta = -0.07$, 95% CI: $-0.18, 0.04$).

In ordinal logistic regression models, only ASAT (OR: 1.77, 95%CI: 1.10–2.84) was associated with higher odds of being in a higher hypertension category, and only ASAT (OR: 1.81, 95% CI: 1.06–3.10) and thigh muscle (OR: 0.37, 95%CI: 0.14–1.01) were associated with odds of being in a higher diabetes category. Though neither the VAT, IMAT, nor TSAT components reached statistical significance, the point estimates and confidence intervals for TSAT suggested a potentially protective effect against diabetes (OR: 0.71, 95%CI: 0.43–1.18).

3.3 | Interactions

There were no statistically significant interactions between tissue components and BMI in continuous risk factor models. However, interactions were identified in type 2 diabetes models for ASAT ($p = 0.0063$) and TSAT ($p = 0.0111$). Estimated probabilities of type 2 diabetes at specified BMI measures and at the mean ± 1 standard deviation of ALR-transformed ASAT or TSAT are depicted in Figure 3. At lower BMIs, having greater ASAT is associated with a greater probability of having type 2 diabetes, but at higher BMIs, this association is attenuated and reversed. In contrast, levels of TSAT do not appear to have a differential impact at lower BMIs but having a greater amount of TSAT is associated with lower probability of type 2 diabetes at higher BMIs.

3.4 | Sensitivity analyses

Models that used only abdominal CT scans (Table 4) or only thigh CT scans (Table 5) showed somewhat different results when compared to main analysis models. Models including only the abdominal composition had slightly attenuated effects for ASAT and slightly larger effects for VAT compared to the main analysis models. For models including only the thigh composition compared to main analysis models, results

TABLE 4 Multivariable-adjusted regressions for abdominal composition tissues only, with continuous risk factors (top) and ordinal risk factors (bottom), ($N = 610$)

Risk Factor	VAT	ASAT
SBP ^a	1.50 (−1.41, 4.41)	2.04 (−1.46, 5.54)
DBP ^a	0.64 (−0.84, 2.13)	0.97 (−0.69, 2.63)
Log glucose ^a	0.02 (−0.02, 0.05)	0.01 (−0.02, 0.05)
Log insulin ^a	0.10 (0.04, 0.17)	0.09 (0.02, 0.17)
Log HOMA-IR ^a	0.12 (0.05, 0.19)	0.11 (0.03, 0.19)
Hypertension categories	0.98 (0.74, 1.31)	1.49 (1.09, 2.03)
Type 2 diabetes categories ^b	1.10 (0.83, 1.47)	1.13 (0.79, 1.62)

Note: Data are reported as the multivariable adjusted β (95% CI) for continuous risk factor data and OR (95% CI) for Ordinal categorical data. All models adjusted for age, BMI, drinking 4+ drinks per week, current smoker, watching television ≥ 14 h/week, hours walked per week for exercise, lipid-modifying medication, family history of diabetes, log ratios of abdominal tissues (with “Other” tissue as referent component), and total measured abdominal volume.

Abbreviations: ASAT, abdominal subcutaneous adipose tissue; BMI, body mass index; DBP, diastolic blood pressure; SBP, systolic blood pressure; VAT, visceral adipose tissue.

^aAdditionally adjusted for antihypertensive or antidiabetic medication use, respectively.

^bPartial proportional odds for lipid-modifying medication.

were more mixed. For TSAT, results for log-insulin and log-HOMA-IR were much stronger in the thigh alone models, while the association with diabetes category was attenuated. For IMAT, the log-insulin and log-HOMA-IR effects were more attenuated in the thigh alone models. And for thigh muscle, associations with glucose and with diabetes category were stronger in the thigh alone models.

Descriptive statistics for estimated components for abdominal muscle and IMAT, as well as thigh muscle attenuation, are included in Table 6. Main analysis results remained consistent in sensitivity analyses which included estimated components for abdominal muscle

