Body Mass Index as a Phenotypic Expression of Adiposity: Quantitative Contribution of Muscularity in a Population-Based Sample

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Abstract

Objective—Although widely applied as a phenotypic expression of adiposity in population and gene-search studies, body mass index (BMI) is also acknowledged to reflect muscularity even though relevant studies directly measuring skeletal muscle (SM) mass are lacking. The current study aimed to fill this important gap by applying advanced imaging methods to test the hypothesis that, after controlling first for adiposity, SM mass is also a significant determinant of BMI in a population-based sample.

Design—Whole-body magnetic resonance imaging scans were completed in CARDIA Study subjects aged 33-45 years. Physical activity (PA) levels, alcohol intake, and adequacy of food intake were assessed by standardized questionnaires.

Subjects—58 African-American (AA) and 78 Caucasian (C) men; 63 AA and 64 C women.

Measurements—Whole-body AT and SM volumes.

Results—AT was significantly predicted by not only BMI, but PA and alcohol intake with total model R^2s of 0.68 (p<0.0001) for men and 0.89 (p<0.0001) for women. Men had more SM than AT at all levels of BMI while SM predominated in women at lower BMIs (C <26 kg/m^2; AA <28 kg/m^2). Both AT and SM contributed a similar proportion of between-subject variation in BMI in men. In contrast, AT contributed ~30% more than SM to the variation in BMI in women. Developed allometric models indicated SM associations with AT, PA, and race after adjusting for

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height. There was little association of age, lifestyle factors, or race with BMI after controlling for both AT and SM.

Conclusion—Variation in muscularity provides a mechanistic basis for the previously observed non-specificity of BMI as a phenotypic expression of adiposity. These quantitative observations have important implications when choosing adiposity measures in population and gene-search studies.

Keywords

Body Composition; Ethnicity; Obesity; Body Mass Index

INTRODUCTION

Body mass index (BMI), weight/height^2, is now the most widely applied phenotypic expression of human adiposity (1). Quetelet in 1842 (2) was the first to observe that weight scales across adult subjects as height^2. Keys et al. (3) largely ended a decades-long debate on the "best" obesity index by showing that among several candidates Quetelet's index had the highest correlations with percent body fat as measured by underwater weighing. Renamed by Keys et al. (3) as BMI, this simple index serves as an important measure of population and individual adiposity.

Close scrutiny of BMI over the years has led to the consistent observation that correlations with adult adiposity are generally modest and that other factors, such as age, race, and physical activity (PA) levels confound the BMI-adiposity relationship (4-14). Other than adipose tissue, skeletal muscle (SM) mass is the largest adult body compartment, and between-subject variability in muscularity is often cited as a reason for the non-specificity of BMI (7, 10-13), although SM is rarely measured. Total body SM mass has traditionally been difficult to quantify, particularly in large population samples, and surrogate muscularity measures have been used to examine BMI-adiposity relations. Skeletal muscle accounts for about one-half of fat-free mass (FFM) (15) and FFM has been used in previous BMI studies as a marker of muscularity (14). However, the proportion of FFM as SM varies with sex, age, race (16), and physical activity levels and thus is not an ideal measure of SM's quantitative impact on BMI. More recently the lean-soft tissue compartment of the extremities as measured by dual-energy x-ray absorptiometry (DXA) has been used as a surrogate marker of muscularity (12, 13), but the same concerns apply to this compartment as a measure of SM as for FFM.

The quantitative impact of muscularity on BMI as a phenotypic marker of population adiposity is thus largely unknown. The recent introduction of magnetic resonance imaging (MRI) as a means of quantifying total body SM volume and mass on a relatively large scale (17) affords the important new opportunity to establish specifically and precisely the relationships between adiposity, muscularity, and BMI. The current study applied MRI to test the hypothesis that, after controlling first for adiposity, SM mass is also a significant and independent determinant of BMI in the population-based Coronary Artery Risk Development in Young Adults (CARDIA) sample (18).

METHODS

Protocol and Subjects

The study hypothesis and related questions were examined using a subset of the bi-racial CARDIA cohort that includes African American and Caucasian men and women who underwent whole body MRI as part of the Fat Redistribution and Metabolic Change in HIV Infection (FRAM) study (21). FRAM was designed to evaluate the prevalence and correlates of changes in fat distribution, insulin resistance, and dyslipidemia in a representative sample of HIV-infected subjects and HIV-seronegative controls in the United States. The methods have been described in detail previously (21, 22).

The group analyzed here were HIV-uninfected control men and women enrolled from two CARDIA research sites (18, 21), one located at Kaiser Permanente, Oakland, CA and the other at the University of Alabama, Birmingham that have followed participants longitudinally enrolled in the Visceral Fat and Metabolic Rate in Young Adults (VIM) ancillary study of CARDIA (23).

CARDIA participants were originally recruited as a population-based sample of healthy 18-33 year old Caucasian and African-American men and women from four cities in 1986 for a longitudinal study of cardiovascular risk factors. The VIM ancillary study recruited participants from two of the four CARDIA Centers in 1995-96. VIM enrolled approximately 100 CARDIA participants from each of the race-gender groups with BMI distributed similarly above and below race-gender specific medians of the population-based CARDIA study. Guidelines for human experimentation in accordance with the US Department of Health and Human Services and the Institutional Review Board of each participating institution were followed in the conduct of the study. Appropriate informed consent was obtained from all study participants.

Subjects had a clinic visit that included a comprehensive history, physical examination, and body composition studies. Whole-body MRI was used to partition body volume into AT, SM, and residual (i.e., bone & organ) compartments (24). Percentage of body weight as adipose tissue (i.e., %AT) was used as an alternative measure of adiposity.

Candidate lifestyle factors included level of physical activity (quartiled by gender), smoking status (current, past, or never), alcohol intake (<1/week, 1-7/week, >7/week, or none), adequate food intake, and illicit drug use (current, past, or never) and were assessed by standardized instruments (18, 25-28). Subjects were also asked to rate their physical activity during the past year on a five-point scale ranging from inactive to very active.

