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ORIGINAL ARTICLE

Visceral adiposity, not abdominal subcutaneous fat area, is associated with high blood pressure in Japanese men: the Ohtori study

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Visceral adiposity is considered to have a key role in cardiometabolic diseases. The purpose of this study is to investigate cross-sectionally the association between intra-abdominal fat area (IAFA) measured by computed tomography (CT) and high blood pressure independent of abdominal subcutaneous fat area (ASFA) and insulin resistance. Study participants included 624 Japanese men not taking oral hypoglycemic medications or insulin. Abdominal, thoracic and thigh fat areas were measured by CT. Total fat area (TFA) was calculated as the sum of abdominal, thoracic and thigh fat area. Total subcutaneous fat area (TSFA) was defined as TFA minus IAFA. Hypertension and high normal blood pressure were defined using the 1999 criteria of the World Health Organization. Multiple-adjusted odds ratios of hypertension for tertiles of IAFA were 2.64 (95% confidence interval, 1.35–5.16) for tertile 2, and 5.08 (2.48–10.39) for tertile 3, compared with tertile 1 after adjusting for age, fasting immunoreactive insulin, diabetes status, ASFA, alcohol consumption, regular physical exercise and smoking habit. IAFA remained significantly associated with hypertension even after adjustment for ASFA, TSFA, TFA, body mass index or waist circumference, and no other measure of regional or total adiposity was associated with the odds of hypertension in models, which included IAFA. Similar results were obtained for the association between IAFA and the prevalence of high normal blood pressure or hypertension. In conclusion, greater visceral adiposity was associated with a higher odds of high blood pressure in Japanese men.
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INTRODUCTION

Many epidemiological studies have reported the association between central obesity, assessed by waist circumference, the ratio of waist-to-hip circumference or the ratio of subscapular-to-triceps skinfold, and cardiometabolic diseases.[1–9] The association between abdominal fat distribution assessed by surface measurements and hypertension has been inconsistent as reported by several epidemiological studies.[3–7] These surface measurements cannot distinguish the contribution of visceral fat from that of subcutaneous abdominal fat. Computed tomography (CT) is an alternative approach that allows the precise separation between the visceral and subcutaneous adipose tissue compartments. In particular, visceral adiposity measured by CT has been reported to be associated with insulin resistance and cardiometabolic diseases.[10–15]

Only a few epidemiological studies have examined the association between visceral adiposity directly measured by CT and hypertension,[13,14,16,17] but the results were inconclusive. In Japanese Americans, the intra-abdominal fat area (IAFA), but not the abdominal subcutaneous fat area (ASFA), was associated with the prevalence and incidence of hypertension.[13,14] Fox *et al.*[16] showed in Caucasians that both visceral and abdominal subcutaneous fat volume were associated with the prevalence of hypertension. On the other hand, Foy *et al.*[17] reported in African-American and Hispanic-American men that ASFA, but not IAFA, was associated with the prevalence of hypertension. Oka *et al.*[18] showed in native Japanese that both visceral and ASFAs were correlated with systolic and diastolic blood pressure. Differences in ethnicity or adjustment for other potentially confounding variables such as insulin resistance or abdominal subcutaneous fat may explain in part these inconclusive findings. The effect of visceral adiposity on hypertension for Asian populations might be more important than for the other ethnic population because Asians and Asian Americans have been reported to have a lower prevalence of obesity by body mass index compared with Caucasians[19,20] but a greater degree of visceral adiposity.[21]

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Therefore, we cross-sectionally examined whether visceral adiposity measured by CT was associated with an increased odds of the prevalence of hypertension and of high normal blood pressure or hypertension in Japanese men independent of other adipose depots and insulin resistance.

METHODS

Study subjects

The Ohtori study. The Ohtori Study is an ongoing cohort investigation designed to examine relationships between body fat distribution and cardiometabolic diseases. Between December 2005 and February 2007, 710 Japanese men (28–76 years old) who visited the Ohtori Health Promotion Center for a medical checkup were enrolled in this study.

For the current analysis, eligible participants consisted of 687 Japanese men not taking oral hypoglycemic medication or insulin. We excluded 29 of the 687 participants because of serum creatinine of 1.5 mg dl^{-1} or more, undergoing renal disease therapy, history of cardiovascular disease or history of cancer. Another 34 persons missing covariate information were also excluded. The analytic cohort consisted of 624 participants.

