The Association of Regional Fat Depots With Hypertension in Older Persons of White and African American Ethnicity

Jingzhong Ding, Marjolein Visser, Stephen B. Kritchevsky, Michael Nevitt, Anne Newman, Kim Sutton-Tyrrell, and Tamara B. Harris

Background: Fat distribution has been shown to be a strong correlate of hypertension, independent of general obesity. However, population-based studies are lacking on the association of regional fat depots with hypertension.

Methods: The present study is a cross-sectional analysis of 2969 individuals in the Health, Aging and Body Composition Study (915 men of white ethnicity and 535 of African American; and 833 women of white ethnicity and 686 of African American) who were 70 to 79 years of age. Fat depots were measured by computed tomography.

Results: The prevalence of hypertension was 57%. Among those with hypertension, 70% reported antihypertensive treatment. In logistic regression analyses, visceral fat was strongly associated with hypertension (odds ratios for each standard deviation increase in the area of visceral fat: 1.28, \(P < .0001\)) after adjustment for age, sex, ethnicity, site, height, smoking status, pack-years of smoking, alcohol consumption status, amount of alcohol consumption, and physical activity. Moreover, the association was the strongest in individuals with the least amount of total body fat. Besides visceral fat, subcutaneous fat and thigh intermuscular fat were also associated with hypertension in African Americans.


Key Words: Hypertension, obesity, epidemiology, aging.
American ethnicity. We postulated that visceral fat is the strongest correlate of hypertension in both white and African American individuals.

Methods

Study Population

The Health, Aging, and Body Composition (Health ABC) Study is a prospective, population-based study to investigate the effects of body composition on morbidity, functional limitations, and mortality. A total of 3075 participants were recruited from a random sample of white and all African American Medicare beneficiaries residing within each ZIP code from the metropolitan areas surrounding Pittsburgh, PA and Memphis, TN, from 1997 to 1998. Participants were eligible if they were 70 years of age; reported no difficulty walking 1/4 mile, climbing up 10 steps, and performing mobility-related activities of daily living; denied radiation treatment or chemotherapy for cancer in the past 3 years; were not enrolled in a trial of a lifestyle intervention; and had no plans to move out of the area in the next 3 years. The study was approved by the institutional review boards of both the University of Pittsburgh and the University of Tennessee, and the participants gave informed consent. Participants with missing information on the fat measures (n = 84) or the hypertension measure (n = 22) were excluded, leaving 2969 (915 men of white ethnicity and 535 of African American; and 833 women of white ethnicity and 686 of African American) for the present analysis. Individuals who were excluded had characteristics similar to those of persons who were included in the present analysis. All variables for the present analysis were assessed at baseline (1997 to 1998).

Hypertension

Trained and certified clinical staff measured blood pressure (BP) in the right arm, using a conventional mercury sphygmomanometer, with the participant in a seated position. Systolic and diastolic BP were defined as the average of two measures. Hypertension was defined on the basis of one of the following: 1) systolic BP ≥140 mm Hg; 2) diastolic BP ≥90 mm Hg; or 3) current use of antihypertensive medication and a self-report of having been diagnosed with hypertension by a physician.

Body Fat Measures

Regional fat depots were assessed from CT scans obtained in Pittsburgh on a General Electric 9800 Advantage (General Electric, Milwaukee, WI) and in Memphis on a Siemens Somatron Plus 4 (Siemens, Erlangen, Germany) or Picker PQ2000S (Marconi Medical Systems, Cleveland, OH). A single axial scan (140 kVp, 300 to 360 mAs, 10-mm thickness) was taken at the disk space between the fourth and fifth lumbar vertebrae. Images were transferred to the Reading Center at the University of Colorado Health Sciences Center on optical disc or magnetic tape. Analyses were performed on a SPARC station II (Sun Microsystems, Mountain View, CA) using IDL development software (RSI Systems, Boulder, CO). An outline was traced surrounding the abdominal cavity. The adipose tissue density range was determined with a bimodal image distribution histogram for each participant. Visceral fat was defined as the area of all adipose tissue within the abdominal cavity, calculated by multiplying the number of pixels within this range by a single pixel area. Abdominal subcutaneous fat was defined as the difference in the area between the entire adipose tissue in the scan and visceral fat. A cross-sectional scan of both legs was also taken at the midpoint between the medial edge of the greater trochanter and the intercondylar fossa. A line was manually drawn along the deep facial plane surrounding the thigh muscles. Intermuscular fat was defined as all pools of fat identified within the deep facial plane surrounding the thigh muscles. Subcutaneous fat was defined as the difference in the area between the thigh external outline and the deep facial plane surrounding the thigh muscles. Thigh subcutaneous fat and thigh intermuscular fat, respectively, were defined as the average of these fat areas in both legs. Muscle attenuation was defined as the average density of muscular areas in both legs, using Hounsfield units (HU) where water was set to zero. Muscle attenuation represents fat within muscle that cannot be quantitated directly as fat pools from CT scans. The lower the HU, the fatter the muscle. To assess the reproducibility of these measurements, 5% of the data was re-read in a blinded fashion. The intra-class correlation coefficients of reliability ranged from 0.93 to 1.00.

