Body Composition and Diabetes Risk in South Asians: Findings From the MASALA and MESA Studies

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OBJECTIVE

South Asians have a higher prevalence of type 2 diabetes compared with other race/ethnic groups. Body composition is associated with the risk for type 2 diabetes. Differences in body composition between South Asians and other race/ethnic groups are one hypothesized mechanism to explain the disproportionate prevalence of type 2 diabetes in this population.

RESEARCH DESIGN AND METHODS

This study used data from the Mediators of Atherosclerosis in South Asians Living in America (MASALA) and the Multi-Ethnic Study of Atherosclerosis (MESA) cohorts to determine whether body composition mediated the elevated prevalence of impaired fasting glucose and type 2 diabetes in South Asians. Participants (n = 2,615) with complete body composition data were included. Ordinal logistic regression models were calculated to determine the odds for glycemic impairment in South Asians compared with the MESA cohort.

RESULTS

In multivariate models, South Asians had a significantly higher prevalence of glycemic impairment and type 2 diabetes compared with all four race/ethnic groups included in the MESA ($P < 0.001$ for all). In unadjusted and multivariate adjusted models, South Asians had higher odds for impaired fasting glucose and type 2 diabetes compared with all other race/ethnic groups ($P < 0.001$ for all). The addition of body composition measures did not significantly mitigate this relationship.

CONCLUSIONS

We did not identify strong evidence that accounting for body composition explains differences in the risk for type 2 diabetes. Future prospective studies of the MESA and MASALA cohorts are needed to understand how adipose tissue impacts the risk for type 2 diabetes and how to best assess this risk.

Type 2 diabetes occurs in the setting of multiple genetic and lifestyle factors and is a priority area for public health efforts in the U.S. and globally (1–4). A previous analysis (5) of the Mediators of Atherosclerosis in South Asians Living in America (MASALA) study and the Multi-Ethnic Study of Atherosclerosis (MESA) showed that, after adjustment for demographic, behavioral, and metabolic risk factors, South Asians have a significantly higher prevalence of type 2 diabetes (26%) compared with whites (6%), Chinese Americans (13%), African Americans (18%), and Hispanics (17%).

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Differences in body composition are associated with the risk for type 2 diabetes (6–9). Body composition characteristics can be assessed by measuring ectopic fat regions, including abdominal visceral fat area, intermuscular fat area, pericardial fat volume, and the presence of significant liver fat (6–9). One hypothesized mechanism for the increased prevalence of type 2 diabetes in South Asians compared with other race/ethnic groups is a higher distribution of adipose tissue in these ectopic regions (10–12). These adipose tissue regions are not well captured by traditional measures of body composition (e.g., BMI) (10). Measures of ectopic fat regions from computed tomography (CT) scans have demonstrated stronger associations with metabolic risk when compared with body weight or BMI in Asians (10,11,13).

Prior studies showed that ectopic fat is associated with insulin resistance and risk for type 2 diabetes (6–9). Studies also showed that South Asians have a more harmful body composition profile as measured by ectopic fat regions. However, no prior studies adequately measured and adjusted for multiple body compartments in multiple race/ethnic groups in order to determine whether elevated risk for type 2 diabetes is mediated by differences in body composition. The purpose of this study was to determine whether differences in body composition explain the differences in the prevalence of impaired fasting glucose and type 2 diabetes among five race/ethnic groups in the United States.

RESEARCH DESIGN AND METHODS

Study Sample

We performed a cross-sectional analysis of harmonized data from two community-based cohorts: MASALA and MESA. Prior analyses have been conducted using these harmonized variables (11). Subgroups of participants from MASALA (n = 747 South Asians) and MESA (n = 745 whites, n = 244 Chinese Americans, n = 394 African Americans, n = 485 Hispanics) with complete data for ectopic fat distribution, assessment of impaired fasting glucose and type 2 diabetes, and relevant covariates, were included in this study. 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 participants.

MASALA Study

The MASALA study, which was modeled on the MESA cohort (14), is a community-based cohort of South Asian adults without known cardiovascular disease (15). 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. Detailed methods for the MASALA study were previously published (15).

Eligibility criteria for the MASALA study included self-identification of South Asian ethnicity, age 40–84 years, and the ability to speak and read English, Hindi, or Urdu (15). The MASALA study used exclusion criteria that were identical to those of the MESA, which included prior 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 lb. Participants were assisted by trained bilingual study staff to complete detailed questionnaires for demographic information and behaviors, including tobacco and alcohol use. Physical activity was assessed using the Typical Week's Physical Activity Questionnaire (16). Blood pressure was measured after a 5-min seated rest using an automated blood pressure machine (V100 Vital Sign Monitor; GE Healthcare, Fairfield, CT). Three blood pressure readings were obtained, and the average of the last two readings was recorded. Systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg or use of any antihypertensive medication was defined as hypertension.