Data collection and measurements

All measurements were made in the Ohtori Health Promotion Center, Sakai, Japan. The protocol for this research was approved by the Human Subjects Review Committee at Osaka City University and signed informed consent was obtained from all the participants. The clinical examination consisted of a medical history; a physical examination; anthropometric measurements; measurements of fasting plasma glucose and immunoreactive insulin levels; measurements of fat areas by CT as described below; and self-administered questionnaires on health-related behaviors. After a 5-min rest in a quiet room, systolic and diastolic blood pressures were measured on the right arm with an automatic sphygmomanometer while the participant was seated (BP-203RV II; Omron Colin, Tokyo, Japan). Spearman's correlation between the former device and a standard mercury sphygmomanometer was 0.973 for diastolic blood pressure and 0.985 for systolic blood pressure in a voluntary sample (n=60). Blood pressure was measured twice at an interval of a few minutes and the subject's blood pressure was defined as the average of the two readings. Blood samples were drawn after an overnight 12-h fast. Plasma glucose was assayed by an automated hexokinase method. The intra- and inter-assay coefficients of variation were 0.8 and 2.0%, respectively. Fasting immunoreactive insulin was measured by a chemiluminescent immunoassay. The intra- and inter-assay coefficients of variation were 2.7 and 3.5%, respectively. Insulin resistance was evaluated by using the homeostasis model assessment-insulin resistance (HOMA IR), calculated as (fasting immunoreactive insulin (μU ml^{-1}))×(fasting plasma glucose (mg dl^{-1}))/405 (Matthews *et al.*[22]). Height and weight were measured in shoeless participants wearing light cloths. We calculated body mass index as weight in kilograms divided by height in meters squared. Waist circumference was measured at the level of the umbilicus while participants were in a standing position.

The questions about usual alcohol consumption included the weekly frequency of alcohol consumption, the type of alcohol beverages and the usual amount consumed per drinking day. The quantity of alcohol consumption was converted to weekly consumed ethanol volume in grams using standard Japanese tables. Regarding regular physical exercise, a detailed questionnaire was administered about the types of leisure-time physical activities they took part in (described as light, moderate or vigorous in accordance with the Centers for Disease Control and Prevention),[23] their weekly activity frequency and time spent in each activity. Participants were classified as engaging in regular leisure-time physical activity at least once weekly if they reported that they engaged in light or more intense activities at least once weekly. Regarding smoking habits, participants were classified as current smokers, past smokers or nonsmokers.

Evaluation of CT imaging

All participants were scanned at the end of inspiration in a supine position with their arms extended above their head and their legs extended using an X Lead (Toshiba Medical, Tokyo, Japan) to measure fat areas (cm^2). In all, 1-cm thick non-contrast-CT slices were acquired in the chest (120 kVp, 100 mA, table speed 10 mm s^{-1}, beam pitch 10 mm and gantry rotation time 1.0 s), at the level of the umbilicus (120 kVp, 200 mA, beam pitch 10 mm and gantry rotation time 1.0 s), and at mid-thigh midway between the greater trochanter and the superior margin of the patella (120 kVp, 200 mA, beam pitch 10 mm and gantry rotation time 1.0 s). The slices at the level of the nipples, the umbilicus and the mid-thighs were used to quantify thoracic subcutaneous fat area, IAFA, ASFA and thigh subcutaneous fat area, respectively. The areas were measured using SliceOmatic 4.2 image analysis software (Tomovision, Montreal, Canada), blinded to all the other measurements of the study participants. We directly estimated visceral adiposity from IAFA at the umbilicus level. This measurement has been reported to have a high correlation with directly ascertained total visceral fat volume measured by using CT or magnetic resonance imaging.[24–26] Total fat area (TFA) was calculated as the sum of IAFA, thoracic and ASFAs, and twice the right thigh subcutaneous fat area. TFA measured by this method was reported to correlate highly with fat mass measured by hydrodensitometry among Japanese Americans (r=0.89–0.94) (McNeely *et al.*[27]). Total subcutaneous fat area (TSFA) was defined as TFA minus IAFA. A single observer measured the IAFA and ASFA of all participants, and another measured the thoracic and mid-thigh subcutaneous fat area of all participants. Inter-reader reproducibility was assessed by two independent readers measuring intra-abdominal, abdominal subcutaneous, thoracic subcutaneous and mid-thigh subcutaneous fat areas on a subset of 50 randomly selected participants. The intraclass correlation coefficients for inter-reader comparisons were 0.989 for IAFA, 0.999 for ASFA, 0.996 for thoracic subcutaneous fat area and 0.998 for mid-thigh subcutaneous fat area. In addition, the intraclass correlation coefficients for intra-reader comparisons was 0.999 for IAFA, 0.999 for ASFA, 0.994 for thoracic subcutaneous fat area and 0.999 for mid-thigh subcutaneous fat area.

