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Association of Abdominal Muscle Area and Density with Glucose Regulation: The Multi-Ethnic Study of Atherosclerosis (MESA)

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Abstract

Aims: Previous characterization of body composition as a type 2 diabetes mellitus (T2DM) risk factor has largely focused on adiposity, but less is known about the independent role of skeletal muscle. We examined associations between abdominal muscle and measures of glucose regulation.

Materials and Methods: Cross-sectional analysis of 1,891 adults enrolled in the Multi-Ethnic Study of Atherosclerosis. Multivariable regression assessed associations between abdominal muscle area and density (measured by computed tomography) with fasting glucose, homeostasis

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model assessment of insulin resistance (HOMA-IR), and prevalent T2DM (fasting glucose ≥126mg/dL or medication use).

Results: In minimally adjusted models (age, sex, race/ethnicity, income), a 1-SD increment in abdominal muscle area was associated with higher HOMA-IR (β=0.20 ± SE 0.03; 95%CI: 0.15, 0.25; *P*<0.01) and odds of T2DM (OR=1.47; 95%CI: 1.18, 1.84; *P*<0.01), while higher density was associated with lower fasting glucose (−4.49 ± 0.90; −6.26, −2.72; *P*<0.01), HOMA-IR (−0.16 ± 0.02; −0.20, −0.12; *P*<0.01), and odds of T2DM (0.64; 0.52, 0.77; *P*<0.01). All associations persisted after adjustment for comorbidities and health behaviors. However, after controlling for height, BMI, and visceral adiposity, increasing muscle area became negatively associated with fasting glucose (−2.23 ± 1.01; −4.22, −0.24; *P*=0.03), while density became positively associated with HOMA-IR (0.09 ± 0.02; 0.05, 0.13; *P*<0.01).

Conclusions: Increasing muscle density was associated with salutary markers of glucose regulation, but associations inverted with further adjustment for body size and visceral adiposity. Conversely, after full adjustment, increasing muscle area was associated with lower fasting glucose, suggesting some patients may benefit from muscle-building interventions.

Keywords

body composition; myosteatosis; fasting glucose; insulin resistance; diabetes; race/ethnicity

INTRODUCTION

In 2015, type 2 diabetes mellitus (T2DM) was the seventh leading cause of death in the United States (U.S.).[1] As the U.S. population ages, T2DM prevalence continues to rise,[2] thereby increasing risk for T2DM-associated comorbidities, complications, and mortality. Further research on the phenotypic differences associated with insulin resistance and hyperglycemia are essential for improved diabetes prevention, early diagnosis, and management.[3]

Previous characterization of body composition as a risk factor for T2DM has largely focused on adipose tissue distribution,[4–7] but less is known about the independent role of skeletal muscle.[8] Among healthy individuals, skeletal muscle meaningfully contributes to insulin-regulated metabolism of glucose, while among individuals with insulin resistance, impaired insulin signaling and post-binding intracellular defects markedly reduce skeletal muscle glucose uptake.[9] Moreover, evidence of skeletal muscle insulin resistance is present long before the onset of clinical diabetes[9] and recent studies suggest ectopic lipid deposits in skeletal muscle, “myosteatosis,” may be relevant to the development of insulin resistance and impaired glucose homeostasis.[5,10,11] Accordingly, myosteatosis assessment could aid in early clinical evaluation of metabolic health, for both prevention and treatment of T2DM.

There is a growing body of literature utilizing imaging modalities such as magnetic resonance imaging (MRI) and computed tomography (CT) to systematically evaluate muscle quantity (i.e., area) and quality (i.e., density), and their role in health and disease. For example, muscle density, assessed by CT, is inversely associated with body fat and fat infiltration of muscle, and positively associated with muscle strength and function.[12]

Notably, there are limitations to the evidence base on associations of muscle and glucose metabolism. Previous studies largely focused on either muscle quantity[13,14] or quality,[15,16] but few included these two variables in the same analyses. Additionally, some studies did not adequately account for potential confounders, such as body mass index (BMI) or visceral adipose tissue (VAT).[13,14,17,18] Finally, some studies did not include both males and females,[13,16,19] or racially/ethnically diverse study populations.[15,16] Therefore, we aimed to test the independence of associations between abdominal muscle area and density with markers of glucose regulation among a multi-ethnic cohort of males and females.

MATERIALS AND METHODS

Participants

The Multi-Ethnic Study of Atherosclerosis (MESA) is a longitudinal cohort study of American adults of African, Chinese, Hispanic, and non-Hispanic White background. Details about the MESA study design have previously been published.[20] In brief, from 2000–2002, 6,814 adults aged 45–84 years were recruited from six U.S. locations. Individuals with a history of the following were excluded: angina, myocardial infarction, heart failure, stroke or transient ischemic attack; coronary artery bypass graft, angioplasty, valve replacement or pacemaker placement. The institutional review board of each study site approved the MESA, and all participants provided written informed consent.

At clinic visits 2 and 3 (2002–2005), a random subset of 1,968 participants were enrolled in an ancillary study on body composition and underwent an abdominal CT scan; approximately half at visit 2 and half at visit 3. Individuals with incident cardiovascular disease after visit 1 were excluded from the ancillary study.