Body Composition

Anthropometric Measurements—All staff were centrally trained and certified for measurements. Subjects wore light clothing or a hospital gown and no shoes. Height was measured to the nearest 0.1 cm and weight was measured to the nearest 0.1 kg on calibrated stadiometers and scales, respectively. Waist circumference was measured immediately below the lowest rib. Hip circumference was measured at the maximum extension of the buttocks as viewed from the side.

Magnetic Resonance Imaging—Body composition was measured by MRI with subjects in the supine position with arms extended over their head (24). Using the inter-vertebral space between the fourth and fifth lumbar vertebrae as the origin, 10 mm thick transverse images were obtained every 40 mm from hands to feet. MRI field strength was standardized at 1.5 Tesla. Image analysis software (Tomovision Inc., Montreal, Canada) was used to segment the cross-sectional images for total area and areas of AT and SM; residual (bone & organs) area was calculated as the difference between total image area and the sum of AT and SM areas. The AT compartment was further segmented into total subcutaneous AT, visceral AT, and AT volume in 4 regions [leg, lower trunk (abdomen and back), upper trunk (chest and back), arm].

All MRI scans were read at the Image Reading Center (IRC) located at the Obesity Research Center, St. Luke's-Roosevelt Hospital, New York, NY. The image acquisition protocol was standardized across sites and visits were conducted by the IRC staff to ensure protocol adherence. Scans were sent to the IRC where AT and SM tissue areas (cm^2) were calculated after segmentation by summing appropriate tissue pixels, then multiplying by individual pixel surface area. The volume of AT and SM in each slice was calculated by multiplying tissue area by thickness. The volume of each tissue for the space between two consecutive slices was calculated via a mathematical algorithm (24).

Percent fat was calculated as 100×0.92 g/$cm^3 \times$ the ratio of total AT volume to body weight, since adipose tissue has a density of ~0.92 g/cm^3 (24). Percent SM was similarly calculated as 100×1.04 g/$cm^3 \times$ the ratio of SM volume to body weight, as SM has a density of ~1.04 g/cm^3.

Statistical Methods

Subject demographic characteristics are reported as median with interquartile range (IQR). Characteristics of African American and Caucasian participants were compared and tested for statistical significance using the Mann-Whitney U test for continuous variables, and Fisher's exact test for categorical variables. Separate analyses for all measures were conducted for men and women. All analyses were conducted using the SAS system, version 9.1 (SAS Institute, Inc., Cary, NC).

The hypothesis and related questions were evaluated in three stages. We first examined the association of BMI and SM with AT in multivariable linear regression analyses adjusting for age, race, and lifestyle factors, with BMI analyzed linearly, but with potentially different slopes in the ranges of <25, 25-30, and >30 kg/m^2. We used a linear spline to model BMI due to the curvilinear relation between BMI and AT. Candidate lifestyle factors included physical activity, smoking, alcohol use, adequate food intake, and illicit drug use. This first series of analyses was aimed at confirming that CARDIA subjects have AT-BMI relations generally similar to those reported in earlier studies (4-14).

In this first set of analyses, we developed AT prediction equations using the simple allometric model (19),

$$y = \alpha \cdot x_1^{\beta_1} x_2^{\beta_2} \cdot exp\left[\sum_{i=3}^{9}(\beta_i x_i)\right] \cdot \varepsilon \quad (1)$$

where y is AT volume, α is the proportionality constant, x_1 is age, x_2 is SM, x_3, x_4, x_5 are BMI linear spline terms, x_6 is ethnicity (African American or Caucasian), x_7, x_8, x_9 are levels of physical activity or alcohol use (vs. the lowest level of activity or drinking), β_i is the scaling exponent or power, and ε is a multiplicative error term. When converted to logarithmic form, the allometric equation can be solved as:

$$log_e y = log_e \alpha + \beta_1 log_e x_1 + \beta_2 log_e x_2 + \left[\sum_{i=3}^{9}(\beta_i x_i)\right] + log_e \varepsilon \quad (2)$$

Allometric model coefficients in equation 2 (α and β_i) were derived using least-squares multiple linear regression analysis and log-transformed data.

In the second set of analyses, SM was modeled as:

$$y = \alpha \cdot x_1^{\beta_1} \cdot x_2^{\beta_2} \cdot x_3^{\beta_3} \cdot exp\left(\beta_4 x_4 + \beta_5 x_5 + \beta_6 x_6 + \beta_7 x_7\right) \cdot \varepsilon \quad (3)$$

where y is SM volume, α is the proportionality constant, x_1 is height, x_2 is age, x_3 is %AT, x_4 is ethnicity (African American or Caucasian), x_5, x_6, x_7 are quartiles of physical activity (vs. the first quartile or lowest level of activity), β_i is the scaling exponent or power, and ε is a multiplicative error term. When converted to logarithmic form, the allometric equation can be solved as:

$$log_e y = log_e \alpha + \beta_1 log_e x_1 + \beta_2 log_e x_2 + \beta_3 log_e x_3 + \left[\sum_{i=4}^{7}(\beta_i x_i)\right] + log_e \varepsilon \quad (4)$$

The third series of analyses, related directly to the study hypothesis, focused on the individual contributions of AT and SM to BMI. Adipose tissue and SM volumes were normalized in this analysis by dividing AT by height-squared, with summaries back-transformed to 1.75 m of height (20) as follows:

$$y_t = (1.75)^2 \cdot \frac{y_{unadj.}}{height^2}$$

where y_{unadj} denotes the unadjusted AT or SM volume, height is in meters, and y_t denotes the back-transformed quantity. This adjustment has the effect of normalizing the AT or SM volume to a standard height, which is useful in comparing subjects in populations with differing heights. We investigated the associations of AT and SM with BMI in multivariable linear regression analyses adjusting for age, race, and candidate lifestyle factors. We also considered visceral AT and the sum of bone plus organ volumes in models, but associations of AT and SM were strongest and were not improved by consideration of other body compartments.

