Title

Associations of abdominal muscle area and density with coronary artery calcium volume and density: The multi-ethnic study of atherosclerosis

Authors

Crawford, Margaret A
Criqui, Michael H
Forbang, Nketi
et al.

Publication Date

2020-06-01

DOI

10.1016/j.metabol.2020.154230

Peer reviewed

HHS Public Access

Author manuscript

Metabolism. Author manuscript; available in PMC 2021 June 01.

Published in final edited form as:

Metabolism. 2020 June ; 107: 154230. doi:10.1016/j.metabol.2020.154230.

Associations of Abdominal Muscle Area and Density with Coronary Artery Calcium Volume and Density: The Multi-Ethnic Study of Atherosclerosis

Margaret A. Crawford, PhD, MPH[a], **Michael H. Criqui, MD, MPH**[b], **Nketi Forbang, MD**[b], **Jonathan T. Unkart, MD, MPH, MS**[b], **Matthew A. Allison, MD, MPH**[b], **Britta A. Larsen, PhD**[b]

[a]University of California, San Diego/San Diego State University Joint Doctoral Program in Public Health, 9500 Gilman Dr., La Jolla, CA 92093-0965

[b]Department of Family Medicine and Public Health, University of California, San Diego, 9500 Gilman Dr., La Jolla, CA 92093-0965

Abstract

Background: Due to the opposing cardiovascular risk profiles of CAC volume and density, we tested the hypothesis that increased abdominal muscle area (AMA) and density (AMD) were significantly associated with lower coronary arterial calcium (CAC) volume and higher CAC density.

Methods: Using data from 787 participants from the Multi-Ethnic Study of Atherosclerosis, Ancillary Body Composition Study, we analyzed abdominal and chest computed tomography (CT) scans. Abdominal scans were scored for muscle area, muscle density (attenuation) and visceral and subcutaneous fat. Chest scans were scored for CAC volume and Agatston values, which were used to derive CAC density scores.

Results: The mean (SD) age and BMI of the participants was 67.8 (9.0) years and 27.9 (4.8) kg/m^2, respectively. Forty-one percent were female, 46% were Caucasian, 60% had hypertension, 17% had diabetes, and 46% had dyslipidemia. AMA was positively associated with CAC volume ($p<0.001$) and inversely associated with CAC density ($p<0.001$). Conversely, AMD was inversely associated with CAC volume and positively associated with CAC density in minimally adjusted models ($p<0.001$), but not significant in confounder adjusted models.

Conclusion: AMA and AMD had differing associations with CAC volume and density, with AMA significantly associated with a higher risk CAC profile (high volume, low density) and

Corresponding Author: Dr. Britta Larsen, Department of Family Medicine and Public Health, University of California, San Diego, School of Medicine, 9500 Gilman Drive, Mail Code 0965, La Jolla, CA 92093-0965, United States, blarsen@ucsd.edu.

Author Contributions: Margaret Crawford: conceptualization, data curation, formal analysis, writing – original draft; Britta Larsen: methodology; supervision; writing – review & editing; Michael Criqui: conceptualization, resources, writing – review & editing; Jonathan Unkart: validation, writing – review & editing; Nketi Forbang: data curation, validation, writing – review & editing; MAA: funding acquisition; methodology; supervision; writing – review & editing.

Conflict of Interest: All authors have approved the final manuscript. The authors have no conflict of interest to disclose.

AMD not significantly associated with CAC volume or density. Future research needs to account for the unique components of both muscle composition and CAC.

Keywords

subclinical atherosclerosis; body composition; cardiovascular risk; Agatston score

1. Introduction

Excess abdominal adiposity is a well-established risk factor for cardiovascular disease (CVD) (1–3). However, less is known about abdominal muscle and CVD. Emerging evidence suggests different components of skeletal muscle may be protective against disease and mortality. Muscle density, a marker of fat infiltration, is inversely associated with mortality, hospitalizations, and frailty in older adults (4–6). However, muscle area, a measure of muscle size, has inconsistent associations with mortality and other outcomes (7, 8). To fully understand the relationship of abdominal composition and CVD risk, it is important to evaluate the contribution of differing components of abdominal muscle (9–11).

Coronary artery calcium (CAC) is a strong risk factor for CVD (12, 13). Typically, CAC is scored using the Agatston method which is a single score combining the volume and density of the calcified plaque (14). However, a recent study that isolated the Agatston score components of CAC volume and density found that volume was positively associated with CVD events, while CAC density was inversely associated with CVD events and appears to be protective (15). Prior to this landmark study, one study found a null association of abdominal muscle area and total Agatston score (10). It is possible that this null finding is driven by different components of muscle being associated with different components of calcified plaque (i.e. density and volume).

In light of the new knowledge of the opposing CVD risk profile of CAC volume and density, we sought to investigate the relationship of abdominal muscle area and density with both CAC volume and density. In the present analysis, we hypothesized that increased abdominal muscle area and density would be significantly associated with lower CAC volume and higher CAC density.