Risk Factor	TSAT	Thigh IMAT	Thigh muscle
SBP ^a	2.60 (-0.70, 5.91)	-0.54 (-4.58, 3.51)	3.13 (-5.64, 11.89)
DBP ^a	0.20 (-1.72, 2.11)	0.05 (-2.20, 2.31)	0.52 (-4.15, 5.19)
Log glucose ^a	0.02 (-0.03, 0.06)	0.02 (-0.04, 0.07)	-0.15 (-0.25, -0.04)
Log insulin ^a	0.15 (0.07, 0.24)	-0.001 (-0.10, 0.10)	0.08 (-0.13, 0.28)
Log HOMA-IR ^a	0.17 (0.07, 0.27)	0.02 (-0.10, 0.13)	-0.07 (-0.33, 0.17)
Hypertension categories	1.10 (0.76, 1.58)	1.49 (0.96, 2.32)	0.76 (0.31, 1.87)
Type 2 diabetes categories ^b	1.01 (0.68, 1.50)	1.26 (0.79, 1.98)	0.25 (0.10, 0.63)

Note: Data are reported as the multivariable adjusted β (95% CI) for continuous risk factor data and OR (95% CI) for Ordinal categorical data. All models adjusted for age, BMI, drinking 4+ drinks per week, current smoker, watching television ≥ 14 h/week, hours walked per week for exercise, lipid-modifying medication, family history of diabetes, log ratios of thigh tissues (with bone volume as referent component), and total measured thigh volumes.

Abbreviations: BMI = body mass index, SBP = systolic blood pressure; DBP = diastolic blood pressure, TSAT = thigh subcutaneous adipose tissue; IMAT = intermuscular adipose tissue

^aAdditionally adjusted for antihypertensive or antidiabetic medication use, respectively

^bPartial proportional odds for lipid-modifying medication

TABLE 5 Multivariable-adjusted regressions for thigh composition tissues only, with continuous risk factors (top) and ordinal risk factors (bottom), (N = 610)

TABLE 6 Additional abdominal and thigh characteristics, overall and by BMI category

Variable	Mean (SD) or Median (IQR)				p-value
	Overall (N = 610)	Normal (N = 177)	Overweight (N = 266)	Obese (N = 167)	
Body composition tissue measures					
Abdominal IMAT volume (cm ³) ^a	27.6 (21.5, 37.0)	21.7 (9.1)	28.4 (23.0, 36.0)	37.0 (28.5, 49.9)	<0.0001
Abdominal muscle volume (cm ³) ^a	165.7 (148.4, 183.6)	153.8 (23.1)	167.7 (24.6)	182.3 (28.2)	<0.0001
Other abdominal volume (cm ³) ^a	115.5 (25.3)	114.0 (26.4)	108.2 (93.7, 127.2)	123.4 (23.8)	0.0007
Thigh muscle attenuation (HU)	43.6 (40.5, 45.6)	43.2 (3.8)	40.1 (37.7, 43.7)	43.1 (39.9, 45.3)	0.1491

^aAbdominal measures in 608 men (264 overweight).

Abbreviation: IMAT, intermuscular adipose tissue.

and IMAT (Table 7) and in models which adjusted for thigh muscle attenuation (Table 8).

4 | DISCUSSION

When using a CoDA approach and when considering both abdominal and thigh compositions, ASAT but not VAT remained the primary depot associated with both hypertension and diabetes in this African Caribbean population. Additionally, inclusion of thigh muscle tissue with other abdominal and thigh tissues was particularly important for models of type 2 diabetes. That simultaneous inclusion of the abdominal and thigh compositions yields different results than either composition alone further underscores the importance of including multiple body regions in analyses of cardiometabolic disease risk and development.

These analyses utilized a novel application of CoDA methodology to body composition imaging data, removing the inherent correlational structure in body imaging data that is ignored in previous approaches. While CoDA methodology is increasing in usage in a

variety of public health fields,²⁵⁻²⁷ its application in the body composition field is admittedly new.^{28,29} Though CoDA interpretations may be new to body composition researchers, it is important to note that many of the current study findings and intuitions are in line with previous reporting of tissue associations. Namely, strong positive associations with ASAT, but not VAT, with cardiometabolic risk factors in this African Caribbean population are in line with findings in other African ancestry populations,^{22,23} as are the inverse associations of muscle with diabetes risk.^{9,13} A unique additional property of CoDA is its scale invariance,³⁹ where the focus on relative tissue amounts makes the total specimen size (i.e. total scanned abdominal or thigh sizes) irrelevant. Given that growth of AT or muscle may contribute to increases in a body region's size, this property allowed for further disentanglement of the effects of body composition from body size.

