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ORIGINAL ARTICLE

Less favorable body composition and adipokines in South Asians compared with other US ethnic groups: results from the MASALA and MESA studies

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BACKGROUND: Small studies have shown that South Asians (SAs) have more total body, subcutaneous, visceral and hepatic fat and abnormal adipokine levels compared with Whites. However, comprehensive studies of body composition and adipokines in SAs compared with other ethnic groups are lacking.

METHODS: Using harmonized data, we performed a cross-sectional analysis of two community-based cohorts: Mediators of Atherosclerosis of South Asians Living in America (MASALA, $n = 906$) and Multi-Ethnic Study of Atherosclerosis (MESA which included 2622 Whites, 803 Chinese Americans, 1893 African Americans and 1496 Latinos). General linear models were developed to assess the ethnic differences in ectopic fat (visceral, intermuscular and pericardial fat; and hepatic attenuation), lean muscle mass and adipokines (adiponectin and resistin). Models were adjusted for age, sex, site, alcohol use, smoking, exercise, education, household income and body mass index. Ectopic fat models were additionally adjusted for hypertension, diabetes, high-density lipoprotein and triglycerides. Adipokine models were adjusted for subcutaneous, visceral, intermuscular and pericardial fat; and hepatic attenuation.

RESULTS: Compared with all ethnic groups in MESA (Whites, Chinese Americans, African Americans and Latinos), SAs had greater intermuscular fat (pairwise comparisons with each MESA group, $P < 0.01$), lower hepatic attenuation ($P < 0.001$) and less lean mass ($P < 0.001$). SAs had greater visceral fat compared with Chinese Americans, African Americans and Latinos ($P < 0.05$) and greater pericardial fat compared with African Americans ($P < 0.001$). SAs had lower adiponectin levels compared with other ethnic groups ($P < 0.01$; except Chinese Americans) and higher resistin levels than all groups ($P < 0.001$), even after adjusting for differences in body composition.

CONCLUSION: There are significant ethnic differences in ectopic fat, lean mass and adipokines. A less favorable body composition and adipokine profile in SAs may partially explain the increased predisposition to cardiometabolic disease. The mechanisms that underlie these differences warrant further investigation.

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INTRODUCTION

With over 3.4 million current residents, South Asians, individuals from India, Pakistan, Nepal, Bangladesh and Sri Lanka, comprise the fastest growing ethnic group in the United States (US).[1] Compared with other race/ethnic groups, South Asians have higher rates of type 2 diabetes (DM)[2] and cardiovascular disease (CVD).[3,4] Some hypothesize that the higher rates of metabolic disorders and CVD are due to differences in body composition with higher amounts of fat in organs and tissues where fat is not intended to be stored (called ectopic fat) and/or lower levels of lean muscle mass.[5]

Compared with Whites, South Asians have higher amounts of total body fat for a given body mass index (BMI).[6] Abnormalities in glucose and lipid metabolism that are seen in Europeans with a BMI of 30 kg m^{-2} are seen at a lower BMI (21–22.5 kg m^{-2}) in South Asians.[7] Furthermore, for a given level of total body fat, South Asians have higher amounts of abdominal adipose tissue including subcutaneous, visceral and hepatic fat, and less lean muscle mass,[8,9] as well as abnormal levels of hormones secreted from adipose tissue (adipokines).[10,11] Compared with Whites, South Asians have a lower capacity to store fat in subcutaneous adipose, and therefore, some have proposed the adipose tissue overflow hypothesis, which states that excess fat overflows to these ectopic compartments.[12] In the Molecular Study of Health and Risk in Ethnic Groups (mol-SHARE), ectopic fat in combination with decreased lean muscle mass and an abnormal adipokine profile was associated with insulin resistance and higher cardiometabolic risk in South Asians with a non-obese BMI.[9]

Prior studies investigating differences in body composition, ectopic fat depots and adipokines in South Asians compared with another ethnic group have been small. None have performed a comprehensive evaluation of several ectopic fat depots, lean muscle mass and adipokines simultaneously among multiple different race/ethnic groups. A comprehensive evaluation of body composition that includes several measures of ectopic fat and lean mass in combination with adipokine levels, serving as measures of

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adipocyte dysfunction, is critical to better assessing the overall metabolic risk in the South Asian population. Therefore, using data from two large well-phenotyped cohorts, Mediators of Atherosclerosis in South Asians Living in America (MASALA) and Multi-Ethnic Study of Atherosclerosis (MESA), we compared body composition and adipokines among five race/ethnic groups. Our hypothesis was that compared with other race/ethnic groups in the US, South Asians would have greater amounts of ectopic fat (visceral fat area, intermuscular fat area, pericardial fat volume and lower hepatic attenuation), less lean muscle mass and a less favorable adipokine profile. In addition, we hypothesized that by controlling for the differences in body composition, we would be able to explain the differences in adipokine levels between South Asians and the other four race/ethnic groups.

