Published in final edited form as:

Arterioscler Thromb Vasc Biol. 2017 December ; 37(12): 2370–2378. doi:10.1161/ATVBAHA.117.309633.

Intermuscular adipose tissue and subclinical coronary artery calcification in midlife: The CARDIA Study

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Abstract

Objective—Excess deposition of fat within and around vital organs and non-adipose tissues is hypothesized to contribute to cardiovascular disease (CVD) risk. We evaluated the association of abdominal intermuscular adipose tissue (IMAT) volume with coronary artery calcification (CAC) in Coronary Artery Risk Development in Young Adults (CARDIA) Study participants.

Approach and Results—We measured IMAT in the abdominal muscles, visceral (VAT) and pericardial (PAT) adipose tissue, and CAC using computed tomography (CT) in 3,051 CARDIA participants (56% women) at the CARDIA year 25 examination (2010–11). Mean IMAT volume and mean IMAT/total muscle volume (IMAT normalized for muscle size) were calculated in a 10-mm block of slices centered at L3–L4. Multivariable analyses included potential confounders and traditional CVD risk factors. Compared to the lowest quartile, the upper quartile of abdominal IMAT volume was associated with higher CAC prevalence [OR (95% CI) 1.6(1.2, 2.1)] after adjusting for CVD risk factors. Results were similar for highest versus lowest quartile of IMAT normalized to total muscle volume [OR (95%CI) 1.5 (1.1, 2.0)]. Significant associations of higher IMAT and normalized IMAT with CAC prevalence persisted when BMI, VAT or PAT were added to the models.

Conclusions—In a large, community-based, cross-sectional study, we found that higher abdominal skeletal muscle adipose tissue volume was associated with subclinical atherosclerosis independent of traditional CVD risk factors and other adipose depots.

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Disclosures: The authors report no conflicts. The views expressed in this manuscript are those of the authors and do not necessarily represent the views of the NHLBI; the National Institutes of Health; or the U.S. Department of Health and Human Services.

Keywords

adipose tissue; muscle; coronary artery calcification; computed tomography

Subject Codes

Obesity; Atherosclerosis; Risk Factors; Epidemiology; Computerized Tomography (CT)

Introduction

Nearly 40% of U.S. adults aged 40 to 59 years have body mass indices ≥30 kg/m^2 and are considered to be clinically obese based on recent National Health and Nutrition Examination Survey (NHANES) data[1]. Obesity, in turn, increases the risk of age-related disability[2] and chronic diseases including diabetes, heart disease and cancer[3].

Coronary heart disease (CHD) risk related to obesity is partially attributable to expansion of visceral adipose tissue (VAT), the adipose depot most closely associated with cardiometabolic risk factors[4]. However, excess adipose tissue may also be deposited within and around non-adipose tissues such as skeletal muscle, potentially altering tissue physiology and causing detrimental cardiovascular effects both locally and systemically[5–8]. Studies that have directly quantified intermuscular adipose tissue (IMAT) using computed tomography (CT) consistently show that higher IMAT is, like VAT, associated with dyslipidemia[7], impaired glucose metabolism[9], metabolic syndrome[10], and inflammation[11]. Although IMAT is associated with cardiometabolic risk factors for atherosclerosis, to date, the few studies that have evaluated the association of directly measured IMAT with subclinical measures of atherosclerosis such as intima-media thickness or arterial calcification provide conflicting information on a role for IMAT[12–16].

The present study directly measured IMAT and other abdominal adipose depots along with coronary artery calcification (CAC) with non-contrast CT in 3,051 participants aged 43–55 in the Coronary Artery Risk Development in Young Adults (CARDIA) Study. We tested the hypothesis that higher abdominal IMAT deposition is directly associated with CAC prevalence independent of traditional CVD risk factors and other measures of adipose deposition.

Materials and Methods

Study population

The Coronary Artery Risk Development in Young Adults (CARDIA) Study began in 1985 with recruitment of 5,115 participants aged 18 to 30 years at field centers located in Birmingham, AL, Chicago, IL, Minneapolis, MN, and Oakland, CA[17]. The current cross-sectional study includes data from participants who agreed to undergo computed tomography (CT) scans at the year 25 CARDIA examination (3,189 of 3,498 year 25 participants; 91%).

Materials and Methods are available in the online-only Data Supplement

Results

Participant Characteristics

Older age, lower education, lower physical activity, and a history of smoking were associated with higher overall abdominal IMAT volume ($p<0.001$ for each comparison) whereas race, sex, and alcohol intake did not significantly differ across IMAT quartiles (Table 1). Diabetes prevalence, glucose, HbA1c and HOMA-IR were each directly associated with IMAT volume ($p<0.001$ for each comparison). CRP, blood pressures and blood pressure treatment, triglycerides, and cholesterol treatment were also associated positively with higher IMAT whereas HDL-c was inversely associated with IMAT ($p<0.001$ for each comparison). Height, BMI, WC, SAT, VAT and PAT were also associated with higher IMAT ($p<0.001$ for each comparison).

Muscle Composition

Individual and overall abdominal muscle composition is shown in Supplemental Table I. Compared to other muscle groups, psoas muscles were relatively lean with lower IMAT volume and IMAT normalized to total muscle volume. Lateral oblique and paraspinous muscles had ~2–5 fold greater IMAT volume than either the rectus or psoas muscles. However, normalized IMAT was higher in rectus muscles (~19% fat on average) than either paraspinous or lateral oblique muscles (11–12% fat).