Though a CoDA approach yielded similar inferences to those found in the literature, greater variability in results were seen when comparing the main analyses results (simultaneous adjustment of both upper and lower body tissues) with upper body or lower body alone analyses. In upper body alone analyses, the effects of VAT were

TABLE 7 Multivariable-adjusted regressions for body composition tissues with continuous risk factors (top) and ordinal risk factors (bottom), including abdominal IMAT and muscle estimates (N = 608)

Risk Factor	VAT	ASAT	Abdominal IMAT	Abdominal Muscle	TSAT	Thigh IMAT	Thigh Muscle
SBP ^a	1.35 (-1.50, 4.21)	4.14 (-0.53, 8.82)	-3.41 (-7.85, 1.03)	0.39 (-7.00, 7.78)	0.03 (-4.33, 4.40)	-0.90 (-5.39, 3.60)	3.41 (-5.42, 12.24)
DBP ^a	0.53 (-1.07, 2.12)	3.00 (0.39, 5.62)	-0.87 (-3.36, 1.61)	-0.08 (-4.21, 4.05)	-1.78 (-4.22, 0.66)	-0.69 (-3.20, 1.83)	0.83 (-4.11, 5.76)
Log glucose ^a	-0.003 (-0.04, 0.03)	0.07 (0.02, 0.12)	0.03 (-0.02, 0.08)	-0.11 (-0.20, -0.02)	-0.03 (-0.08, 0.01)	-0.01 (-0.06, 0.03)	-0.05 (-0.14, 0.04)
Log insulin ^a	0.11 (0.04, 0.18)	0.05 (-0.06, 0.17)	-0.06 (-0.17, 0.04)	0.16 (-0.01, 0.34)	0.08 (-0.02, 0.19)	-0.06 (-0.17, 0.05)	0.10 (-0.11, 0.31)
Log HOMA-IR ^a	0.10 (0.02, 0.19)	0.13 (0.01, 0.24)	-0.03 (-0.15, 0.08)	0.05 (-0.17, 0.28)	0.05 (-0.07, 0.17)	-0.08 (-0.19, 0.04)	0.05 (-0.22, 0.32)
Hypertension categories	0.93 (0.69, 1.27)	1.77 (1.08, 2.92)	0.87 (0.54, 1.40)	0.93 (0.41, 2.11)	0.81 (0.51, 1.29)	1.25 (0.76, 2.04)	1.02 (0.39, 2.64)
Type 2 diabetes categories ^b	0.94 (0.69, 1.30)	2.05 (1.17, 3.60)	1.10 (0.66, 1.82)	0.37 (0.16, 0.85)	0.66 (0.40, 1.10)	1.02 (0.61, 1.70)	0.41 (0.15, 1.14)

Note: Data are reported as the multivariable adjusted β (95% CI) for continuous risk factor data and OR (95% CI) for Ordinal categorical data. All models adjusted for age, BMI, drinking 4+ drinks per week, current smoker, watching television ≥ 14 h/week, hours walked per week for exercise, lipid-modifying medication, family history of diabetes, log ratios of abdominal tissues (with "Other" tissue as referent component), log ratios of thigh tissues (with bone volume as referent component), and total measured abdominal and thigh volumes.

Abbreviations: BMI = body mass index; SBP = systolic blood pressure; DBP = diastolic blood pressure; ASAT = abdominal subcutaneous adipose tissue; VAT = visceral adipose tissue; TSAT = thigh subcutaneous adipose tissue; IMAT = intermuscular adipose tissue

^aAdditionally adjusted for antihypertensive or antidiabetic medication use, respectively.

^bPartial proportional odds for lipid-modifying medication.

more extreme, while the effects of ASAT were more attenuated, as compared to analyses adjusting for both regions. In the lower body alone analyses, TSAT was positively associated with cardiometabolic risk factors, whereas in the main analyses it was inversely associated. As there were no collinearity issues identified in these models, these discrepant results are likely due to the confounding effects of one region on another, highlighting the importance of including multiple metabolically-relevant body regions in cardiometabolic risk assessment.