Data collection

Standardized questionnaires were used to obtain information on socio-demographics, medical history and medication usage. Participants self-reported frequency of sedentary behavior and physical activity using the Typical Week Physical Activity Survey (adapted from the Cross-Cultural Activity Participation Study).[21]

Height and weight were measured to the nearest 0.1cm and 0.5kg, respectively, and used to calculate BMI in kg/m^2. An automated monitor measured blood pressure (BP) after five minutes of seated rest; the last two of three readings were averaged and recorded. Hypertension was defined as systolic BP≥130mmHg, diastolic BP≥80mmHg, or use of antihypertensives.[22]

Laboratory

At the visit concomitant to CT scans, venous blood was collected after a 12-hour fast. Participants were instructed to take their usual medications before the visit. Total and high-density lipoprotein (HDL) cholesterol, triglycerides, creatinine, glucose, and insulin were measured as previously reported.[20] Insulin resistance was estimated by the homeostasis model assessment of insulin resistance (HOMA-IR) = fasting insulin (mIU/L) x fasting glucose (mg/dL)/405.[23] Diabetes was defined as fasting glucose ≥126mg/dL or

use of insulin or oral hypoglycemic medication. Dyslipidemia was defined as Total/HDL cholesterol ratio >5.0 or use of cholesterol-reducing medication.[24,25] Estimated glomerular filtration rate (eGFR) was calculated according to the CKD-Epi Equation.[26]

Abdominal muscle and fat measurements

To measure abdominal muscle and fat, a single CT slice at L4-L5 was processed using the Medical Imaging Processing Analysis and Visualization software version 4.1.2 (NIA/NIH, Bethesda, MD).[27] Tissue was categorized by Hounsfield units (HU): −190 to −30HU was considered fat, 0 to 100HU lean muscle, and the intervening HU range mixed connective tissue.[28–30] Bilateral oblique, rectus abdominus, paraspinal, and psoas muscles were defined within their unique facial planes and grouped into muscles of stabilization (oblique, rectus abdominus, paraspinal) and locomotion (psoas). When muscles of stabilization and locomotion were considered together, this was termed *total* abdominal muscle.

For each muscle, area was determined by summing the number of pixels from 0 to 100HU within that muscle's fascial plane. A similar process was completed for visceral and subcutaneous fat. Muscle density was defined by the average HU value (between 0–100) within the muscle's fascial plane. As muscle density increases (i.e., higher average HU), fatty infiltration of the muscle decreases (i.e., higher muscle "quality"). Staff blinded to participants' clinical information analyzed all CT imaging. Inter- and intrarater reliability for abdominal, subcutaneous, and visceral fat were 0.99 for all measurements. Inter- and intrarater reliability for muscle groups ranged from 0.93 to 0.98.[28]

Statistical analysis

Of the 1,968 participants enrolled in the ancillary study, 70 were missing muscle data and 7 were missing fasting glucose or insulin data. These 77 individuals were excluded, resulting in a final analytic sample of 1,891 participants.

Continuous variables were examined for normality. HOMA-IR was natural logarithm (ln) transformed due to positive skewness. Descriptive statistics of population characteristics were described with mean and standard deviation (SD) for continuous variables, and count and percentage for categorical. To examine differences in clinical and demographic characteristics across muscle quartiles, we used analysis of variance (ANOVA) for continuous variables and Chi-square test for categorical. ANOVA post hoc analyses were conducted using Tukey's HSD (honestly significant difference) test.

Pearson correlation assessed unadjusted associations between total abdominal muscle area and density with fasting glucose and HOMA-IR. ANOVA was used to compare mean muscle area and density between participants with diabetes (T2DM+) and without diabetes (T2DM−); with eta squared presented to estimate effect size.

We used linear regression models to assess associations between muscle area and density with fasting glucose and HOMA-IR, and logistic regression models for diabetes status. To compare muscle area and density, given their different units of cm^2 and HU, respectively, we used standardized z-scores for both variables. Muscle area and density were first analyzed separately and then included simultaneously in the same models to explore

potential confounding or unmasking of associations. We performed multivariable modeling starting with age, sex, race/ethnicity, and income (Model 1); then subsequently adjusted for dyslipidemia, hypertension, eGFR, use of diabetes medication (when fasting glucose or HOMA-IR were outcomes), moderate-to-vigorous physical activity, and sedentary behavior (Model 2); and then finally height, BMI, and visceral fat area (Model 3). In multivariable regression models, BMI was a continuous covariate. For subgroup analyses, BMI was a categorical variable with three levels: 18.5≤BMI<25 (normal weight), 25≤BMI<30 (overweight), BMI≥30 (obese).[31,32]

We performed sensitivity analyses to examine the above associations by specific muscle group (locomotion, stabilization, total). Additionally, to evaluate possible effects of diabetes medications on fasting glucose and HOMA-IR, we excluded individuals who reported diabetes medication use and then re-ran models with diabetes status defined only as a fasting glucose ≥126mg/dL. Finally, to examine if a non-linear or threshold relationship existed, muscle variables were grouped into quartiles and regression models were re-run comparing first quartiles of area or density, respectively, to progressively higher quartiles.

To assess for possible effect modification, we *a priori* stratified the cohort by sex, diabetes status, BMI category, and race/ethnicity, then re-ran fully adjusted association models (Model 3) using group-specific standardized z-scores for muscle area and density. In sensitivity analyses, we examined using alternative BMI cut-points for Chinese Americans: BMI<23 (normal weight), 23≤BMI<27.5 (overweight), BMI≥27.5 (obese).[33]

A two-tailed P value <0.05 was considered statistically significant. All statistical analyses were conducted using SPSS Statistics (Version 25).

RESULTS

The mean cohort age was 64.6 years and 50% were female. Approximately 40% of participants were non-Hispanic White, 13% Chinese, 21% African, and 26% Hispanic American. The mean (SD) for total abdominal muscle area and density were 98.3 cm^2 (27.6 cm^2) and 42.2 HU (5.5 HU), respectively.