Laboratory Tests

Fasting plasma glucose was measured by the hexokinase method (Quest Laboratories, San Jose, CA). Type 2 diabetes was defined as fasting plasma glucose ≥126 mg/dL or the use of a glucose-lowering medication. Impaired fasting glucose was defined as fasting plasma glucose ≥100 and <126 mg/dL, and normal fasting glucose was defined as <100 mg/dL. Total cholesterol, triglycerides, and HDL cholesterol were measured by enzymatic methods (Quest, Chicago, IL), and LDL cholesterol was calculated. Adiponectin and resistin were measured using the Millipore Luminex adipokine A panel (EMD Millipore, Billerica, MA). The interassay coefficient of variation was 2.3–4.1% for adiponectin and 3.3–5.5% for resistin.

Body Composition

Weight was measured on a standard balance-beam scale or digital weighing scale. Height was measured using a stadiometer. BMI was calculated as kilograms per square meter. 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 recorded as the final measurement.

CT scans of the abdomen (Philips Medical Systems, Andover, MA; Toshiba Medical Systems, Tustin, CA; Siemens Medical Solution, Malvern, PA) were used to calculate abdominal visceral fat area and abdominal intermuscular fat area. A CT technician obtained a lateral scout image of the abdomen to establish position between the L4 and L5 vertebrae, and a single abdominal CT slice was obtained at this level. Medical Image Processing, Analysis, and Visualization (MIPAV) software was used to measure abdominal visceral fat at the University of California, San Diego, body composition reading center (17). Visceral fat was demarcated by pixels with the appropriate Hounsfield unit (HU) range inside the visceral cavity. As described previously, the four abdominal/back muscle groups from which abdominal intermuscular fat was measured included the psoas, paraspinous, oblique, and rectus muscles (18). These muscles were highlighted by the readers and then deleted from the calculation of the subcutaneous fat area.

Noncontrast cardiac CT images were used to quantify pericardial fat and liver fat attenuation using a cardiac-gated CT scanner (UCSF: Philips 16D scanner or Toshiba MSD Aquilion 64; NWU: Siemens

Sensation Cardiac 64 Scanner). The same reading center staff, under the supervision of J.J.C., performed all measurements of pericardial fat volume and liver fat attenuation. The CT scan range encompassed the entire heart and provided information on 45 mm of adipose tissue encasing the proximal coronary arteries. First, the 45-mm *z*-axis volume containing the proximal coronary arteries was defined. Next, the technician assessed regions of interest relevant to pericardial fat within the 45-mm volume along with regions within the calibration phantom to determine the range of HU for each ectopic fat depot. The heart was segmented from the thorax by removing areas outside the lung using a deformable model-based edge detection method (i.e., active contours or live wires) to detect the boundary between the lung and pericardial fat (19–21).

CT images for liver fat attenuation were interrogated using the MIPAV software at the vertebral level of T12–L1. Within homogeneous portions of the liver and avoiding any vascular structures or other liver pathology, nine regions of interest across two levels were read. Measurement methods were similar to those used in the MESA (22). Fatty liver was defined as having $<$40 HUs.

MESA

The study design, eligibility, and methods for the MESA were previously published (14). The MESA includes individuals from four racial/ethnic groups (whites, Chinese Americans, African Americans, and Hispanics) living in Forsyth County, NC; Chicago, IL; Baltimore, MD; Los Angeles County, CA; St. Paul, MN; and New York, NY. 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. Data from the baseline MESA examination (2000–2002) were used for hepatic fat attenuation and pericardial fat volume measurements; data from ancillary studies that included random subsets of participants from examinations 2 (2002–2004) and 3 (2004–2005) were used for the abdominal visceral fat, abdominal intermuscular fat, and adipokine measurements. Both studies used the same reading centers and protocols for measuring abdominal visceral fat area, pericardial fat volume, and hepatic fat attenuation for ease of data harmonization.

