nature publishing group

Visceral Fat and Prevalence of Hypertension Among African Americans and Hispanic Americans: Findings From the IRAS Family Study

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BACKGROUND

We examined the relationship between visceral adipose tissue (VAT), independent of overall adiposity, and prevalent hypertension among adults enrolled in the Insulin Resistance Atherosclerosis (IRAS) Family Study. We also examined the role of insulin sensitivity (S_I) upon hypertension. This was a cross-sectional epidemiological study in which African-American and Hispanic-American families were recruited from three clinical sites. The main outcome measure was prevalent hypertension, as defined by standardized protocol.

METHODS

The relationship between VAT and prevalent hypertension was examined in adjusted marginal models among 1,582 participants. All continuous variables were standardized.

RESULTS

A significant VAT by gender interaction prompted separate analyses for VAT according to gender. Further adjustment for S_I was performed to determine its potential roles in the VAT–hypertension relationship. The mean age (s.d.) of the sample was 41.3 (13.8) years, with a mean body mass index (BMI) (s.d.) of 28.7 (6.0) kg/m^2. Women comprised 58.5% of the sample ($N = 925$), and Hispanic Americans comprised 69.2% of the sample ($N = 1,095$). One in five participants (21.2%) had prevalent hypertension. In women, VAT was significantly associated with hypertension, independent of BMI (odds ratio (OR) = 1.49, $P = 0.006$). African-American women demonstrated increased odds of prevalent hypertension compared to Hispanic-American women (OR = 3.08, $P < 0.001$). Among men, VAT was not associated with hypertension independent of BMI, and BMI explained a significant amount of the variation in hypertension.

CONCLUSIONS

A significant relationship may exist between VAT and hypertension among women, but not among men. The relationship between VAT and hypertension in women was not associated with insulin resistance.

Am J Hypertens 2008; **21**:910-916

Abdominal obesity, a component of the metabolic syndrome, represents a substantial public health challenge, particularly among African Americans and Hispanic Americans, and its prevalence is expected to increase in the United States over the next 20 years.[1] Because individuals with abdominal obesity also exhibit high prevalence of hypertension, another component of the metabolic syndrome,[2] studying the association between these detrimental and often concurrent cardiovascular disease risk factors is warranted.

Early studies relied upon waist circumference and waist-to-hip ratio as measures of abdominal obesity.[3,4] However, precise measurements of visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT) also are relevant in examining the relationship between obesity and hypertension, because adipose tissue is an endocrine organ, and VAT has been demonstrated to secrete adipocytokines that contribute to the development and progression of cardiovascular and metabolic disease.[5,6] Moreover, VAT, independent of total body fat, has been shown to be associated with hypertension among Caucasian Americans[7] and Japanese Americans.[8] However, relatively few studies have studied this relationship among African Americans and Hispanic Americans.[9] Also, several aspects of the fat deposition–hypertension relationship remain unanswered, including the possible role of insulin sensitivity (S_I), and the potential moderating relationship of gender upon fat deposition.

Consequently, the purpose of this study was to investigate the cross-sectional relationship between computed tomography–measured VAT, SAT, and hypertension among African-American and Hispanic-American participants in the

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Received 5 July 2007; first decision 11 August 2007; accepted 5 May 2008; advance online publication 19 June 2008. doi:10.1038/ajh.2008.213

Insulin Resistance Atherosclerosis (IRAS) Family Study. The IRAS Family Study design allowed us to explore this question within a large biethnic sample with equal representation according to gender, while using direct, standardized measures for glucose tolerance, S_I, blood pressure, and abdominal adipose tissue.