Table 1 presents unadjusted study cohort characteristics across muscle quartiles. For both muscle area and density, nearly all demographic and physiologic variables differed significantly across quartiles. Notably, for both muscle indices, participants in the third and fourth quartiles spent significantly more time in physical activity compared to the first and second quartiles (all P<0.05). Participants in the fourth quartile of muscle area also had significantly higher HOMA-IR, BMI and visceral fat levels compared to the first quartile (all P<0.05). Conversely, participants in the fourth quartile of muscle density had the lowest prevalence of diabetes, and significantly lower fasting glucose, HOMA-IR, BMI and visceral fat levels compared to the first quartile (all P<0.05).

Associations of abdominal muscle with measures of glucose metabolism

Preliminary unadjusted analyses showed that total abdominal muscle area was weakly correlated with HOMA-IR (r=0.10, P<0.01), but not fasting glucose (r=0.03, P=0.27),

while density was weakly inversely correlated with fasting glucose (r= −0.07, *P*<0.01) and HOMA-IR (r= −0.10, *P*<0.01). Compared to participants without diabetes, participants with diabetes had significantly higher mean total muscle area (T2DM+ 102.0 cm^2, T2DM− 97.8 cm^2, *P*=0.02, Eta Squared= 0.003) and lower density (T2DM+ 41.4 HU, T2DM− 42.3 HU, *P*=0.01, Eta Squared=0.003).

In multivariable regression models controlling for age, sex, race/ethnicity, and income (Model 1), a 1-SD increment in total abdominal muscle area was associated with higher HOMA-IR (β=0.20 [22%] ± SE 0.03; 95%CI: 0.15, 0.25; *P*<0.01) and odds of having diabetes (OR=1.47; 95%CI: 1.18, 1.84; *P*<0.01) (Table 2). In contrast, a 1-SD increment in density was associated with lower fasting glucose (−4.49 ± 0.90; −6.26, −2.72; *P*<0.01), HOMA-IR (−0.16 ± 0.02; −0.20, −0.12; *P*<0.01), and odds of diabetes (0.64; 0.52, 0.77; *P*<0.01). All associations persisted after adjustment for medical comorbidities and health behaviors (Model 2), with some reduction in effect size. However, after additionally controlling for height, BMI, and visceral fat area (Model 3), muscle area became negatively associated with fasting glucose (−2.23 ± 1.01; −4.22, −0.24; *P*=0.03), while density became positively associated with HOMA-IR (0.09 ± 0.02; 0.05, 0.13; *P*<0.01). There were no significant associations with prevalent diabetes.

In sensitivity analyses of specific muscle groups (Supplemental Table 1), associations with both stabilization and locomotion muscle density mirrored those presented above for total density. For muscle area, after full adjustment, only locomotion muscle area was significantly associated with lower fasting glucose (−3.00 ± 1.06; −5.08, −0.91; *P*=0.01), but not stabilization muscle area (−1.49 ± 0.90; −3.26, 0.27; *P*=0.10).

After excluding 211 individuals who self-reported diabetes medication use, 49 participants met criteria for diabetes based on fasting glucose alone. When we re-ran analyses among this subgroup of 1,680 participants, the above-mentioned associations for total muscle density did not change: density became associated with higher HOMA-IR in fully adjusted models. However, area was no longer significantly associated with lower fasting glucose (−1.18 ± 0.80; −2.74, 0.38; *P*=0.14) (Supplemental Table 2).

In sensitivity analyses comparing quartiles of area or density, observed associations mirrored those described above and there was no evidence of non-linearity.

Group differences in associations

For females, in fully adjusted models (Model 3), a 1-SD increment of both muscle area (SD 17.4 cm^2; 0.07 ± 0.02; 0.02, 0.11; *P*=0.01) and density (SD 5.2 HU; 0.09 ± 0.03; 0.04, 0.15; *P*<0.01) were positively associated with HOMA-IR (Figure 1). For males, a 1-SD increment of area (23.9 cm^2) was associated with lower fasting glucose (−2.28 ± 1.13; −4.50, −0.05; *P*=0.05) (Figure 2) and HOMA-IR (−0.05 ± 0.02; −0.10, <0.01; *P*=0.05) (Figure 1), while a 1-SD increment of density (4.9 HU) was associated with higher HOMA-IR (0.08 ± 0.03; 0.03, 0.13; *P*<0.01).

Among participants with diabetes, a 1-SD increment of muscle area (28.3 cm^2) was associated with lower fasting glucose (−10.95 ± 5.64; −22.07, 0.17; *P*=0.05) (Figure 2),

but there were no significant associations with density. For participants without diabetes, a 1-SD increment of density (5.5 HU) was positively associated with both fasting glucose (0.81 ± 0.37; 0.08, 1.54; P=0.03) (Figure 2) and HOMA-IR (0.10 ± 0.02; 0.06, 0.14; P<0.01) (Figure 1).

When we stratified participants by BMI category, a 1-SD increment in muscle density was associated with higher HOMA-IR among both overweight (SD 5.3 HU; 0.09 ± 0.03; 0.04, 0.15; P<0.01) and obese (SD 5.7 HU; 0.15 ± 0.04; 0.07, 0.23; P<0.01) participants (Figure 1). There were no significant associations for the normal weight subgroup. In sensitivity analyses using modified BMI cut-points for Chinese Americans, our findings did not change.

Lastly, a 1-SD increment in muscle area was associated with lower fasting glucose only among Hispanic Americans (SD 28.6 cm^2; −5.34 ± 2.44; −10.14, −0.54; P=0.03) (Figure 2). A 1-SD increment in density was associated with higher HOMA-IR for Whites (SD 5.3 HU; 0.08 ± 0.03; 0.02, 0.14; P=0.01), African Americans (SD 5.6 HU; 0.11 ± 0.05; 0.01, 0.21; P=0.04), and Hispanic Americans (SD 5.5 HU; 0.10 ± 0.04; 0.03, 0.18; P=0.01) (Figure 1), but lower odds of diabetes only among Chinese Americans (SD 5.4 HU; 0.38; 0.16, 0.88; P=0.02) (Figure 3).