Diagnosis of hypertension and type 2 diabetes

Hypertension was defined as systolic blood pressure $\geqslant$140 mm Hg, diastolic blood pressure $\geqslant$90 mm Hg or the use of antihypertensive medications.[28] High normal blood pressure was defined as no history of hypertension and systolic blood pressure $\geqslant$130 and $<$140 mm Hg or diastolic blood pressure $\geqslant$85 and $<$90 mm Hg.[28] Normotension was defined as no history of hypertension, systolic blood pressure $<$130 mm Hg and diastolic blood pressure $<$85 mm Hg.[28] Type 2 diabetes was defined as a fasting plasma glucose level $\geqslant$126 mg dl^{-1} or if participants were taking oral hypoglycemic medications or insulin.[29] Impaired fasting glucose was defined as no history of diabetes and a fasting plasma glucose level $\geqslant$110 and $<$126 mg dl^{-1}. Normal fasting glucose was defined as no history of diabetes and a fasting plasma glucose level $<$110 mg dl^{-1}.

Statistical analysis

Multiple logistic regression analysis was used to estimate the odds ratio for the prevalence of hypertension and of high normal blood pressure or hypertension. Nonlinear effects of continuous independent variables were evaluated using quadratic, square-root and log transformations. The presence of effect modification was tested by the insertion of first-order interaction terms into appropriate regression models. Multicollinearity was assessed by using the variance inflation factor.[30] A variance inflation factor exceeding 10 is regarded as indicating serious multicollinearity, and values $>$5.0 may be a cause for concern.[30] We calculated the 95% confidence interval for each odds ratio. All P-values were two-tailed. All statistical analyses were performed using the PASW Statistics 17.0 (SPSS, Chicago, IL, USA).

RESULTS

The characteristics of the study participants are shown in Table 1. Among the 624 eligible men, we confirmed 148 (24%) cases of hypertension and 137 (22%) cases of high normal blood pressure. Of all participants with hypertension, 66 (44.6%) were taking antihypertensive medications. Study participants on average were not obese with a mean body mass index of 24.0 kg m^{-2}. Participants with high normal blood pressure or hypertension had higher mean values of IAFA and ASFA than those with normotension (Table 1).

Table 1 Characteristics of study participants

Characteristics	*Total (n=624)*	*Normotension (n=339)*	*High normal blood pressure (n=137)*	*Hypertension (n=148)*
Age (years)	49.4 ± 9.0	47.4 ± 8.7	48.7 ± 8.7	54.9 ± 7.7
Metabolic variables				
Fasting immunoreactive insulin ($\mu U\,ml^{-1}$)	5.52 ± 3.53	4.91 ± 2.97	6.35 ± 4.04	6.13 ± 3.93
HOMA IR	1.45 ± 1.08	1.25 ± 0.82	1.69 ± 1.31	1.68 ± 1.27
Fasting plasma glucose ($mg\,dl^{-1}$)	103.6 ± 19.2	101.5 ± 19.6	105.0 ± 20.4	107.3 ± 16.4
Diabetes status				
Normal fasting glucose (%)	81.4	87.0	81.0	68.9
Impaired fasting glucose (%)	13.1	9.7	12.4	21.6
Type 2 diabetes (%)	5.4	3.2	6.6	9.5
Adipose variables				
Intra-abdominal fat area (cm^2)	80.7 ± 40.4	68.9 ± 36.9	86.0 ± 39.1	103.0 ± 39.2
Abdominal subcutaneous fat area (cm^2)	122.7 ± 55.0	116.0 ± 55.4	132.1 ± 55.2	129.3 ± 52.3
Total subcutaneous fat area (cm^2)	284.7 ± 108.7	274.0 ± 111.5	302.1 ± 109.4	293.3 ± 98.8
Total fat area (cm^2)	365.4 ± 135.3	342.7 ± 137.6	388.0 ± 134.7	396.3 ± 121.1
Body mass index ($kg\,m^{-2}$)	24.0 ± 3.1	23.4 ± 3.0	24.8 ± 3.1	24.7 ± 3.0
Waist circumference (cm)	86.0 ± 8.2	84.3 ± 8.2	87.3 ± 8.2	88.7 ± 7.1
Alcohol consumption (g ethanol per week)	213.7 ± 239.7	162.1 ± 194.3	244.7 ± 256.0	303.4 ± 284.4
Drinking habit (%)	82.7	79.6	84.7	87.8
Regular physical exercise (%)	47.4	45.1	46.0	54.1
Smoking habit				
Nonsmokers (%)	36.4	37.2	32.1	38.5
Past smokers (%)	20.7	16.2	24.8	27.0
Current smokers (%)	42.9	46.6	43.1	34.5

Abbreviation: HOMA IR, homeostasis model assessment-insulin resistance.
Data are mean ± s.d. or %.