2. Patients and Methods

Details regarding the objectives, design, and recruitment for the Multi-Ethnic Study of Atherosclerosis (MESA) have been published previously (16). Briefly, eligible participants were aged 45–84 years, and self-reported African-American, Chinese, Non-Hispanic White, or Hispanic race/ethnicity. Exclusion criteria included clinically recognized CVD (defined as history of heart attack, angina, CVD procedures, heart failure, cerebrovascular disease), active treatment for non-skin cancers, or pregnancy.

In total, 6,814 participants enrolled from 6 centers across the US and underwent a baseline study visit (exam 1; 2000– 2002) that included a chest computed tomography (CT) scan. Participants returned for 2 sequential follow-up visits approximately 18 months (visit 2) and 36 months (visit 3) after baseline and were randomly assigned to undergo follow-up chest

CT at one of these follow-up visits. At these times, participants were invited to participate in an ancillary study that extended the CT scan to include the abdominal region, concurrent with the timing of their follow-up chest CT. 1,974 individuals participated in the abdominal body composition ancillary study, and the abdominal CT scans were subsequently analyzed for body composition.

The chest CT scans were used to assess CAC volume and density. Since CAC density only has meaning in those with non-zero calcium volume, this study includes only participants who have non-zero CAC volume. Our analytic sample of 787 participants consists of participants who have non-zero CAC volume and complete data for included covariates.

2.1 Study Measurements.

Standardized questionnaires at Visits 1, 2, & 3 gathered data on demographics, tobacco use, education, income, medical history, and anti-hypertensive, glucose-lowering, and cholesterol-lowering medications. Height was measured using a stadiometer. Moderate and vigorous physical activity (MVPA; METS-min/week) was estimated using the MESA Typical Week Physical Activity Survey (TWPAS), adapted from the Cross-Cultural Activity Participation Study (17, 18). After 5 minutes of rest, seated blood pressure was measured 3 times using a Dinamap automated oscillometric sphygmomanometer (model Pro 100; Critikon, Tampa, Florida); the last 2 measurements were averaged and used in analysis. Participants' hypertension (SBP ≥140, DBP ≥90, or taking blood pressure medication), diabetes (fasting blood glucose ≥126, A1C ≥7, or taking diabetes medication), and dyslipidemia (triglyceride:HDL ratio > 5 or taking cholesterol medication) status was obtained from the visit corresponding to their abdominal CT scans (i.e. Visit 2 or 3).

Abdominal muscle and fat areas were determined using *Medical Imaging Processing Analysis and Visualization (MIPAV)* software, version 4.1.2. For each participant who participated in the ancillary body composition study at visit 2 or 3, two image slices were analyzed at each of the disc spaces at L2/L3, L3/L4, and L4/L5. Area within the fascial planes for each muscle group were categorized into one of 3 tissue types based on Hounsfield Units (HU); 0 to 100 were considered muscle, −190 to −30 were considered fat, and intervening HU were considered mixed connective tissue such as fascia (which was not included in the computation for either fat or muscle).

Muscle area was calculated for each muscle group by multiplying the number of pixels of the appropriate HU range within the fascial plane of the given muscle by the pixel area. Total abdominal muscle area (cm^2) was calculated by summing the muscle area of the four muscle groups (see Figure 1). Stabilization-specific abdominal muscle area was calculated by summing the areas of the rectus abdominis, paraspinis, and obliques, while locomotion-specific abdominal muscle area was limited to that of the psoas. Average muscle density was calculated by summing the average densities (HU) of the included muscle groups and dividing by the number of muscles in these groups. Using these rules, area and density were calculated for the psoas, rectus abdominis, paraspinis, and oblique muscle groups, in addition to stabilization-specific, locomotion-specific, and total abdominal muscle.

Visceral fat (adipose tissue inside the abdominal wall) and subcutaneous fat (outside the abdominal wall) areas we calculated using similar rules to muscle area. Imputed values for subcutaneous fat area were utilized for 80 participants, who had part of their subcutaneous compartments truncated in their CT scans due to large body size. Gender and race specific regression equations were developed for subcutaneous area imputation that included each participant's BMI, height, WHR, and waist circumference at the corresponding CT scan visit.

Fasting venous blood obtained contemporaneous to the clinic visit when the CT scan was performed was assayed for glucose, triglycerides, total cholesterol, and high-density lipoprotein cholesterol (HDL). Adiposity-associated inflammatory markers (C-reactive Protein [CRP], interleukin-6 [IL6], tumor necrosis factor – alpha [TNF-a], resistin, leptin, and adiponectin), as well as markers of kidney function (eGFR, renin, and aldosterone) were also measured using these samples.

Agatston CAC scores were obtained from visits 2 or 3, depending on when the participant underwent the abdominal CT scan. The formulas for calculating CAC density scores have previously been published (13). In brief, the volume of CAC (in cubic millimeters) was divided by the appropriate slice thickness (2.5mm or 3mm depending on the CT scan site), resulting in an area "score". The formula for the density score was: Density score = Agatston score/area score. CAC density scores ranged from 1–4.