DISCUSSION

Among a large, diverse cohort of adult males and females, we found that increasing abdominal muscle density was associated with lower fasting glucose, HOMA-IR, and odds of prevalent diabetes. However, after adjusting for height, BMI, and visceral fat, associations with fasting glucose and diabetes were attenuated, while increasing muscle density became associated with higher HOMA-IR. With regard to muscle area, in unadjusted and minimally adjusted models, we found that increasing abdominal muscle area was associated with higher HOMA-IR and odds of prevalent diabetes. Then, after controlling for body size and visceral fat, muscle area became associated with lower fasting glucose and was no longer associated with HOMA-IR or diabetes.

Previous findings on muscle density and insulin resistance are mixed. In contrast to our findings, Miljkovic, et al.[16] found that abdominal myosteatosis was positively associated with HOMA-IR, independent of VAT, although this study only examined Caucasian males without diabetes. Similar to our study, in minimally adjusted models Therkelsen, et al.[15] found that as abdominal muscle density increased, glucose and HOMA-IR decreased. Though after adjusting for VAT, associations between density and glucose became null, while associations between density and HOMA-IR inverted. The authors postulated that collinearity could partially explain this change in association. In our study, we observed only a modest correlation between total abdominal muscle density and VAT (r= −0.29), making collinearity less likely. However, controlling for visceral fat in muscle density models may be considered an over-adjustment, as both variables are markers of ectopic lipid deposition.

Other studies have found evidence of this unexpected inverse association between intramuscular lipid accumulation and insulin resistance among endurance athletes.[34,35]

Exercise increases diacylglycerol acyltransferase, which catalyzes triglyceride production and actually protects against insulin resistance.[36] These findings may be less applicable to our study, however, since the MESA cohort was recruited from the community and is likely less physically active than endurance athletes. Future research is needed to better understand associations between muscle density and insulin resistance, particularly among a diverse, community-dwelling population.

Our results suggest higher muscle area may be associated with lower fasting glucose, independent of body size or VAT. If replicated in longitudinal studies, this finding could have clinical and public health implications. Behavioral interventions for diabetes prevention have predominantly focused on weight loss.[37] However, some patients, such as Hispanics or males as identified by our subgroup analyses, may benefit from interventions that additionally maintain or increase muscle area. For example, resistance exercise training[38] with a hypocaloric diet and adequate protein intake,[39] fruits and vegetables[40] can support muscle area as part of weight-loss therapy. Moreover, our sensitivity analyses suggest interventions specifically targeting muscles of locomotion may be most efficacious. Finally, although BMI is currently used to clinically estimate body size as a health risk factor, BMI does not differentiate between fat and muscle. In the future, clinicians may consider utilizing more comprehensive estimates of body composition, such as dual-energy X-ray absorptiometry,[41] to better inform their evaluation of patient health. Of note, MESA enrolled participants between 45–84 years; therefore, the majority of females were postmenopausal. Menopause is associated with higher VAT, decreased bone mass density and muscle mass,[42] which may have biased associations towards the null among females and help explain why increased muscle mass was associated with lower fasting glucose only among males.

In contrast to findings from the Third National Health and Nutrition Examination Survey (NHANES) suggesting higher muscle mass, estimated by bioelectrical impedance, was associated with lower rates of pre- or overt diabetes,[43] we did not find significant associations between muscle and prevalent diabetes among the general cohort in fully adjusted regression models. Of note, NHANES used different muscle measures and only adjusted for generalized and central obesity, but not visceral fat. Similar to our work, in their longitudinal cohort study, Larsen et al.[44] found higher abdominal muscle area was associated with greater risk of developing diabetes in unadjusted analyses. However, this relationship was no longer significant after adjusting for demographics and body size, again emphasizing that adiposity may confound measures of abdominal muscle.

Nonetheless, in subgroup analyses stratified by race/ethnicity, we found that Chinese Americans with higher muscle density had significantly lower odds of prevalent diabetes, independent of body size or VAT. Previous studies have shown that at similar BMIs, Asian Americans have a higher prevalence of diabetes compared to Whites,[45] which has partly been explained by some Asian Americans' propensity to develop visceral rather than subcutaneous fat.[46] Muscle density captures ectopic fat deposition, and therefore, similar to visceral adiposity may play a role in the pathophysiology for these patients.

Our study has limitations. First, the cross-sectional design limits causal inference due to lack of temporality. Second, we defined diabetes cases by fasting glucose or medication use,

but we did not have hemoglobin A1c or oral glucose tolerance testing data. Diagnosis by fasting glucose alone is less sensitive than these other measures, particularly among Asian Americans,[33] which could have led to misclassification of some participants to the group without diabetes. Moreover, euglycemic-hyperinsulinemic clamp is the gold standard for measuring whole body insulin resistance, but is invasive and expensive. As such, HOMA-IR serves as a non-invasive, clinically useful assessment.[47] Nonetheless, it is thought HOMA-IR predominantly estimates central or hepatic insulin resistance,[47] which could limit the relationship of these data and peripheral or muscle insulin resistance. Third, we excluded 70 individuals missing muscle data because their entire visceral cavity could not be captured within the CT scan view of interest. This small excluded subgroup had more males and higher BMIs, but otherwise was comparable to participants included in the analytic sample. Although this was a rare occurrence, excluding these larger participants could have impacted results. Fourth, our study only examined abdominal muscle but did not assess ectopic lipid depositions in other muscle regions or organs. Finally, the majority of participants had fasting glucose <100mg/dL and HOMA-IR <2.0, which fall within the range of normal, respectively, and thus may have biased our findings towards the null.