Candidate lifestyle factors were tested in all models in a stepwise fashion, with p=0.05 for entry and retention. Interactions of race and age with other factors in the model were also assessed and included if they reached statistical significance. The linearity assumption was tested for continuous measures by adding quadratic terms to the models. We tested for colinearity for body compartments in the model and found that it was not substantial between AT and SM; therefore, both compartments were kept in the final model. Confidence intervals were determined using the bias-corrected accelerated bootstrap method with p-values defined as the one minus the highest confidence level that still excluded zero (29); this procedure was necessary as the error residuals appeared to be non-Gaussian.

RESULTS

Subjects

Body composition studies were available on 263 subjects from the CARDIA study and the characteristics for each sex and race group are presented in Table 1. There were 136 men (58 African Americans; 78 Caucasians) and 127 women (63 African Americans; 64 Caucasians). The Caucasian subjects were slightly older than their African American counterparts by a median of 1-2 years and the IQR was expectedly small (~37-44 yrs) as subjects were enrolled in CARDIA with an age spread of only 12 years.

Both groups of men were, on average, within the overweight range (i.e., BMI 25 to < 30 kg/m^2) with median BMI in African Americans at 27.2 kg/m^2 and Caucasians at 26.2 kg/m^2. About two-thirds of the men were overweight or obese (African Americans 69% and Caucasians 67%, p=0.86). Although total and subcutaneous AT were similar between the two groups of men, African Americans had about one-half the amount of visceral AT compared to the Caucasian men (p=0.0003). Of note, African-American men had much higher SM and slightly higher BMI, but lower VAT and slightly lower %AT compared with Caucasian men.

The African American women were, as a group, obese (i.e., BMI 30 kg/m^2) while the Caucasian women were normal weight (i.e., BMI 25 kg/m^2) with respective median BMIs of 31.6 kg/m^2 and 23.5 kg/m^2. The proportion of African American women who were overweight or obese (78%) was significantly larger (p<0.001) than the proportion of overweight or obese Caucasian women (42%). However, as in men, African-American women had much higher SM. In women, VAT was higher in African-Americans, while in men, VAT was higher in Caucasians. The racial differences in total and regional adipose tissue compartment volumes paralleled between-race group differences in BMI.

Physical activity levels were similar overall in African American and Caucasian men (p=0.58), although African-American men were somewhat more likely to be in the most active quartile compared with Caucasian men (28% vs. 19%). Among women, although the difference in self-reported physical activity did not reach statistical significance, African Americans had relatively more subjects in the least active physical activity quartile 1 (29% vs. 22% in Caucasians) and Caucasian women more in quartile 4 (34% vs. 18%), suggesting that the Caucasian women tended to be more physically active.

Overall, nearly 80% of the men and women in this analysis self-reported being moderately to very physically active.

Adiposity-BMI Associations

This first series of analyses were designed to characterize the associations of BMI with adiposity.

BMI was strongly associated with height-normalized AT in all four sex and ethnic groups (Figure 1, p<0.0001), although the proportion of BMI variation explained in men (African American, R^2=0.71; Caucasian, R^2=0.64) was lower than the proportion observed in the women (African American, R^2=0.84; Caucasian, R^2=0.92).

The corresponding associations between BMI and %AT are plotted in Figure 2. All four correlations were statistically significant (all p<0.001) in men and women. However, according to these analyses, BMI is only modestly associated with percent adiposity, particularly in men (African American, $R^2 = 0.46$; Caucasian, $R^2 = 0.24$), but also in women (African American, $R^2 = 0.55$; Caucasian, $R^2 = 0.72$).

The simple univariate BMI-AT analyses presented in Figure 1 were extended in the multivariable models shown in Table 2 to determine factors associated with AT (i.e., adiposity). Increasing BMI was independently associated with higher AT in both men and women (p<0.0001), with stronger associations seen for those in the normal BMI range (<25 kg/m^2). By comparison, increasing SM was associated with lower AT in men (p=0.036) with a weaker negative association in women (p=0.25). In men, the BMI effect was stronger in African Americans compared with Caucasians (p = 0.002, test for interaction). However, we elected to report results from the combined model in men since BMI was positively associated with AT in both African Americans and Caucasians.

Age showed little association with AT in men or women. Among lifestyle factors, greater physical activity in men and alcohol use in women remained associated with lower AT. The sex-specific multivariable models accounted for 68% of between-individual differences in AT among men and 89% in women. A model of %AT gave similar results.

Skeletal Muscle Associations

This next set of analyses examined the associations between BMI and SM or %SM as well as the determinants of between-individual differences in SM.

The associations of BMI with SM were also significant in both men and women, but the patterns differed. Men had relatively more SM than AT throughout the entire range of evaluated BMIs, but the amount of AT approached SM at larger BMIs (Figure 1). Women had more SM than AT in the normal BMI range, but AT exceeded SM at higher BMIs (Caucasian >26 kg/m^2; African-American >28 kg/m^2).

The correlation between BMI and %SM in African American and Caucasian men was negative but weak (r=-0.127, p=0.14; Figure 2), although the correlation was somewhat stronger and statistically significant in African American men compared with Caucasian

men. The correlation between BMI and %SM was negative and statistically significant (r=-0.52, p<0.0001) in both African American and Caucasian women (Figure 2). Regardless of race, the correlations were much stronger in women than in men.

The multivariable SM prediction models are presented in Table 3. Height was strongly associated with SM (p<0.0001) and height alone explained 13% of the SM variation in men and 16% in women. Skeletal muscle volume in the composite models scaled to height with powers in the range of ~1.3-1.6 (Table 3). Absolute AT volume alone explained 19% of the SM variation in men and 38% in women. Adipose tissue volume in the composite models was independently associated with SM in both men and women. Greater physical activity levels were associated with a larger SM. Age showed little association with SM in men (p=0.41) and contributed to the SM prediction model only weakly in women (p=0.085). After multivariable adjustment for height, age, and lifestyle factors, being African American was associated with approximately 10-11% greater SM (p<0.0001) compared with being Caucasian. The fully adjusted models for men and women accounted for 43% and 60% of between-individual differences in SM volume, respectively. Ethnicity, adiposity, and physical activity levels all thus accounted for between-individual differences in SM even after controlling first for height.