Statistical Analysis

Descriptive statistics and *t* tests were calculated in order to compare demographic and clinical characteristics, including ectopic fat distributions, between race/ethnic groups. Pearson correlation coefficients were calculated to determine the correlations among measures of body composition. Univariate logistic regression models were calculated to determine the associations between each ectopic fat region (i.e., abdominal visceral fat area, hepatic fat attenuation, abdominal intermuscular fat area, and pericardial fat volume) and type 2 diabetes overall and then within each race/ethnic group. Prevalence of impaired fasting glucose and type 2 diabetes with 95% CI was calculated. The first estimate of prevalence did not include any covariates, the second estimate included demographic and clinical covariates (i.e., age, sex, study site, education level, income level, prior and current smoking status, alcohol use, exercise, BMI, HDL, triglycerides, and hypertension), and the final estimate also included measures of ectopic fat. Ordinal logistic regression was used to assess for differences in the associations between body composition and glycemic status (i.e., impaired fasting blood glucose, type 2 diabetes) between race/ethnic groups with South Asians as the reference group. Models were adjusted for demographic and clinical covariates (i.e., age, sex, study site, education level, income level, smoking status, alcohol use, exercise level, BMI, HDL, triglycerides, hypertension) followed by ectopic fat regions and finally, two adipokines (i.e., adiponectin, resistin), in order to determine whether these variables mediated the associations between body composition and glycemic status. For ease of interpretation, odds ratios (ORs) and CIs are reported as the inverse (i.e., 1/OR). All analyses were performed using SAS version 9.4 (SAS Institute, Inc., Cary, NC).

RESULTS

A total of 2,615 participants were included in the analysis (*n* = 747 South Asians, *n* = 745 whites, *n* = 244 Chinese Americans, *n* = 394 African Americans, *n* = 485 Hispanics). In South Asians, the mean abdominal visceral fat area was 159 ± 75 cm^2, hepatic fat attenuation was 61 ± 12 HUs, abdominal intermuscular fat area was 28 ± 12 cm^2, and pericardial fat volume was 85 ± 46 cm^3 (Table 1).

All body composition measures were associated with glycemic impairment in the five race/ethnic groups overall ($P <$ 0.001 for all) except abdominal intermuscular fat area and type 2 diabetes (P = 0.32) (Table 2). For South Asians, in multivariate adjusted models, abdominal visceral fat area (OR 1.43 [95% CI 1.10, 1.86]) was positively associated with impaired fasting glucose. Abdominal visceral fat area (OR 1.66 [95% CI 1.26, 2.18]) and pericardial fat area (1.73 [95% CI 1.26, 2.38]) were positively associated with type 2 diabetes. Hepatic fat attenuation was negatively associated with type 2 diabetes (1.50 [95% CI 0.38, 0.66]), and abdominal intermuscular fat area was not significantly associated with glycemic impairment (Table 2).

South Asians have a significantly higher prevalence of impaired fasting glucose and type 2 diabetes compared with all four race/ethnic groups included in the MESA. The crude prevalence of impaired fasting glucose was 22%, and 21% of participants had type 2 diabetes (Fig. 1). After adjustment for demographic and clinical characteristics, the prevalence increased to 24% (95% CI 21%, 26%) with impaired fasting glucose and 30% (95% CI 24%, 35%) with type 2 diabetes (Fig. 1) ($P <$ 0.001 for all). In fully adjusted models that included demographic and clinical characteristics and all body composition measures, the prevalence of impaired fasting glucose in South Asians was 23% (95% CI 21%, 25%), and 27% of participants had type 2 diabetes (95% CI 22%, 32%) (Fig. 1) ($P <$ 0.001 for all).

In multivariate ordinal logistic regression models for glycemic impairment, South Asians had significantly higher odds for impaired fasting glucose and type 2 diabetes compared with all four MESA race/ethnic groups (ORs: 7.04 compared with whites, 3.60 compared with Chinese Americans, 3.44 compared with African Americans, 6.94 compared with Hispanics; $P <$ 0.001 for all) (Table 3). The addition of body composition measures showed that South Asians are still at significantly greater risk for glycemic impairment compared with the