Despite these limitations, our study offers a robust analysis of multiple outcomes as proxies for glucose regulation and comprehensive measures of body composition among a racially/ethnically diverse cohort of males and females, increasing generalizability of findings. Our study suggests higher abdominal muscle density, a marker of less fat infiltration, is associated with salutary glucose regulation, but this association is significantly confounded by other measures of body composition. In contrast, higher abdominal muscle area may be independently associated with lower fasting glucose, particularly among Hispanics and males. Future studies should evaluate the efficacy of muscle-building interventions in these patient populations and expand research to include other racial/ethnic minority groups.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data Availability Statement:

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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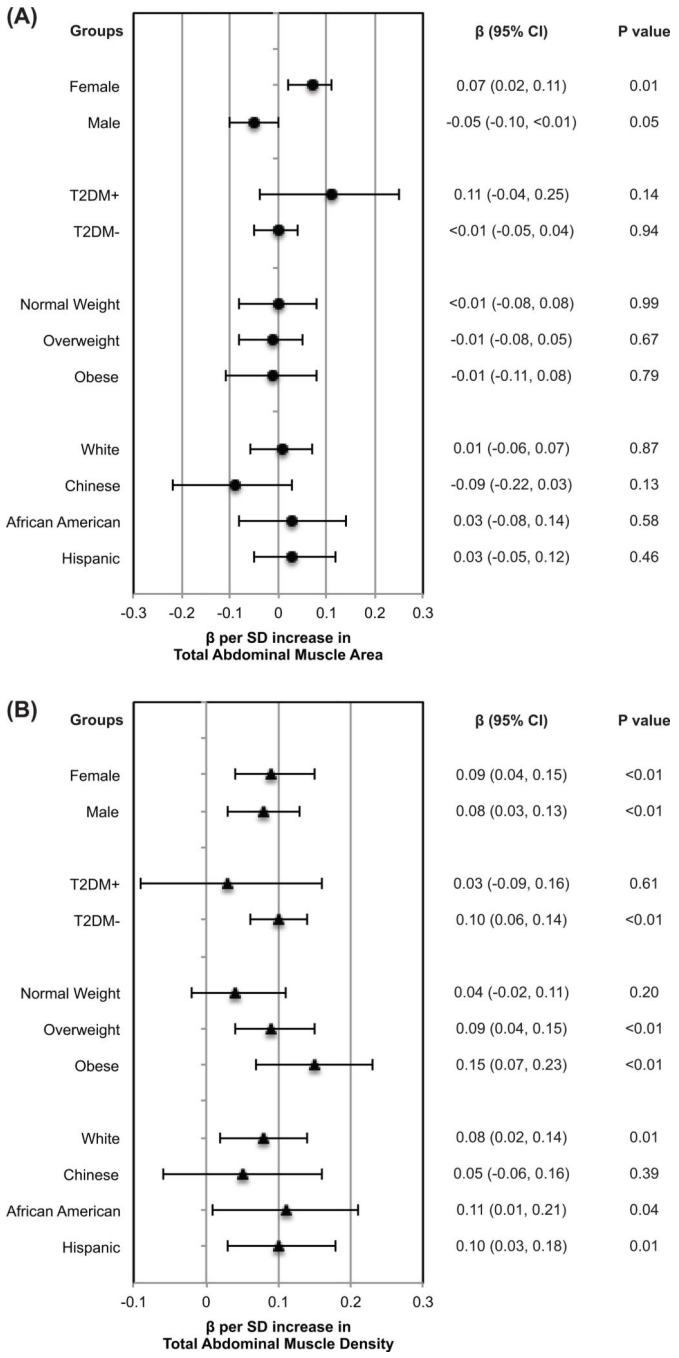

Figure 1:

Forest plot depicting the association (beta coefficient, β) of **(A)** total abdominal muscle area and **(B)** density with HOMA-IR, stratified by subgroups. T2DM+ = participants with diabetes; T2DM− = participants without diabetes. The natural logarithm (ln) of HOMA-IR is shown. Fully adjusted results shown, controlling for age, sex (except when stratified by variable), race/ethnicity (except when stratified by variable), annual family income, dyslipidemia, hypertension, eGFR, use of diabetes medication, physical activity, sedentary behavior, height, BMI (except when stratified by variable) and visceral fat area. Subgroup

sizes (*n*): Females 948, Males 943; T2DM+ 260, T2DM− 1,631; Normal Weight 544, Overweight 770, Obese 567; White 758, Chinese American 249, African American 395, Hispanic American 489.