Contributions of AT and SM to BMI

The third group of analyses examined the determinants of BMI after controlling first for AT. Adipose tissue and SM were both strongly and independently associated with BMI in men and women (each p<0.0001, Table 4) in multivariable models adjusting for demographic and lifestyle factors. Furthermore, a large proportion of the between-subject variation in BMI was now explained in both men (86%) and women (94%).

In men, both AT and SM contributed to a similar proportion of the between-subject variation in BMI as established by developing the model with either AT or SM alone along with ethnicity and age as covariates. In contrast, AT in women contributed to nearly 30% more of the variation in BMI compared with SM. In men, a one liter increase in SM was associated with a larger increase in BMI than a one liter increase in AT (0.46 vs. 0.32, p = 0.0042), but in women the SM relationship with BMI was not statistically larger than the AT relationship with BMI (0.40 vs. 0.34, p = 0.34). Furthermore, after controlling for both AT and SM, there was little association of age, race, or lifestyle factors (data not shown) with BMI.

DISCUSSION

The expanding global prevalence of obesity (30) and increasing search for weight-related genetic markers (31) highlight the important need for simple adiposity measures that can be applied to large population samples. A wealth of experimental data supports the use of BMI in this context, but reported BMI-adiposity associations are modest and "muscularity" is often cited as a factor that confounds this relationship (7, 8, 12-14, 32). The present study is the first to report direct SM estimates in a population sample that provides quantitative estimates of the extent to which BMI reflects variation in muscularity.

Our findings in the CARDIA sample show that SM is a major factor determining between-subject differences in BMI, equal to that of AT in men and normal weight women. Additionally, the results of the current study show that factors predicting BMI after controlling for AT, such as age, race, and activity levels, are largely accounted for by their association with SM.

BMI as a Measure of Adiposity

As shown in earlier studies, after controlling for BMI, other factors add to AT prediction, including age (4, 5), race (6, 7), body build (7), and physical activity levels (8). Age had only a small effect in our adiposity prediction models, but the age range of our subjects was relatively narrow (33-45 yrs). Others have found greater %AT with older age even after adjusting first for BMI (5). The relative increase in AT with aging corresponds to a parallel loss of SM (17, 33).

A critical issue for setting universal BMI ranges is the stability of BMI-adiposity relations across different race and ethnic groups. Deurenberg et al. (10, 11) and Rush et al. (12, 13) have reported ethnic variation in BMI-adiposity relationships and have attributed these findings to differences in body build, extremity proportions, and muscularity as defined by DXA estimates of extremity lean soft tissue. Our study extends these earlier observations using advanced whole-body MRI-AT and SM measurements and strongly supports the hypothesis that differences in muscularity account for the observed variation in BMI-AT relationships across African American and Caucasian subjects even after controlling for age and lifestyle factors, including physical activity levels and alcohol intake. The important implication of these findings is that BMI, when applied across race groups, may provide a biased measure of adiposity secondary to race differences in muscularity.

The lower adiposity after controlling first for BMI in physically active subjects is consistent with earlier studies (8) and is in part attributable to exercise-induced effects on body composition, notably SM. At the same BMI, physically active subjects have a lower AT and larger SM mass, an effect that was more evident in men. While young "athletes" may have a high BMI due to lean mass rather than fat, we focus here on subjects with "average" physical activity whose age range and BMI make them important candidates for screening and lifestyle interventions.

Skeletal Muscle as a Source of BMI Variation

A central feature of our study is the presentation of an allometric SM prediction model that provides new insights into BMI-AT associations. We focused our analysis specifically on SM rather than the substantially larger and heterogeneous FFM compartment often considered when critically evaluating BMI as a measure of adiposity.

We developed our SM model *a priori* by considering factors known to associate with muscle mass including height, mechanical loading conditions (i.e., adiposity, physical activity level)(8), ethnicity (34), and age (17, 33). Other as yet less well defined factors may be involved, but we based our model on established relations. As expected, we observed

positive associations between height and SM, although the correlations were generally weak, with only 11-15% of the variation explained in men, and 19-20% in women.

A striking observation emerging as part of our SM model development is that SM represented a larger fraction of body mass than AT in men throughout the entire range of evaluated BMIs. In contrast, SM was larger in women whose BMI on average was ~26-28 kg/m^{2}or lower; above that level AT predominated as a fraction of body mass. These observations in a population-based sample of adults underscore a prominent sex difference in body structure in relation to BMI and adiposity. Accordingly, in men, SM and AT roughly accounted equally for between-individual differences in BMI. This is distinct from the women in whom AT was a predominant determinant of between individual differences in BMI, driven primarily by those who are obese.

A second related observation emerging from our SM models is that all of the entered predictors collectively only accounted for 43% of between individual differences in SM among the men and a somewhat larger percentage (60%) in women. Race remained an independent SM predictor in our models even after controlling for height and physical activity levels. Baumgartner et al. (33) developed similar models for an older 96% non-Hispanic white cohort using extremity lean soft tissue measured by DXA as a proxy for SM mass. Free testosterone and IGF-1 levels added to the SM prediction model for men (total R^2, 0.57) in the study by Baumgartner et al, including controlling for knee height and the presence of cardiovascular disease. The corresponding model in women had an R^2 of 0.52 and included knee height, fat mass, and physical activity as predictor variables; hormones did not enter the SM prediction model for the women. Thus, a large proportion of the variance in SM remains unexplained, suggesting that there are other important as yet unmeasured factors leading to between-subject differences in muscularity. Our measure of self-reported physical activity was also qualitative and more advanced accurate methods of estimating non-resting energy expenditure are available and should be considered for in future studies.

A limitation of our study is that the age range of CARDIA subjects is relatively small (33-45 years old) compared to the general adult population. Variation in SM relative to BMI may play a smaller role when considered across the entire adult lifespan.