Table 1—Demographic and clinical characteristics

Characteristic	Overall (*n* = 2,615)	South Asian (*n* = 747)	Caucasian (*n* = 745)	Chinese American (*n* = 244)	African American (*n* = 394)	Hispanic (*n* = 485)	*P* value overall
Age (years)	61 ± 10	57 ± 9	63 ± 10	62 ± 10	62 ± 10	61 ± 10	<0.001
Male sex	1,310 (50.10)	386 (51.7)	383 (51.4)	128 (52.5)	170 (43.2)	243 (50.1)	0.05
Study site							<0.001
NWU (MASALA)	329 (12.6)	329 (44.0)	0	0	0	0	
UCSF	418 (16.0)	418 (56.0)	0	0	0	0	
WFU	393 (15.0)	0	226 (30.3)	0	167 (42.4)	0	
COL	384 (14.7)	0	77 (10.3)	2 (0.8)	118 (30.0)	187 (38.6)	
JHU	0	0	0	0	0	0	
UMN	380 (14.5)	0	213 (28.6)	0	0	167 (34.4)	
NWU (MESA)	379 (14.5)	0	180 (24.2)	119 (48.8)	80 (20.3)	0	
UCLA	332 (12.7)	0	49 (6.6)	123 (50.4)	29 (7.4)	131 (27.0)	
Current smoker	264 (10.1)	25 (3.4)	90 (12.1)	12 (4.9)	74 (18.8)	63 (13.0)	<0.001
Alcohol use ≥1 drink/week	1,210 (46.6)	244 (32.7)	486 (66.0)	55 (22.7)	188 (48.1)	237 (49.1)	<0.001
Diabetes							<0.001
Normal blood glucose	1,814 (69.4)	416 (55.7)	607 (81.5)	174 (71.3)	278 (70.6)	339 (69.9)	
Impaired fasting glucose	439 (16.8)	178 (23.8)	95 (12.8)	45 (18.4)	51 (12.9)	70 (14.4)	
Type 2 diabetes	362 (13.8)	153 (20.5)	43 (5.8)	25 (10.2)	65 (16.5)	76 (15.7)	
BMI (kg/m^2)	27.4 ± 4.9	25.9 ± 4.3	27.6 ± 4.7	24.3 ± 3.0	29.5 ± 5.3	29.4 ± 4.9	<0.001
Waist circumference (cm)	96.3 ± 13.0	92.6 ± 10.1	98.5 ± 13.8	87.2 ± 9.2	99.9 ± 14.2	100.4 ± 12.7	<0.001
Hip circumference (cm)	103.8 ± 10.2	102.6 ± 8.4	105.0 ± 10.0	94.9 ± 6.4	108.2 ± 11.6	104.8 ± 10.8	<0.001
Systolic blood pressure (mmHg)	127 ± 20	126 ± 16	125 ± 20	124 ± 21	133 ± 22	127 ± 23	<0.001
Diastolic blood pressure (mmHg)	73 ± 10	73 ± 10	71 ± 10	72 ± 9	75 ± 11	72 ± 10	<0.001
Hypertension	1,168 (44.7)	322 (43.1)	311 (41.7)	95 (38.9)	232 (58.9)	208 (42.9)	<0.001
HDL (mg/dL)	51 ± 14	51 ± 13	52 ± 16	50 ± 13	54 ± 16	48 ± 13	<0.001
Triglycerides (mg/dL)	134 ± 78	132 ± 73	139 ± 84	137 ± 90	99 ± 55	154 ± 79	<0.001
Fasting glucose (mg/dL)	99 ± 28	104 ± 25	91 ± 17	98 ± 26	97 ± 27	104 ± 40	<0.001
HbA_{1c} (%)	5.8 ± 1.0	6.1 ± 0.9	5.5 ± 0.7	5.8 ± 1.0	5.8 ± 1.0	6.0 ± 1.3	<0.001
HOMA-IR	2.81 ± 3.66	3.49 ± 5.95	2.32 ± 1.99	2.32 ± 1.60	2.62 ± 2.33	2.98 ± 2.59	<0.001
HOMA-β	130.66 ± 94.65	121.78 ± 88.33	140.11 ± 84.07	116.98 ± 76.25	131.44 ± 132.24	135.27 ± 88.98	<0.001
Body composition							
Abdominal visceral fat area (cm^2)	144 ± 65	136 ± 56	158 ± 75	116 ± 49	126 ± 58	163 ± 65	<0.001
Hepatic fat attenuation (HUs)	60 ± 13	55 ± 11	62 ± 13	62 ± 12	66 ± 10	60 ± 14	<0.001
Abdominal intermuscular fat area (cm^2)	24 ± 11	22 ± 9	28 ± 12	19 ± 8	21 ± 12	26 ± 12	<0.001
Pericardial fat volume (cm^3)	74 ± 39	59 ± 29	87 ± 46	75 ± 30	63 ± 30	87 ± 42	<0.001
Adipokines							
Total adiponectin (ng/mL)	18.4 ± 12.5	12.2 ± 6.7	24.1 ± 14.1	17.1 ± 12.7	18.3 ± 12.5	19.8 ± 11.7	<0.001
Resistin (ng/mL)	17.9 ± 9.9	21.7 ± 12.2	16.0 ± 5.3	18.1 ± 13.9	16.2 ± 6.8	15.1 ± 7.2	<0.001

Data are means ± SD or *n* (%) unless otherwise indicated. COL, Columbia University; HOMA-IR, HOMA of insulin resistance; JHU, Johns Hopkins University; UCLA, University of California, Los Angeles; UMN, University of Minnesota; WFU, Wake Forest University.