2.2 Statistical Analysis.

Descriptive statistics were generated as means with standard deviations for continuous variables, and frequencies with percentages for categorical variables. We performed ANCOVA adjusted for age, gender and race to determine the mean values of the cohort characteristics by quartiles of CAC volume and above and below the median of CAC density, as well as by quartiles of total abdominal muscle area and average abdominal muscle density.

Univariable and multivariable linear regression were used to examine the association of abdominal muscle area with standardized CAC volume with adjustment for age, gender, race, ethnicity, CAC density and average abdominal muscle density (model 1). Subsequent models adjusted for: weekly moderate & vigorous physical activity levels, income, education, visceral fat, subcutaneous area, and height (model 2); hypertension, diabetes, dyslipidemia, smoking status, total cholesterol, and HDL cholesterol, CRP, IL6, TNF-a, resistin, leptin, adiponectin, eGFR, renin, and aldosterone in model 3.

Similarly, staged multivariable linear regressions were used to examine the associations of average abdominal muscle *density* with standardized CAC volume, then abdominal muscle area with CAC *density*, and abdominal muscle density with CAC *density*. In order to test for independent associations, all models with ln CAC volume as an outcome were adjusted for CAC density, and vice versa. Similarly, all models with abdominal muscle area as a predictor variable were adjusted for average abdominal muscle density, and vice versa. The same analytic plan was used to evaluate the aforementioned associations separately for stabilization muscles and locomotion muscles.

Six separate, unadjusted models evaluated possible interactions between: abdominal muscle area and gender, abdominal muscle area and race group, abdominal muscle area and diabetes status, abdominal muscle density and gender, abdominal muscle area and race group, and abdominal muscle density and diabetes status. Standardized coefficients were reported for regression results. P values <0.05 were considered statistically significant and SAS 9.4 was used for all analyses.

3. Results

The mean (SD) age and BMI of the 787 participants was 67.8 (9.0) years and 27.9 (4.8) kg/m^2, respectively. Forty-one percent were female, 46% were Caucasian, 14% were Chinese American, 17% were African American, and 23% were Hispanic American. Sixty percent had hypertension, 17% had diabetes, and 46% had dyslipidemia. The mean total abdominal muscle area was 99.1 (27.4) mm^3 and the mean average muscle density was 41.8 (5.5) HU. The median CAC volume was 95.7 (range: 2.4– 3263.7) mm^3, the mean ln CAC volume was 4.5 (1.6), and the mean CAC density was 2.7 (0.7) HU. Compared to the overall MESA population, the analytic study population had fewer African Americans (17% vs 28%) and a lower percentage of females (41% vs. 53%), but higher rates of dyslipidemia (46% compared to 34.6%), diabetes (17% vs. 12.4%), and hypertension (60% vs. 45.0%).

Table 1 shows the distribution of cohort characteristics across quartiles of abdominal muscle area and abdominal muscle density. After adjustment and compared to individuals in lower quartiles of muscle area, individuals in higher quartiles were significantly younger, participated in more physical activity, and had larger body size as measured by BMI, height, and body surface area. The highest quartile of muscle area was composed of only 3% females. Similarly, individuals in higher quartiles of muscle density were significantly younger, had lower BMIs and body surface areas, and lower rates of hypertension and diabetes.

Abdominal muscle *area* was strongly correlated with abdominal muscle density ($r = 0.62$, $p < 0.01$), moderately correlated with visceral fat ($r= 0.23$, $p < 0.01$), and weakly correlated with CAC volume, CAC density, and subcutaneous area (all $r < 0.15$, $p = 0.37$, <0.01, <0.05 respectively), while abdominal muscle *density* was moderately and inversely correlated with visceral fat and subcutaneous fat ($r= -0.20$ and -0.27 respectively, $p < 0.01$ for both). CAC density was strongly correlated with ln CAC volume ($r = 0.64$, $p< 0.01$), but weakly correlated with abdominal muscle area and density ($r=-0.15$, $p <0.01$ and $r= -0.08$, $p <0.05$, respectively), visceral fat, and subcutaneous area ($r = -0.10$, $p= <.01$ and $r= -0.15$ and $p <0.01$, respectively).

Multiple linear regression analyses were conducted to evaluate associations between AMA and AMD with CAC density and CAC volume. In age, sex, and race/ethnicity adjusted models (Table 2), total abdominal muscle *area* was significantly associated with *higher* CAC volume (beta = 0.28 per SD, $p <0.001$) but *lower* CAC density (beta = −0.32 per SD, $p = <0.001$). Results were similar in fully adjusted models. Separate models evaluating these associations for abdominal locomotion muscle area and stabilization muscle area yielded similar results.

In age, sex, and race/ethnicity adjusted models (Table 3b), higher average abdominal muscle *density* was significantly associated with *lower* CAC volume (beta = −0.14 per SD, p <0.001) and *higher* CAC density (beta= 0.12 per SD, p <0.001). Adjusting for covariates attenuated the associations such that they were no longer significant (beta = −0.05 per SD, p = 0.22 and beta= 0.00, p=0.95 respectively). Separate models evaluating these associations for abdominal locomotion muscle density and stabilization muscle density were not significant.