Implications

As in other reports (3-14), our findings support the observation that BMI is a modest surrogate measure of adiposity at the individual level. Some of our subjects evaluated in a population-based sample who were classified as "obese" by BMI, and thus having excess adiposity (35), had actual %AT levels similar to those of subjects within the "normal" BMI range (Figure 2). The potential for diagnosing subjects as obese, a condition defined by "excess" adipose tissue, is particularly present in men who have greater variation in muscularity and related adiposity than women. Another important finding is that when both AT and SM are used to predict BMI, race, age and lifestyle factors are no longer associated with BMI.

Those individuals most at risk for classification as overweight or obese based on BMI in the absence of excess adipose tissue are young males, particularly those who are physically active and African American. Similarly, BMI is also a measure of adiposity with limited predictive value in non-obese women, notably those who are African American. These predictions are consistent with reports examining the question of optimum means of recruiting and retaining military personnel in an environment with clear weight/BMI criteria (36, 37).

Similar concerns apply when considering BMI as a measure of adiposity at the population level. In particular, misinterpretations may prevail when applying BMI as a phenotypic marker of adiposity across populations differing in age, race, and activity levels, factors shown in the present report to associate with variation in muscularity. The search for obesity genes continues to grow with genome wide association studies typically based on BMI as a measure of adiposity. Our findings suggest that BMI can equally represent SM in men and normal weight women.

While BMI has several favourable characteristics as a screening tool for evaluating individual and population adiposity, our findings strongly argue for cautious interpretation in selected contexts. When practical, a second tier evaluation should be considered that provides improved resolution on health risk prediction (e.g., waist circumference estimates or even blood tests) and direct adiposity measures (e.g., DXA estimates of body fat). While additional measures beyond BMI add cost and complexity to evaluations, their improved resolution of health risks and adiposity may add substantial value depending on the context.

Conclusions

Body mass index, growing in worldwide use and promoted as a measure of adiposity, not only represent a subject or group's adiposity, but their level of muscularity as well. Muscularity at the population level, as defined the current report, is influenced to varying degrees by age, race, and lifestyle factors. In addition to a cautionary note regarding the application and interpretation of BMI, our findings encourage the continued development of other means of quantifying body composition and establishing health risks in individual subjects and populations.
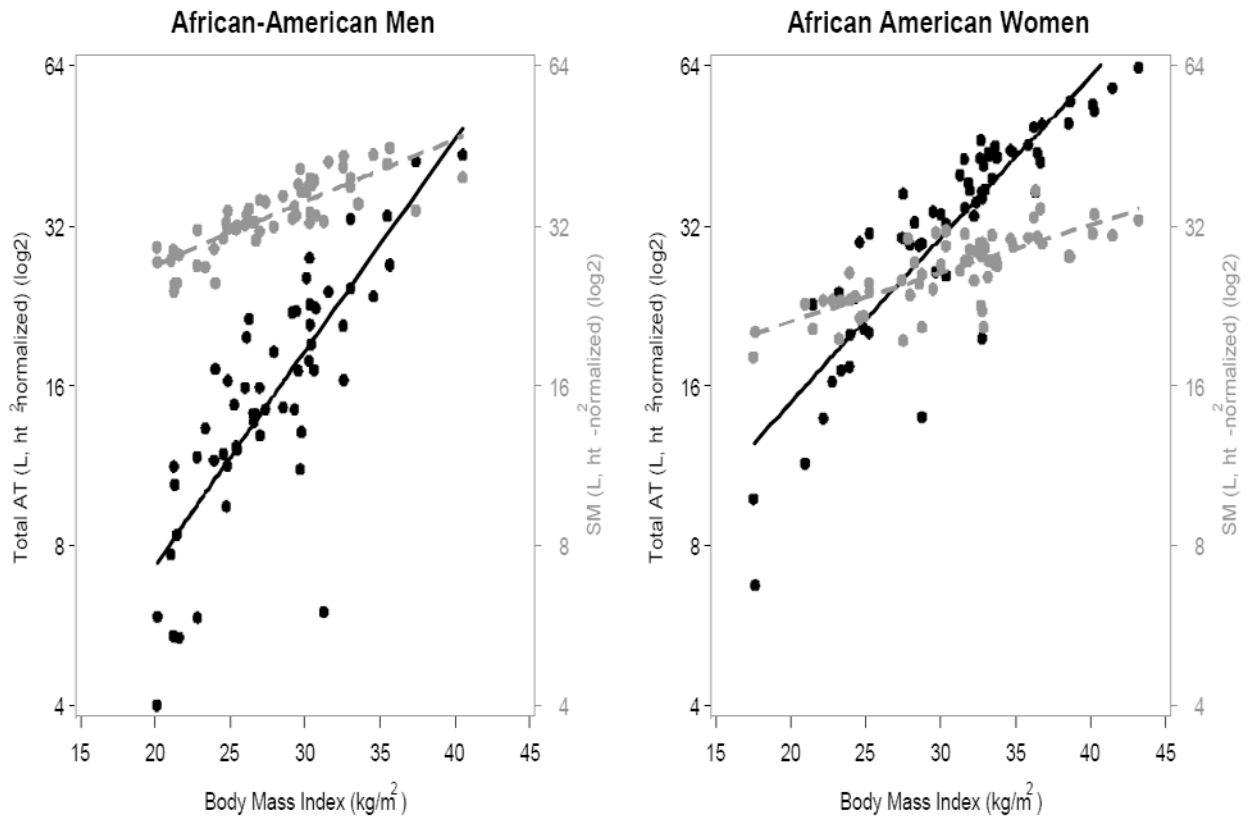
Acknowledgments