Table 2—ORs for glycemic impairment for each body composition measure for study sample overall and by race/ethnic group

	Impaired fasting glucose[1]			Type 2 diabetes[2]		
	OR*	*P* value	95% CI	OR*	*P* value	95% CI
Overall (*N* = 2,615)						
Abdominal visceral fat area	**1.39**	**<0.001**	**1.23, 1.57**	**1.39**	**<0.001**	**1.21, 1.59**
Liver fat attenuation	**0.70**	**<0.001**	**0.62, 0.79**	**0.63**	**<0.001**	**0.56, 0.72**
Abdominal intermuscular fat area	**1.20**	**0.001**	**1.08, 1.34**	1.06	0.37	0.92, 1.21
Pericardial fat volume	**1.34**	**<0.001**	**1.18, 1.52**	**1.32**	**<0.001**	**1.15, 1.51**
South Asian (*n* = 747)						
Abdominal visceral fat area	**1.43**	**0.008**	**1.10, 1.86**	**1.66**	**<0.001**	**1.26, 2.18**
Liver fat attenuation	0.88	0.34	0.68, 1.14	**0.50**	**<0.001**	**0.38, 0.66**
Abdominal intermuscular fat area	1.24	0.12	0.95, 1.62	1.12	0.46	0.84, 1.49
Pericardial fat volume	1.28	0.13	0.93, 1.77	**1.73**	**<0.001**	**1.26, 2.38**
White (*n* = 745)						
Abdominal visceral fat area	**1.41**	**0.002**	**1.13, 1.76**	**2.30**	**<0.001**	**1.66, 3.17**
Liver fat attenuation	**0.65**	**<0.001**	**0.52, 0.82**	**0.68**	**0.02**	**0.50, 0.94**
Abdominal intermuscular fat area	**1.42**	**0.001**	**1.16, 1.74**	**1.70**	**<0.001**	**1.31, 2.22**
Pericardial fat volume	**1.36**	**0.005**	**1.10, 1.68**	**1.59**	**0.001**	**1.21, 2.10**
Chinese American (*n* = 244)						
Abdominal visceral fat area	1.55	0.15	0.86, 2.80	**2.42**	**0.01**	**1.24, 4.71**
Liver fat attenuation	**0.53**	**0.003**	**0.35, 0.81**	0.77	0.34	0.44, 1.32
Abdominal intermuscular fat area	0.76	0.44	0.38, 1.52	1.45	0.35	0.66, 3.16
Pericardial fat volume	1.73	0.09	0.93, 3.22	**4.75**	**<0.001**	**2.25, 10.02**
African American (*n* = 394)						
Abdominal visceral fat area	1.39	0.08	0.97, 2.01	1.09	0.62	0.77, 1.55
Liver fat attenuation	0.76	0.20	0.50, 1.16	**0.57**	**0.003**	**0.40, 0.82**
Abdominal intermuscular fat area	1.25	0.14	0.93, 1.67	**0.71**	**0.044**	**0.50, 0.99**
Pericardial fat volume	**1.58**	**0.045**	**1.01, 2.46**	1.12	0.60	0.73, 1.74
Hispanic (*n* = 485)						
Abdominal visceral fat area	**1.88**	**<0.001**	**1.39, 2.55**	1.23	0.22	0.89, 1.70
Liver fat attenuation	0.77	0.06	0.59, 1.01	**0.76**	**0.03**	**0.58, 0.98**
Abdominal intermuscular fat area	**1.56**	**<0.001**	**1.21, 2.00**	**1.33**	**0.037**	**1.02, 1.73**
Pericardial fat volume	**2.01**	**<0.001**	**1.48, 2.74**	**1.44**	**0.024**	**1.05, 1.97**

ORs are scaled by SD for each body composition measure. [1]Compared with normal glucose tolerance. [2]Compared with impaired fasting glucose. *Adjusted for age, sex, study site, education, income, smoking, alcohol, exercise, HDL, triglycerides, and hypertension. Statistically significant values are in bold ($P < 0.05$).

other four race/ethnic groups (ORs: 6.41 compared with whites, 3.28 compared with Chinese Americans, 2.26 compared with African Americans, 4.00 compared with Hispanics; $P < 0.001$ for all) (Table 3). When we further adjusted for adiponectin and resistin, the ORs did not notably change for South Asians compared with Chinese Americans (OR 3.29), African Americans (OR 2.31), and Hispanics (OR 4.31) ($P < 0.001$ for all) (Table 3). However, for South Asians compared with whites, the association (OR 7.04) was similar to what was observed in the multivariate adjusted model without measures of ectopic fat (Table 3). We checked for collinearity among all of the body composition measures and found weak to moderate evidence for correlations overall; the strongest correlation was between abdominal visceral fat area and pericardial fat volume ($r = 0.67$) (Table 4).