METHODS

The IRAS Family Study is designed to study the genetics of insulin resistance and visceral adiposity.[9] Three sites recruited and examined members of large families of Hispanic (San Antonio, TX, and San Luis Valley, CO) or African-American ethnicity (Los Angeles, CA) over a 2.5-year period, 2000–2002. In general, probands were identified from the IRAS study,[10] the parent study of the IRAS Family Study, as those who had self-reported a large family structure on a family medical history questionnaire. The exclusion criteria for the IRAS probands were (i) conditions that would interfere with the measurement or interpretation of S_I, and (ii) conditions that would limit a person's ability to participate in a 4-h examination. This collection was supplemented with large, non-IRAS families, recruited via probands from the general population. These non-IRAS probands were not selected with regard to the presence of absence of the disease, and met the same eligibility criteria as the IRAS probands. In both cases, participants were required to have a self-reported ethnicity of either Hispanic or non-Hispanic African American, and were required to be 18 years of age or older. Individuals were excluded from the CT exam for excessively large body size or pregnancy.[9] All participants provided written informed consent to participate in the study, and all procedures were conducted with the approval of the Institutional Review Boards at all institutions. Participants with pharmacologically treated diabetes (i.e., insulin use or oral hypoglycemic agents) were excluded from analyses in this investigation; however, we retained participants with diabetes who were not pharmacologically treated.

Outcome variable. Resting seated blood pressure was measured three times using a mercury manometer, after a 5-min rest by centrally trained technicians using identical equipment. Blood pressure technicians participated in monthly reproducibility studies within center; and the inter-rater coefficient of variation for repeat diastolic and systolic blood pressure measures among 22 pairs of readings was 3 and 2%, respectively. The mean of the last two measurements was used to calculate blood pressure.

For this analysis, we dichotomized the continuous variables of systolic and diastolic blood pressure, and the categorical variable of current medication for blood pressure (yes/no) into a new categorical variable denoting hypertension (yes/no). Hypertension was defined as the presence of one of the following: systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg, or current pharmaceutical treatment for hypertension.[11]

Independent variable

VAT and SAT: Abdominal fat mass was measured at the L2/L3 and L4/L5 vertebral region by computed tomography under a common protocol at each of the three sites. Scans were read

Table 1 | Descriptive characteristics of participants at baseline

	African Americans (*N* = 487)						Hispanic Americans (*N* = 1,095)					
	Men (*n* = 208)			Women (*n* = 279)			Men (*n* = 449)			Women (*n* = 646)		
	No HTN (*n* = 154)	HTN (*n* = 54)	*P*	No HTN (*n* = 205)	HTN (*n* = 74)	*P*	No HTN (*n* = 348)	HTN (*n* = 101)	*P*	No HTN (*n* = 540)	HTN (*n* = 106)	*P*
Age[a]	39.1 (1.3)	52.7 (1.5)	<0.001	36.5 (1.1)	53.2 (1.3)	<0.001	37.8 (0.8)	48.1 (10.6)	<0.001	39.4 (0.7)	56.0 (1.5)	<0.001
BMI (kg/m^2)[a]	27.5 (0.5)	29.8 (0.7)	<0.001	29.0 (0.6)	33.4 (0.8)	<0.001	27.8 (0.4)	30.4 (0.5)	<0.001	28.4 (0.3)	31.0 (0.5)	<0.001
VAT (cm^2)[a]	83.8 (4.7)	136.5 (7.6)	<0.001	67.9 (3.5)	122.2 (6.7)	<0.001	114.3 (3.4)	155.2 (6.4)	<0.001	90.8 (2.6)	144.1 (5.3)	<0.001
SAT (cm^2)[a]	235.5 (13.9)	295.7 (21.9)	<0.001	387.8 (18.0)	492.0 (19.2)	<0.001	261.0 (8.6)	310.3 (14.3)	0.002	370.4 (7.9)	422.7 (13.4)	<0.001
VAT/SAT[a]	0.39 (0.02)	0.50 (0.03)	<0.001	0.18 (0.01)	0.27 (0.02)	<0.001	0.47 (0.01)	0.56 (0.03)	<0.001	0.25 (0.01)	0.35 (0.01)	<0.001
Waist circumference (cm)[a]	90.40 (1.13)	98.96 (1.84)	<0.001	84.34 (1.22)	97.25 (1.62)	<0.001	92.66 (0.81)	99.49 (1.04)	<0.001	84.52 (0.82)	91.56 (1.07)	<0.001
Waist-to-hip ratio[a]	0.86 (0.01)	0.91 (0.01)	<0.001	0.77 (0.01)	0.83 (0.01)	<0.001	0.91 (0.003)	0.95 (0.006)	<0.001	0.79 (0.003)	0.83 (0.006)	0.003
Impaired fasting glucose or type 2 diabetes[b,c]	41 (27)	28 (51.9)	<0.008	26 (12.7)	41 (55.4)	<0.001	81 (23.3)	37 (37.0)	<0.03	77 (14.3)	37 (35.6)	<0.001
Type 2 diabetes[b]	2 (1.3)	*N* = 1 (1.8)	0.43[d]	2 (1.0)	8 (10.8)	<0.001[d]	11 (2.5)	9 (9.0)	0.01	6 (1.1)	4 (3.8)	0.05[d]
Insulin sensitivity ($10^{-4} \times min^{-1} \times \mu U^{-1} \times ml^{-1}$)	1.9 (0.1)	1.1 (0.1)	<0.001	1.7 (0.1)	1.0 (0.1)	<0.001	2.2 (0.1)	1.4 (0.2)	0.007	2.3 (0.1)	1.2 (0.1)	<0.001
Taking antihypertensive medications[b,e]	—	33 (61.1)	—	—	58 (78.4)	—	—	26 (25.7)	—	—	51 (48.1)	—