MATERIALS AND METHODS

Study populations

We performed a cross-sectional analysis of harmonized data from two community-based cohorts: MASALA and MESA. As we did not detect a strong correlation between age and body composition variables ($r \leqslant 0.35$), all individuals in the MASALA study (ages 40–84 years) were included for the purposes of this analysis ($n = 906$) and were compared with the four MESA racial/ethnic groups. Data from the MESA baseline exam were used for pericardial fat volume and hepatic attenuation analyses and included 2622 Whites, 803 Chinese Americans, 1893 African Americans and 1496 Latinos. Data from an ancillary study from MESA Exams 2 and 3 were used for abdominal fat, intermuscular fat, lean mass and adipokine analyses, which included a random sample from each of the four race/ethnic groups with a total of 785 Whites, 251 Chinese Americans, 407 African Americans and 501 Latinos.

The institutional review boards at the sites conducting both the MASALA and MESA studies approved both study protocols. Informed consent was obtained from all study subjects.

MASALA study

The MASALA study is a community-based cohort of South Asian adults without known CVD, which was modeled on MESA.[13,14] Study participants were sampled from two geographic locations, the nine counties of the San Francisco Bay Area and the greater Chicago area. Clinical sites for the study were at the University of California, San Francisco (UCSF) and Northwestern University (NWU). A total of 906 subjects were recruited between October 2010 and March 2013. We have previously published detailed methods for the MASALA Study.[14]

Eligibility criteria for MASALA included self-identification of South Asian ethnicity, age between 40 and 84 years, and ability to speak and read English, Hindi or Urdu.[14] MASALA used identical exclusion criteria as the MESA Study, which included a diagnosis of a heart attack, stroke or transient ischemic attack, heart failure, angina, nitroglycerin medication use, any prior cardiovascular procedures, current atrial fibrillation, cancer treatment, shortened life expectancy, impaired cognition, plans to move out of the geographic vicinity of the study site in the next 5 years, living in a nursing home or weight >300 lbs.[14]

Participants were assisted by trained bilingual study staff to complete detailed questionnaires for demographic information and behaviors (including tobacco and alcohol use).[14] Physical activity was assessed using the Typical Week's Physical Activity Questionnaire.[15]

Blood pressure was measured after a 5-min seated rest using an automated blood pressure machine (V100 Vital Sign Monitor; GE Healthcare, Fairfield, CT, USA). Three blood pressures were recorded and the average of the last two readings used as mean systolic and diastolic blood pressure. A systolic blood pressure $\geqslant 140$ mm Hg and/or diastolic blood pressure $\geqslant 90$ mm Hg or use of any anti-hypertensive medication was used to define hypertension.

After a requested 12-h fast, fasting blood samples were obtained. We measured total cholesterol, triglycerides, high-density lipoprotein cholesterol using enzymatic methods and low-density lipoprotein was calculated. Fasting plasma glucose was measured by the hexokinase method (Quest Labs, San Jose, CA, USA). We used the American Diabetes Association criteria to define DM, by fasting glucose $\geqslant 126$ mg dl^{-1} and/or use of a DM medication.[16] We measured adiponectin and resistin using Millipore Luminex adipokine A panel (EMD Millipore, Billerica, MA, USA). Inter-assay coefficient of variation was 2.3–4.1% for adiponectin and 3.3–5.5% for resistin.

Body composition. We measured participant weight on a standard balance-beam scale or digital weighing scale. Height was measured using a stadiometer. BMI was calculated by weight in kilogram divided by height in (meters)^2. Trained study coordinators measured waist circumference using a flexible tape measure at the site of maximum waist circumference midway between the lower ribs and the anterior superior iliac spine. The average of two measurements was used for analysis.