Total body fat was measured by dual-energy x-ray absorptiometry using a Hologic QDR4500A Scanner (Logic, Waltham, MA) with software version 8.21 for analysis. Scans of phantoms were performed to monitor machine performance daily and for cross-calibration purposes annually across sites.

Other Covariates

Age, sex, ethnicity, clinic site, smoking status, and alcohol consumption status were attained by interviewer-administered questionnaire. Height was measured with a Harpenden stadiometer (Holtain, Crosswell, United Kingdom) with the participant in a standing position. Pack-years of smoking was defined as the average number of packs of cigarettes smoked per day multiplied by the number of years smoking. Amount of alcoholic drinking was categorized on a scale of 1 to 4 (none to heavy), according to alcohol consumption in the past year. The time and intensity level of all physical activity performed in the past 7 days, including climbing stairs, walking for exercise, walking for other purposes, aerobics, weight training, and other activities of high and medium intensity, were assessed by questionnaire to create an overall physical activity score in kilocalories per week.
Statistical Analysis

The differences in proportions and means of the baseline characteristics between participants with and without hypertension were examined with χ² test and t test for categorical and continuous variables, respectively. Means and standard deviations (SD) of fat measures were presented by sex and ethnicity. Pearson correlation coefficients of total body fat with the other fat measures were also calculated by sex and ethnicity.

Logistic regression analysis was used to assess the association of fat measures with hypertension in all participants after adjusting for age, sex, ethnicity, site, height, smoking status, pack-years of smoking, alcohol consumption status, amount of alcohol consumption, and physical activity. Because the association was approximately linear, fat measures were used as continuous variables. As the unit of measurement, 1 SD of each fat measure was used so that the strength of the associations of fat measures with hypertension could be compared with one another. Linear regression analysis was used to assess the associations of fat measures with systolic and diastolic BP only in participants who did not report use of any antihypertensive medication (n = 1539). Because of the different fat distributions among the four sex and ethnicity subgroups, the association of fat measures with hypertension was also examined separately within each subgroup. Finally, to delineate the independent contribution of visceral fat to hypertension, we assessed the association of visceral fat with hypertension within each sex- and ethnicity-specific tertile of total body fat.

Results

The prevalence of hypertension was 57% in the study sample. Among the subjects with hypertension, 70% reported antihypertensive treatment. Subjects with hypertension were more likely to be female, to be African American, and to report lower levels of physical activity than subjects without hypertension (Table 1).

Of four sex and ethnicity subgroups, men of white ethnicity had the largest amount of visceral fat, whereas women of African American ethnicity had the largest amounts of abdominal and thigh subcutaneous fat as well as total body fat (Table 2). In Pearson correlation analyses,
total body fat was correlated with all regional fat depots within each of four sex and ethnicity subgroups (Table 3).

Visceral fat, abdominal subcutaneous fat, thigh intermuscular fat, and total body fat were consistently associated with hypertension, based on logistic regression analysis, and with systolic and diastolic BP, based on linear regression analysis (Table 4). With each increase in unit of SD, visceral fat, among these fat measures, had the greatest odds ratio of hypertension and largest regression coefficients of systolic and diastolic BP. In the logistic regression analysis, further adjustment for diabetic status, fasting glucose and insulin levels, high-density lipoprotein cholesterol, and triglycerides levels reduced the odds ratio for visceral fat from 1.28 (95% confidence interval: 1.18 to 1.39) to 1.23 (95% confidence interval: 1.12 to 1.35).

In sex- and ethnicity-stratified analyses, visceral fat was the primary correlate of hypertension in subjects of white ethnicity (Table 5). In fact, visceral fat was the only fat measure associated with hypertension in white men (P < .05). In African Americans, visceral fat, subcutaneous fat, and thigh intermuscular fat were all associated with hypertension (P < .05). Furthermore, African American men had greater odds ratios of hypertension for each increase in unit of SD of all fat measures except thigh intermuscular fat and muscle attenuation than did the other sex and ethnicity subgroups. However, the association of regional fat depots with hypertension was not statistically different between subjects of white and African American ethnicity except in the case of thigh subcutaneous fat (for interaction terms, P > .05).