Muscle Correlations with Measures of Adiposity

IMAT volume was correlated with BMI, WC, SAT, VAT, and PAT across all muscle groups (Supplemental Table II) with Pearson correlation coefficients ranging from 0.40 to 0.73 (all paired correlations $p<0.001$). Normalized IMAT was also significantly associated with anthropometric and CT measures of adipose tissue with correlations ranging from 0.25 to 0.64 (all correlations $p<0.001$). Total muscle volume was correlated with height, BMI, WC and VAT across all muscle groups ($r=0.21–0.66$, all correlations $p<0.001$). Individual muscle IMAT volumes were correlated with each other ($r=0.56–0.77$, all correlations $p<0.001$). Also, IMAT volume was correlated with total muscle volume with correlations ranging from $r=0.32$ for paraspinous to $r=0.58$ for lateral oblique (all correlations $p<0.001$).

IMAT and CAC Prevalence

CAC prevalence and scores were associated with overall abdominal IMAT volume ($p<0.0001$) in univariate analysis (Figure 2). CAC prevalence (CAC>0 Agatston Units) was approximately 20% in the lowest quartile compared to 38% in the highest quartile of IMAT. CAC scores ≥100 Agatston Units were present in 6.6% of participants having IMAT in the lowest quartile compared to 12.5% of participants within the highest quartile for IMAT.

IMAT volume and normalized IMAT were significantly associated with CAC prevalence after adjusting for potential confounding variables in multivariable logistic regression (model 1, Table 2). In model 1, continuous IMAT volume and normalized IMAT were directly associated with CAC prevalence ($p_{trend}<0.0001$), but when quartiles IMAT and normalized IMAT were substituted in the model, CAC prevalence was ~2-fold higher in the 4^{th} quartile compared to the 1^{st} quartile suggesting a threshold effect. Including traditional

CVD risk factors (model 2) attenuated these findings, but associations of CAC prevalence with IMAT volume (OR=1.61, 95% CI 1.22–2.13) and normalized IMAT (OR=1.52, 95% CI 1.14–2.03) remained statistically significant. BMI, VAT, and PAT were separately added to model 2 to test the influence of generalized and regional adiposity on the association of IMAT with CAC. Adding BMI, VAT, or PAT to model 2 did not substantially change the association of higher IMAT and normalized IMAT with prevalent CAC ($p<0.05$ for all comparisons of 4^{th} versus 1^{st} quartile). In 2,661 participants without diabetes, we tested whether insulin resistance might explain associations between IMAT volume and normalized IMAT with prevalent CAC (Supplemental Table III). Comparing models 1 and 2, addition of HOMA-IR, along with other model 2 covariates, attenuated the association of both IMAT and normalized IMAT with prevalent CAC, but the upper quartile of IMAT was still significantly associated with ~1.5-fold more prevalent CAC than the lowest quartile. Adding BMI or VAT to model 2 did not attenuate associations of higher IMAT volume or normalized IMAT with CAC prevalence. Adding PAT to model 2 attenuated the association of the highest quartile of IMAT or normalized IMAT with CAC, but continuous IMAT measures remained significantly associated with higher CAC prevalence ($p<0.02$).

Associations of CAC prevalence with IMAT in individual muscles are presented in Supplemental Tables IV and V. Findings for individual muscle groups generally reflected those for overall IMAT; however, the associations of paraspinous IMAT with CAC prevalence appeared to be more robust than those in other muscle groups. Higher quartiles of paraspinous IMAT or normalized IMAT remained significantly associated with CAC prevalence in the fully adjusted models including other adipose measures ($p<0.05$ for comparisons of 4^{th} quartile to 1^{st} quartile in each model).

IMAT and CAC Score

Probabilities of CAC scores across IMAT (Figures 3a–3d) and normalized IMAT (Figures 4a–4d) quartiles were determined using multinomial logistic regression. As shown in panel 3a, CAC scores varied significantly across IMAT quartiles after adjusting for CVD risk factors ($p=0.008$ for test with 9 degrees of freedom). Adjusting for BMI attenuated associations between IMAT and CAC scores to borderline significance ($p=0.066$; panel 3b). However, the association of CAC scores with IMAT remained significant when either VAT or PAT was included in the model (both $p<0.05$; panels 3c and 3d). CAC score probabilities across normalized IMAT quartiles, shown in Figures 4a–4d, were similar in patterning to those for IMAT volume. CAC scores varied significantly across quartiles of normalized IMAT in the CVD risk factor adjusted model ($p=0.001$; panel 4a), but additional adjustment for BMI, VAT or PAT made little difference in probability distributions ($p<0.01$ for all models; panels 4b–4d).

Discussion

In this community-based, cross-sectional study of more than 3,000 middle-aged participants, we found that higher IMAT within the abdominal musculature was positively associated with CAC, an indicator of subclinical atherosclerotic plaque burden. Moreover, associations of higher IMAT with CAC were consistent across sex and race strata and persisted after

adjusting for traditional CVD risk factors and other adipose measures. In our knowledge, this is the first large-scale population-based study to demonstrate that higher abdominal IMAT, directly measured using CT, is associated with subclinical atherosclerosis after adjusting for body composition, including the major ectopic depots of VAT and PAT.

Skeletal muscle is critical to glucose metabolism, accounting for ~80% of glucose utilization in healthy individuals[18]. Impaired glucose clearance in response to insulin, or insulin resistance, represents a key component in the development of type 2 diabetes and important contributor to cardiovascular risk[18]. Clinical studies have shown that IMAT accumulation is strongly associated with insulin resistance[9,10,13,19]. The present data and previous studies show that IMAT is directly correlated with VAT and PAT volume and the latter are strongly associated with adverse CVD risk factor profiles[20–23]. In CARDIA, we have recently shown that higher PAT is associated with diabetes prevalence even after controlling for BMI and VAT[24]. Higher VAT is also associated with prevalent subclinical atherosclerosis in the preponderance of studies, though it remains unclear as to whether this relationship is independent of cardiometabolic risk factors and overall obesity[15,25–28]. PAT is associated with both CAC and incident CVD and these associations appear to be independent from traditional risk factors and other measures of obesity[15,16,22,29]. Although IMAT contributes a relatively small proportion to the total abdominal adipose tissue stores, it is strongly associated with established CVD risk factors including insulin resistance, dyslipidemia, hypertension, hyperinflammatory states, and type 2 diabetes[9–11,13,19]. Moreover, a recent report in 1,063 older men demonstrated an association of lower calf muscle attenuation (a marker of higher IMAT levels) with all-cause and CVD mortality that was not explained by traditional risk factors including diabetes and dyslipidemia[30].