Computed tomography (CT) scans of the abdomen (Philips Medical Systems, Andover, MA, USA; Toshiba Medical Systems, Tustin, CA, USA; Siemens Medical Solution, Malvern, PA, USA) were used to calculate abdominal visceral and subcutaneous fat area intermuscular fat area, and abdominal lean muscle mass area. A CT technician obtained a lateral scout image of the abdomen to establish the position between the L4 and L5 vertebrae. A single abdominal CT slice was obtained at this level and Medical Image Processing, Analysis and Visualization (MIPAV) software was used to measure the visceral and subcutaneous abdominal fat[17] at the University of California, San Diego body composition-reading center. Visceral fat was demarcated by readers as those pixels with the appropriate Hounsfield Unit range inside the visceral cavity. Subcutaneous fat was defined as the tissue outside the visceral cavity but inside the body contour. Muscle segmentation was carried out as previously described.[18] The four abdominal/back muscle groups from which fat and lean mass measurements were obtained included the psoas, paraspinous, oblique and rectus muscles. These muscles were highlighted by the readers and then deleted from the calculation of subcutaneous fat. Measurements from all four abdominal and back muscle groups were summed to obtain total intermuscular fat area and total lean muscle mass area.

Non-contrast cardiac CT images were obtained to quantify pericardial fat and hepatic attenuation using a cardiac-gated CT scanner: at UCSF, a Phillips 16D scanner or a Toshiba MSD Aquilion 64 and at NWU, a Siemens Sensation Cardiac 64 Scanner (Siemens Medical Solutions, Malvern, PA, USA) was used. The same reading center staff under the supervision of Dr Jeffrey Carr performed all measurements of pericardial fat volume and hepatic attenuation. The CT scan range encompassed the entire heart and provided information on 45 mm of adipose tissue encasing the proximal coronary arteries. We first defined the 45 mm *z* axis volume containing the proximal coronary arteries. The technician follows a set of regions of interest pertaining to subcutaneous and pericardial fat within the 45 mm volume along with regions in the calibration phantom to calculate the range of Hounsfield units for adipose tissue. The technician segments the heart from the thorax by removing tissues beyond the lung using a deformable model-based edge detection method such as active contours or live wires to detect the boundary between the lung and fat around the heart.[19–21]

CT images for hepatic attenuation were also interrogated using the MIPAV software at vertebral level T12-L1. Nine regions of interest within homogenous portions of the liver at two levels were read, avoiding any vascular structures or other liver pathology. Measurement methods were similar to those used in MESA.[22] Fatty liver was defined as having Hounsfield units <40.

MESA study

The study design, eligibility and methods for MESA have been previously published.[13] MESA includes individuals from four racial/ethnic groups (Whites, African Americans, Chinese Americans and Latinos) living in Forsyth County, NC, USA; Chicago, IL, USA; Baltimore, MD, USA; Los Angeles County, CA, USA; St Paul, MN, USA and New York, NY, USA. Data from the baseline MESA examination (2000–2002) were used for hepatic attenuation and pericardial fat volume measurements; data from a body composition ancillary study performed during exam 2 (2002–2004) and 3 (2004–2005) were used for the abdominal fat, intermuscular fat, lean mass and adipokine measurements. Identical questionnaires for assessing sociodemographic characteristics and behaviors and identical protocols for seated blood pressure, anthropometry, and abdominal and cardiac CT scanning were used as described above for the MASALA study. Both studies used the same reading centers and protocols for measuring abdominal body composition, pericardial fat volume and hepatic attenuation for ease of data harmonization.

Serum glucose was measured from fasting samples by the glucose oxidase method (Ortho Clinical Diagnostics, Johnson & Johnson Clinical Diagnostics, New Brunswick, NJ, USA). Similar assays were used to measure

adiponectin and resistin (Millipore Luminex adipokine panel A) as for the MASALA study, and these adipokines measurement were conducted at the same research laboratory.

Statistical analysis

Harmonized data from the MASALA and MESA study cohorts were used. Age- and sex-adjusted baseline characteristics of the MASALA participants and each of the MESA race/ethnic groups were obtained using regression standardization.

Multivariate general linear models were developed to examine the association between race/ethnicity and the following: subcutaneous fat area, visceral fat area, total intermuscular fat area, pericardial fat volume, hepatic attenuation, total lean muscle mass area, adiponectin and resistin. For the body fat measures, the models were adjusted in a stepwise manner: first for age, sex, site, alcohol use, smoking history, education, household income, exercise and BMI; then for hypertension and DM; and finally for high-density lipoprotein and triglycerides. The total lean muscle mass model and adipokine models were adjusted for age, sex, site, alcohol use, smoking history, education, household income, exercise and BMI. The adipokine models were additionally adjusted for visceral fat area, total intermuscular fat area, subcutaneous fat area, pericardial fat volume and hepatic attenuation. In addition, to account for race/ethnic differences in height, a sensitivity analysis was carried out where the models were adjusted for height instead of BMI. Sex interaction by race was also investigated and sex-stratified analyses were also performed. For the pericardial fat volume and hepatic attenuation models, baseline covariate data from the MESA study was used for sequential adjustments. For the abdominal fat, intermuscular fat, lean mass and adipokine models, updated MESA covariate data from exam 2 and 3 were used for sequential adjustments.