We stratified participants according to median values of ASFA, TSFA, TFA, body mass index and waist circumference to examine the association between IAFA and the prevalence of hypertension and of high normal blood pressure or hypertension (Table 2). Greater visceral adiposity was associated with higher prevalence of hypertension in all groups (Table 2). On the other hand, after participants were stratified according to IAFA, no measure of ASFA, TSFA, TFA, body mass index or waist circumference was associated with a higher prevalence of hypertension stratified by IAFA tertiles (Table 2). Similar results were obtained for the prevalence of high normal blood pressure or hypertension (Table 2).

In multiple logistic regression analysis, insertion of quadratic, square-root or log transformations of all continuous variables except IAFA into all models did not result in an improvement in fit compared with the linear model. As only IAFA showed a nonlinear association with the prevalence of hypertension in all models, we fit a model by using IAFA categorized into tertiles to account for this nonlinearity (Tables 3 and 4). We examined the significance of the first-order interaction terms in all models of Table 3 between IAFA and the other adipose variables or fasting immunoreactive insulin. None of these interactions was significant. Correlation coefficients between IAFA and ASFA, TSFA, TFA, waist circumference or body mass index were 0.537, 0.554, 0.744, 0.642 and 0.748, respectively. Correlation coefficients between fasting immunoreactive insulin or HOMA IR and IAFA, ASFA, TSFA, TFA, waist circumference or body mass index were as follows: for fasting immunoreactive insulin they were 0.460, 0.482, 0.487, 0.529, 0.534 and 0.563, respectively, and for HOMA IR 0.459, 0.440, 0.444, 0.494, 0.512 and 0.529, respectively. Evidence for multicollinearity was absent because the variance inflation factor for independent variables in all models in Tables 3 and 4 was <4.0.

We tested several regression models to assess whether body fat distribution was associated with an increased odds of hypertension (Table 3). IAFA was associated with an increased odds of hypertension after adjusting for age, alcohol consumption, regular physical exercise and smoking habit (model 1, Table 3). IAFA was associated with an increased odds of hypertension even after adjusting for age, alcohol consumption, regular physical exercise, smoking habit, ASFA, fasting immunoreactive insulin and diabetes status (model 2, Table 3). Models 3–6 of Table 3 were identical to model 2, with the exception that a different adipose variable was substituted for ASFA. Model 7 was identical to model 2, with the exception that HOMA IR was substituted for fasting immunoreactive insulin. In all of these models, the relationships of IAFA to hypertension did not substantially change (models 1–7, Table 3). Also, neither other measures of regional or total adiposity nor insulin resistance indices emerged as significantly related to hypertension (models 1–7, Table 3).

We tested several regression models to assess whether body fat distribution was associated with an increased odds of high normal blood pressure or hypertension (Table 4). The results of the association between IAFA and high normal blood pressure or hypertension were similar to those between IAFA and hypertension (Table 4). Fasting immunoreactive insulin and HOMA IR were associated with a higher odds of high normal blood pressure or hypertension, but not hypertension (Tables 3 and 4).

Table 2 Prevalence of hypertension and of high normal blood pressure or hypertension according to intra-abdominal fat area, abdominal subcutaneous fat area, total subcutaneous fat area, total fat area, body mass index and waist circumference