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African-American Men / African American Women — scatter plots of Total AT (L, ht² normalized) (log2) and SM (L, ht⁻² normalized) (log2) versus Body Mass Index (kg/m²)
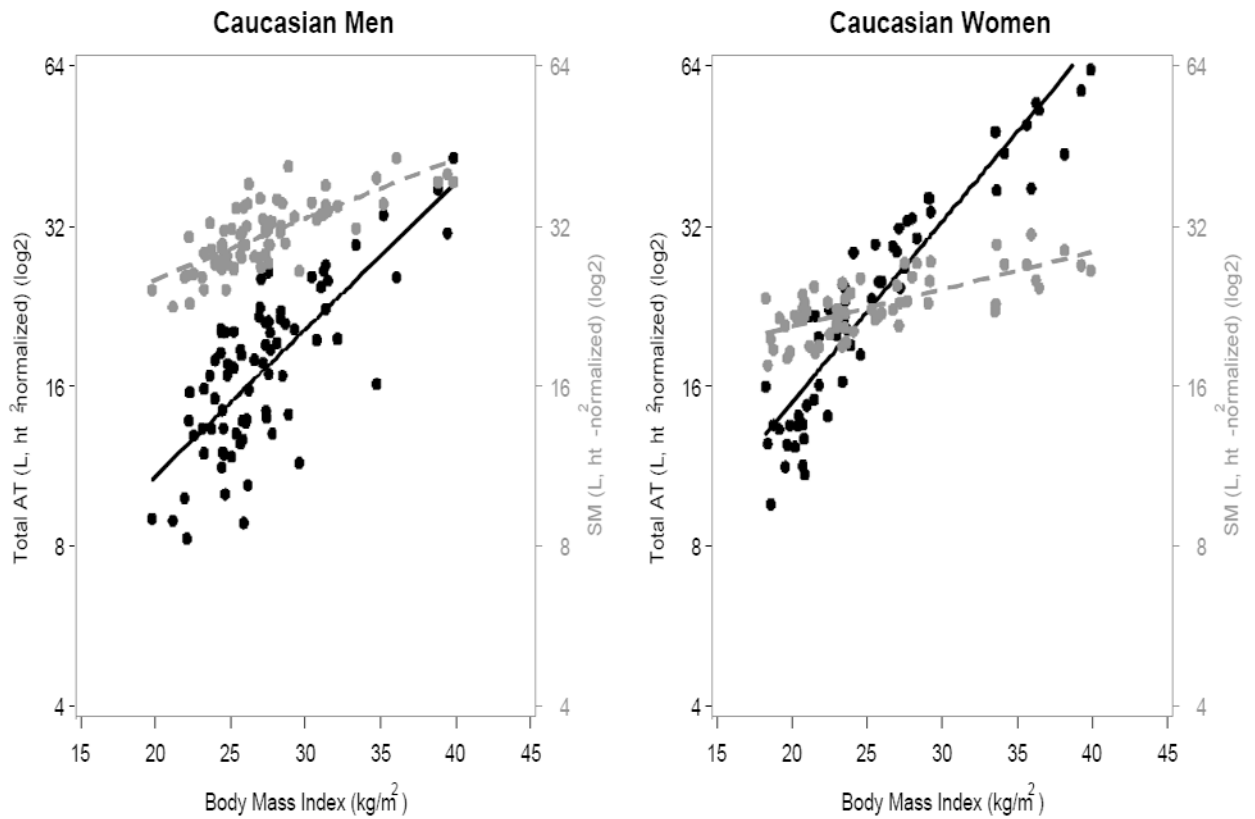
Figure 1.
(A) African-Americans; (B) Caucasians. Association of BMI with AT and SM volumes, expressed as ratios to height^2, in men (left) and women (right). Black symbols and whole lines denote AT, and grey symbols and dashed lines denote SM. [AT men: African American, y=-26.9+1.6x (R^2, 0.71, p<0.0001); Caucasian, y=−17.0+1.3x (R^2, 0.64, p<0.0001). AT women: African American, y=−19.8+1.5x+0.011x^2 (R^2, 0.84, p<0.0001); Caucasian, y=-25.8+1.9x+0.007x^2 (R^2, 0.92, p<0.0001)]
[SM men: African American, y=8.4+0.92x (R^2, 0.68, p<0.0001); Caucasian, y=8.3+0.83x (R^2, 0.58, p<0.0001). SM women: African American, y=10.0+0.55x (R^2, 0.56, p<0.0001); Caucasian, y=13.0+0.38x (R^2, 0.53, p<0.0001)].
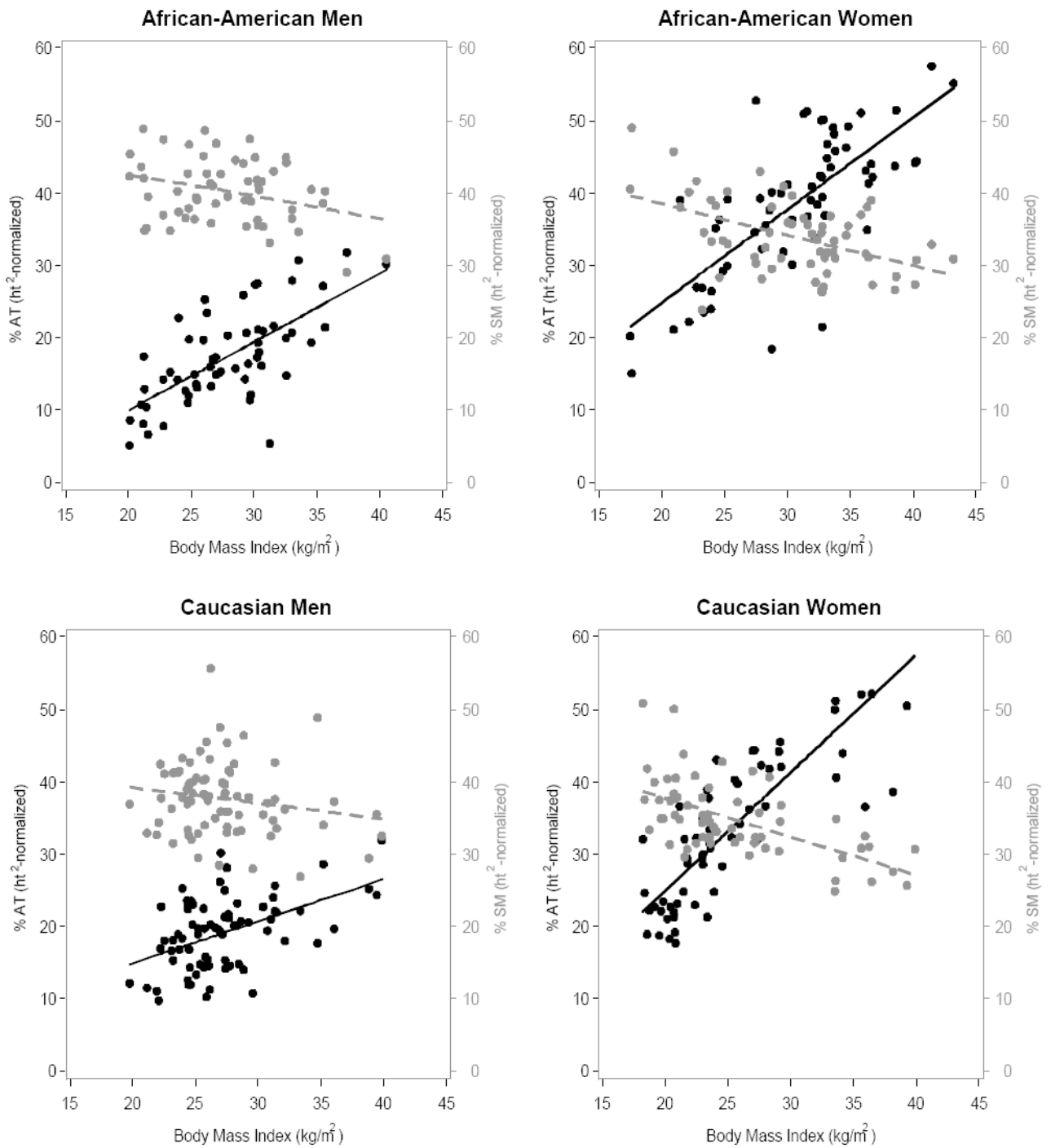
Figure 2.
(A) African-Americans; (B) Caucasians. Association of BMI with %AT and %SM , expressed as 100×0.92 g/cm^3 × the ratio of total height^2-normalized AT volume to body weight and 100×1.04 g/cm^3 × the ratio of total height^2-normalized SM volume to body weight in men (left) and women (right). Black symbols and whole lines denote %AT, and grey symbols and dashed lines denote %SM.