The present study suggests that higher abdominal IMAT is associated with CAC development which is, in turn, a well-established non-invasive imaging marker for risk of incident CHD and CVD[31,32]. Previous studies that are directly comparable to the present study are few and may have been limited in power[15,16]. In a small MESA substudy (n=398) that used the present CT methods, IMAT was associated with CAC in univariate analysis, but this association did not persist in multivariable models[15]. A second study in African Americans with diabetes (n=422), found no significant associations of IMAT volume with calcified plaque in the coronary, carotid, or aortic arteries[16]. A number of previous studies should also be discussed in context with the present CARDIA data as those studies suggest that a higher proportion of lean muscle is associated with lower atherosclerosis[12–14,33]. In a study that included 100 participants, higher thigh muscle attenuation (indicative of leaner tissue) was associated with lower carotid intima-media thickness and the association persisted after adjustment for age, diabetes, insulin resistance, and VAT[13]. Higher proportion of lean abdominal muscle was associated with lower likelihood of thoracic aorta calcification in 394 participants, but the authors noted there were no significant associations of muscle composition with carotid, coronary, abdominal aorta, or iliac calcifications, nor was IMAT *per se* associated with higher calcification in any artery bed[14]. Recently, Ko and colleagues reported that higher total skeletal muscle mass measured using bioelectrical impedance was inversely associated with CAC in more than 31,000 South Korean adults, and these findings remained significant after adjusting for insulin resistance and other potential risk mediators[33]. In the study by Ko et al., it is important to note that skeletal

muscle mass was inversely associated with BMI; in fact, in the highest quartile of muscle mass only 12% of participants were obese compared to 49% of participants in the lowest quartile of muscle mass[33]. Therefore, the data from Ko and colleagues suggest that it is higher lean muscle mass that is associated with healthier arteries[33]. The present study shows that higher abdominal IMAT, directly quantified using CT, is associated with the prevalence and extent of subclinical atherosclerosis in midlife. Moreover, these associations persist in multivariable models including CVD risk factors and other adipose measures.

Potential Mechanisms

Although IMAT accumulation is strongly associated with hypertension, diabetes, and dyslipidemia, and these are plausible intermediaries for the association between IMAT and CAC development, adjustment for these and other traditional risk factors did not explain the association of IMAT with CAC in the present study. CARDIA clinical evaluations (e.g. blood pressure, anthropometric measures) and laboratory measures (e.g. lipids, glucose) were thoughtfully designed and have been performed with consistency and precision over the study's decades-long existence[17]. Diabetes was carefully defined based on fasting glucose, post-challenge glucose, and HbA1c or use of diabetes medications. Moreover, we performed a sub-analysis in non-diabetics that included adjustment for HOMA-IR, yet none of these traditional CVD risk factors fully explained the association of abdominal IMAT with CAC. Still, the present cross-sectional study relies on measures performed at a single visit. Previous studies in CARDIA have shown that in early life, between 18 and 30 years of age, exposure to even slightly elevated glucose and LDL-cholesterol (below clinical thresholds) is more strongly associated with CAC 15 years later than concurrent measures[34]. Moreover, CARDIA participants receive feedback on multiple risk factors making it likely that abnormal values are detected earlier in life and possibly treated sooner than in the general population. Though we adjusted for known CVD risk factors and treatment for diabetes, hypertension, and hypercholesterolemia, we cannot be sure that our cross-sectional study captures integrated risk factor exposure over a lifetime.

Excess muscle fat accumulation may be pro-inflammatory as suggested by Beasley and colleagues who found that IMAT was directly associated with IL-6 concentration[11]. Haam et al. found that CT-quantified IMAT was directly associated with circulating monocyte chemoattractant protein-1 (MCP-1), a pro-inflammatory chemotactic factor for monocytes and T-cells[35]. These studies, along with other lines of laboratory and clinical evidence, suggest that IMAT has the potential to promote and sustain an inflammatory microenvironment[11,18,35]. Moreover, as an activator of monocytes, MCP-1 has the potential to promote monocyte adherence to vascular endothelium and subsequent monocyte migration into the vessel wall where they are hypothesized to play a role in atherogenesis via differentiation into macrophages and ultimately foam cells[36,37]. Although circulating MCP-1 and other cytokines are associated with prevalent and incident CVD, it remains unclear if their roles are independent from traditional risk factors[38–40]. In the present cross-sectional study, the chronic inflammation marker CRP did not explain the association between IMAT and CAC. We did not measure IL-6 nor any of the myriad other chemokines that may explain the association of IMAT with subclinical atherosclerosis. Regardless, chronic inflammation is a plausible mechanism for development of atherosclerosis that has

been linked to IMAT and other ectopic adipose depots[4,18]. Moreover, based on previous studies[11,35], it is possible that the contribution of higher IMAT to risk for atherosclerosis extends beyond its correlation with other ectopic adipose depots. The association of CAC progression with cumulative exposure to central obesity has been documented in CARDIA[41], and the present study suggests that excess IMAT may be one component of the risk associated with central obesity.