BMI, body mass index; HTN, hypertension; SAT, subcutaneous adipose tissue; VAT, visceral adipose tissue.
[a]Data are reported as mean (s.e.). [b]Data are reported as *N*(%). [c]Participants with impaired fasting glucose (defined as fasting glucose >100 mg/dl at clinical examination), or participants with type 2 diabetes (defined as >126 mg/dl at clinical examination) not taking medication. [d]Fisher's exact test. [e]Among participants with hypertension.

centrally at the University of Colorado Health Sciences Center, Department of Radiology, for VAT and SAT. Bowel fat was subtracted out from the VAT. The L4/L5 measures were used in these analyses. However, 45 (2.8%) participants were missing the L4/L5 data but had L2/L3 data. Because SAT and VAT areas at the L2/L3 and L4/L5 regions are very highly correlated, in these latter participants we imputed the L4/L5 data from the L2/L3 data using a simple linear model.

S_I was assessed by the frequently sampled intravenous glucose-tolerance test,[9] with minimal model analyses[10] as previously described. An injection of insulin was used to ensure adequate plasma insulin levels for the accurate computation of insulin resistance across a broad range of glucose tolerance.[9] Also, a reduced sampling protocol, requiring 12 plasma samples,[9] was used because of the large number of subjects. Glucose in the form of a 50% solution (0.3 g/kg) and regular human insulin (0.03 μ/kg) were injected through an intravenous line at 0 and 20 min, respectively. Blood was collected at −5, 2, 4, 8, 19, 22, 30, 40, 50, 70, 100, and 180 min for the determination of plasma glucose and insulin concentrations. Plasma glucose was measured using the glucose oxidase technique on an automated autoanalyzer (YSI, Yellow Springs, OH); and insulin was assessed by radioimmunoassay.

Demographic and clinical variables: Height and weight were measured in duplicate to the nearest 0.5 cm and 0.1 kg, respectively. Body mass index (BMI) was calculated as weight/height^2 (kg/m^2) and was used as an estimate of overall adiposity. Ethnicity and gender were obtained by self-report. Glucose values were obtained after a minimum 8-h fast, and diabetes was diagnosed using the American Diabetes Association criteria of fasting plasma glucose value of ≥126 mg/dl.[12] Impaired fasting glucose was defined as fasting glucose value of >100 mg/dl.[12] As noted earlier, participants who had pharmacologically treated diabetes were excluded from these analyses. Because of the small number of participants with diabetes that was not pharmacologically treated (n = 43 or 2.7%), we combined participants into a grouping of impaired fasting glucose or type 2 diabetes.

Statistical analyses. Descriptive summary statistics were generated for the sample to determine the characteristics of each gender and ethnic group. Spearman correlations were performed among the measures of adiposity. The collinear nature of BMI and SAT (r^2 = 0.89 to 0.92; **Table 2**) prohibited the simultaneous adjustment of both fat measures in the same model.