CONCLUSIONS

Prior studies reported a higher prevalence of type 2 diabetes in South Asians compared with other race/ethnic groups (5,23,24). Although there are known genetic risk factors for type 2 diabetes that are common in South Asians (25–30), the reasons for the elevated risk in this population are not fully understood. Our prior study (5) showed that traditionally measured risk factors for type 2 diabetes (e.g., age, sex, BMI, lipids) did not explain the disproportionately high prevalence of impaired fasting glucose and type 2 diabetes in South Asians compared with other race/ethnic groups. Differences in body composition, assessed by measuring ectopic fat distributions, are the one hypothesized mechanism to explain this disparity (10–13,31–33). In the current study, we used harmonized data on body composition from the MASALA study and the MESA to determine whether the presence of ectopic fat explains the higher prevalence of glycemic impairment in South Asians compared with the four race/ethnic groups included in the MESA. The associations between race/ethnicity and glycemic impairment were moderately decreased with the addition of body composition variables to the models. The reduction in risk for South Asians was greatest in comparison with whites and Hispanics followed by African Americans. There was very little change in the risk for South Asians compared with Chinese Americans. These findings suggest that differences in body composition may be important for understanding the observed increased risk for type 2 diabetes in South Asians compared with whites more than the other race/ethnic groups.

Consistent with prior observations (7–9), all four measures of ectopic fat were associated with glycemic impairment in the study sample overall. However, these associations were not consistent among South Asians. Only abdominal visceral fat area was associated with the presence of impaired fasting glucose. Abdominal visceral fat area, liver fat attenuation, and pericardial fat volume were associated with the presence of type 2 diabetes. Our goal was to determine whether overall body composition mediated the higher prevalence of glycemic impairment in South Asians. Individual measures of body composition were moderately correlated. However, the lack of association between abdominal intermuscular fat and glycemic impairment was unlikely to be the result of collinearity, given a variance inflation factor of 1.8. An alternative explanation is that abdominal intermuscular fat is the smallest of the fat depots and therefore is unlikely to have a large effect. These inconsistencies in how ectopic fat relates to glycemic impairment among South Asians may be one reason for the observation from this study that body composition moderately decreases the differences in risk for type 2 diabetes in South Asians compared with other race/ethnic groups.

Although several studies showed that body composition characteristics are associated with risk for type 2 diabetes (7–9), there are some inconsistencies. A prior study (34) of white, Filipina, and African American women showed the highest prevalence of type 2 diabetes