Limitations

The present study is limited by a cross-sectional design that does not permit us to establish definitively the temporal nature of the associations; however, it seems unlikely that calcified atherosclerosis is driving IMAT accumulation. Though we adjusted for known cardiometabolic risk factors believed to contribute to associations between IMAT and CAC, it is possible that emerging risk factors for CAC, such as circulating calcium-phosphorous product, contribute to associations as well[42]. The measurement of muscle composition was performed at the L3–L4 vertebral level and VAT volume was measured at the L4–L5 level, but we do not believe this would have a meaningful impact on our results. The composition of the abdominal muscles at these respective lumber levels is similar and highly correlated. Indeed, we chose to measure muscle composition at the L3–L4 level to avoid the pelvic bones that may prevent clear visualization of the lateral oblique muscles in some participants at the L4–L5 level. We primarily focused on overall abdominal IMAT in the present study, but we also measured specific muscle groups. Paraspinous and psoas muscles have often been the focus of prior studies due to their relative ease of measurement. The paraspinous muscles have a relatively high proportion of Type I (slow twitch) fibers and provide postural support along the spine, whereas the other abdominal muscles we measured are relatively enriched in Type II fibers and function in movement[43–45]. Regardless of these histological and functional differences, trends were similar across all muscle groups in the individual analyses. Since we only measured abdominal muscles in the present study, we cannot address any potential associations of IMAT in peripheral skeletal muscles with CAC. The CARDIA study has many important attributes including its multicenter design with the large number of participants including approximately equal numbers of white and black men and women of varying socioeconomic status and lifestyles. However, these cross-sectional findings require independent confirmation in other populations and we cannot address whether the present CARDIA data are applicable to populations including other age ranges or ethnicities.

Conclusion

Higher abdominal IMAT volume was associated with prevalent CAC and higher CAC scores in this cross-sectional study in middle-age participants. These associations persisted after accounting for traditional CVD risk factors and visceral adiposity. Although prospective studies are needed, these cross-sectional findings raise the possibility that ectopic deposition of fat within abdominal skeletal muscles contributes to the role of adiposity as an adverse CVD risk factor.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The Authors would like to thank the investigators, the staff, and the participants of the CARDIA study for their dedication and highly valued contributions. This manuscript has been reviewed by CARDIA for scientific content.

Sources of Funding: The Coronary Artery Risk Development in Young Adults Study (CARDIA) is conducted and supported by the National Heart, Lung, and Blood Institute (NHLBI) in collaboration with the University of Alabama at Birmingham (HHSN268201300025C & HHSN268201300026C), Northwestern University (HHSN268201300027C), University of Minnesota (HHSN268201300028C), Kaiser Foundation Research Institute (HHSN268201300029C), Johns Hopkins University School of Medicine (HHSN268200900041C) and Vanderbilt School of Medicine (R01-HL098445). CARDIA is also partially supported by the Intramural Research Program of the National Institute on Aging (NIA) and an intra-agency agreement between NIA and NHLBI (AG0005).

Abbreviations

BMI	body mass index
CAC	coronary artery calcification
CARDIA	Coronary Artery Risk Development in Young Adults
CT	computed tomography
IMAT	intermuscular adipose tissue
PAT	pericardial adipose tissue
SAT	subcutaneous adipose tissue
VAT	visceral adipose tissue
WC	waist circumference

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Highlights

- Abdominal intermuscular adipose tissue (IMAT) was associated with coronary artery calcification (CAC) prevalence and score in 3,048 community-dwelling participants
- The IMAT and CAC association was not explained by traditional cardiovascular disease risk factors
- Body mass index and visceral adipose tissue partially attenuated, but did not explain, associations of abdominal IMAT with CAC