	Intra-abdominal fat area (cm^2)			
	Tertile 1 (⩽61.28)	*Tertile 2 (61.29–93.69)*	*Tertile 3 (93.70⩽)*	*Total*
Prevalence of hypertension according to intra-abdominal fat area, abdominal subcutaneous fat area, total subcutaneous fat area, total fat area, body mass index and waist circumference				
Total	17/208 (11.5)	48/208 (32.4)	83/208 (56.1)	148/624 (23.7)
Abdominal subcutaneous fat area (cm^2)				
⩽114.20	14/168 (8.3)	20/90 (22.2)	31/55 (56.4)	65/313 (20.8)
>114.20	3/40 (7.5)	28/118 (23.7)	52/153 (34.0)	83/311 (26.7)
Total subcutaneous fat area (cm^2)				
⩽271.53	14/171 (8.2)	25/93 (26.9)	26/48 (54.2)	65/312 (20.8)
>271.53	3/37 (8.1)	23/115 (20.0)	57/160 (35.6)	83/312 (26.6)
Total fat area (cm^2)				
⩽358.12	15/185 (8.1)	25/100 (25.0)	14/27 (51.9)	54/312 (17.3)
>358.12	2/23 (8.7)	23/108 (21.3)	69/181 (38.1)	94/312 (30.1)
Body mass index ($kg\,m^{-2}$)				
⩽23.75	14/179 (7.8)	20/92 (21.7)	23/41 (56.1)	57/312 (18.3)
>23.75	3/29 (10.3)	28/116 (24.1)	60/167 (35.9)	91/312 (29.2)
Waist circumference (cm)				
⩽86.0	14/190 (7.4)	21/94 (22.3)	19/37 (51.4)	54/321 (16.8)
>86.0	3/18 (16.7)	27/114 (23.7)	64/171 (37.4)	94/303 (31.0)
Prevalence of high normal blood pressure or hypertension according to intra-abdominal fat area, abdominal subcutaneous fat area, total subcutaneous fat area, total fat area, body mass index and waist circumference				
Total	57/208 (27.4)	88/208 (42.3)	140/208 (67.3)	285/624 (45.7)
Abdominal subcutaneous fat area (cm^2)				
⩽114.20	46/168 (27.4)	39/90 (43.3)	42/55 (76.4)	127/313 (40.6)
>114.20	11/40 (27.5)	49/118 (41.5)	98/153 (64.1)	158/311 (50.8)
Total subcutaneous fat area (cm^2)				
⩽271.53	49/171 (28.7)	43/93 (46.2)	35/48 (72.9)	127/312 (40.7)
>271.53	8/37 (21.6)	45/115 (39.1)	105/160 (65.6)	158/312 (50.6)
Total fat area (cm^2)				
⩽358.12	52/185 (28.1)	46/100 (46.0)	21/27 (77.8)	119/312 (38.1)
>358.12	5/23 (21.7)	42/108 (38.9)	119/181 (65.7)	166/312 (53.2)
Body mass index ($kg\,m^{-2}$)				
⩽23.75	47/179 (26.3)	38/92 (41.3)	29/41 (70.7)	114/312 (36.5)
>23.75	10/29 (34.5)	50/116 (43.1)	111/167 (66.5)	171/312 (54.8)
Waist circumference (cm)				
⩽86.0	50/190 (26.3)	41/94 (43.6)	27/37 (73.0)	118/321 (36.8)
>86.0	7/18 (38.9)	47/114 (41.2)	113/171 (66.1)	167/303 (55.1)

Data are *n* (%).

DISCUSSION

These cross-sectional data demonstrated that greater visceral adiposity was associated with an increased odds of the prevalence of hypertension in Japanese men. These findings were independent of age, fasting immunoreactive insulin, diabetes status, alcohol consumption, regular physical exercise, smoking habit and other measures of regional or total adiposity. On the other hand, no other measure of regional or total adiposity was associated with an increased odds of the prevalence of hypertension after adjusting for IAFA. Similar results were obtained for the association between IAFA and the prevalence of high normal blood pressure or hypertension.

Table 3 Multivariable models of prevalence of hypertension in relation to intra-abdominal fat area, other adipose depots and insulin resistance indices