We performed a stepwise sensitivity analysis to understand the attenuation in the association between average abdominal muscle *density* and CAC *density* between models 1 and 2 (Model 1: beta = 0.12 per SD, p= <0.001; Model2: beta = 0.03, p = 0.64). Adding visceral fat to Model 1 attenuated the association by 50% (beta = 0.06 per SD, p= 0.14).

We tested for interactions between both muscle area and density with gender, race/ethnicity and diabetes status (separately) for CAC volume and density. None were significant (for all p>0.2).

4. Discussion

In this cross-sectional study of individuals from 4 racial/ethnic groups and 5 different locations in the United States, we found higher abdominal muscle *area* was significantly associated with higher CAC volume and lower CAC density. Additionally, we found that abdominal muscle density was associated with lower CAC volume and higher CAC density, however, these associations were insignificant after multivariable adjustment. Contrary to our hypothesis, these results suggest that higher abdominal muscle area is associated with a more harmful CAC profile, i.e. greater CAC volume and lower CAC density.

Our hypotheses on the associations of abdominal muscle area with CAC volume and density were based on the assumption that people who are more physically active will have greater muscle area and density, as well as lower levels of CVD risk factors (19). Our hypothesis was further shaped by Criqui et. al's finding that CAC volume is positively associated with CVD events, while CAC density is inversely associated with CVD events (11). Since the presence and extent of CAC has been shown to be significantly associated with higher levels of CVD risk factors, we believed greater muscle area would be associated with lower CAC volume but greater CAC density. However, when investigating health status by quartiles of abdominal muscle area that were adjusted for age, gender, and race/ethnicity, we found that people with greater muscle area also had higher rates of diabetes and dyslipidemia, higher BMI, and lower HDL cholesterol. Similarly, our regression results indicate that muscle area is positively associated with CAC volume, which suggests an association with cardiovascular disease risk (15), even when adjusted for existing cardiometabolic diseases and inflammatory markers.

Higher muscle density is positively associated with lower mortality, less hospitalization, and less frailty in older adults (4–6). In our sample, and compared to the lower quartiles of muscle density, participants in the higher quartiles of muscle density had lower rates of diabetes, hypertension and dyslipidemia, lower BMI, and higher HDL cholesterol. In our

minimally adjusted model, higher muscle density was associated with a more cardioprotective CAC profile, i.e. lower CAC volume and higher CAC density. Despite this, the associations of muscle density with CAC volume and CAC density were non-significant after multivariable adjustment. In our sensitivity analysis, we found that the presence of visceral fat attenuates the association of abdominal muscle density and CAC density by 50% and results in significant attenuation toward the null. Thus, higher muscle density may be a proxy measure for less visceral fat.

Results from previous studies provide possible insights into our results demonstrating the opposite of our hypothesis. Notably, in a study that classified muscle tissue between 35–100 HU as “normal density” and between 0– 34 HU as “low density” (20), higher muscle volume in obese individuals was due entirely to increased “low density muscle.” Additionally, this study found decreased muscle density to be significantly associated with higher rates of diabetes. These findings may help explain the increase in disease prevalence with increased quartiles of abdominal muscle area found in our study. That is, the higher area may be linked to less dense muscle and, thereby, higher CVD risk. A number of studies have shown that lifestyle change increases muscle density and metabolic markers without changing muscle size (21, 22), and others have shown greater risk of hypertension and CVD risk factors with greater muscle size (23–25). At this point it is unclear whether greater muscle is truly associated with increased CVD morbidity, or whether larger muscle size serves as a proxy measure for larger overall body size.

Results were quite consistent across muscles of stabilization and locomotion. Associations between muscle density and CAC volume and density were initially stronger for muscles of stabilization, yet these associations were attenuated in the final model. This may be due to adjustment for markers of inflammation in the final model, which have shown differing associations with muscles of stabilization vs. locomotion (26).

The strengths of this study include the large, multi-ethnic study sample, CT-derived measures of both abdominal body composition and CAC, and availability of measures of important confounders like physical activity. Limitations of this study include our population being focused on individuals who have nonzero CAC volume, and potential bias due to missing the measure of subcutaneous area for the largest people in the population due to size-restrictions of the CT scanner. Additionally, it is possible that there is a systematic error in the CT measures of muscle density, since the CT beam attenuates as it traverses layers of adipose tissue and CT beam attenuation has been shown to increase with body size (27, 28). Finally, this study was cross-sectional which prevents us from evaluating the temporality of these associations.

5. Conclusions

In conclusion, these data show that greater abdominal muscle area is associated with a more harmful CAC profile. Moreover, our results support recent studies showing that CAC density and volume are independent. These results build on this literature by showing that density and volume of muscle appear to likewise be independent, and have divergent associations with CAC volume and density. As with CAC, the growing field examining the role of muscle

in morbidity and mortality should fully examine associations with both volume and density, and explore possible mechanisms for the association between greater muscle area and cardiovascular risk factors.