All analyses were conducted using SAS version 9.4 (SAS Institute, Inc., Cary, NC, USA).

RESULTS

South Asians in MASALA were younger (55 ± 9 years for MASALA vs 62 ± 10 years in MESA) and MASALA included fewer women (46% women in MASALA vs 52% in MESA) compared with those in other race/ethnic groups in MESA. Therefore, age- and sex-adjusted baseline characteristics of participants in the MASALA and MESA studies by race/ethnic group are shown in Table 1. Compared with other MESA groups, South Asians had a significantly higher level of education, higher household income, lower prevalence of smoking and alcohol use (except compared with Chinese Americans), and were less physically active. South Asians also had a higher prevalence of DM and hypertension (except compared with African Americans), lower adiponectin levels and higher resistin levels. South Asians had a lower BMI, weight and waist circumference compared with most other MESA groups, except compared with Chinese Americans who had the lowest means for these anthropometric indices.

Figures 1a–e (and Supplementary Table 1) depict the mean ectopic fat measures after adjusting for age, sex, socioeconomic status, behavioral factors, BMI and metabolic factors (DM, hypertension, high-density lipoprotein and triglycerides). Compared with African Americans, South Asians had less subcutaneous fat. South Asians had higher levels of visceral fat compared with Chinese Americans, African Americans and Latinos but similar amounts compared with Whites. South Asians had higher levels of intermuscular fat and hepatic fat (that is, lower hepatic attenuation) compared with all other race/ethnic groups. South Asians had less pericardial fat volume compared with Whites and Chinese Americans, but greater pericardial fat volume than African Americans. Pericardial fat volume was similar between South Asians and Latinos.

Analyses of lean muscle mass, adjusting for age, sex, socioeconomic status, behavioral factors and BMI showed that South Asians had significantly less total lean abdominal/back muscle mass compared with all other ethnic groups after full adjustment (Figure 1f and Supplementary Table 1).

Adiponectin levels were lower in South Asians after adjusting for age, sex, socioeconomic status, behavioral factors, BMI and all ectopic fat measures compared with all MESA groups except for Chinese Americans. However, resistin levels remained higher in South Asians compared with all other ethnic groups after full adjustment for all ectopic fat depots (Figure 2 and Supplementary Table 1).

To adjust for body size differences without possibly overadjusting for fat or lean body mass, we performed a sensitivity analysis adjusting for height instead of BMI (Supplementary Table 2). Similar results were obtained for the analyses of lean mass, adipokines and hepatic attenuation and only some slight but statistically significant differences were noted in the other ectopic fat measures.

Given evidence of sex interaction by race for several of the ectopic fat measures and adipokines, sex-stratified analyses were performed (Supplementary Table 3). With few exceptions, body composition and adipokine patterns across ethnicities were similar in men and women, although similar levels of significance were not always observed.

DISCUSSION

In this cross-sectional study of two community-based cohort studies of multiple ethnic groups residing in the US and without CVD, South Asians overall had less favorable body composition and adipokine profiles compared with most other US race/ethnic groups. Interestingly, while South Asians did not consistently have higher levels of subcutaneous and visceral fat area compared with other race/ethnic groups, they had greater total intermuscular fat area, lower hepatic attenuation and less total lean muscle mass compared with all other ethnic groups. Furthermore, even after adjusting for all measures of ectopic fat, South Asians had lower adiponectin levels compared with all other ethnic groups, except Chinese Americans, and higher resistin levels compared with all other groups.