Variables in the models	*Multiple-adjusted odds ratios (95% CI)*	P-*value*	*Further adjustment for fasting insulin or HOMA IR, odds ratios (95% CI)*	P-*value*
Model 1[a]				
Intra-abdominal fat area				
Tertile 1 (−61.28)	1.00 (reference)		—	—
Tertile 2 (61.29–93.69)	2.73 (1.46–5.10)	0.002	—	—
Tertile 3 (93.70–)	5.50 (3.01–10.05)	<0.001	—	—
Model 2[b]				
Intra-abdominal fat area				
Tertile 1 (−61.28)	1.00 (reference)		1.00 (reference)	
Tertile 2 (61.29–93.69)	2.68 (1.38–5.23)	0.004	2.64 (1.35–5.16)	0.004
Tertile 3 (93.70–)	5.28 (2.61–10.68)	<0.001	5.08 (2.48–10.39)	<0.001
Abdominal subcutaneous fat area	0.99 (0.76–1.29)	0.934	0.96 (0.73–1.27)	0.787
Fasting immunoreactive insulin	—	—	1.08 (0.85–1.38)	0.522
Diabetes status				
Normal fasting glucose	1.00 (reference)		1.00 (reference)	
Impaired fasting glucose	1.21 (0.68–2.13)	0.514	1.15 (0.64–2.08)	0.634
Type 2 diabetes	1.28 (0.56–2.91)	0.564	1.20 (0.51–2.80)	0.678
Model 3: same variables as model 2, except total subcutaneous fat area is substituted for abdominal subcutaneous fat area[c]				
Intra-abdominal fat area				
Tertile 1 (−61.28)	1.00 (reference)		1.00 (reference)	
Tertile 2 (61.29–93.69)	2.90 (1.48–5.66)	0.002	2.84 (1.45–5.57)	0.002
Tertile 3 (93.70–)	5.97 (2.90–12.28)	<0.001	5.69 (2.74–11.83)	<0.001
Total subcutaneous fat area	0.90 (0.69–1.19)	0.475	0.87 (0.65–1.17)	0.355
Fasting immunoreactive insulin	—	—	1.11 (0.87–1.42)	0.403
Model 4: same variables as model 2, except total fat area is substituted for abdominal subcutaneous fat area[c]				
Intra-abdominal fat area				
Tertile 1 (−61.28)	1.00 (reference)		1.00 (reference)	
Tertile 2 (61.29–93.69)	2.86 (1.43–5.73)	0.003	2.84 (1.42–5.71)	0.003
Tertile 3 (93.70–)	5.94 (2.62–13.47)	<0.001	5.83 (2.56–13.28)	<0.001
Total fat area	0.93 (0.68–1.27)	0.632	0.89 (0.64–1.24)	0.483
Fasting immunoreactive insulin	—	—	1.10 (0.86–1.41)	0.434
Model 5: same variables as model 2, except body mass index is substituted for abdominal subcutaneous fat area[c]				
Intra-abdominal fat area				
Tertile 1 (−61.28)	1.00 (reference)		1.00 (reference)	
Tertile 2 (61.29–93.69)	2.76 (1.41–5.41)	0.003	2.74 (1.40–5.38)	0.003
Tertile 3 (93.70–)	5.54 (2.66–11.54)	<0.001	5.41 (2.58–11.32)	<0.001
Body mass index	0.96 (0.73–1.26)	0.761	0.91 (0.68–1.23)	0.555
Fasting immunoreactive insulin	—	—	1.11 (0.86–1.43)	0.439
Model 6: same variables as model 2, except waist circumference is substituted for abdominal subcutaneous fat area[c]				
Intra-abdominal fat area				
Tertile 1 (−61.28)	1.00 (reference)		1.00 (reference)	
Tertile 2 (61.29–93.69)	2.76 (1.38–5.56)	0.004	2.77 (1.37–5.56)	0.004
Tertile 3 (93.70–)	5.54 (2.52–12.19)	<0.001	5.46 (2.48–12.06)	<0.001
Waist circumference	0.96 (0.71–1.31)	0.802	0.92 (0.66–1.28)	0.617
Fasting immunoreactive insulin	—	—	1.10 (0.85–1.41)	0.466
Model 7: same variables as model 2, except HOMA IR is substituted for fasting immunoreactive insulin[d]				
Intra-abdominal fat area				
Tertile 1 (−61.28)	—	—	1.00 (reference)	
Tertile 2 (61.29–93.69)	—	—	2.67 (1.37–5.21)	0.004
Tertile 3 (93.70–)	—	—	5.22 (2.56–10.62)	<0.001
Abdominal subcutaneous fat area	—	—	0.98 (0.74–1.29)	0.873
HOMA IR	—	—	1.03 (0.80–1.33)	0.793

Abbreviations: CI, confidence interval; HOMA IR, homeostasis model assessment-insulin resistance.
Odds ratios for continuous variables reflect a 1-SD-magnitude increase.
[a]Model 1 was adjusted for age, alcohol consumption, regular physical exercise and smoking habit (nonsmokers, past smokers and current smokers).
[b]Model 2 includes age, alcohol consumption, regular physical exercise and smoking habit (nonsmokers, past smokers and current smokers) in addition to all variables shown in model 2 of the Table 3.
[c]Models 3–6 were identical to model 2, with the exception that a different adipose variable was substituted for abdominal subcutaneous fat area.
[d]Model 7 was identical to model 2, with the exception that HOMA IR was substituted for fasting immunoreactive insulin.

Table 4 Multivariable models of high normal blood pressure or hypertension in relation to intra-abdominal fat area, other adipose depots and insulin resistance indices

