

SUPPLEMENTAL MATERIAL

Supplementary Appendix Methods

All biomarkers reported here have been measured previously and the analytical methods described: fructosamine (1), N-terminal pro-B-type natriuretic peptide (NT-pro BNP) (1), lymphotoxin β receptor (LT β R) (2), and soluble endothelial cell-selective adhesion molecule (sESAM) (3), soluble intercellular adhesion molecule (sICAM) (3), soluble vascular cell adhesion molecule (sVCAM) (3), myeloperoxidase (MPO)(4), matrix metalloproteinase-9 (MMP-9) (4), tumor necrosis factor receptor alpha-1 (TNFR1A)(4), peptidoglycan recognition protein-1(PGYLRP-1) (5), soluble receptor for advanced glycation end products (sRAGE) (6), soluble CD40 ligand (sCD40L) (7), growth differentiation factor-15 (GDF-15) (8), cystatin C (9), osteoprotegerin (OPG) (10), monocyte chemoattractant protein-1 (MCP-1) (11), B-type natriuretic peptide (BNP) (12), interleukin-18 (IL-18) (13), lipoprotein-associated phospholipase A2 activity (LP-PLA2) (14), highly-sensitive troponin T (cTnT) (15), caspase-3 (16), CCL11 (17), CXCL1 (17), and CXCL2 (17).

Supplementary Appendix Table 1. Baseline Characteristics of Participants in the Entire Cohort (n=1200) Stratified by Inclusion or Exclusion in the Analysis of Biomarkers and Lipoproteins (n=942)

Variable	Excluded (n=258)	Included (n=942)	p-value
Age (yrs)	51 (45, 58)	42 (35, 50)	<0.0001
Men	36%	38%	0.52
White	25%	25%	0.87
Body Mass Index (kg/m ²)	35.2 (32.6, 39.7)	34.8 (32.0, 38.8)	0.09
Total Body Fat (%)	0.41 (0.32, 0.44)	0.39 (0.30, 0.44)	0.09
Subcutaneous Adipose Tissue (kg)	7.1 (5.5, 9.5)	6.5 (4.9, 8.7)	0.003
Visceral Adipose Tissue (kg)	1.7 (1.4, 2.1)	1.6 (1.2, 2.0)	0.01
Hypertension	68%	36%	<0.0001
Diabetes	50%	8%	<0.0001
Low HDL Cholesterol	50%	52%	0.62
Metabolic Syndrome	75%	51%	<0.0001

Data are presented as median (25th, 75th percentile) or proportion (%) where appropriate

Supplementary Appendix Table 2. Unadjusted Spearman Correlation Coefficients between VAT/BSA or SAT/BSA and Biomarkers

Variable	VAT/BSA	SAT/BSA
<i>Demographics</i>		
Age (years)	0.25*	-0.03
BMI (kg/m ²)	-0.02	0.69*
Waist Circumference (cm)	0.28*	0.44*
Hip Circumference (cm)	-0.16*	0.73*
Waist/Hip ratio	0.53*	-0.33*
<i>DEXA Fat Measures</i>		
Fat Mass (kg)	-0.15*	0.80*
Lean Mass (kg)	0.24*	-0.37*
Total Body Fat (%)	-0.23*	0.81*
Lower Fat (kg)	-0.39*	0.68*
Truncal Fat (kg)	0.07	0.76*
<i>Insulin Resistance</i>		
Glucose (mg/dL)	0.26*	0.002
Insulin (μU/mL)	0.17*	0.18*
HOMA-IR	0.23*	0.17*
Fructosamine (μmol/L)	0.10*	-0.22*
<i>Adipokines</i>		
Leptin (μg/L)	-0.29*	0.73*
Adiponectin (ng/mL)	-0.13*	0.11*
<i>Lipids</i>		
Total Cholesterol (mg/dL)	0.13*	-0.05
LDL-C (mg/dL)	0.08	-0.01
LDL particle no. (nmol/L)	0.25*	-0.13*
LDL size (nm)	-0.34*	0.26*
Triglycerides (mg/dL)	0.35*	-0.18*
VLDL particle no. (nmol/L)	0.32*	-0.20*
VLDL size (nm)	0.15*	-0.02
HDL-C (mg/dL)	-0.26*	0.17*
HDL particle no. (μmol/L)	-0.003	0.12*
HDL size (nm)	-0.33*	0.22*
<i>Inflammation</i>		
hs-CRP (mg/L)	-0.02	0.42*
OPG (ng/mL)	-0.02	0.16*
MCP-1 (pg/mL)	0.08	0.06
MMP-9 (ng/mL)	-0.004	0.07
CCL11 (pg/mL)	0.12*	-0.12*
CXCL1 (ng/mL)	-0.06	0.08
CXCL2 (ng/mL)	-0.05	0.03
LTBR (ng/mL)	0.06	0.19*
PGLYP-1 (ng/mL)	0.10	0.16*