The prevalence of obesity-related diseases such as DM, hypertension and coronary artery disease is high in South Asians.[23] A recent comparison of the MASALA and MESA cohorts found that US South Asians have a higher prevalence of DM compared with other ethnic groups.[2] In the MASALA pilot study, we showed that although South Asians only had a modestly elevated BMI (mean 26.1 kg m^{-2}), they had relatively high levels of total and regional adiposity, including subcutaneous, visceral and hepatic fat.[24] Studies in South Asians have demonstrated that visceral adiposity is associated with insulin resistance, increased inflammatory markers, the metabolic syndrome and cardiovascular risk.[25,26] Therefore, it is thought that despite having a non-obese BMI, having greater amounts of ectopic fat contributes to an increased risk of obesity-related diseases in South Asians.[23]

Although our findings show that there are some race/ethnic differences in visceral and subcutaneous fat, our observations differ from what has been reported in other South Asian studies conducted in Europe and Canada. The M-CHAT study found that compared with Europeans, South Asians had greater amounts of subcutaneous adipose tissue and visceral adipose tissue for a given amount of total body fat, although at extremely high values of body fat mass, no differences were detected.[8] South Asian men and women also had greater total body fat and abdominal fat for a given BMI compared with Europeans and Pacific Islanders.[27] And differences in metabolic risk factors were explained by greater visceral adipose tissue in South Asians compared with Europeans.[28] Some studies conducted in the US have also found that compared with Whites, Asian Indians have higher levels of subcutaneous adipose tissue and visceral adipose tissue for a given BMI.[29,30] Our findings may differ from prior studies because of differences in age and socioeconomic, immigration and behavioral differences between South Asians and Whites in the US vs those in Europe or Canada.

Table 1. Age- and sex-adjusted baseline characteristics[a] of MASALA and MESA[b] study participants by race/ethnicity

Characteristics	*South Asian (n = 906)*	*White (n = 2622)*	P-*value*	*Chinese American (n = 803)*	P-*value*	*African American (n = 1893)*	P-*value*	*Latino (n = 1496)*	P-*value*	*Overall* P-*value*
Socioeconomic status										
Education (⩾ Bachelor's degree)	85 (83-88)	50 (49-52)	< 0.001	39 (36–43)	< 0.001	35 (33–37)	< 0.001	10 (8–11)	< 0.001	< 0.001
Household Income (⩾ $75 000)	66 (63–69)	37 (35–39)	< 0.001	17 (15–20)	< 0.001	17 (15–18)	< 0.001	7 (6–8)	< 0.001	< 0.001
Behavioral factors										
Ever smoker	17 (14–19)	56 (54–58)	< 0.001	25 (22–28)	< 0.001	55 (53–58)	< 0.001	46 (44–48)	< 0.001	< 0.001
Alcohol (⩾ 1 drink per week)	31 (28–33)	65 (63–66)	< 0.001	21 (19–24)	< 0.001	53 (51–55)	< 0.001	47 (44–49)	< 0.001	< 0.001
Exercise (MET-min per week)	1246 (95)	2646 (55)	< 0.001	1780 (99)	< 0.001	2747 (64)	< 0.001	2107 (72)	< 0.001	< 0.001
Clinical and metabolic factors										
Systolic blood pressure (mmHg)	129.3 (0.7)	122.5 (0.4)	< 0.001	123.8 (0.7)	< 0.001	131.0 (0.4)	0.03	126.7 (0.5)	0.002	< 0.001
Diastolic blood pressure (mmHg)	72.9 (0.3)	70.3 (0.2)	< 0.001	72.0 (0.3)	0.06	74.7 (0.2)	< 0.001	71.5 (0.2)	0.001	< 0.001
Hypertension	51 (48–54)	37 (35–38)	< 0.001	36 (33–39)	< 0.001	58 (56–60)	< 0.001	42 (39–44)	< 0.001	< 0.001
Fasting glucose (mmol l^{-1})	5.79 (0.06)	5.01 (0.03)	< 0.001	5.43 (0.06)	< 0.001	5.50 (0.04)	< 0.001	5.71 (0.04)	0.22	< 0.001
Diabetes	24 (21–28)	6 (5–7)	< 0.001	13 (10–15)	< 0.001	17 (16–19)	< 0.001	18 (16–20)	< 0.001	< 0.001
Total cholesterol (mmol l^{-1})	4.86 (0.03)	5.06 (0.02)	< 0.001	4.99 (0.03)	0.004	4.89 (0.02)	0.33	5.12 (0.02)	< 0.001	< 0.001
LDL cholesterol (mmol l^{-1})	2.86 (0.03)	3.03 (0.02)	< 0.001	2.98 (0.03)	0.002	3.01 (0.02)	< 0.001	3.09 (0.02)	< 0.001	< 0.001
HDL cholesterol (mmol l^{-1})	1.33 (0.01)	1.35 (0.01)	0.23	1.28 (0.01)	0.002	1.34 (0.01)	0.40	1.23 (0.01)	< 0.001	< 0.001
Triglycerides (mmol l^{-1})	1.47 (0.03)	1.50 (0.02)	0.31	1.61 (0.03)	0.002	1.19 (0.02)	< 0.001	1.77 (0.02)	< 0.001	< 0.001
Adiponectin (ng ml^{-1})	12.8 (0.4)	23.5 (0.4)	< 0.001	16.6 (0.7)	< 0.001	17.3 (0.5)	< 0.001	19.4 (0.5)	< 0.001	< 0.001
Resistin (ng ml^{-1})	22.4 (0.3)	15.7 (0.3)	< 0.001	14.9 (0.6)	< 0.001	17.7 (0.5)	< 0.001	16.0 (0.4)	< 0.001	< 0.001
Anthropometric measures										
Body mass index (kg m^{-2})	25.8 (0.2)	27.8 (0.1)	< 0.001	24.0 (0.2)	< 0.001	30.2 (0.1)	< 0.001	29.4 (0.1)	< 0.001	< 0.001
Weight (kg)	67.9 (0.5)	79.5 (0.3)	< 0.001	63.0 (0.6)	< 0.001	85.9 (0.4)	< 0.001	77.5 (0.4)	< 0.001	< 0.001
Height (cm)	162.4 (0.2)	169.1 (0.1)	< 0.001	161.6 (0.2)	0.01	168.9 (0.1)	< 0.001	161.8 (0.2)	0.04	< 0.001
Waist circumference (cm)	93.2 (0.5)	97.9 (0.3)	< 0.001	87.0 (0.5)	< 0.001	101.2 (0.3)	< 0.001	100.6 (0.3)	< 0.001	< 0.001