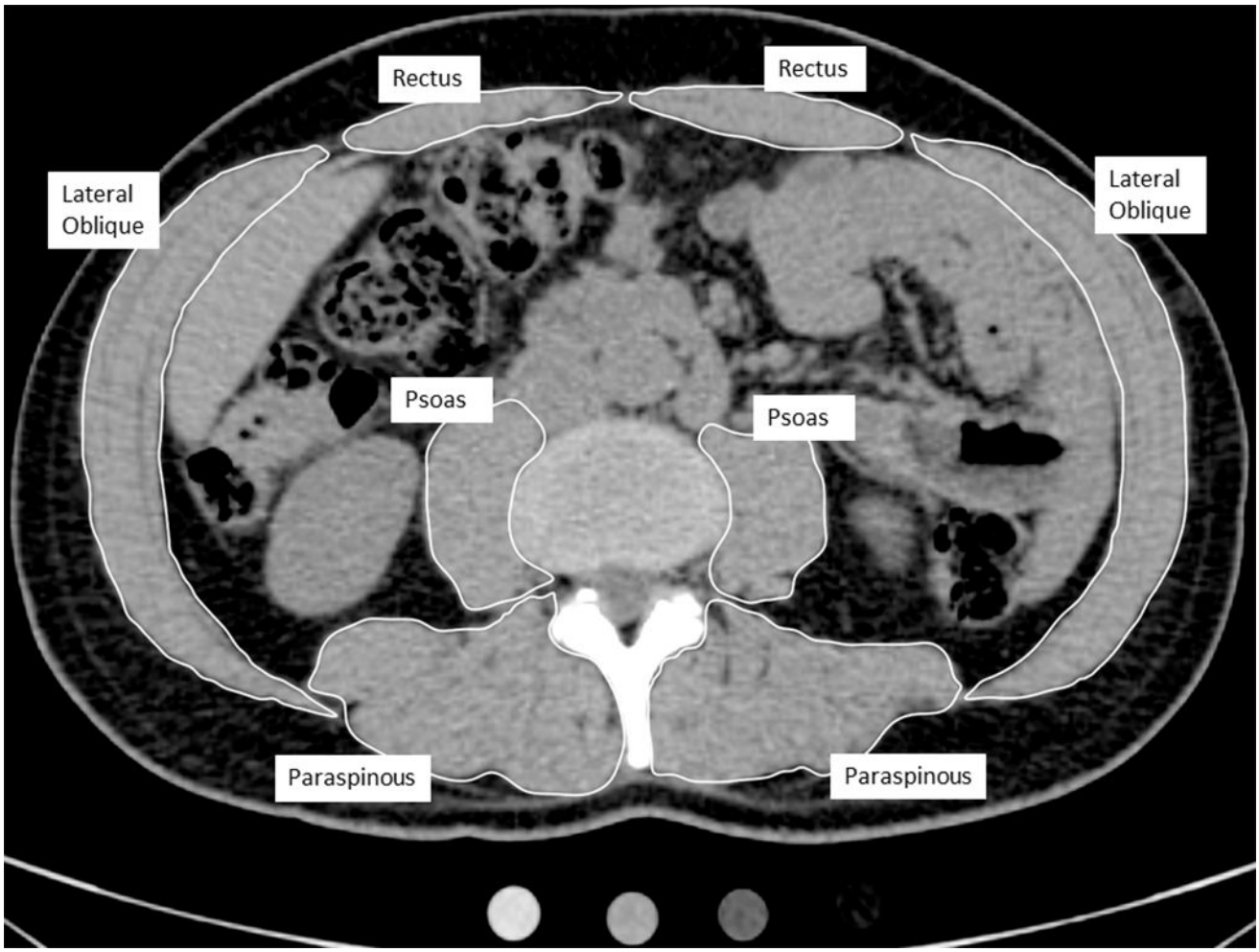

Figure 1.
Single CT slice through the abdomen at the L3–L4 lumbar level. Right and left muscle groups are indicated. Left and right sides were averaged for analyses.

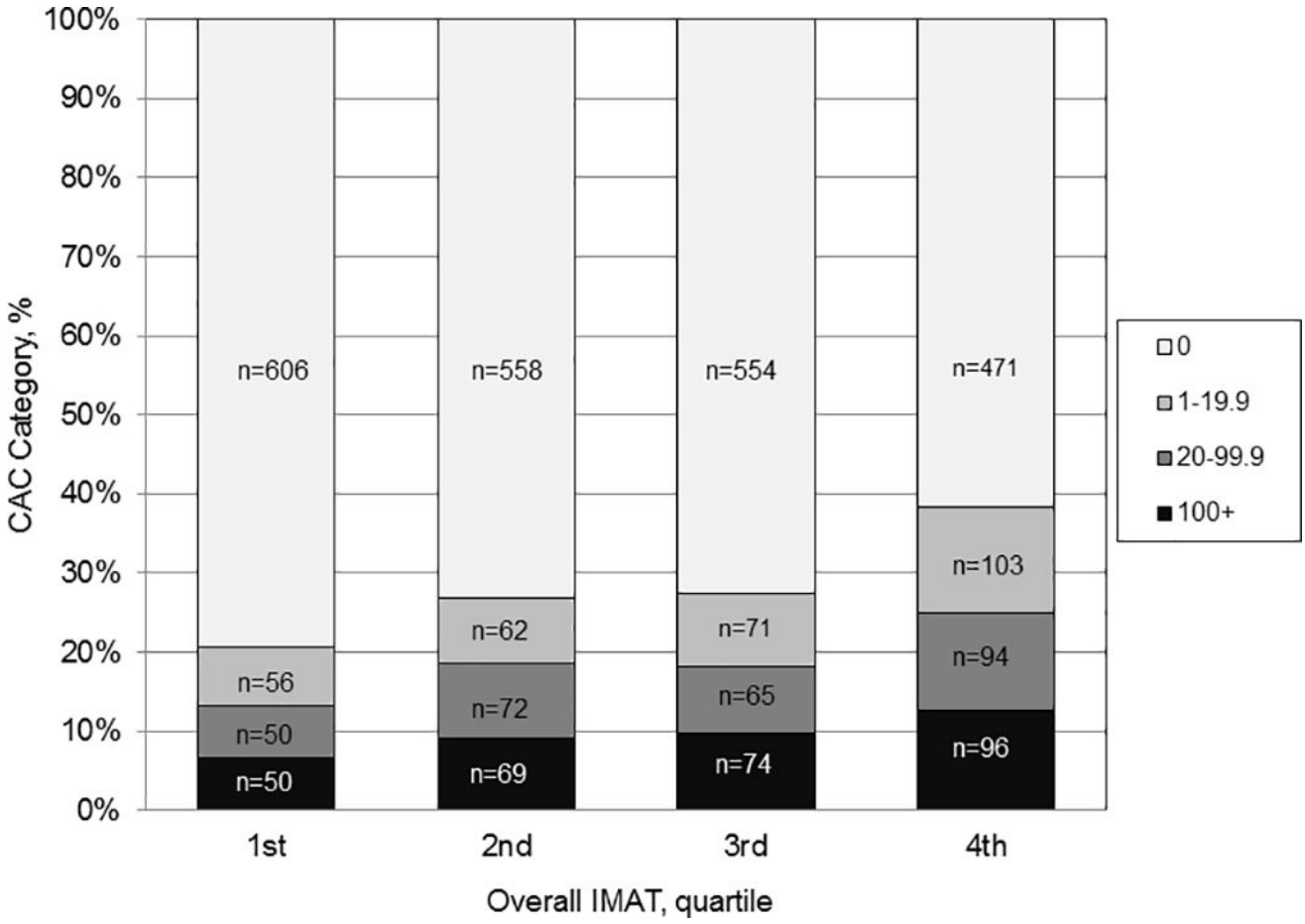

Figure 2.
Unadjusted Agatston CAC scores by quartiles of overall IMAT volume (chi square analysis p<.0001).