The IRAS Family Study sample consists of highly correlated data between family members. Thus, the relationship between abdominal fat deposition and hypertension was also examined using the generalized estimating equation[13] approach using the SAS (Cary, NC) PROC GENMOD procedure. The models account for familial correlation using a sandwich estimator of the variance under exchangeable correlation. The α-level for testing the significance of main effects in each model was set a priori at $P < 0.05$, and the significance level for the interaction term was set at $P < 0.10$.

The initial strategy consisted of testing the relationship between VAT and hypertension adjusting for demographic, metabolic, and anthropometric variables, and two-way interactions between VAT with gender, ethnicity, age, and BMI. Specifically, the full model tested the relationship between VAT and hypertension adjusted for age, gender, ethnicity, glucose dysregulation (impaired fasting glucose or type 2 diabetes vs. normal fasting glucose (reference)), BMI, S_I, and interactions between VAT with gender, ethnicity, age, and BMI. In this model, the VAT by ethnicity, VAT by age, and VAT by BMI interactions were not significant (odds ratio (OR) = 0.90, P = 0.56; OR = 0.95, P = 0.48; OR = 0.95, P = 0.56, respectively); only

Table 2 | Spearman bivariate correlations among total sample, partitioned by gender and ethnicity* (1 s.d. as unit of measurement)

	VAT	SAT	BMI	Waist	S_I	Age
African-American men						
VAT	—	0.65	0.59	0.77	−0.63	0.58
SAT	0.65	—	0.89	0.87	−0.59	0.16 *(P = 0.02)*
BMI	0.59	0.89	—	0.88	−0.54	0.09 *(P = 0.16)*
Waist	0.77	0.87	0.88	–	−0.64	0.35
S_I	−0.63	−0.59	−0.54	−0.64	–	−0.26
Age	0.58	0.16	0.09 *(P = 0.16)*	0.35	−0.26	–
African-American women						
VAT	–	0.66	0.70	0.83	−0.57	0.66
SAT	0.66	–	0.92	0.88	−0.49	0.25
BMI	0.70	0.92	–	0.93	−0.51	0.27
Waist	0.83	0.88	0.93	–	−0.57	0.41
S_I	−0.57	−0.49	−0.51	−0.57	–	−0.27
Age	0.66	0.25	0.27	0.41	−0.28	–
Hispanic Men						
VAT	–	0.61	0.64	0.76	−0.63	0.45
SAT	0.61	–	0.89	0.87	−0.61	0.003 *(P = 0.95)*
BMI	0.64	0.89	–	0.91	−0.62	0.05 *(P = 0.32)*
Waist	0.76	0.87	0.91	—	−0.69	0.21
S_I	−0.63	−0.61	−0.62	−0.69	—	−0.26
Age	0.45	0.002 *(P = 0.95)*	0.05 *(P = 0.32)*	0.21	−0.26	—
Hispanic Women						
VAT	—	0.63	0.69	0.77	−0.62	0.53
SAT	0.63	—	0.89	0.85	−0.53	0.13
BMI	0.69	0.90	—	0.91	−0.60	0.14
Waist	0.77	0.85	0.91	—	−0.64	0.19
S_I	−0.62	−0.53	−0.60	−0.64	—	−0.23
Age	0.53	0.13	0.14	0.19	−0.23	—

BMI, body mass index; SAT, subcutaneous adipose tissue; S_I, insulin sensitivity; VAT, visceral adipose tissue.
*Unless otherwise indicated, significant at the $P < 0.01$ level .