Abbreviations: HDL, high-density lipoprotein; LDL, low-density lipoprotein; MET, metabolic equivalent. [a]Data are presented as percent (95% confidence interval) or mean (standard error). Using South Asians as the reference group, pairwise comparisons were carried out using logistic model and analysis of variance (ANOVA). [b]Analyses carried out using data from baseline exam.

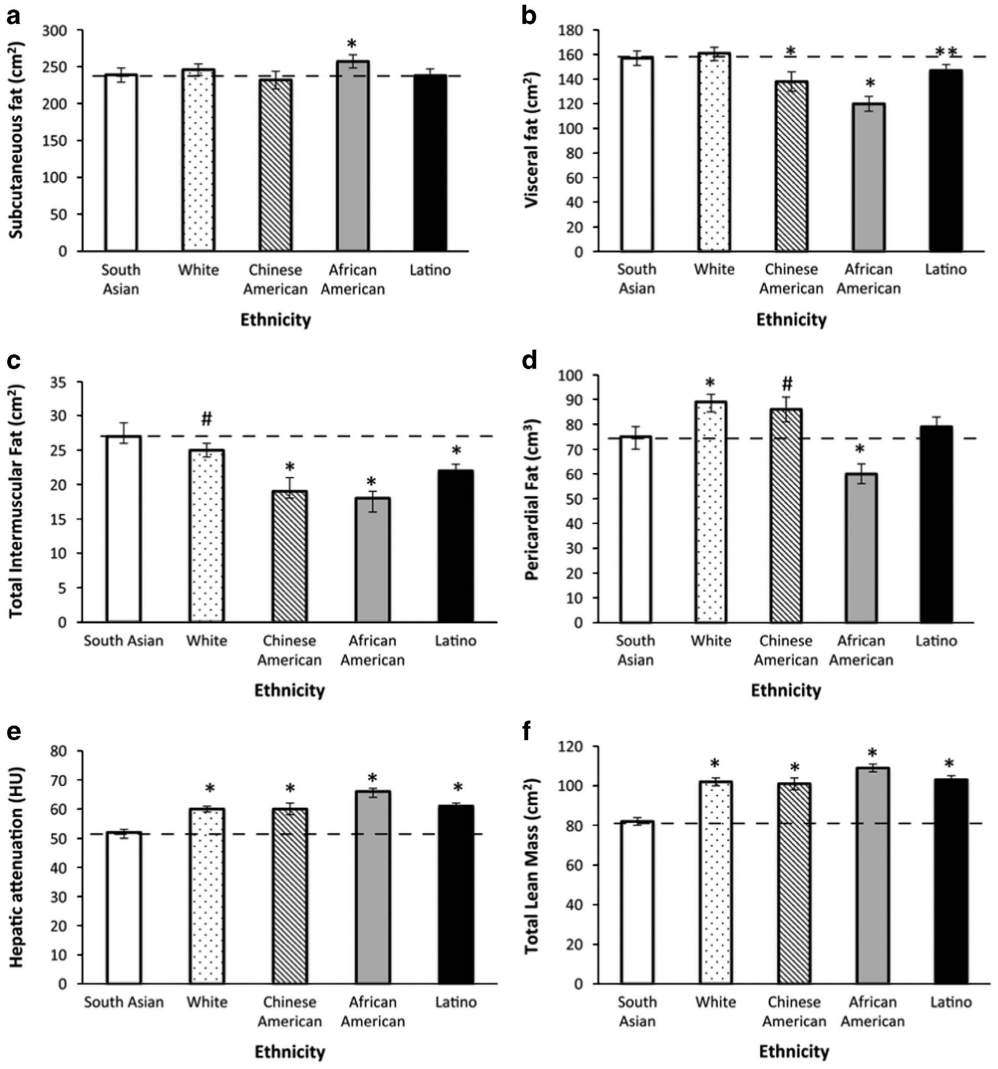

Figure 1. (**a**–**f**) Fully adjusted body composition measures across ethnic groups. Body composition was compared across ethnic groups in a multivariate model. Covariates included: age, sex, study site, alcohol use, smoking history, socioeconomic status, exercise and BMI. For abdominal and ectopic fat measures, additional covariates included: DM, hypertension, high-density lipoprotein and triglycerides. Data represent mean and 95% confidence interval. (**a**) Subcutaneous fat area, (**b**) Visceral fat area, (**c**) Total intermuscular fat area, (**d**) Pericardial fat volume, (**e**) Hepatic attenuation, (**f**) Total lean muscle mass area. For pericardial fat and hepatic attenuation analyses, *N* for MESA ethnic groups are as follows: White, 2622; Chinese American, 803; African American, 1893 and Latino, 1496. For subcutaneous fat area, visceral fat area, total intermuscular fat area and total lean muscle mass area analyses, *N* for MESA ethnic groups are as follows: Whites, 785; Chinese Americans, 251; African Americans, 407 and Latino, 501. $^{*}P < 0.001$: Results of pairwise comparisons of body composition between South Asians and each of the other race/ethnic groups. $^{**}P < 0.05$: Results of pairwise comparisons of body composition between South Asians and each of the other race/ethnic groups. $^{\#}P < 0.01$: Results of pairwise comparisons of body composition between South Asians and each of the other race/ethnic groups.