Financial Support:

This work was supported by the National Institutes of Health/National Heart, Lung and Blood Institute (N01-HC-95159 through N01-HC-95169). Margaret A. Crawford and Jonathan T. Unkart were supported during the preparation of this article by a research and training grant from the National Institutes of Health (NIH)/National Heart, Lung, and Blood Institute (NHLBI) (5T32HL079891-06-MAC, 2T32HL079891- JTU). Britta A. Larsen was supported by K01DK101650 from the National Institutes of Health/NIDDK.

REFERENCES

1. Wilson PWF, D'Agostino RB, Sullivan L, Parise H, Kannel WB. Overweight and obesity as determinants of cardiovascular risk - The Framingham experience. Archives of Internal Medicine. 2002;162:1867–1872. [PubMed: 12196085]
2. Kannel WB, Cupples LA, Ramaswami R, Stokes J, Kreger BE, Higgins M. REGIONAL OBESITY AND RISK OF CARDIOVASCULAR-DISEASE - THE FRAMINGHAM-STUDY. Journal of Clinical Epidemiology. 1991;44:183–190. [PubMed: 1995775]
3. Rexrode KM, Buring JE, Manson JE. Abdominal and total adiposity and risk of coronary heart disease in men. International Journal of Obesity. 2001;25:1047–1056. [PubMed: 11443505]
4. Cawthon PM, Fox KM, Gandra SR, Delmonico MJ, Chiou CF, Anthony MS, Sewall A, Goodpaster B, Satterfield S, Cummings SR, Harris TB, Hlth A, Body Composition S. Do Muscle Mass, Muscle Density, Strength, and Physical Function Similarly Influence Risk of Hospitalization in Older Adults? Journal of the American Geriatrics Society. 2009;57:1411–1419. [PubMed: 19682143]
5. Cesari M, Leeuwenburgh C, Lauretani F, Onder G, Bandinelli S, Maraldi C, Guralnik JM, Pahor M, Ferrucci L. Frailty syndrome and skeletal muscle: results from the Invecchiare in Chianti study. American Journal of Clinical Nutrition. 2006;83:1142–1148.
6. Newman AB, Kupelian V, Visser M, Simonsick EM, Goodpaster BH, Kritchevsky SB, Tylavsky FA, Rubin SM, Harris TB, Hlth Aging Body Composition S. Strength, but not muscle mass, is associated with mortality in the health, aging and body composition study cohort. Journals of Gerontology Series a-Biological Sciences and Medical Sciences. 2006;61:72–77.
7. Saji M, Lim DS, Ragosta M, LaPar DJ, Downs E, Ghanta RK, Kern JA, Dent JM, Ailawadi G. Usefulness of Psoas Muscle Area to Predict Mortality in Patients Undergoing Transcatheter Aortic Valve Replacement. Am J Cardiol. 2016;118:251–257. [PubMed: 27236254]
8. McDermott MM, Liu K, Tian L, Guralnik JM, Criqui MH, Liao Y, Ferrucci L. Calf muscle characteristics, strength measures, and mortality in peripheral arterial disease: a longitudinal study. J Am Coll Cardiol. 2012;59:1159–1167. [PubMed: 22440216]
9. Jensky NE, Criqui MH, Wright CM, Wassel CL, Alcaraz JE, Allison MA. The Association Between Abdominal Body Composition and Vascular Calcification. Obesity. 2011;19:2418–2424. [PubMed: 21475146]
10. Jensky NE, Allison MA, Loomba R, Carnethon MR, de Boer IH, Budoff MJ, Burke GL, Criqui MH, Ix JH. Null association between abdominal muscle and calcified. atherosclerosis in community-living persons without clinical cardiovascular disease: The multi-ethnic study of atherosclerosis. Metabolism-Clinical and Experimental. 2013;62:1562–1569. [PubMed: 23916063]
11. Alexandersen P, Tanko LB, Bagger YZ, Jespersen J, Skouby SO, Christiansen C. Associations between aortic calcification and components of body composition in elderly men. Obesity. 2006;14:1571–1578. [PubMed: 17030968]
12. Hou ZH, Lu B, Gao Y, Jiang SL, Wang Y, Li W, Budoff MJ. Prognostic Value of Coronary CT Angiography and Calcium Score for Major Adverse Cardiac Events in Outpatients. Jacc-Cardiovascular Imaging. 2012;5:990–999. [PubMed: 23058065]