Table 3 | Adjusted odds ratios of hypertension for visceral adipose tissue (1 s.d. as unit) among participants, stratified by gender

	Model 1 (*N* = 925)	*P*	Model 2 (*N* = 920)	*P*	Model 3a (*N* = 915)	*P*	Model 3b (*N* = 920)	*P*	Model 4 (*N* = 849)	*P*
Women										
VAT	1.98 (1.58, 2.47)	<0.001	1.77 (1.37, 2.30)	<0.001	1.49 (1.12, 1.99)	0.006	1.52 (1.16, 2.01)	0.003	1.47 (1.09, 1.99)	0.01
African American vs. Hispanic American (ref)	3.67 (2.14, 6.32)	<0.001	3.37 (1.94, 5.85)	<0.001	2.92 (1.65, 5.15)	0.0002	2.99 (1.69, 5.28)	0.002	2.71 (1.48, 4.98)	0.001
Age	3.49 (2.59, 4.70)	<0.001	3.37 (2.50, 4.55)	<0.001	3.77 (2.77, 5.13)	<0.001	3.74 (2.75, 5.09)	<0.001	3.93 (2.79, 5.53)	<0.001
IFG or DM2 vs. NFG	—	—	1.70 (1.07, 2.67)	0.02	1.59 (1.00, 2.52)	0.05	1.61 (1.02, 2.56)	0.04	1.50 (0.92, 2.44)	0.10
BMI	—	—	—	—	1.27 (1.04, 1.56)	0.02	—	—	1.20 (0.96, 1.51)	0.11
SAT	—	—	—	—	—	—	1.33 (1.06, 1.66)	0.01	—	—
S_I	—	—	—	—	—	—	—	—	0.84 (0.60, 1.17)	0.30
	Model 1 (*N* = 657)	***P***	**Model 2 (*N* = 654)**	***P***	**Model 3a (*N* = 652)**	***P***	**Model 3b (*N* = 631)**	***P***	**Model 4 (*N* = 607)**	***P***
Men										
VAT	1.57 (1.30, 1.89)	<0.001	1.48 (1.21, 1.81)	0.0001	1.08 (0.85, 1.42)	0.58	1.24 (0.97, 1.58)	0.08	1.03 (0.76, 1.38)	0.86
African American vs. Hispanic American (ref)	1.28 (0.79, 2.07)	0.31	1.27 (0.78, 2.04)	0.34	1.08 (0.66, 1.77)	0.75	1.16 (0.71, 1.91)	0.55	1.07 (0.65, 1.77)	0.79
Age	1.80 (1.47, 2.20)	<0.001	1.82 (1.49, 2.23)	<0.001	2.24 (1.78, 2.83)	<0.001	2.07 (1.66, 2.59)	<0.001	2..34 (1.83, 2.99)	<0.001
IFG or DM2 vs. NFG	—	—	1.28 (0.84, 1.94)	0.26	1.19 (0.77, 1.84)	0.42	1.23 (0.80, 1.88)	0.34	1.05 (0.66, 1.67)	0.84
BMI	—	—	—	—	1.79 (1.31, 2.44)	0.003	—	—	1.93 (1.30, 2.88)	0.001
SAT	—	—	—	—	—	—	1.51 (1.12, 2.03)	0.006	—	—
Si	—	—	—	—	—	—	—	—	0.93 (0.59, 1.49)	0.77

Each model displays all variables included in the model.
BMI, body mass index; DM2, type 2 diabetes; IFG, impaired fasting glucose; NFG, normal fasting glucose; SAT, subcutaneous adipose tissue; S_I, insulin sensitivity; VAT, visceral adipose tissue.

the VAT by gender interaction was significant (OR = 1.34, P = 0.053), supporting subsequent stratification by gender. Similar models were conducted that tested the relationship between VAT-to-SAT ratio on hypertension (not presented).

Within each gender, subsequent models tested the relationship between VAT and hypertension. Model 1 tested the association between VAT and hypertension adjusted for ethnicity and age. Model 2 added glucose-tolerance status to model 1. Model 3a represented model 2 with the addition of BMI. In model 3b, BMI was replaced by SAT as a measure of overall adiposity. Finally, model 4 was characterized by model 3a with the addition of S_I to determine its effect.