We next examined whether there was an interaction between visceral fat and total body fat. The association of visceral fat with hypertension was statistically different between two lower tertiles and the highest tertile of total body fat (for interaction terms, P < .05). Visceral fat was significantly associated with hypertension only in two lower tertiles of total body fat (P < .05) (Fig. 1). Furthermore, subjects in the highest tertile of visceral fat but the lowest tertile of total body fat had the highest odds of hypertension.

**Discussion**

The present study, to our knowledge, is the first population-based study to address the association of regional fat depots with hypertension. In accordance with previous studies in individuals of white and Asian ethnicity, it is the present study found that visceral fat was of primary importance with regard to associated hypertension, especially

### Table 3. Correlation of total body fat with other fat measures by sex and ethnicity

<table>
<thead>
<tr>
<th></th>
<th>White</th>
<th>African American</th>
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<tbody>
<tr>
<td>Visceral fat</td>
<td>0.67 (0.0001)</td>
<td>0.67 (0.0001)</td>
</tr>
<tr>
<td>Abdominal subcutaneous fat</td>
<td>0.81 (0.0001)</td>
<td>0.85 (0.0001)</td>
</tr>
<tr>
<td>Thigh subcutaneous fat</td>
<td>0.75 (0.0001)</td>
<td>0.78 (0.0001)</td>
</tr>
<tr>
<td>Thigh intermuscular fat</td>
<td>0.67 (0.0001)</td>
<td>0.63 (0.0001)</td>
</tr>
<tr>
<td>Muscle attenuation</td>
<td>−0.55 (0.0001)</td>
<td>−0.50 (0.0001)</td>
</tr>
</tbody>
</table>

Data are Pearson correlation coefficients, with P values in parentheses.

### Table 4. Association of fat measures (1 SD as the unit) with hypertension and systolic and diastolic blood pressure

<table>
<thead>
<tr>
<th></th>
<th>Hypertension (N = 2969)</th>
<th>Regression Coefficients (95% CI)†</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Systolic BP (N = 1539)</td>
<td>Diastolic BP (N = 1539)</td>
</tr>
<tr>
<td>Visceral fat</td>
<td>1.28 (1.18, 1.39)</td>
<td>1.60 (0.56, 2.63)</td>
</tr>
<tr>
<td>Abdominal subcutaneous fat</td>
<td>1.21 (1.11, 1.32)</td>
<td>1.32 (0.19, 2.44)</td>
</tr>
<tr>
<td>Thigh subcutaneous fat</td>
<td>1.07 (0.97, 1.19)</td>
<td>0.27 (−1.11, 1.66)</td>
</tr>
<tr>
<td>Thigh intermuscular fat</td>
<td>1.20 (1.10, 1.30)</td>
<td>1.24 (0.27, 2.20)</td>
</tr>
<tr>
<td>Muscle attenuation</td>
<td>0.87 (0.80, 0.94)</td>
<td>−0.47 (−1.52, 0.57)</td>
</tr>
<tr>
<td>Total body fat</td>
<td>1.20 (1.11, 1.30)</td>
<td>1.13 (0.07, 2.19)</td>
</tr>
</tbody>
</table>

BP = blood pressure; CI = confidence interval.

* Logistic regression analyses, adjusting for age, sex, ethnicity, site, height, smoking status, pack-years of smoking, drinking status, amount of drinking, and physical activity; † Linear regression analyses were limited to subjects not taking antihypertensive medication; same adjustment as above.
pared with subcutaneous fat. Third, visceral fat may have a higher expression of angiotensinogen in visceral fat compared with subcutaneous fat.13 Because of a higher lipolytic activity in visceral fat than in subcutaneous fat,18 the excess free fatty acids released from visceral adipose tissue lead to increased hepatic insulin extraction and skeletal muscle sensitivity to insulin in the individuals with excess amounts of visceral fat.19,20 Second, visceral fat may cause greater activity of the renin-angiotensin system due to a higher expression of angiotensinogen in visceral fat compared with subcutaneous fat.13 Third, visceral fat may raise intrarenal pressures by increasing intra-abdominal pressures and penetrating into the renal medullary sinuses.15

Several mechanisms may underlie these associations. First, visceral fat may raise BP by increasing sympathetic nervous system activity, enhancing activation of the renin-angiotensin system, and possibly even causing physical compression of the kidneys.15 Visceral fat may increase sympathetic nervous system activity through associated insulin resistance.16,17 Because of a higher lipolytic activity in visceral fat than in subcutaneous fat and because of a direct connection between visceral fat and liver through the portal venous system, release of free fatty acids is more rapid in visceral fat than in subcutaneous fat.18 The excess free fatty acids released from visceral adipose tissue lead to decreased hepatic insulin extraction and skeletal muscle sensitivity to insulin in the individuals with excess amounts of visceral fat.19,20 Second, visceral fat may cause greater activity of the renin-angiotensin system due to a higher expression of angiotensinogen in visceral fat compared with subcutaneous fat.13 Third, visceral fat may raise intrarenal pressures by increasing intra-abdominal pressures and penetrating into the renal medullary sinuses.15

It is noteworthy that the association of visceral fat with hypertension was strongest in subjects with the least amounts of total body fat. This observation is consistent with a previous Health ABC report that, even in individuals with normal body weight, visceral fat was positively associated with insulin resistance.21 In fact, the highest risk for cardiovascular disease was found in lean individuals with a high waist-hip ratio, a surrogate of visceral fat.22 Although the underlying mechanisms are unknown, this finding provides the basis for targeting lean individuals with larger visceral fat depots for the prevention of hypertension.