Relatively high correlations between ASAT and TSAT components were identified. While both are forms of subcutaneous AT, there are functional and metabolic differences between ASAT and TSAT which may contribute to their opposing roles in cardiometabolic health.¹ The findings of opposing associations with fasting glucose are consistent with previous reports from Health ABC,⁸ and are further supported by their opposing associations with type 2 diabetes categories. However, both ASAT and TSAT were similarly positively associated with insulin, though only ASAT was associated with insulin resistance. A few studies suggest that having more TSAT is associated with better insulin sensitivity⁹⁻¹²; while an inverse relationship between TSAT and insulin resistance was not observed in this study, this may be due in part to differences in insulin resistance/sensitivity estimations, or may also be due to racial/ethnic differences between study populations since African ancestry individuals tend to have higher HOMA-IR compared to hyperinsulinemic clamp-matched European ancestry individuals.⁴⁰ TSAT, while not statistically significantly so, was inversely associated with DBP and hypertension categories. Previous reports, which did not include simultaneous adjustments of TSAT and ASAT,^{5,6} indicated that TSAT may be positively associated with hypertension and blood pressure; these results are similar to this study's sensitivity analyses which did not adjust the thigh tissues for abdominal tissues, demonstrating that the inclusion of both upper- and lower-body composition measures may be essential for understanding associations of tissues with cardiometabolic health.

Interestingly, while IMAT was strongly correlated with ASAT and TSAT, its associations with insulin and HOMA-IR were opposite of the SATs. The high correlation between SAT and IMAT is not unexpected; previous studies^{16,41} demonstrated that increases in IMAT mirror increases in total adiposity, of which SAT is a major component. However, the role of IMAT in insulin resistance remains understudied. IMAT can secrete factors that induce insulin resistance in neighboring muscles,⁴² indicating that it could play a direct role in insulin resistance pathology. For example, increased calf IMAT volume is associated with incident diabetes.¹⁶ Still, it may be that IMAT is only a marker of overall adiposity and metabolic dysfunction,³⁸ future work is needed to elucidate the roles of IMAT in type 2 diabetes.

Thigh muscle tissue was inversely associated with glucose and diabetes categories, which is in line with previous results in the literature^{9,13,43-46} and speaks to the role of skeletal muscle as a major site for glucose uptake. Still, the use of CT derived measures of muscle size is complicated by the fact that increasing muscle can

TABLE 8 Multivariable-adjusted regressions for body composition tissues with continuous risk factors (top) and ordinal risk factors (bottom), including thigh muscle density ($N = 610$)

Risk factor	VAT	ASAT	TSAT	Thigh IMAT	Thigh muscle volume	Thigh muscle density (per SD Increase)
SBP ^a	1.03 (−1.93, 3.99)	4.01 (−1.16, 9.18)	−0.48 (−4.51, 3.55)	−1.65 (−6.29, 3.00)	4.26 (−5.45, 13.97)	0.40 (−1.75, 2.55)
DBP ^a	0.51 (−1.02, 2.03)	3.32 (0.78, 5.86)	−2.00 (−4.43, 0.44)	−1.04 (−3.70, 1.61)	1.46 (−3.68, 6.59)	−0.14 (−1.37, 1.09)
Log glucose ^a	0.001 (−0.03, 0.03)	0.06 (−0.01, 0.11)	−0.03 (−0.07, 0.02)	0.005 (−0.05, 0.06)	−0.08 (−0.17, 0.02)	0.01 (−0.02, 0.04)
Log insulin ^a	0.10 (0.03, 0.17)	0.06 (−0.05, 0.16)	0.03 (−0.07, 0.14)	0.03 (−0.09, 0.14)	0.01 (−0.21, 0.23)	0.10 (0.04, 0.15)
Log HOMA-IR ^a	0.10 (0.02, 0.18)	0.12 (0.002, 0.23)	0.01 (−0.11, 0.12)	0.03 (−0.10, 0.16)	−0.06 (−0.33, 0.21)	0.10 (0.04, 0.16)
Hypertension categories	0.91 (0.68, 1.23)	1.70 (1.05, 2.75)	0.77 (0.49, 1.22)	1.39 (0.82, 2.36)	0.92 (0.35, 2.47)	1.15 (0.89, 1.48)
Type 2 diabetes categories ^b	0.95 (0.70, 1.28)	1.77 (1.03, 3.04)	0.70 (0.42, 1.16)	1.16 (0.67, 2.00)	0.33 (0.11, 0.97)	1.08 (0.84, 1.38)

Note: Data are reported as the multivariable adjusted β (95% CI) for continuous risk factor data and OR (95% CI) for Ordinal categorical data. All models adjusted for age, BMI, drinking 4+ drinks per week, current smoker, watching television ≥ 14 h/week, hours walked per week for exercise, lipid-modifying medication, family history of diabetes, log ratios of abdominal tissues (with “Other” tissue as referent component), log ratios of thigh tissues (with bone volume as referent component), total measured abdominal and thigh volumes, and average thigh muscle density.