Ectopic fat stores including intermuscular fat, hepatic fat and pericardial fat are also important for cardiometabolic risk. Intermuscular adipose tissue is implicated in metabolic dysfunction and insulin resistance.[31] We found that South Asians had the highest total intermuscular fat area compared with all other groups. Only one other study has investigated differences in intermuscular fat between South Asians and other ethnic groups and found that South Asians had less or similar amounts of thigh intermuscular fat compared with Europeans.[32] As we measured abdominal front and back wall intermuscular fat, these findings are not directly comparable with our findings.

Non-alcoholic fatty liver disease is associated with several features of the metabolic syndrome in South Asians.[33] We found that South Asians had lower hepatic attenuation (greater hepatic fat content) compared with all other ethnic groups. There are few studies comparing liver attenuation in South Asians with other ethnic groups. The mol-SHARE study found that South Asians had more liver fat than Caucasians.[9] However, this ethnic difference was attenuated after adjustment for adipocyte size and fat distribution.[9] Studies evaluating other ethnic groups, including prior studies of the MESA cohort, have found that compared with Whites, Hispanics had a higher odds and African Americans had a lower odds of fatty liver.[22,34] These race/ethnic differences are thought to be due to differences in lifestyle, insulin resistance, genetics and distribution of adiposity.[34]

Interestingly, we found that South Asians had less or similar pericardial fat volume compared with all ethnic groups except African Americans. To our knowledge, this is the first study to investigate pericardial fat in South Asians. Pericardial fat is associated with obesity-related insulin resistance,[35] which has