Variable	VAT/BSA	SAT/BSA
MPO (ng/mL)	0.03	0.06
IL-18 (ng/mL)	0.14*	-0.04
GDF-15m(ng/mL)	0.18*	-0.002
LP-PLA2 activity (nmol/min/ml)	0.28*	-0.28*
TNFR1A (ng/mL)	0.08	0.05
sRAGE (ng/mL)	0.06	-0.08
<i>Endothelial Function</i>		
sESAM (ng/mL)	0.15*	0.11*
sVCAM (ng/mL)	0.06	0.02
sICAM (ng/mL)	0.04	0.00
<i>Cardiac Structure and Function</i>		
cTnT (ng/mL)	0.18*	-0.18*
BNP (pg/mL)	-0.07	0.10*
NT-Pro BNP (pg/mL)	-0.09	0.18*
<i>Thrombosis</i>		
D-Dimer (ng/mL)	-0.16*	0.28*
sCD40L (ng/mL)	0.06	-0.05
<i>Renal Function</i>		
eGFR (ml/min/1.73 m2)	-0.10*	0.13*
CystatinC (mg/L)	0.16*	0.04
<i>Miscellaneous</i>		
Caspase-3 (ng/mL)	-0.01	0.11*
Uric Acid (mg/L)	0.28*	-0.21*
Liver Fat (%)	0.40*	0.03
<i>Atherosclerosis</i>		
CAC (Agatston units)	0.25*	-0.07
APB (%)	0.21*	-0.08
AWT (mm)	0.30*	-0.13*

* $p < 0.0016$

Abbreviations: APB, aortic plaque burden; AWT, aortic wall thickness; BMI, body-mass index; BNP, B-type natriuretic peptide; BSA, body surface area; CAC, coronary artery calcium; CCL11, chemokine (c-c motif) ligand 11; cTnT, highly sensitive cardiac troponin T; CXCL1, chemokine (c-x-c motif) 1; CXCL2, chemokine (c-x-c motif) 2; eGFR, estimated glomerular filtration rate; GDF-15, growth differentiation factor-15; HDL-C, high-density lipoprotein cholesterol; hs-CRP, high-sensitivity C-reactive protein; HOMA-IR, homeostasis model assessment of insulin resistance; IL-18, interleukin 18; LDL-C, low-density lipoprotein cholesterol; LP-PLA2, lipoprotein-associated phospholipase A2; LT β R, lymphotoxin β receptor; MCP-1, monocyte chemoattractant protein-1; MMP-9, matrix metalloproteinase-9; MPO, myeloperoxidase; NT-Pro BNP, N-terminal Pro-B-type natriuretic peptide; OPG, osteoprotegerin; PGLYRP-1, peptidoglycan recognition protein-1; SAT, subcutaneous adipose tissue; sCD40L, soluble CD40 Ligand; sESAM, soluble endothelial cell-selective molecule; sICAM, soluble intracellular adhesion molecule; sRAGE, soluble receptor for advanced glycation end products; sVCAM, soluble vascular cell adhesion molecule; TNFR1A, tumor necrosis factor alpha-1 receptor; VAT, visceral adipose tissue

Supplementary Appendix Table 3. Multivariable-Adjusted Linear Regression Models of Relation of VAT or SAT to Other Biomarkers: Standardized β coefficient of VAT/BSA or SAT/BSA

Variable	VAT/BSA	SAT/BSA
<i>Inflammation</i>		
OPG (ng/mL)	0.07	0.09
MCP-1 (pg/mL)	0.02	0.10
MMP-9 (ng/mL)	0.07	0.03
CCL11 (pg/mL)	-0.01	-0.20
CXCL1 (ng/mL)	-0.05	-0.01
CXCL2 (ng/mL)	-0.02	-0.02
PGLYP-1 (ng/mL)	0.11	0.15
MPO (ng/mL)	0.07	0.05
IL-18 (ng/mL)	0.004	0.15
GDF-15m(ng/mL)	0.02	0.03
LP-PLA2 activity (nmol/min/ml)	0.08	-0.01
TNFR1A (ng/mL)	0.03	0.11
sRAGE (ng/mL)	-0.05	-0.16
<i>Endothelial Function</i>		
sVCAM (ng/mL)	0.04	0.03
sICAM (ng/mL)	-0.01	-0.04
<i>Cardiac Structure and Function</i>		
cTnT (ng/mL)	-0.02	-0.04
BNP (pg/mL)	-0.09	0.09
NT-Pro BNP (pg/mL)	-0.07	0.09
<i>Thrombosis</i>		
D-Dimer (ng/mL)	0.02	0.10
sCD40L (ng/mL)	0.03	0.03
<i>Renal Function</i>		
eGFR (ml/min/1.73 m ²)	0.09	0.07
CystatinC (mg/L)	-0.02	0.13
<i>Miscellaneous</i>		
Caspase-3 (ng/mL)	0.11	0.11
Uric Acid (mg/L)	0.09	0.08