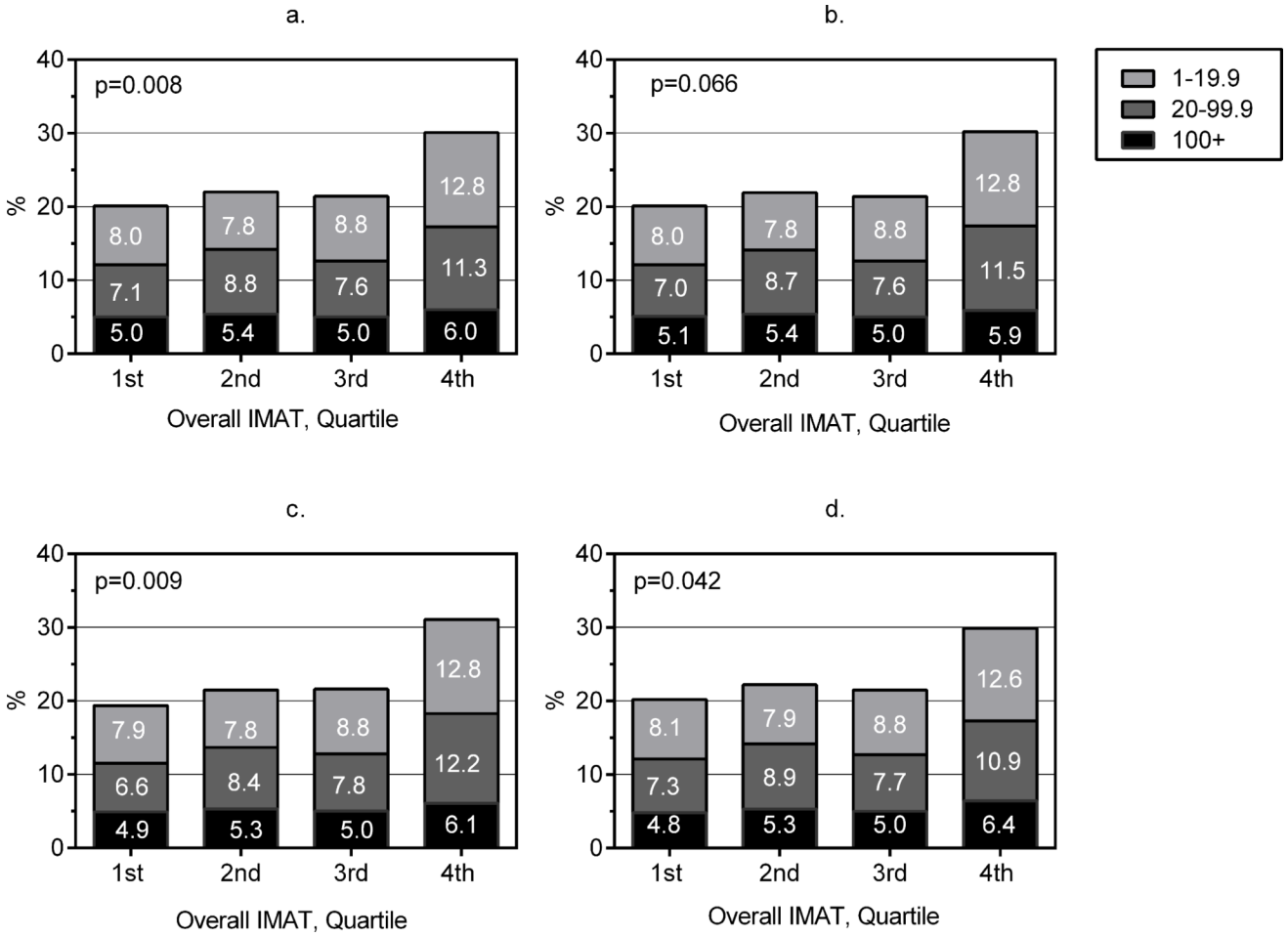

Figure 3.

a–d. Probability of positive CAC scores of 1–19.9, 20–99.9, and ≥100 Agatston Units across quartiles of IMAT volume derived using multivariable multinomial logistic regression. Probabilities are adjusted for age, sex, race, sex*race, center, height (except when BMI is included), education, physical activity, alcohol consumed, smoking history, diabetes, systolic BP, BP med use, HDL cholesterol, triglycerides, cholesterol med use, and CRP (panel 3a) with or without BMI (panel 3b) or VAT (panel 3c) or PAT (panel 3d). P-value is based on multinomial logistic regression model.