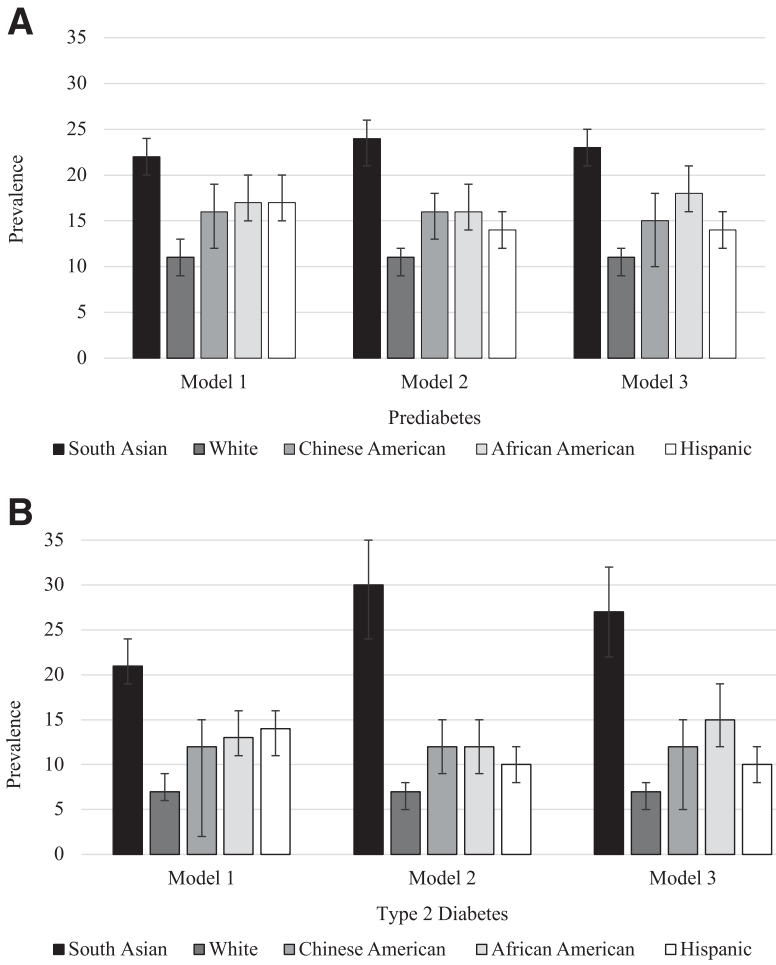

Figure 1—Prevalence of impaired fasting glucose and type 2 diabetes by race/ethnic group. Panel *A* shows the unadjusted and multivariate adjusted prevalence of impaired fasting glucose. Panel *B* shows the unadjusted and multivariate adjusted prevalence of type 2 diabetes. Error bars show 95% CI. Model 1 did not adjust for any covariates. Model 2 is adjusted for age, sex, study site, education level, income level, prior and current smoking status, alcohol use, exercise, BMI, HDL cholesterol, triglycerides, and hypertension. Model 3 includes all variables in model 2 and hepatic fat attenuation, abdominal visceral fat area, abdominal intermuscular fat area, and pericardial fat volume.

in Filipinas as well as high measures of abdominal visceral fat. However, the abdominal visceral fat levels failed to explain the differences in prevalence of type 2 diabetes between race/ethnic groups. Similarly, a prior study of the MASALA and MESA cohorts showed that South Asians had the highest burden of pericardial fat and the highest prevalence of coronary artery calcium, which is a marker of cardiovascular disease risk (35). However, the differences in body composition in this study failed to explain the elevated risk for cardiovascular disease in South Asians compared with the four other race/ethnic groups. Differences in how body composition is best assessed and how ectopic fat relates to risk for type 2 diabetes and related conditions may vary substantially by race/ethnicity, sex, age, and other characteristics. These differences could explain the observed inconsistencies between studies and support further investigation about the impact of body composition across heterogeneous populations.

Adiponectin and resistin, which are adipokines, are measured to assess adipocyte function rather than adipose tissue volume. Low levels of adiponectin and high levels of resistin are associated with insulin resistance, an important precursor to type 2 diabetes (36–38). The Molecular Study of Health and Risk in Ethnic Groups (mol-SHARE) showed that adipokines are useful for the identification of insulin resistance in South Asians, even those with a normal BMI (12). In the current study, we confirmed that South Asians have lower levels of adiponectin and higher resistin levels compared with the four race/ethnic groups in the MESA cohort (11). This profile has previously been linked to insulin resistance and increased risk for type 2 diabetes in South Asians (36,37,39,40). An alternative explanation for the observation that higher distributions of ectopic fat in South Asians did not mediate the higher prevalence of glycemic impairment is related to the metabolic impact of fat in these regions. Both adiponectin and resistin showed low correlation coefficients with measures of body composition in our study sample. In order to determine whether adipocyte function, in addition to adipose tissue volume, mediated the higher prevalence of glycemic impairment in South Asians, we added adiponectin and resistin to a final ordinal logistic regression model for glycemic impairment. For South Asians compared with whites, the estimate of the odds for glycemic impairment was stronger (OR 7.04 [95% CI 4.40, 11.24] with adipokines versus without adipokines (OR 6.41 [95% CI 4.41, 10.10]). The association was also

Table 3—ORs for abnormal glucose tolerance, comparing South Asians to each MESA race/ethnic group

Race/ethnic group	Model 1	Model 2	Model 3	Model 4
White	3.50 (2.77, 4.41)	7.04 (4.53, 10.99)	6.41 (4.05, 10.10)	7.04 (4.41, 11.24)
Chinese American	1.99 (1.46, 2.71)	3.60 (2.32, 5.56)	3.28 (2.10, 5.13)	3.29 (2.10, 5.18)
African American	1.77 (1.38, 2.28)	3.44 (2.13, 5.56)	2.26 (1.39, 3.70)	2.31 (1.41, 3.79)
Hispanic	1.75 (1.38, 2.30)	6.94 (2.96, 6.94)	4.00 (2.58, 6.21)	4.31 (2.76, 6.71)

Data are OR (95% CI). Each OR represents the risk for glycemic impairment for South Asians compared with each race/ethnic group in the MESA. Model 1 was unadjusted. Model 2 was adjusted for age, sex, study site, education level, income level, prior and current smoking status, alcohol use, exercise, BMI, HDL cholesterol, triglycerides, and hypertension. Model 3 includes all variables in model 2 and hepatic fat attenuation, abdominal visceral fat area, abdominal intermuscular fat area, and pericardial fat volume. Model 4 includes all variables in model 3 and adiponectin and resistin.