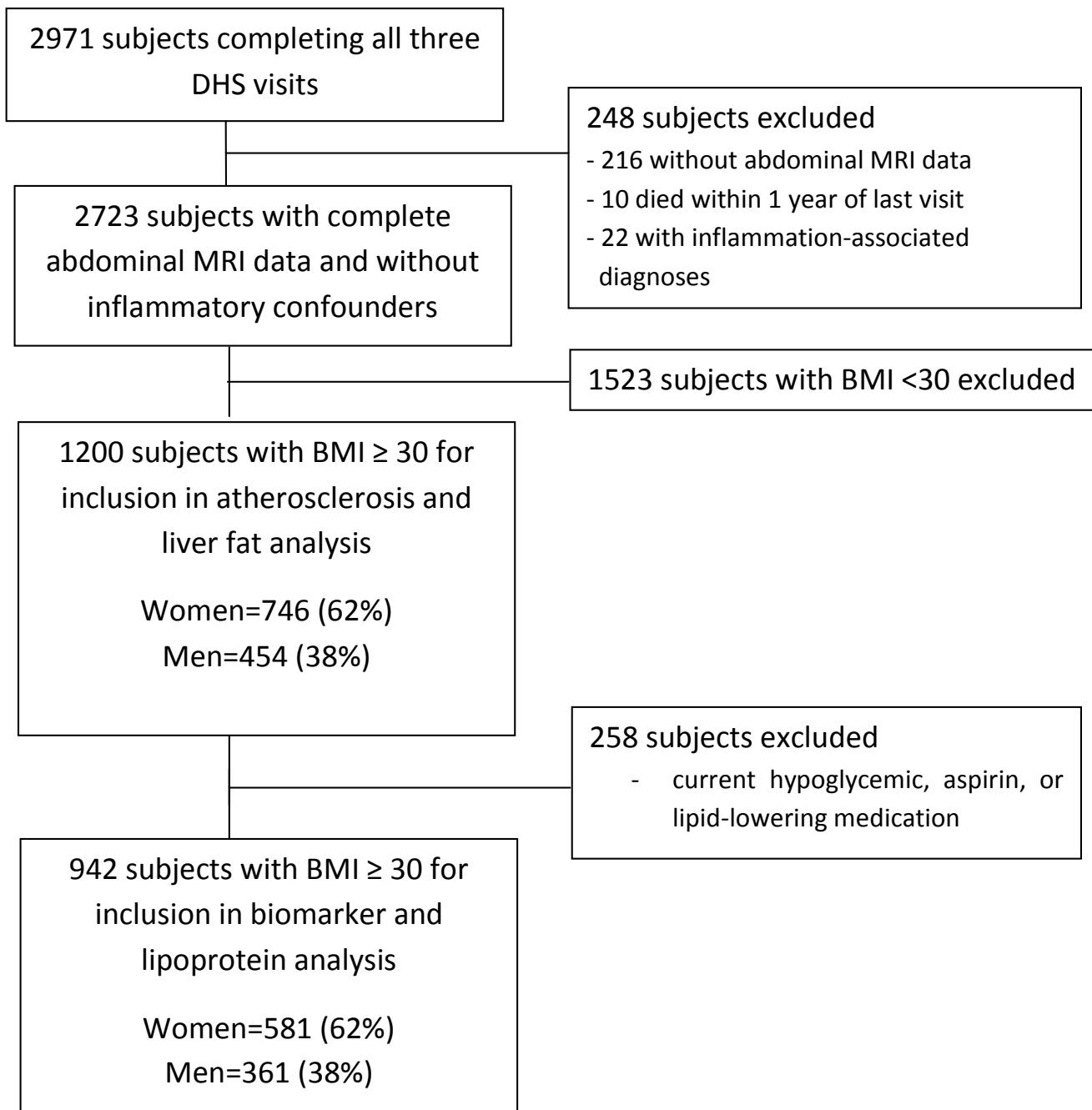
* $p < 0.0016$

Model adjusted for age + sex + race + menopausal status (women only) + BMI+ VAT/BSA + SAT/BSA

Data presented are β coefficients that represent the estimated unit change in 1 standard deviation of the log-transformed biomarker for a 1 standard deviation increase in the fat parameter.