Variables in the models	*Multiple-adjusted odds ratios (95% CI)*	P-*value*	*Further adjustment for fasting insulin or HOMA IR, odds ratios (95% CI)*	P-*value*
Model 1[a]				
Intra-abdominal fat area				
Tertile 1 (−61.28)	1.00 (reference)		—	—
Tertile 2 (61.29–93.69)	1.71 (1.11–2.64)	0.016	—	—
Tertile 3 (93.70–)	4.48 (2.87–7.00)	<0.001	—	—
Model 2[b]				
Intra-abdominal fat area				
Tertile 1 (−61.28)	1.00 (reference)		1.00 (reference)	
Tertile 2 (61.29–93.69)	1.50 (0.93–2.44)	0.100	1.41 (0.86–2.30)	0.170
Tertile 3 (93.70–)	3.70 (2.14–6.42)	<0.001	3.20 (1.82–5.61)	<0.001
Abdominal subcutaneous fat area	1.12 (0.90–1.40)	0.305	1.01 (0.80–1.28)	0.934
Fasting immunoreactive insulin	—	—	1.37 (1.09–1.71)	0.007
Diabetes status				
Normal fasting glucose	1.00 (reference)		1.00 (reference)	
Impaired fasting glucose	1.04 (0.61–1.79)	0.878	0.90 (0.52–1.57)	0.707
Type 2 diabetes	1.76 (0.77–4.01)	0.181	1.46 (0.62–3.43)	0.382
Model 3: same variables as model 2, except total subcutaneous fat area is substituted for abdominal subcutaneous fat area[c]				
Intra-abdominal fat area				
Tertile 1 (−61.28)	1.00 (reference)		1.00 (reference)	
Tertile 2 (61.29–93.69)	1.62 (1.00–2.64)	0.051	1.52 (0.93–2.48)	0.097
Tertile 3 (93.70–)	4.13 (2.35–7.29)	<0.001	3.57 (2.01–6.36)	<0.001
Total subcutaneous fat area	1.04 (0.83–1.30)	0.763	0.92 (0.72–1.17)	0.492
Fasting immunoreactive insulin	—	—	1.41 (1.12-1.77)	0.003
Model 4: same variables as model 2, except total fat area is substituted for abdominal subcutaneous fat area[c]				
Intra-abdominal fat area				
Tertile 1 (−61.28)	1.00 (reference)		1.00 (reference)	
Tertile 2 (61.29–93.69)	1.58 (0.94–2.64)	0.082	1.53 (0.91–2.57)	0.106
Tertile 3 (93.70–)	3.91 (2.03–7.54)	<0.001	3.69 (1.90–7.15)	<0.001
Total fat area	1.06 (0.82–1.38)	0.658	0.92 (0.70–1.21)	0.548
Fasting immunoreactive insulin	—	—	1.40 (1.12–1.77)	0.004
Model 5: same variables as model 2, except body mass index is substituted for abdominal subcutaneous fat area[c]				
Intra-abdominal fat area				
Tertile 1 (−61.28)	1.00 (reference)		1.00 (reference)	
Tertile 2 (61.29–93.69)	1.32 (0.81-2.16)	0.270	1.29 (0.79–2.12)	0.308
Tertile 3 (93.70–)	2.94 (1.65-5.24)	<0.001	2.78 (1.55–4.97)	0.001
Body mass index	1.29 (1.02-1.63)	0.032	1.14 (0.88–1.47)	0.326
Fasting immunoreactive insulin	—	—	1.30 (1.03–1.65)	0.029
Model 6: same variables as model 2, except waist circumference is substituted for abdominal subcutaneous fat area[c]				
Intra-abdominal fat area				
Tertile 1 (−61.28)	1.00 (reference)		1.00 (reference)	
Tertile 2 (61.29–93.69)	1.51 (0.90–2.53)	0.119	1.49 (0.89–2.51)	0.134
Tertile 3 (93.70–)	3.68 (1.96–6.90)	<0.001	3.47 (1.84–6.54)	<0.001
Waist circumference	1.10 (0.86–1.42)	0.448	0.95 (0.72–1.25)	0.718
Fasting immunoreactive insulin	—	—	1.39 (1.10–1.75)	0.005
Model 7: same variables as model 2, except HOMA IR is substituted for fasting immunoreactive insulin[d]				
Intra-abdominal fat area				
Tertile 1 (−61.28)	—	—	1.00 (reference)	
Tertile 2 (61.29–93.69)	—	—	1.43 (0.87–2.33)	0.157
Tertile 3 (93.70–)	—	—	3.25 (1.85–5.70)	<0.001
Abdominal subcutaneous fat area	—	—	1.02 (0.81–1.29)	0.872
HOMA IR	—	—	1.39 (1.07–1.79)	0.014

Abbreviations: CI, confidence interval; HOMA IR, homeostasis model assessment-insulin resistance.
Odds ratios for continuous variables reflect a 1-SD-magnitude increase.
[a]Model 1 was adjusted for age, alcohol consumption, regular physical exercise and smoking habit (nonsmokers, past smokers and current smokers).
[b]Model 2 includes age, alcohol consumption, regular physical exercise and smoking habit (nonsmokers, past smokers and current smokers) in addition to all variables shown in model 2 of the Table 4.
[c]Models 3 to 6 were identical to model 2, with the exception that a different adipose variable was substituted for abdominal subcutaneous fat area.
[d]Model 7 was identical to model 2, with the exception that HOMA IR was substituted for fasting immunoreactive insulin.