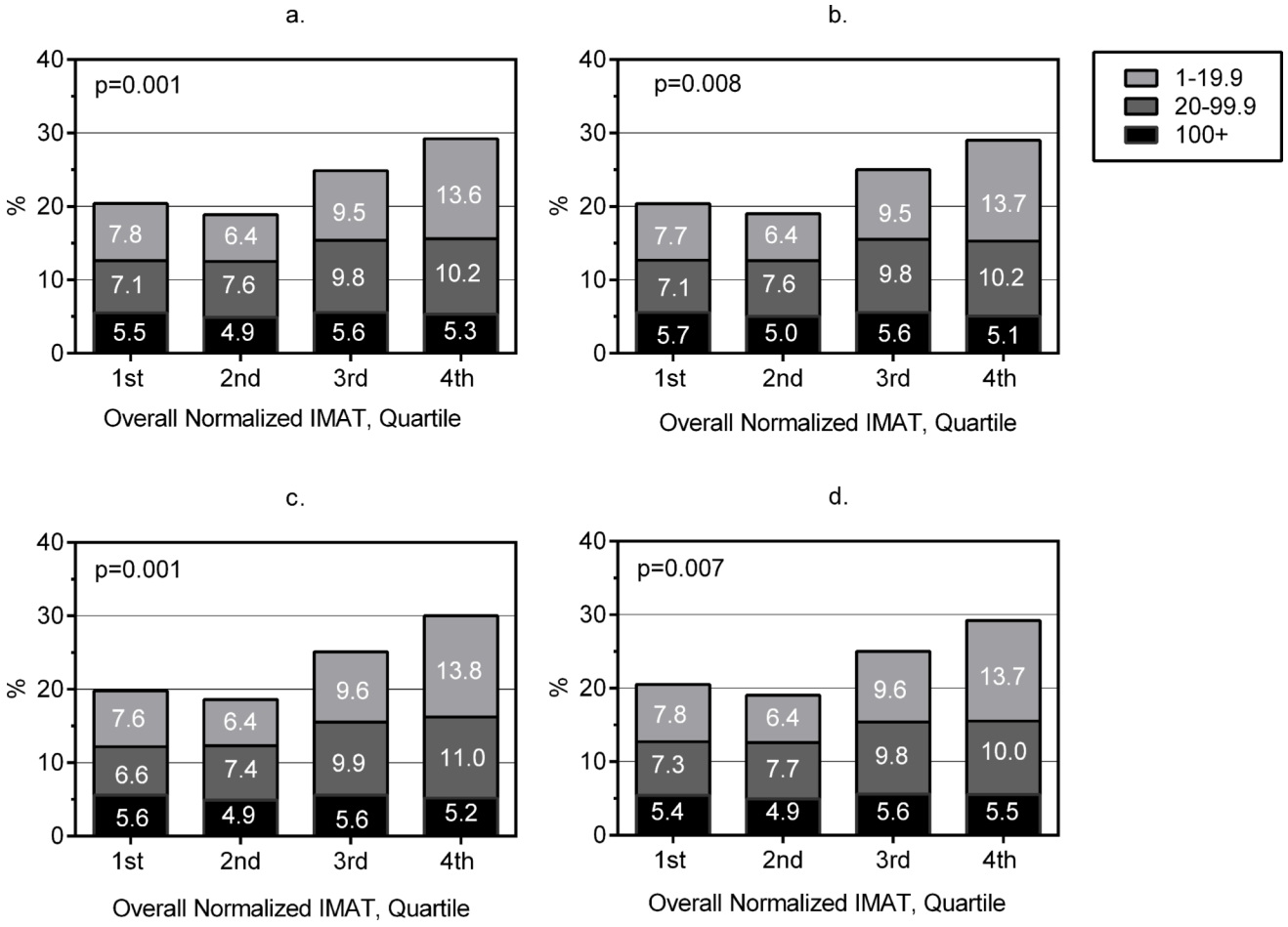

Figure 4.

a–d. Probability of positive CAC scores of 1–19.9, 20–99.9, and ≥100 Agatston Units across quartiles of normalized IMAT derived using multivariable multinomial logistic regression. Probabilities are adjusted for age, sex, race, sex*race, center, height (except when BMI is included), education, physical activity, alcohol consumed, smoking history, diabetes, systolic BP, BP med use, HDL cholesterol, triglycerides, cholesterol med use, and CRP (panel 4a) with or without BMI (panel 4b) or VAT (panel 4c) or PAT (panel 4d). P-value is based on multinomial logistic regression model.

Table 1

Participant characteristics [(mean(SD), median(25th, 75th percentile) or %(n)] by sex-specific quartiles overall IMAT volume

Characteristic	All Participants (n=3051)	IMAT Volume (cm^3), quartiles*				
		<1.27 (n=762)	1.27 – <1.90 (n=761)	1.90 – <2.92 (n=764)	≥2.92 (n=764)	p
Age, years	50.1(3.6)	49.3(3.6)	50.2(3.6)	50.5(3.6)	50.5(3.6)	<.0001
Female Sex	56.2%(1716)	58.7% (447)	54.3% (413)	56.5% (432)	55.5% (424)	0.241
Black Race	47.2% (1441)	45.7% (348)	46.5% (354)	46.5% (355)	50.3% (384)	0.161
Education, years	15.6(2.6)	16.0(2.6)	15.7(2.6)	15.4(2.5)	15.2(2.5)	<.0001
Physical Activity, units	277 (126–486)	330 (158–547)	306 (144–509)	264 (115–467)	216 (97–403)	<.0001
Smoking						
Never	60.9% (1859)	67.3% (513)	58.6% (446)	61.1% (467)	56.7% (433)	
Ever	21.8% (665)	17.6% (134)	23.9% (182)	22.4% (171)	23.3% (178)	
Current	17.3% (527)	15.1% (115)	17.5% (133)	16.5% (126)	20.0% (153)	0.001
Alcohol Intake, ml/day	2.4 (0–14.7)	2.7 (0–14.5)	2.7 (0–17.0)	2.4 (0–14.3)	2.4 (0–14.7)	0.295
Diabetes	12.3% (375)	5.2% (40)	9.3% (71)	11.6% (89)	22.9% (175)	<.0001
Glucose	99.4(28.5)	92.1(19.4)	97.2(29.7)	99.8(25.5)	108.6(34.9)	<.0001
HbA1c, %	5.7(1.0)	5.5(0.7)	5.7(1.0)	5.7(0.9)	6.0(1.2)	<.0001
CRP, mg/l	1.4 (0.6–3.5)	0.8 (0.4–1.7)	1.1 (0.5–2.5)	1.7 (0.8–3.8)	3.1 (1.4–6.5)	<.0001
HOMA-IR†	1.9 (1.1–3.1)	1.2 (0.8–1.9)	1.6 (1.0–2.6)	2.2 (1.4–3.2)	3.0 (2.0–4.5)	<.0001
Systolic BP, mmHg	119.8(16.0)	115.8(15.1)	119.0(15.1)	120.5(16.4)	123.9(16.4)	<.0001
Diastolic BP, mmHg	75.0(11.2)	71.1(10.6)	73.7(11.1)	75.9(10.7)	79.3(10.6)	<.0001
BP Treatment	27.3% (833)	18.0% (137)	24.3% (185)	26.2% (200)	40.7% (311)	<.0001
Total cholesterol, mg/dl	192.6(36.9)	190.3(33.1)	193.3(38.3)	194.8(38.0)	191.9(37.7)	0.099
LDL-c, mg/dl	112.1(32.8)	107.7(29.8)	112.8(33.1)	115.0(33.6)	112.9(34.0)	0.0001
HDL-c, mg/dl	58.0(18.0)	64.9(19.0)	58.8(18.2)	55.5(16.3)	52.8(16.3)	<.0001
Triglycerides, mg/dl	93 (68–134)	75 (58–103)	88 (65–126)	100 (76–144)	112 (80–161)	<.0001
Cholesterol Treatment	15.8% (481)	10.2% (78)	13.9% (106)	17.8% (136)	21.1% (161)	<.0001
Height, cm	170.3(9.4)	168.8(8.8)	170.5(9.2)	170.6(9.7)	171.5(9.7)	<.0001
BMI, kg/m^2	30.2(7.1)	24.9(4.1)	27.9(4.7)	30.9(5.1)	37.2(7.4)	<.0001
WC, cm	94.6(15.8)	81.0(9.9)	89.4(10.4)	96.8(10.8)	111.1(13.5)	<.0001