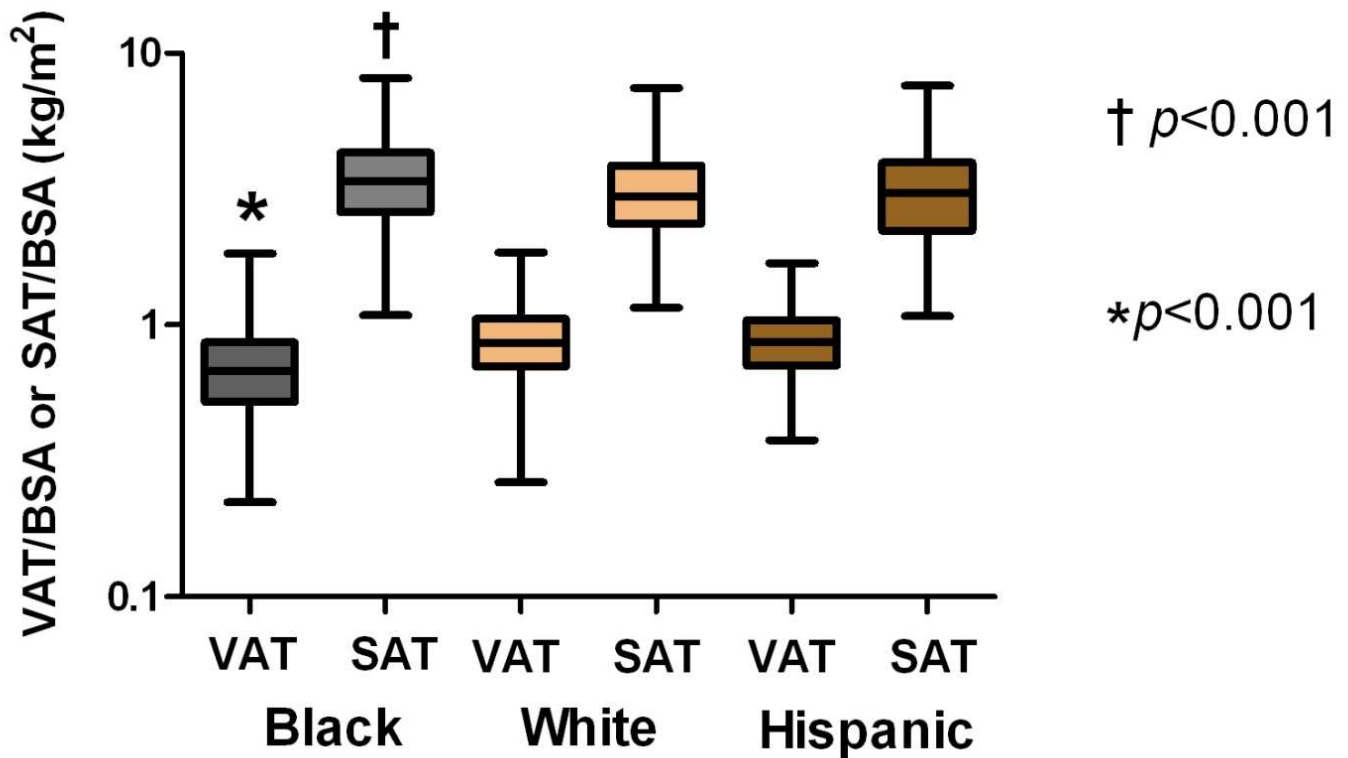
Abbreviations same as in Supplementary Appendix Table 2

Supplementary Appendix Figure 1. Subject Selection Diagram



BMI, body mass index; DHS, Dallas Heart Study; MRI, magnetic resonance imaging

Supplementary Appendix Figure 2. VAT and SAT by Race in Obese Adults



Box-and-whiskers plot represents median value, 25th and 75th percentile, and maximum/minimum values for VAT/BSA or SAT/BSA

**p*-value for Wilcoxon rank-sum test for comparisons of VAT between Black and White and Black and Hispanic
 †*p*-value for Wilcoxon rank-sum test for comparisons of SAT between Black and White and Black and Hispanic

BSA, body surface area; SAT, subcutaneous adipose tissue; VAT, visceral adipose tissue

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