In African American individuals, especially men, subcutaneous fat and thigh intermuscular fat contributed to hypertension to a similar degree as visceral fat. The underlying mechanisms of this phenomenon are unknown. One possibility is that regional fat depots in individuals of African American ethnicity are more highly correlated with each other than in persons of white ethnicity, making it more difficult to assess contributions of individual fat depot. Alternatively, regional fat depots in African Americans may have different physiologic function than those in whites, which predispose African Americans to hypertension. For example, sympathetic nervous system activity in African American men may be higher than in white men with comparable levels of obesity.23 This notion can partially explain why there is a higher prevalence of hypertension in African Americans compared with whites, even though African Americans have a relatively smaller amount of visceral fat than whites.

The fat area from a single scan was used as a surrogate of the fat volume. Although the correlation between the subcutaneous fat area from a single scan and the subcutaneous fat volume is still unknown, the correlation coefficients between the visceral fat area at the fourth and fifth lumbar vertebrae and the visceral fat volume are >0.97 (P < .001) in both sexes24 and the intermuscular fat area at the mid-thigh explains >80% of the variance of the intermuscular fat volume in women (P. Kuznia, unpublished data, 2003). The prevalence/incidence bias may affect the present study. If the risk of mortality is greater in individuals with both larger amounts of visceral fat and hyper-

### Table 5. Association of fat measures (1 SD as the unit) with hypertension, stratified by sex and ethnicity

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Visceral fat</td>
<td>1.22 (1.07, 1.39)</td>
<td>1.30 (1.10, 1.52)</td>
<td>1.35 (1.10, 1.64)</td>
<td>1.31 (1.06, 1.60)</td>
</tr>
<tr>
<td>Abdominal subcutaneous fat</td>
<td>1.19 (0.98, 1.46)</td>
<td>1.13 (0.96, 1.32)</td>
<td>1.41 (1.12, 1.78)</td>
<td>1.21 (1.04, 1.41)</td>
</tr>
<tr>
<td>Thigh subcutaneous fat</td>
<td>0.85 (0.62, 1.15)</td>
<td>1.08 (0.91, 1.28)</td>
<td>1.65 (1.09, 2.52)</td>
<td>1.06 (0.91, 1.23)</td>
</tr>
<tr>
<td>Thigh intermuscular fat</td>
<td>1.03 (0.90, 1.18)</td>
<td>1.34 (1.10, 1.63)</td>
<td>1.24 (1.04, 1.48)</td>
<td>1.29 (1.10, 1.52)</td>
</tr>
<tr>
<td>Muscle attenuation</td>
<td>0.95 (0.82, 1.10)</td>
<td>0.81 (0.70, 0.95)</td>
<td>0.88 (0.72, 1.08)</td>
<td>0.84 (0.70, 1.00)</td>
</tr>
<tr>
<td>Total body fat</td>
<td>1.12 (0.94, 1.32)</td>
<td>1.23 (1.05, 1.44)</td>
<td>1.40 (1.13, 1.75)</td>
<td>1.16 (1.00, 1.35)</td>
</tr>
</tbody>
</table>

Data are odds ratios, with 95% confidence intervals in parentheses. Data are based on logistic regression analyses, adjusting for age, site, height, smoking status, pack-years of smoking, drinking status, amount of drinking, and physical activity.
tension, the present study may underestimate the real association of visceral fat with hypertension. As with all cross-sectional studies, whether the appearance of regional fat depots preceded the development of hypertension cannot be determined in the present study. However, waist circumference, a surrogate of visceral fat, is a risk factor for the development of hypertension in longitudinal studies.25

In conclusion, our findings are consistent with the results from previous studies with regard to the primary importance of visceral fat in hypertension, and extend these findings to a population-based sample of older adults. Moreover, the prevention of hypertension needs to be targeted to lean individuals with larger visceral fat depots who have an increased risk of hypertension. Further epidemiologic and physiologic studies are needed to examine whether subcutaneous fat and intermuscular fat, besides visceral fat, are also contributors to hypertension in African American individuals, particularly in men.

References