Characteristic	All Participants (n=3051)	IMAT Volume (cm^3), quartiles*				
		<1.27 (n=762)	1.27 – <1.90 (n=761)	1.90 – <2.92 (n=764)	≥2.92 (n=764)	p
SAT, cm^3	335.0(169.4)	211.0(115.0)	289.4(131.4)	362.2(141.6)	476.8(160.9)	<.0001
VAT, cm^3	132.1(73.7)	74.8(41.4)	109.7(48.7)	146.2(59.2)	197.4(76.8)	<.0001
PAT, cm^3	56.8(33.7)	35.6(17.6)	48.1(23.2)	60.2(28.6)	83.1(40.6)	<.0001

*Quartiles based on overall IMAT volume (cm^3) averaged across left and right sides for all abdominal muscles measured in the study (rectus, lateral oblique, psoas and paraspinous);

†HOMA-IR is reported for the 2,661 non-diabetics

Significance tests from ANOVA (continuous variables) or chi square analysis (categorical variables)

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Table 2

Logistic regression models for association of overall IMAT volume and normalized overall IMAT with CAC prevalence [Odds Ratio(95% Confidence Interval)]

Measure	Quartile	CAC (cases/total)	Model 1	Model 2	BMI	Model 2 plus VAT	PAT
IMAT Volume	<1.27	156/762	reference	reference	reference	reference	reference
	1.27 – <1.90	203/761	1.22 (0.95,1.58)	1.11 (0.85,1.45)	1.10(0.84,1.44)	1.14(0.88,1.51)	1.11(0.85,1.45)
	1.90 – <2.92	210/764	1.22 (0.95,1.58)	1.06 (0.81,1.39)	1.06(0.79,1.41)	1.13(0.84,1.51)	1.06(0.80,1.40)
	≥2.92	293/764	**2.10 (1.64,2.69)**	**1.61 (1.22,2.13)**	**1.60(1.13,2.25)**	**1.79(1.29,2.49)**	**1.58(1.16,2.17)**
		P_{trend}	<0.0001	0.008	0.014	0.001	0.047
	Continuous		1.27 (1.17,1.38)*	1.14 (1.04,1.25)	1.11 (0.98,1.26)	1.17 (1.04,1.30)	1.12(1.00,1.24)
Normalized IMAT	<0.067	201/763	reference	reference	reference	reference	reference
	0.067 – <0.097	189/763	1.03 (0.80,1.33)	0.91 (0.70,1.18)	0.90 (0.70,1.18)	0.94 (0.72,1.23)	0.91(0.70,1.18)
	0.097 – <0.144	228/761	**1.47 (1.14,1.89)**	1.26 (0.97,1.65)	1.24 (0.94,1.63)	**1.34 (1.00,1.78)**	1.25(0.95,1.66)
	≥0.144	244/764	**1.96 (1.51,2.54)**	**1.52 (1.14,2.03)**	**1.46 (1.04,2.03**)	**1.65 (1.18,2.31)**	**1.48(1.07,2.05)**
		P_{trend}	<0.0001	0.002	0.015	0.001	0.034
	Continuous		1.29 (1.18,1.41)	1.16 (1.05,1.28)	1.14 (0.99,1.29)	1.19 (1.06,1.34)	1.13(1.01,1.27)

Prevalence based 0 or >0 Agatston Units; normalized IMAT = IMAT volume/total muscle volume ratio Model 1: age, sex, race, sex*race, center, height (except when BMI is included), and education; Model 2: model 1 + physical activity, alcohol consumed, smoking history, diabetes, systolic BP, BP med use, HDL cholesterol, triglycerides, cholesterol med use, and CRP.

*estimate per SD IMAT volume (1.63 cm^3) or normalized IMAT (0.06 cm^3); **Bold** indicates odds ratio differs significantly (p<.05) from Quartile 1 (reference). P_{trend} is based on modeling continuous IMAT.