Additional analyses were conducted within each gender to determine the collective relationship of VAT and BMI and prevalent hypertension. Participants were categorized into intragender tertiles according to their standardized VAT and BMI levels, and further classified into nine categorizes based upon BMI-VAT tertile combination. For each gender, using participants in the lowest VAT-BMI tertile combination (i.e., VAT tertile 1 and BMI tertile 1) as a reference, the association of the other VAT-BMI tertile combinations with prevalent hypertension was examined using the SAS PROC GENMOD procedure, adjusting for age, ethnicity, and glucose tolerance.

RESULTS

Table 1 displays descriptive statistics for the sample, partitioned by gender, ethnicity, and hypertension status. The values for VAT/SAT ratio and waist-to-hip ratio are rounded to the nearest 0.01 or lower to demonstrate the differences between means and standard errors more clearly. Collectively, among both African-American and Hispanic-American men and women, participants with hypertension were older than those with normal blood pressure, and had higher mean BMI, VAT, SAT, and VAT-to-SAT ratio. In addition, among both ethnicities, those with hypertension demonstrated lower mean S_I levels. We also conducted subgroup analyses among participants with hypertension in which we assessed S_I among participants who were taking antihypertensive medications vs. those who were not taking medication. Participants who were taking antihypertensive medications had significantly lower mean S_I (least square mean (s.e.) = 1.03 (0.09)) compared to those who not taking medications (1.50 (0.15); $P < 0.001$).

Table 2 illustrates the Spearman bivariate correlations among VAT, SAT, BMI, and waist circumference and S_I, partitioned by ethnicity and gender. For both ethnicities and genders, these four estimates of adiposity are highly correlated. We also sought to determine whether there

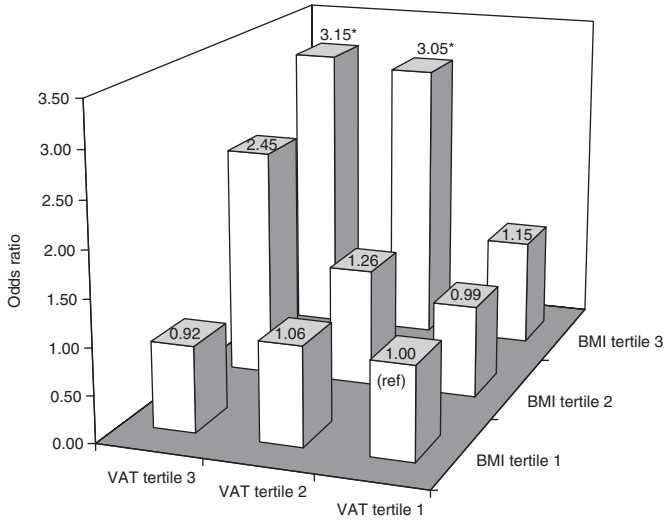

Figure 1 | Adjusted odds ratios for hypertension by visceral adipose tissue (VAT) and body mass index (BMI) tertile among women. †Adjusted for age, ethnicity, and glucose tolerance status (impaired fasting glucose or type 2 diabetes vs. normal fasting glucose (reference). *Significant at the $P < 0.05$ level. VAT tertile 1 range (10.00–69.68 cm^2); VAT tertile 2 range (69.77–118.63 cm^2); VAT tertile 3 range (118.67–342.28 cm^2). BMI tertile 1 range (15.37–25.47 kg/m^2); BMI tertile 2 range (25.49–30.42 kg/m^2); BMI tertile 3 range (30.45–58.09 kg/m^2).