13. Criqui MH, Denenberg JO, McClelland RL, Allison MA, Ix JH, Guerci A, Cohoon KP, Srikanthan P, Watson KE, Wong ND. Abdominal aortic calcium, coronary artery calcium, and cardiovascular morbidity and mortality in the Multi-Ethnic Study of Atherosclerosis. Arterioscler Thromb Vasc Biol. 2014;34:1574–1579. [PubMed: 24812323]
14. Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M, Detrano R. QUANTIFICATION OF CORONARY-ARTERY CALCIUM USING ULTRAFAST COMPUTED-TOMOGRAPHY. Journal of the American College of Cardiology. 1990;15:827–832. [PubMed: 2407762]
15. Criqui MH, Denenberg JO, Ix JH, McClelland RL, Wassel CL, Rifkin DE, Carr JJ, Budoff MJ, Allison MA. Calcium Density of Coronary Artery Plaque and Risk of Incident Cardiovascular Events. Jama-Journal of the American Medical Association. 2014;311:271–278.
16. Bild DE, Bluemke DA, Burke GL, Detrano R, Roux AVD, Folsom AR, Greenland P, Jacobs DR, Kronmal R, Liu K, Nelson JC, O'Leary D, Saad MF, Shea S, Szklo M, Tracy RP. Multi-ethnic study of atherosclerosis: Objectives and design. American Journal of Epidemiology. 2002;156:871–881. [PubMed: 12397006]
17. Ainsworth BE, Irwin ML, Addy CL, Whitt MC, Stolarczyk LM. Moderate physical activity patterns of minority women: The cross-cultural activity participation study. Journal of Womens Health & Gender-Based Medicine. 1999;8:805–813.
18. Ainsworth BE, Haskell WL, Whitt MC, Irwin ML, Swartz AM, Strath SJ, O'Brien WL, Bassett DR, Schmitz KH, Emplaincourt PO, Jacobs DR, Leon AS. Compendium of Physical Activities: an update of activity codes and MET intensities. Medicine and Science in Sports and Exercise. 2000;32:S498–S516. [PubMed: 10993420]
19. Warburton DER, Nicol CW, Bredin SSD. Health benefits of physical activity: the evidence. Canadian Medical Association Journal. 2006;174:801–809. [PubMed: 16534088]
20. Kelley DE, Slasky BS, Janosky J. SKELETAL-MUSCLE DENSITY - EFFECTS OF OBESITY AND NON-INSULIN-DEPENDENT DIABETES-MELLITUS. American Journal of Clinical Nutrition. 1991;54:509–515.
21. Prior SJ, Joseph LJ, Brandauer J, Katzel LI, Hagberg JM, Ryan AS. Reduction in midthigh low-density muscle with aerobic exercise training and weight loss impacts glucose tolerance in older men. J Clin Endocrinol Metab. 2007;92:880–886. [PubMed: 17200170]
22. Shaibi GQ, Cruz ML, Ball GD, Weigensberg MJ, Salem GJ, Crespo NC, Goran MI. Effects of resistance training on insulin sensitivity in overweight Latino adolescent males. Medicine and Science in Sports and Exercise. 2006;38:1208–1215. [PubMed: 16826016]
23. Ye S, Zhu C, Wei C, Yang M, Zheng W, Gan D, Zhu S. Associations of Body Composition with Blood Pressure and Hypertension. Obesity (Silver Spring). 2018;26:1644–1650. [PubMed: 30260578]
24. Tucker AM, Vogel RA, Lincoln AE, Dunn RE, Ahrensfield DC, Allen TW, Castle LW, Heyer RA, Pellman EJ, Strollo PJ, Jr., Wilson PW, Yates AP. Prevalence of cardiovascular disease risk factors among National Football League players. JAMA. 2009;301:2111–2119. [PubMed: 19470988]
25. Berge HM, Isern CB, Berge E. Blood pressure and hypertension in athletes: a systematic review. Br J Sports Med. 2015;49:716–723. [PubMed: 25631543]
26. RB VANH, Cushman M, Schlueter EF, Allison MA. Abdominal Muscle Density Is Inversely Related to Adiposity Inflammatory Mediators. Med Sci Sports Exerc. 2018;50:1495–1501. [PubMed: 29401141]
27. Stanford W, Burns TL, Thompson BH, Witt JD, Lauer RM, Mahoney LT. Influence of body size and section level on calcium phantom measurements at coronary artery calcium CT scanning. Radiology. 2004;230:198–205. [PubMed: 14695394]
28. Schindera ST, Tock I, Marin D, Nelson RC, Raupach R, Hagemeister M, von Allmen G, Vock P, Szucs-Farkas Z. Effect of Beam Hardening on Arterial Enhancement in Thoracoabdominal CT Angiography with Increasing Patient Size: An in Vitro and in Vivo Study. Radiology. 2010;256:528–535. [PubMed: 20656839]

Highlights

- Abdominal muscle density (AMD) and area (AMA) were measured in adults with no CVD
- Coronary artery calcium (CAC) Agatston scores were divided into volume and density
- AMA was associated with higher CAC volume and lower CAC density
- AMD was associated with lower CAC volume and higher CAC density
- AMA and AMD are unique and opposing predictors of CAC profiles