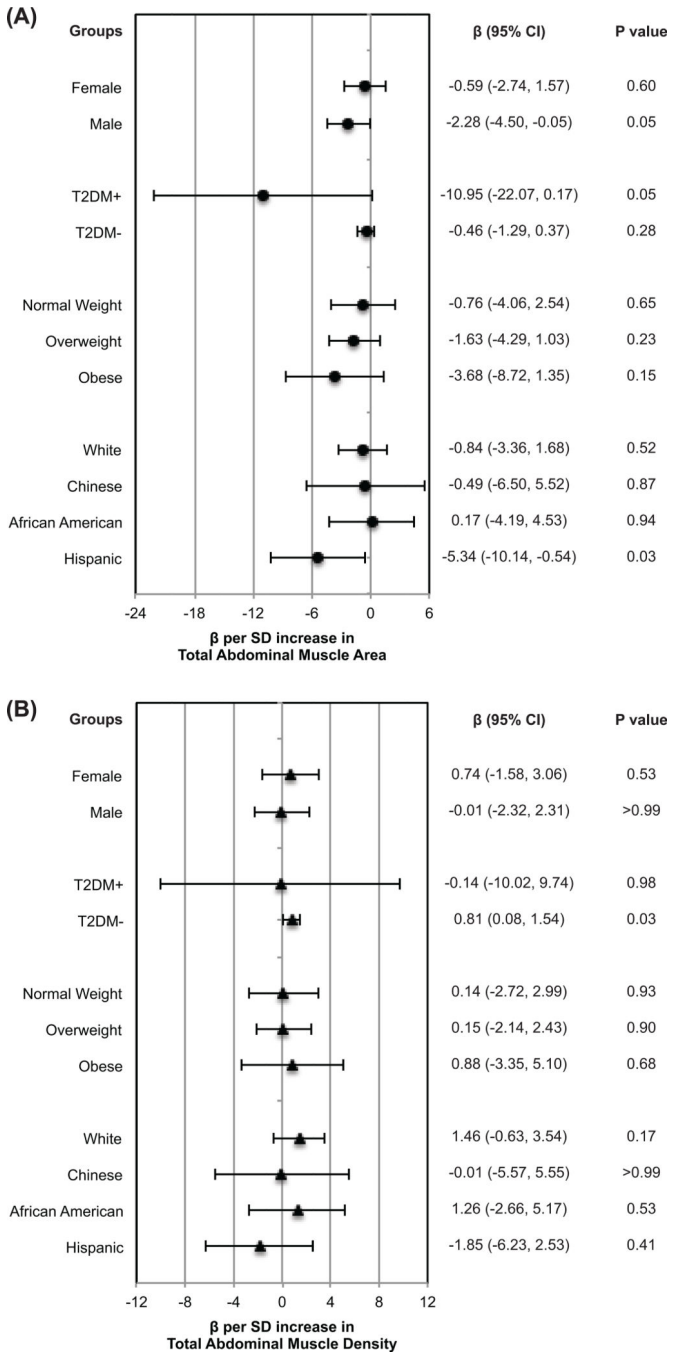

Figure 2:

Forest plot depicting the association (beta coefficient, β) of **(A)** total abdominal muscle area and **(B)** density with fasting glucose, stratified by subgroups. T2DM+ = participants with diabetes; T2DM− = participants without diabetes. Results are expressed in mg/dL. Fully adjusted results shown, controlling for age, sex (except when stratified by variable), race/ethnicity (except when stratified by variable), annual family income, dyslipidemia, hypertension, eGFR, use of diabetes medication, physical activity, sedentary behavior, height, BMI (except when stratified by variable) and visceral fat area. Subgroup sizes (*n*):

Females 948, Males 943; T2DM+ 260, T2DM− 1,631; Normal Weight 544, Overweight 770, Obese 567; White 758, Chinese American 249, African American 395, Hispanic American 489.