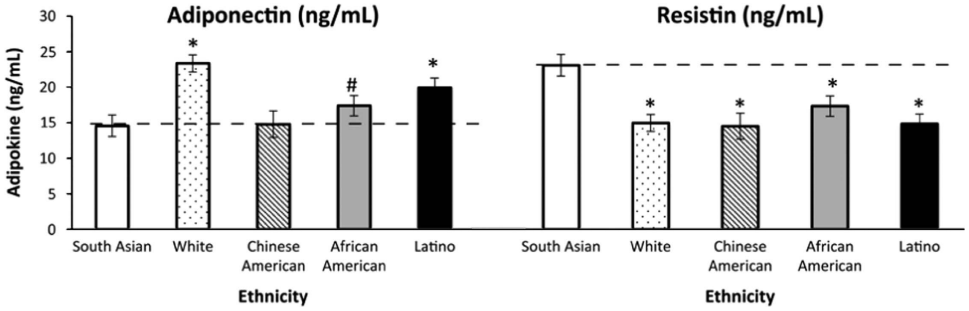

Figure 2. Fully-adjusted adipokine levels across ethnic groups. Left: Adiponectin (ng ml^{-1}). Right: Resistin (ng ml^{-1}). Adipokine levels were compared across ethnic groups in a multivariate model. Covariates included: age, sex, study site, alcohol use, smoking history, socioeconomic status, exercise, BMI, subcutaneous fat area, visceral fat area, total intermuscular fat area, pericardial fat volume and hepatic attenuation. Data represent mean and 95% confidence interval. For these analyses, *N* for MESA ethnic groups are as follows: Whites, 785; Chinese Americans, 251; African Americans, 407 and Latino, 501. *$P < 0.001$: Results of pairwise comparisons of adipokine levels (adiponectin and resistin) between South Asians and each of the other race/ethnic groups. #$P < 0.01$: Results of pairwise comparisons of body composition between South Asians and each of the other race/ethnic groups.

also been shown in the MESA cohort.[36] Ongoing investigations will examine pericardial fat associations with metabolic and CVD outcomes in the MASALA cohort.

Although increased adiposity increases the risk of metabolic disorders and CVD, lower lean mass also has a role. As lean mass is predominantly skeletal muscle mass, a target for insulin action, higher levels of lean mass are associated with greater insulin sensitivity[37] and reduced muscle mass has been associated with decreased insulin sensitivity in Asian Indian men.[23] We found that South Asians had the lowest total lean mass area compared with all other ethnic groups. These findings are consistent with those from prior studies,[27,29,38] including the mol-SHARE study, which found that South Asian men and women had less total body lean mass compared with Caucasians.[9] Why South Asians have less lean muscle mass than other race/ethnic groups and understanding the role of physical activity, the biology of lean muscle mass and its role in metabolic risk are key areas for future investigation.

Adipokines are associated with metabolic risk as low levels of adiponectin and high levels of resistin have been implicated in insulin resistance and obesity.[39,40] We found that adiponectin was lower in South Asians compared with Whites, African Americans and Latinos while resistin was higher in South Asians compared with all other groups. These findings are consistent with those from prior studies.[41–43] The mol-SHARE study found that South Asians had lower adiponectin levels than Whites, although this difference was accounted for by increased adipocyte area in South Asians vs Whites.[9] To our knowledge, other studies comparing resistin levels between South Asians and other ethnic groups have not been conducted. We expected that accounting for differences in body composition would explain the differences in adipokine levels between South Asians vs other groups, however, the differences remained significant. The robust differences in these adipokine levels among South Asians suggest that adipokines may independently influence downstream metabolic risk.

This study has several strengths as it is the first study to perform a comprehensive analysis of body composition and adipokines among five ethnic groups in the US using data from two large cohorts with harmonized data. In addition, it includes several radiographic measures of body composition including novel measures of ectopic fat. Limitations include the inability to adjust for comparable measures of dietary intake between the two cohorts to determine the role of diet in body composition differences although measures of socioeconomic status may serve as a surrogate for diet. In addition, the prevalence of obesity in 2000–2005 during the MESA data collection and 2010–2013 for the MASALA data collection may be different and may have introduced some differences between the two cohorts. Finally, although the MASALA Study does not include a nationally representative sample of South Asians, it is representative of the middle-older aged South Asian population in the US. However, our findings may not be generalizable to the younger US South Asian population or to South Asians in other diaspora settings.

In conclusion, US South Asians have high levels of intermuscular and hepatic fat, less lean muscle mass and less favorable adipokine profiles compared with other US race/ethnic groups. These differences may partially account for the increased predisposition to insulin resistance, metabolic disorders and DM in South Asians. Prospective follow-up of the MASALA study cohort will provide additional insight into how these ethnic differences in body composition and adipokines influence differences in the development of type 2 DM and CVD.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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