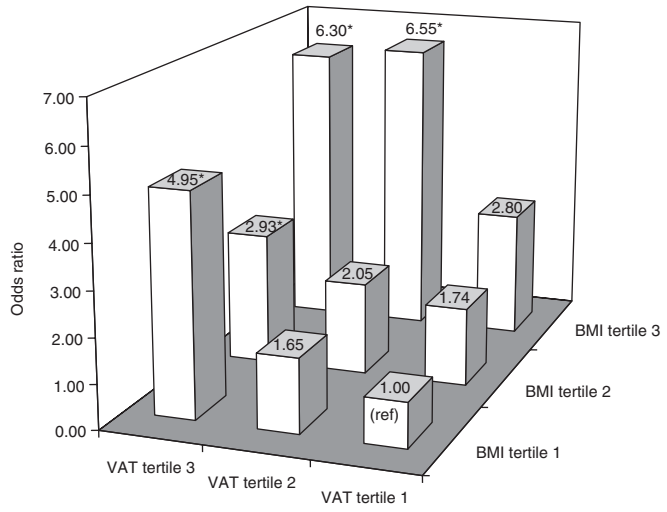

Figure 2 | Adjusted odds ratios for hypertension by visceral adipose tissue (VAT) and body mass index (BMI) tertile among men. †Adjusted for age, ethnicity, and glucose tolerance status (impaired fasting glucose or type 2 diabetes vs. normal fasting glucose (reference). *Significant at the $P < 0.05$ level. VAT tertile 1 range (10.00–69.61 cm^2); VAT tertile 2 range (69.80–118.56 cm^2); VAT tertile 3 range (118.69–363.34 cm^2).
BMI tertile 1 range (17.58–25.45 kg/m^2); BMI tertile 2 range (25.51–30.44 kg/m^2); BMI tertile 3 range (30.46–46.65 kg/m^2).

were significant differences between the following sets of correlations: (i) BMI and SAT vs. BMI and VAT; (ii) SAT and BMI vs. SAT and VAT; (iii) waist circumference and SAT vs. waist circumference and VAT; and (iv) SAT and waist circumference vs. SAT and VAT. Because testing whether a correlation coefficient is 0 is equivalent to testing whether the corresponding regression coefficient is 0 and the conventional correlation coefficient comparison does not take into account the correlated family structure, we conducted a Z statistic to compare the regression coefficients from two generalized estimating equation models for each comparison. All the tests were significant (P value < 0.05) except when comparing the correlation between BMI and SAT and the correlation between BMI and VAT in African-American women (P value = 0.2556).

Table 3 displays the relationship between VAT and hypertension among women and men. VAT was significantly associated with an increased odds of hypertension for both men and women adjusted for ethnicity and age (model 1: women, OR = 1.98; men, OR = 1.57, both $P < 0.001$). This significant relationship persisted in women after additional adjustment for fasting glucose status (OR = 1.77, $P < 0.001$) and BMI (OR = 1.49, $P = 0.006$). Substituting SAT for BMI as a measure of total adiposity had minimal effect on the main effect. S_I did not attenuate the VAT–hypertension relationship in model 4 (VAT OR = 1.47, $P = 0.01$). Among men, the VAT–hypertension relationship was attenuated by adjustment for BMI (model 3A: OR = 1.08, $P = 0.58$) or for SAT (model 3A: OR = 1.24, $P = 0.08$).

Figures 1 and **2** display the results of additional analyses that examined the collective relationship of VAT and BMI with hypertension among men and women participants. **Figure 1** demonstrates that among women, increases in both VAT and BMI were associated with increased odds of hypertension, whereas **Figure 2** illustrates a less consistent pattern among men, with participants in the higher BMI tertiles exhibiting markedly higher odds of hypertension.

DISCUSSION

This cross-sectional investigation was designed to determine whether VAT and total body adiposity were associated with prevalent hypertension in a large sample of African-American and Hispanic-American adults. A secondary purpose entailed examining the role of S_I in this relationship. We also considered several demographic and metabolic covariates in our models. Collectively, we found that VAT is associated with hypertension, independent of total body adiposity, and that this association is moderated by gender. To our knowledge, this is the first report of this finding. Specifically, we found that among women, VAT is significantly associated with hypertension, independent of total body adiposity, and that this association persisted after inclusion of S_I in an additional model. Among men, the association between VAT and hypertension was not significant after adjustment for BMI or SAT.

Our findings are consistent with those of other reports. Hayashi *et al.*,[8] studied the relationship between visceral adiposity, described as intraabdominal fat area, and prevalent hypertension among 563 Japanese Americans with normal or impaired glucose tolerance or diabetes. Results indicated that visceral adiposity was a significant predictor of hypertension prevalence, even after adjustment for total subcutaneous fat, abdominal subcutaneous fat, or BMI. Ding *et al.*[7] examined the cross-sectional relationship between regional fat deposition, measured using computed tomography, and prevalent

hypertension among 2,969 participants in the Health, Aging, and Body Composition (Health ABC) Study. In logistic regression analyses, VAT was associated with hypertension, after adjustment for several demographic and behavioral covariates. Indeed, the authors found that the association between VAT and hypertension was strongest in individuals with the least amount of total body fat.