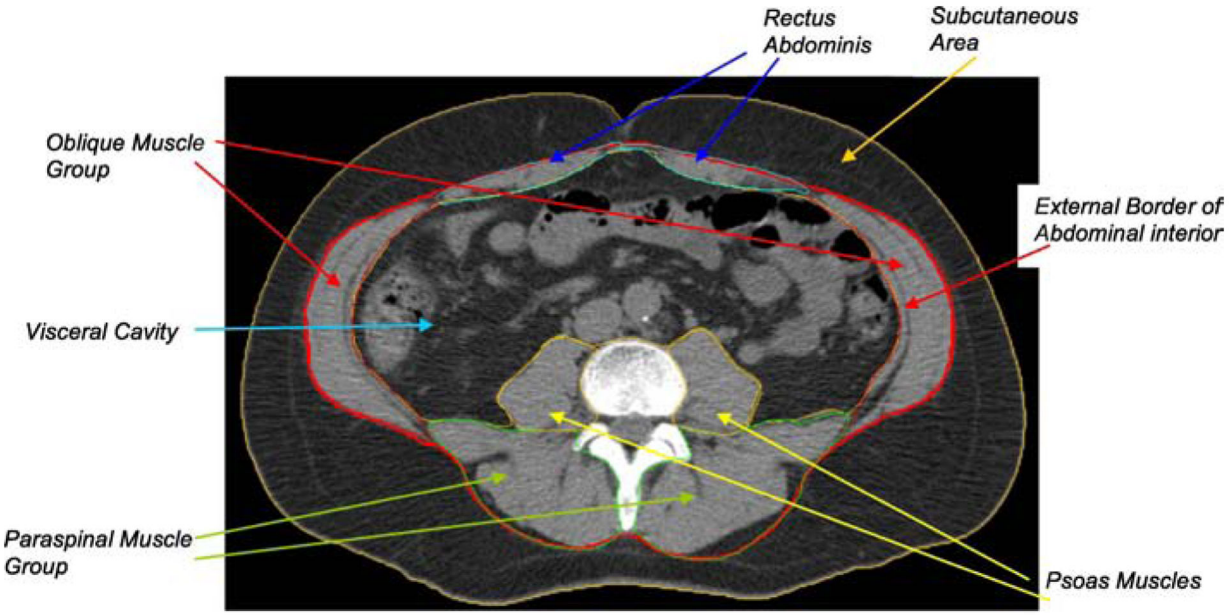

Figure 1.

Sample abdominal CT slice showing: rectus abdominis muscles (light blue), oblique muscles (red), paraspinal muscles (green), and psoas muscles (yellow). The thick red line represents the outer border of the interior abdominal cavity; tissue outside of this is considered the subcutaneous area.

Table 1.

Cohort characteristics across Abdominal Muscle Area (AMA) and Abdominal Muscle Density (AMD) Quartiles in Men and Women with Nonzero CAC Scores in the MESA-Abdominal Body Composition Ancillary Study (n=787).

	Abdominal Muscle Area Quartiles					Abdominal Muscle Density Quartiles				
	I (n=197)	II (n=197)	III (n=197)	IV (n=196)	p-value	I (n=197)	II (n=196)	III (n=197)	IV (n=197)	p-value
Quartile Range *	40.58–77.76	77.77–96.56	96.57–117.96	117.97–183.04		26.55–37.65	37.66–42.07	42.08–45.96	45.97–55.42	
Quartile mean	66.13	87.38	106.82	136.21		34.48	39.86	44.09	48.55	
Age, y	74.27	69.60	65.54	61.72	<0.001	73.14	69.57	67.14	62.32	<0.001
Women, %	90%	49%	21%	3%	<0.001	69%	55%	29%	12%	<0.001
Race, % white	44%	47%	45%	48%	0.83	49%	50%	41%	43%	0.18
High education %	59%	65%	64%	74%	0.02	62%	62%	62%	75%	0.01
High income, %	40%	52%	60%	67%	<0.001	42%	49%	57%	71%	<0.001
MVPA, MET-min/week	3632.3	4183.3	4818.1	5526.2	<0.05	4079.6	4578.3	4422.3	5024.0	0.18
Ever Smoker, %	43%	66%	62%	67%	<0.001	56%	52%	65%	66%	<0.01
BMI, kg/m2	26.17	26.77	28.56	29.97	<0.001	30.17	28.01	27.32	25.96	<0.001
Height, cm	164.50	166.62	167.04	169.95	<0.001	166.33	167.42	167.15	167.20	0.50
Body surface area, m^2	1.77	1.82	1.89	1.98	<0.001	1.91	1.88	1.85	1.81	<0.001
Total cholesterol	193.10	184.71	185.06	182.90	0.10	183.60	184.26	187.15	190.75	0.29
HDL cholesterol	54.74	51.99	49.28	46.69	<0.001	47.70	50.07	51.52	53.41	<0.01
Hypertension, %	66%	61%	55%	56%	0.09	75%	61%	54%	49%	<0.001
Diabetes, %	14%	15%	17%	20%	0.34	18%	16%	21%	12%	0.10
Dyslipidemia, %	40%	44%	47%	54%	0.06	47%	45%	47%	45%	0.91
CRP, mg/L	2.99	3.09	3.28	3.45	0.94	4.19	3.40	2.81	2.39	0.06
IL6, pg/mL	2.40	2.58	2.42	2.72	0.36	3.04	2.76	2.31	2.01	<0.001
TNF-α, pg/mL	4.24	7.00	5.92	7.27	0.07	5.80	5.90	5.55	7.17	0.49
Adiponectin	23.48	22.38	18.12	17.54	<0.001	22.71	21.25	18.90	18.67	0.01
Resistin	16.12	16.31	17.21	17.04	0.55	18.06	16.76	15.73	16.12	0.02
Leptin	16.78	16.27	21.18	22.80	0.02	24.86	18.52	18.37	15.27	<0.001
EGFR, mL/min/1.73m^2	77.82	78.68	75.88	71.57	<0.01	75.82	77.08	78.00	73.06	0.02
Renin	1.53	1.43	1.80	2.21	0.39	2.11	1.66	1.86	1.33	0.37
Aldosterone	155.03	159.62	148.47	144.22	0.52	151.07	154.75	153.16	148.41	0.92
Visceral fat, cm^2	145.46	147.61	156.57	177.17	<0.01	197.25	167.39	143.46	118.67	<0.001
Subcutaneous area, cm^2	264.93	248.20	282.21	291.20	<0.01	315.94	280.45	265.18	224.83	<0.001
Total AMA, cm^2	69.84	88.21	105.38	133.08	<0.001	88.35	96.98	101.87	109.13	<0.001
Total AMD, HU	38.66	41.22	42.66	44.48	<0.001	34.79	40.00	44.00	48.21	<0.001
Locomotion AMA, cm^2	20.16	22.64	24.97	28.69	<0.001	22.61	23.36	24.21	26.26	<0.001