[%AT men: African American, y = -9.0 + 0.95x (R^2=0.46, p<0.0001); Caucasian, y = 3.1 + 0.59x, (R^2=0.24, p<0.0001). %AT women: African American, -0.73 + 1.28x (R^2=0.55, p<0.0001); Caucasian, y = -7.6 + 1.63x (R^2=0.72, p<0.0001)]

[%SM men: African American, y = 48.5 - 0.30x (R^2=0.098, p = 0.018); Caucasian, y =43.5 - 0.22x (R^2=0.031, p = 0.13). %SM women: African American, y = 46.9 - 0.43x (R^2=0.23, p<0.0001); Caucasian, y = 48.3 - 0.53x (R^2=0.35, p<.0001)]

Table 1

Subject characteristics.

	Men			Women		
	African American (n = 58)	Caucasian (n = 78)	P-value	African American (n = 63)	Caucasian (n = 64)	P-value
Age (y)	39.0 (37.0-42.0)	41.0 (38.0-43.0)	0.023	41.0 (37.0-43.0)	42.0 (38.5-44.0)	0.050
Weight (kg)	86.1 (75.9-98.5)	82.4 (77.7-93.0)	0.43	85.6 (72.7-92.1)	65.9 (58.6-77.7)	<0.0001
Height (cm)	179 (175-181)	178 (175-183)	0.92	164 (160-171)	165 (162-171)	0.43
BMI (kg/m^2)	27.2 (24.6-30.4)	26.2 (24.5-28.5)	0.35	31.6 (25.3-33.7)	23.5 (20.9-28.2)	<0.0001
Phys. Activity						
Quartile **1**	25.9%	23.1%	0.58	29.0%	21.9%	0.20
2	22.4%	29.5%		27.4%	20.3%	
3	24.1%	28.2%		25.8%	23.4%	
4	27.6%	19.2%		17.7%	34.4%	
WC (cm)	91.3 (86.2-97.8)	91.3 (86.8-98.2)	0.74	92.3 (82.3-99.2)	75.9 (69.6-86.6)	<0.0001
HC (cm)	102 (98-110)	101 (98-107)	0.23	112 (104-118)	102 (96-110)	0.0002
WHR	0.89 (0.84-0.91)	0.91 (0.88-0.94)	0.004	0.82 (0.77-0.86)	0.75 (0.73-0.79)	<0.0001
%AT	17.4 (14.7-22.8)	20.6 (15.6-23.4)	0.080	36.4 (32.3-41.1)	30.7 (22.3-36.8)	0.004
Total AT (L) *	15.9 (11.8-22.0)	17.5 (13.3-21.1)	0.34	37.6 (26.9-45.1)	23.6 (15.5-35.0)	0.0001
UTr-AT (L)	2.9 (2.0-4.1)	3.1 (2.4-4.0)	0.40	7.0 (4.2-8.6)	3.3 (2.1-5.4)	<0.0001
LTr-AT (L)	5.3 (3.9-7.2)	5.5 (4.2-7.5)	0.48	13.0 (10.0-16.5)	8.6 (5.7-12.8)	0.0001
Leg AT (L)	4.6 (3.7-6.1)	4.3 (3.7-5.4)	0.40	11.5 (8.8-15.2)	9.2 (6.5-11.4)	0.002
Arm AT (L)	1.1 (0.7-1.4)	1.1 (0.9-1.3)	0.17	2.5 (1.9-3.1)	1.8 (1.3-2.6)	0.004
SAT (L)	14.6 (10.5-19.4)	14.5 (11.6-18.0)	0.68	35.7 (25.6-43.3)	23.2 (15.2-32.7)	<0.0001
VAT (L)	1.4 (0.9-2.3)	2.4 (1.6-3.1)	0.0003	1.3 (0.6-2.0)	0.6 (0.4-1.5)	0.026
SM (L)	33.5 (31.3-37.9)	30.7 (27.7-33.7)	0.001	27.1 (23.2-29.8)	22.4 (20.8-25.1)	<0.0001
Bone & Organ (L)	21.4 (19.5-23.1)	21.6 (19.7-23.1)	0.57	20.9 (19.8-22.8)	20.8 (19.2-22.1)	0.27

Data are presented as Median (IQR). Test of African American versus Caucasian for men and women (Wilcoxon's rank-sum test for continuous variables and Fisher's exact test for categorical variables.