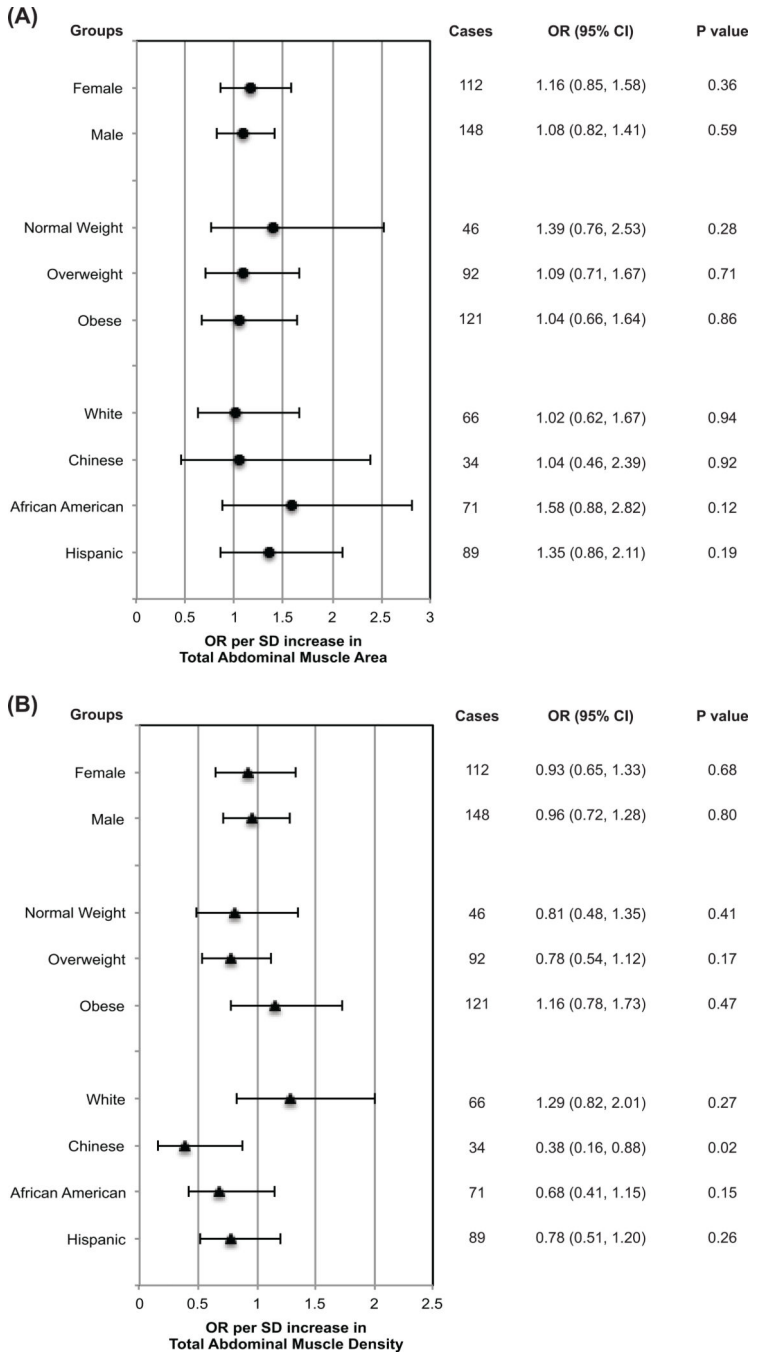

Figure 3:

Odds ratio (OR) of prevalent diabetes by **(A)** total abdominal muscle area and **(B)** density, stratified by subgroups. Fully adjusted results shown, controlling for age, sex (except when stratified by variable), race/ethnicity (except when stratified by variable), annual family income, dyslipidemia, hypertension, eGFR, physical activity, sedentary behavior, height, BMI (except when stratified by variable) and visceral fat area. Subgroup sizes (*n*): Females

948, Males 943; Normal Weight 544, Overweight 770, Obese 567; White 758, Chinese American 249, African American 395, Hispanic American 489.

Table 1.

Characteristics by quartiles of total abdominal muscle area and density (*N*=1,891): The multi-ethnic study of atherosclerosis (2002–2005).[†]

	Quartile 1	Quartile 2	Quartile 3	Quartile 4	*p*[‡]
Total Abdominal Muscle Area					
Range (cm^2)	35–77	77–95	95–117	117–227	
n	471	473	473	474	
Age (yr)	69.0 (8.9)	65.8 (9.7)	64.0 (9.2)	59.8 (8.4)	<0.01
Females	440 (93.4)	320 (67.7)	160 (33.3)	28 (5.9)	<0.01
Race/ethnicity					<0.01
Non-Hispanic White	190 (40.3)	205 (43.3)	177 (37.4)	186 (39.2)	
Chinese American	86 (18.3)	65 (13.7)	66 (14.0)	32 (6.8)	
African American	67 (14.2)	93 (19.7)	112 (23.7)	123 (25.9)	
Hispanic American	128 (27.2)	110 (23.3)	118 (24.9)	133 (28.1)	
Annual Income ≥$50,000[§]	132 (28.8)	164 (37.3)	182 (40.2)	240 (53.1)	<0.01
Physical Activity					
MVPA (MET min/wk)[¶]	3686 (3520)[a]	4268 (3949)[a]	5242 (4691)	6614 (5963)	<0.01
Sedentary (MET min/wk)[¶]	1826 (1126)[a]	1715 (1110)[ab]	1604 (1132)[bc]	1572 (989)[bc]	<0.01
Comorbidities					
Dyslipidemia	156 (33.1)	171 (36.2)	190 (40.2)	208 (43.9)	<0.01
Hypertension	298 (63.3)	272 (57.5)	276 (58.4)	283 (59.7)	0.28
eGFR (mL/min per 1.73 m^2)[//]	76.0 (17.8)	79.4 (17.6)[a]	80.3 (17.7)[ab]	81.0 (15.9)[ab]	<0.01
Glucose metabolism					
Prevalent Diabetes	52 (11.0)	60 (12.7)	73 (15.4)	75 (15.8)	0.10
Fasting Glucose (mg/dL)	96.2 (25.6)[a]	97.6 (27.7)[ab]	100.5 (33.5)[abc]	98.5 (23.2)[abc]	0.12
Insulin (mU/L)	6.2 (4.3)[a]	7.7 (14.7)[ab]	7.2 (4.8)[abc]	7.7 (6.5)[abc]	0.04
HOMA-IR	1.6 (1.5)[a]	1.9 (3.2)[ab]	1.9 (1.7)[abc]	2.0 (2.0)[bc]	0.04
Body composition					
Subcutaneous fat area (cm^2)[#]	281.4 (120.6)	256.3 (128.7)[a]	246.9 (115.4)[ab]	232.0 (99.5)[b]	<0.01
Visceral fat area (cm^2)[††]	132.9 (62.8)[a]	137.8 (67.0)[ab]	148.6 (69.3)[b]	166.6 (69.0)	<0.01
Height (cm)	158.9 (7.5)	163.5 (8.4)	168.7 (8.6)	174.0 (8.0)	<0.01
BMI (kg/m^2)	27.6 (6.1)[a]	27.3 (5.3)[a]	28.2 (4.7)[ab]	29.0 (4.0)[b]	<0.01
Waist circumference (cm)	97.2 (16.6)[a]	95.7 (14.4)[a]	98.1 (12.7)[a]	100.6 (10.8)	<0.01
Total Abdominal Muscle Density					
Range (HU)	26–38	38–43	43–46	46–57	
n	473	472	472	474	
Age (yr)	70.3 (8.8)	66.5 (9.1)	63.2 (8.8)	58.6 (7.9)	<0.01
Females	351 (74.2)	282 (59.7)	211 (44.7)	104 (21.9)	<0.01