Table 4—Pearson correlation coefficients for each body composition measure for the overall study sample (n = 2,615)

	Abdominal visceral fat area	Hepatic fat attenuation	Abdominal intermuscular fat area	Pericardial fat volume	Total adiponectin	Resistin
Abdominal visceral fat area	1.00000	−0.27755/<0.0001	0.51934/<0.0001	0.66748/<0.0001	−0.24988/<0.0001	0.04049/0.0388
Hepatic fat attenuation	−0.27755/<0.0001	1.00000	−0.09821/<0.0001	−0.18316/<0.0001	0.24077/<0.0001	−0.07173/0.0002
Abdominal intermuscular fat area	0.51934/<0.0001	−0.09821/<0.0001	1.00000	0.45543/<0.0001	0.10484/<0.0001	0.06610/0.0007
Pericardial fat volume	0.66748/<0.0001	−0.18316/<0.0001	0.45543/<0.0001	1.00000	−0.05202/0.0079	−0.00786/0.6885
Total adiponectin	−0.24988/<0.0001	0.24077/<0.0001	0.10484/<0.0001	−0.05202/0.0079	1.00000	−0.03879/0.0478
Resistin	0.04049/0.0388	−0.07173/0.0002	0.06610/0.0007	−0.00786/0.6885	−0.03879/0.0478	1.00000

Data are Pearson correlation coefficients/P value.

stronger for South Asians compared with Hispanics with adipokines (OR 4.31 [95% CI 2.76, 6.71]) versus without adipokines (OR 4.00 [2.58, 6.21]). These findings suggest that adipokines represent some overlapping prediction of risk for type 2 diabetes between South Asians and whites and Hispanics, whereas the shared risk prediction may be lower for South Asians with Chinese Americans and African Americans.

This study has a number of strengths, including comprehensive analysis of body composition and adipokines among five ethnic groups in the U.S. using data from two large cohorts with harmonized data. In addition, we included several radiographic measures of body composition including rigorous measures of ectopic fat. The study protocols for both the MESA and the MASALA study were identical; however, there may be unmeasured confounders from both studies given the different dates of data collection and differences in socioeconomic status and acculturation between groups. This was a descriptive, cross-sectional study, which prevents inferences about the mechanisms that underlie risk for type 2 diabetes across race/ethnic groups. However, we did include measures of adipokines to explore the possible functional impact of adipose tissue in addition to volume. The overall prevalence of obesity may have changed between 2000 and 2005 (MESA data collection) and between 2010 and 2013 (MASALA data collection), which is a potential source of bias between the two cohorts. The MASALA study is representative of the middle-aged to older South Asian population in the U.S.; however, our findings may not be generalizable to the younger U.S. South Asian population.

This study and others (11,31–33, 41–43) have identified a higher level of ectopic fat and more harmful adipokine levels in South Asians; however, this did not account for the higher prevalence of glycemic impairment in this population. The differences in impaired fasting glucose and diabetes prevalence were greater for whites and Hispanics than for African Americans and Chinese Americans compared with South Asians. Future prospective studies of the MESA and MASALA study cohorts are needed in order to understand how adipose tissue impacts the risk for type 2 diabetes in South Asians and how to best assess this risk (e.g., adipokine biomarkers vs. measures of body composition).

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Author Contributions. E.F. designed the study, interpreted the results, and had primary responsibility for writing the manuscript. F.L. performed statistical analyses. N.R.K. is the co-principal investigator of the MASALA cohort that provided data for this study. M.A. conducted the ancillary studies in the MESA and MASALA study for abdominal visceral and intermuscular fat areas. J.J.C. performed radiographic data collection included in this study. J.D. conducted the ancillary studies in the MESA for pericardial fat area and liver fat attenuation. R.S. provided expertise on the interpretation of body composition measures. K.L. and D.H. are MESA and MASALA study coinvestigators. A.M.K. is the co-principal investigator of the MASALA cohort that provided data for this study, provided overall scientific guidance of the study design and analysis, and had secondary responsibility for writing the manuscript. E.F. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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