Abbreviations: ASAT, abdominal subcutaneous adipose tissue; BMI, body mass index; DBP, diastolic blood pressure; IMAT, intermuscular adipose tissue; SBP, systolic blood pressure; TSAT, thigh subcutaneous adipose tissue; VAT, visceral adipose tissue.

^aAdditionally adjusted for antihypertensive or antidiabetic medication use, respectively.

^bPartial proportional odds for lipid-modifying medication.

alternatively indicate an adaptation to help support heavier weights in obesity or greater fatty infiltration. To address the first scenario, interaction analyses did not find the effects of thigh muscle to vary across BMI. Thus, independent of other abdominal and thigh tissues and body size, the increase or maintenance of skeletal muscle tissue remains an important consideration for diabetes prevention. To address the second scenario, a sensitivity analysis which further adjusted models for a qualitative measure of intramuscular lipid accumulation (thigh muscle CT attenuation) found that this did not significantly impact glucose or diabetes estimates. Interestingly, higher thigh muscle attenuation (indicating lesser intramuscular lipid accumulation⁴⁷) was associated with higher insulin and insulin resistance, and its inclusion in models attenuated those associations with thigh muscle and IMAT. While individuals with obesity and type 2 diabetes have more low-attenuation muscle area,⁴⁸ the mechanistic relationship between intramuscular lipids and insulin resistance is still not well understood, with increased intramyocellular lipids possibly representing increased fuel storage or reflecting accumulation of lipid species which mediate insulin resistance.⁴⁹ Previous work in the Tobago population demonstrated that while calf skeletal muscle density decreased with aging, it was actually increased calf IMAT that was associated with incident type 2 diabetes.¹⁶ It may be that increases in intramyocellular triglycerides may be preferable in older age to increases in IMAT, or that the impacts of intramuscular lipid accumulation differ by muscle and anatomical location; future work is needed to better understand the effects of regional muscle fat accumulation.

This study has a few limitations. First, direct measures of total abdominal muscle and IMAT were not available at the L4-L5 intervertebral space, and as a result these tissues were collapsed with

remaining abdominal tissues into a singular ‘other’ variable. However, in sensitivity analyses that estimated abdominal muscle and IMAT, these estimated abdominal components did not substantially change results. Second, these analyses were cross-sectional in nature, and so causality cannot be determined. Still, the use of ordinal logistic regression models allows for some stronger evidence for the reported effects. Third, these analyses were limited to men, and thus may not be generalizable to women. Additionally, glycemic control was only assessed using fasting glucose, and measures of long-term control such as HbA1c were not available. This study also has several strengths. This study is novel in its use of a compositional data analytic approach, which allows for appropriate modeling of compositional data. In line with this, this study also mutually adjusted for several abdominal and thigh tissues that often are not included simultaneously in traditional modeling. Further, this study included a high-risk population of individuals with African ancestry, who are underrepresented in analyses involving abdominal and thigh CT scans.

In conclusion, simultaneous assessment of abdominal and thigh compositions in African Caribbean men support previous findings of adverse effects from higher levels of ASAT for both hypertension and type 2 diabetes, and the protective effect of thigh muscle for type 2 diabetes. These findings indicate the importance of incorporating regional body compositions when assessing cardiometabolic risk, and the benefits of utilizing compositional data analytic approaches in body composition analyses.

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CONFLICT OF INTEREST

The authors declared no conflict of interest.

AUTHOR CONTRIBUTIONS

Curtis Tilves and Iva Miljkovic had full access to the data and take responsibility for the integrity of the data and the accuracy of the data analysis. Iva Miljkovic and Joseph M. Zmuda were responsible for the overall study design and received funding to complete the research. Curtis Tilves and Iva Miljkovic conceived and designed the analysis leading to this manuscript submission. John Jeffrey Carr, James G. Terry, and Sangeeta Nair acquired the data and performed the Curtis Tilves scan analyses. Victor Wheeler provided local oversight of the study implementation. Victor Wheeler and Allison L. Kuipers participated in data collection. Curtis Tilves, Joseph M. Zmuda, Shyamal Peddada, and Iva Miljkovic played important roles in interpreting the data. Curtis Tilves performed the analyses and drafted the manuscript. All authors aided in revision of the manuscript and approved the final version.

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