	Quartile 1	Quartile 2	Quartile 3	Quartile 4	p ‡
Race/ethnicity					<0.01
Non-Hispanic White	220 (46.5)	202 (42.8)	179 (37.9)	157 (33.1)	
Chinese American	46 (9.7)	62 (13.1)	58 (12.3)	83 (17.5)	
African American	65 (13.7)	84 (17.8)	106 (22.5)	140 (29.5)	
Hispanic American	142 (30.0)	124 (26.3)	129 (27.3)	94 (19.8)	
Annual Income ≥ $50,000 §	132 (29.0)	153 (34.2)	195 (43.0)	238 (53.1)	<0.01
Physical Activity					
MVPA (MET min/wk) ¶	3919 (3833) *a*	4470 (4322) *ab*	5036 (4715) *b*	6385 (5613)	<0.01
Sedentary (MET min/wk) ¶	1926 (1172)	1724 (1127) *a*	1629 (1083) *a*	1437 (926)	<0.01
Comorbidities					
Dyslipidemia	192 (40.6)	187 (39.6)	173 (36.7)	173 (36.5)	0.46
Hypertension	347 (73.4)	291 (61.7)	249 (52.8)	242 (51.1)	<0.01
eGFR (mL/min per 1.73 m^2) //	74.2 (17.9)	78.6 (17.7) *a*	80.8 (16.7) *ab*	83.1 (15.9) *b*	<0.01
Glucose metabolism					
Prevalent Diabetes	78 (16.5)	69 (14.6)	65 (13.8)	48 (10.1)	0.04
Fasting Glucose (mg/dL)	101.6 (32.4) *a*	97.7 (24.7) *ab*	98.0 (31.3) *abc*	95.6 (21.0) *bc*	0.01
Insulin (mU/L)	8.1 (14.4) *a*	7.1 (5.3) *ab*	6.9 (5.7) *abc*	6.7 (5.7) *bc*	0.05
HOMA-IR	2.1 (3.5) *a*	1.8 (1.6) *ab*	1.7 (1.6) *bc*	1.6 (1.7) *bc*	0.01
Body composition					
Subcutaneous fat area (cm^2) #	303.1 (132.7)	265.8 (114.7) *a*	249.9 (116.2) *a*	207.8 (88.5)	<0.01
Visceral fat area (cm^2) ††	173.3 (73.9)	152.8 (70.5)	138.1 (60.0)	122.1 (56.8)	<0.01
Height (cm)	161.7 (9.3)	165.2 (9.6)	167.2 (9.4)	171.0 (8.9)	<0.01
BMI (kg/m^2)	30.2 (6.1)	27.8 (4.9) *a*	27.5 (4.7) *a*	26.6 (3.8)	<0.01
Waist circumference (cm)	104.4 (15.7)	98.0 (13.6) *a*	96.1 (12.6) *a*	93.1 (10.6)	<0.01

Abbreviations: BMI, body mass index; eGFR, estimated glomerular filtration rate; HOMA-IR, homeostatic model assessment of insulin resistance; HU, Hounsfield units; MET, metabolic; min, minute; MVPA, moderate-to-vigorous physical activity; wk, week; yr, year.

† Mean (SD) or count (column percentages, %) shown.

‡ ANOVA used for continuous traits, Chi-square test used for categorical traits.

§ Data available for *N*=1,804.

¶ Data available for *N*=1,889.

// Data available for *N*=1,881.

Data available for *N*=1,612.

†† Data available for *N*=1,884.

a,b,c Superscript letters demonstrate which quartiles varied significantly from one another in Tukey's HSD (honestly significant difference) post hoc analyses. For example, if a value has no superscript letter, it is significantly different from all of the other quartiles (P<0.05). In contrast, if two values share a superscript value (*a*, e.g.), then those two values did *not* vary significantly from another (P≥0.05) or were statistically similar.

Table 2:

Multivariable linear and logistic regression of total abdominal muscle area and density with glycemic control.

	Fasting Glucose†		HOMA-IR‡		Diabetes Status	
	ß (SE, 95% CI)	*P*	ß (SE, 95% CI)	*P*	OR (95% CI)	*P*
Total Abdominal Muscle Area						
Model 1	1.53 (1.08, −0.58 to 3.64)	0.16	0.20 (0.03, 0.15 to 0.25)	<0.01	1.47 (1.18 to 1.84)	<0.01
Model 2	0.06 (0.97, −1.84 to 1.96)	0.95	0.17 (0.02, 0.13 to 0.22)	<0.01	1.42 (1.12 to 1.80)	<0.01
Model 3	−2.23 (1.01, −4.22 to −0.24)	0.03	0.01 (0.02, −0.03 to 0.06)	0.55	1.19 (0.92 to 1.53)	0.18
Total Abdominal Muscle Density						
Model 1	−4.49 (0.90, −6.26 to −2.72)	<0.01	−0.16 (0.02, −0.20 to −0.12)	<0.01	0.64 (0.52 to 0.77)	<0.01
Model 2	−2.30 (0.80, −3.86 to −0.73)	<0.01	−0.12 (0.02, −0.16 to −0.08)	<0.01	0.70 (0.57 to 0.86)	<0.01
Model 3	0.49 (0.89, −1.25 to 2.24)	0.58	0.09 (0.02, 0.05 to 0.13)	<0.01	0.91 (0.72 to 1.14)	0.41

Abbreviations: ß, beta-estimate; CI, confidence interval; HOMA-IR, homeostatic model assessment of insulin resistance; OR, odds ratio; SE, standard error.

Total abdominal muscle area and density were expressed as standardized z-scores and included in the same multivariable regression models.

Model 1: age, sex, race/ethnicity, and annual family income.

Model 2: Model 1 + dyslipidemia, hypertension, eGFR, use of diabetes medication (when fasting glucose or HOMA-IR were outcome), physical activity, and sedentary behavior.

Model 3: Model 2 + height, body mass index (BMI), and visceral fat area.

†Results are expressed as mg/dL.

‡Natural logarithm (ln) transformed values were used.