There are several possible mechanisms that may explain the relationship between VAT and prevalent hypertension. For instance, Alvarez *et al.*[14] found that visceral fat has been shown to be associated with increased sympathetic nervous system activity, which is associated with elevations in blood pressure. Moreover, VAT contributes free-fatty acids through the portal vein, which may result in increased insulin resistance.[15] Park *et al.*[16] found that intraabdominal fat was associated with increased insulin resistance in a small sample of young men. Insulin resistance, in turn, has been shown to be associated with prevalent[17] and incident hypertension[18] in previous IRAS investigations. Similarly, we conducted an additional model which tested the relationship between S_I and prevalent hypertension adjusted for age, gender, ethnicity, and glucose tolerance, without measures of adiposity. In this model, the OR for S_I was 0.61 ($P = 0.002$).

Increases in VAT may be associated with increased levels of angiotensinogen,[19] which could in turn result in increased activation of the renin–angiotensin system and increased blood pressure.[20–22] There is also emerging evidence regarding a relationship between C-reactive protein and hypertension.[23,24] In addition, Park *et al.*[25] provide a biologically plausible rationale for a relationship between VAT and C-reactive protein, because VAT donates free-fatty acids via the portal vein to the liver, which in turn is the primary site of C-reactive protein production.

In our subgroup analyses, we found that gender moderated the relationship between VAT and hypertension. Specifically, VAT was associated with hypertension among women, but not among men, although **Table 1** demonstrates that women exhibited lower levels of VAT and VAT/SAT ratio compared to men. There are several possible explanations for this finding. VAT and hypertension increase with age among both genders[25] and **Table 1** demonstrates that women with hypertension had higher mean ages compared to men with hypertension, particularly among Hispanic Americans. Also, as women with hypertension had a mean age of >50 years, it is possible that a large percentage of these participants were postmenopausal. Matsuzawa *et al.*[26] found that among women, the correlation between age and VAT, although significant, was of a lower magnitude among premenopausal women compared to postmenopausal women.

The study herein included several strengths, including equal representation according to gender among two ethnic groups, and direct assessment of hypertension and other covariates. Although we did adjust for several variables in our models, yet other variables may moderate the relationship between abdominal fat and hypertension, such as dietary patterns, smoking habits or history, physical activity or alcohol consumption, or hormonal or catecholamine levels or levels of perceived stress. We did not consider intramuscular fat, and our measurements did not distinguish between superficial and deep subcutaneous fat.[27] We were not able to definitively disentangle the effects of age and menopausal status among the female participants. In addition, our cross-sectional design prohibits us from inferring causal relationships. Also, it must be noted that the significant VAT by gender interaction may have been the result of chance, residual confounding, or bias.

The high prevalence of hypertension prohibits us from inferring that the ORs are representative of risk ratios in this study population. **Table 1** reveals that Hispanic Americans appeared to demonstrate higher levels of VAT compared to African Americans. Thus, the relationship between ethnicity and body fat distribution is worthy of further inquiry.

These results suggest that VAT, independent of total body adiposity, is associated with prevalent hypertension. These results are consistent with previous studies, and suggest that VAT may be particularly associated with hypertension among women. The results also suggest that behaviors that reduce VAT, such as regular physical activity and healthy dietary patterns, will have a beneficial effect upon blood pressure. Further epidemiological studies and trials are needed to determine the relationship of ethnicity and total body adiposity upon hypertension, and whether gender moderates the association between visceral fat and hypertension.

Acknowledgments: This research was supported in part by the National Institutes of Health grant HL060944 (to C.G.F., F.C.H., S.H., J.N., J.I.R., M.B.-A., Y.I.C., L.E.W.).

Disclosure: The authors declared no conflict of interest.

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