	Abdominal Muscle Area Quartiles					Abdominal Muscle Density Quartiles				
	I (n=197)	**II (n=197)**	**III (n=197)**	**IV (n=196)**	**p-value**	**I (n=197)**	**II (n=196)**	**III (n=197)**	**IV (n=197)**	**p-value**
Locomotion AMD, HU	47.57	49.61	50.79	51.76	<0.001	44.30	48.74	51.88	54.79	<0.001
Stabilization AMA, cm^2	49.68	65.57	80.41	104.39	<0.001	65.74	73.62	77.66	82.87	<0.001
Stabilization AMD, HU	35.69	38.42	39.94	42.05	<0.001	31.62	37.08	41.37	46.01	<0.001
CAC Volume (mm^3)	220.52	264.24	296.58	303.97	0.49	296.37	319.13	250.78	219.10	0.16
Ln CAC Volume	4.31	4.45	4.59	4.71	0.33	4.70	4.55	4.34	4.47	0.18
CAC Density (HU)	2.87	2.72	2.71	2.51	<0.01	2.78	2.61	2.68	2.73	0.09

All models adjusted for age, gender, and race (age, gender, and race models not adjusted for themselves).

Abbreviations: CAC= coronary artery calcium, HU= Hounsfield Unit, EGFR= Estimated Glomerular Filtration Rate

*Abdominal Muscle Area unit= cm^2, Abdominal Muscle Density= Hounsfield Unit.

Table 2.

Regression results for association of abdominal muscle area (AMA) and abdominal muscle density (AMD) with Coronary Artery Calcium (CAC) volume and density from the MESA Cohort Study (n=787).

	Total AMA		Locomotion AMA		Stabilization AMA	
Model	**β**	**p-value**	**β**	**p-value**	**β**	**p-value**
			Outcome: ln CAC Volume*			
1	0.28	<0.001	0.21	<0.001	0.23	<0.001
2	0.22	<0.001	0.17	<0.001	0.19	<0.001
3	0.20	<0.001	0.18	<0.001	0.16	<0.001
			Outcome: CAC Density*			
1	−0.32	<0.001	−0.23	<0.001	−0.27	<0.001
2	−0.23	<0.001	−0.15	<0.001	−0.19	<0.001
3	−0.21	<0.001	−0.17	<0.001	−0.17	<0.001
	Total AMD		**Locomotion AMD**		**Stabilization AMD**	
Model	**β**	**p-value**	**β**	**p-value**	**β**	**p-value**
			Outcome: ln CAC Volume*			
1	−0.14	<0.001	−0.06	0.05	−0.14	<0.001
2	−0.08	<0.05	−0.01	0.82	−0.09	<0.05
3	−0.05	0.22	0.01	0.86	−0.05	0.20
			Outcome: CAC Density*			
1	0.12	<0.001	0.07	<0.05	0.11	<0.01
2	0.04	0.64	0.01	0.80	0.04	0.35
3	0.00	0.95	−0.01	0.75	0.00	0.94

Model 1: adjusted for abdominal muscle density (AMA models), abdominal muscle area (AMD models), age, gender, ethnicity.

Model 2: Adjusted for model 1 variables plus moderate & vigorous physical activity, education, income, height, visceral fat, and subcutaneous area.

Model 3: Adjusted for model 2 variables plus hypertension, diabetes, smoking status (never/ever/current), total cholesterol, HDL cholesterol, CRP, IL-6, TNF-α, resistin, leptin, adiponectin, EGFR, renin, and aldosterone.

* Models with outcome of CAC Volume are adjusted for CAC Density; models with outcome of CAC

Density area adjusted for CAC Volume

All β are standardized coefficients.