Abbreviations: AT, adipose tissue; BMI, body mass index; HC, hip circumference; IQR, interquartile range; LTr, lower trunk; SM, skeletal muscle; SAT, subcutaneous adipose tissue; AT, adipose tissue; Tr, trunk; UTr, upper trunk; VAT, visceral adipose tissue; WC, waist circumference; WHR, waist to hip circumference ratio.

*
Note that all MRI measures are height^2-normalized and back-transformed.

Table 2

Allometric multivariable associations with AT volume [*].

	Men			Women		
	Estimate	95%CI	P-value	Estimate	(95%CI)	P-value
Intercept	0.68	(-1.8, 2.8)	0.58	2.06	(-0.78, 3.7)	0.11
African-American vs. Caucasian	-0.065	(-0.19, 0.025)	0.16	-0.074	(-0.18, 0.001)	0.052
BMI <25 (m²/kg) [**]	0.18	(0.14, 0.24)	<0.0001	0.14	(0.11, 0.16)	<0.0001
BMI 25-30 (m²/kg)	0.082	(0.030, 0.12)	<0.0001	0.070	(0.032, 0.095)	<0.0001
BMI >30 (m²/kg)	0.085	(0.067, 0.10)	<0.0001	0.054	(0.043, 0.064)	<0.0001
Skeletal Muscle (ln, L)	-0.90	(-1.56, -0.076)	0.036	-0.35	(-0.79, 0.37)	0.25
Age (ln, years)	0.17	(-0.22, 0.57)	0.38	-0.27	(-0.66, 0.18)	0.21
Physical Activity						
2nd **Quartile vs. 1st**	-0.10	(-0.22, -0.011)	0.032			
3rd **Quartile vs. 1st**	-0.073	(-0.18, 0.019)	0.12			
4th **Quartile vs. 1st**	-0.16	(-0.34, -0.035)	0.012			
Alcohol use (per week)						
<1 **vs. none**				-0.076	(-0.17, -0.013)	0.019
1-7 **vs. none**				-0.081	(-0.19, -0.018)	0.011
>7 **vs. none**				-0.081	(-0.21, 0.008)	0.074
SEE			0.24			0.17
Adjusted R²			0.68			0.89

[*] Outcome analyzed is natural log (ln) transformed adipose tissue volume (AT, L) from multivariable linear regression analyses. SEE, standard error of the estimate.

Estimates are slopes (β$_j$) from the allometric model. AT and SM (skeletal muscle volume) are height²-normalized.

[**] BMI analyzed using linear spline.

Table 3

Allometric multivariable associations with SM volume [*].

	Men			Women		
	Estimate	95%CI	P-value	Estimate	(95%CI)	P-value
Intercept	-3.49	(-6.6, -0.24)	0.034	-6.51	(-9.43, -3.74)	<0.0001
African-American vs. Caucasian	0.10	(0.06, 0.14)	<0.0001	0.11	(0.05, 0.14)	<0.0001
Height (ln, cm)	1.31	(0.65, 1.91)	<0.0001	1.58	(1.02, 2.11)	<0.0001
Age (ln, yrs)	-0.11	(-0.35, 0.14)	0.41	0.21	(-0.03, 0.46)	0.085
AT (ln, L)	0.13	(0.10, 0.16)	<0.0001	0.14	(0.12, 0.17)	<0.0001
Physical Activity						
2nd Quartile vs. 1st	0.03	(-0.03, 0.10)	0.33	0.01	(-0.05, 0.07)	0.71
3rd Quartile vs. 1st	0.06	(-0.00, 0.12)	0.070	0.04	(-0.01, 0.10)	0.11
4th Quartile vs. 1st	0.11	(0.04, 0.17)	0.001	0.07	(0.02, 0.13)	0.013
SEE	0.12			0.11		
Full Model Adjusted R^2	0.43			0.60		
Adjusted R^2 (height only)	0.13			0.16		
Adjusted R^2 (AT only)	0.19			0.38		

[*] Outcome analyzed is natural log (ln) transformed skeletal muscle (SM, L) from multivariable linear regression analyses. SEE, standard error of the estimate.

Estimates are slopes (β_j) from the allometric model. AT, adipose tissue volume.

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Table 4

Multivariable associations with BMI [*].

	Men			Women		
	Estimate	95%CI	P-value	Estimate	(95%CI)	P-value
Intercept	6.4	(2.8, 9.2)	<0.0001	6.3	(2.4, 12.5)	<0.00001
African-American vs. Caucasian	-0.35	(-0.92, 0.25)	0.26	0.51	(-0.19, 1.75)	0.15
Age (per decade)	0.17	(-0.39, 0.85)	0.58	0.28	(-0.77, 1.20)	0.60
AT (L, ht²-normalized)	0.32	(0.26, 0.36)	<0.0001	0.34	(0.31, 0.36)	<0.0001
Skeletal Muscle (L, ht²-norm.)	0.46	(0.40, 0.53)	<0.0001	0.40	(0.28, 0.48)	<0.0001
SEE			1.59			1.58
Full Model Adjusted R²			0.86			0.94
Adjusted R² with SM & without AT			0.62			0.62
Adjusted R² with AT & without SM			0.67			0.90

[*] Outcome analyzed is BMI from multivariable linear regression analyses. SEE, standard error of the estimate.

Estimates are slopes (β_j) from the model.