Only limited cross-sectional studies and only one prospective study have investigated associations between CT-measured visceral adiposity and hypertension.[13,14,16,17] In 1995, it was reported in the Japanese Americans Community Diabetes Study that the effects of visceral adiposity on blood pressure were of statistical or borderline statistical significance in both second- and third-generation Japanese Americans, but after further adjustment for body mass index, these associations were diminished in the younger generation.[31] In 2003, it was reported in cross-sectional data from the same population that greater visceral adiposity was associated with a higher prevalence of hypertension independent of other measures of total or regional adiposity and fasting plasma insulin.[13] The reason for these different results was described to be partly because of the fact that in the earlier report, participants taking antihypertensive medication or having type 2 diabetes were not included, which by possibly truncating the upper range for blood pressure may have underestimated these relationships.[13,14] A subsequent prospective analysis from the same cohort showed that greater IAFA, but not ASFA, was associated with the incidence of hypertension after adjustment for fasting plasma insulin.[14] Fox *et al.*[16] showed in the Framingham Heart Study that among Caucasians, both visceral and abdominal subcutaneous fat volumes were associated with prevalence of hypertension. They did not report whether visceral fat volume was associated with the prevalence of hypertension independent of abdominal subcutaneous fat volume and fasting plasma insulin. On the other hand, Foy *et al.*[17] reported in the Insulin Resistance Atherosclerosis Study that among African-American and Hispanic-American men, ASFA, but not IAFA, was significantly associated with the prevalence of hypertension. Our findings of greater visceral adiposity associated with an increased odds of the prevalence of hypertension independent of ASFA and insulin resistance in native Japanese men were consistent with previous reports in Japanese Americans.[13,14] Differences in body composition by ethnicity might have a key role in explaining the inconsistent results in the literature on the association between intra-abdominal fat and hypertension. Asians and Asian Americans have been reported to have a lower prevalence of obesity by body mass index compared with Caucasians or African Americans but have greater visceral adiposity at the same body mass index or waist circumference level as Caucasians or African Americans.[19–21,32,33]

In this study, ASFA was not associated with an increased odds of the prevalence of hypertension in the models that included both IAFA and insulin resistance. This finding was consistent with previous reports in Japanese Americans.[13,14] Although Oka *et al.*[18] showed in native Japanese that both intra-abdominal fat and ASFA were independently correlated with systolic and diastolic blood pressure, they did not control for confounders such as insulin resistance.

There are several possible mechanisms that may explain the relationship between visceral adipose tissue and prevalence of high blood pressure. This pathophysiological link may be partly mediated by insulin resistance.[34–37] In this study, as the association between visceral adiposity and hypertension was independent of insulin resistance, visceral adiposity may affect hypertension through mechanisms unrelated to fasting plasma insulin.

Increasing evidence has suggested that adipocyte-derived substances, such as tumor necrosis factor-α, plasminogen-activator inhibitor type 1 or adiponectin, are involved in the development of hypertension.[38–40] Visceral fat has been reported to have a more important role in producing some of these substances than subcutaneous fat.[41–43] Therefore, adipocyte-derived circulating factors may be involved in part in the pathogenesis of high blood pressure associated with visceral adiposity. The role of visceral adiposity in the pathogenesis of hypertension requires further investigation.

Our study has several limitations. First, we cannot draw conclusions about cause-and-effect relationships because of the cross-sectional nature of our data. Second, we adjusted our analysis for multiple potential confounding variables, including age, fasting immunoreactive insulin, diabetes status, measures of regional and total adiposity, alcohol consumption, regular physical exercise, and smoking habit. However, other unknown or unmeasured confounding variables might explain the relationship of visceral adiposity to high blood pressure for which we did not account. Third, we used a limited single-slice visceral fat area at the umbilicus level to estimate total visceral fat volume. However, this measurement has been reported to have a high correlation with directly ascertained total visceral fat volume.[24–26] Fourth because we studied a single ethnic group of men, our results may not apply to the general population but may apply to Japanese-American men and also possibly other Asian-American and native Asian men. Fifth, anti-hypertensive medication might have some effect on the association between visceral adiposity and the prevalence of hypertension. However, even if some anti-hypertensive medications decreased visceral fat area, results from our study would underestimate the association between visceral adiposity and the prevalence of hypertension.

In conclusion, these results provide evidence that greater visceral adiposity is associated with an increased odds of high blood pressure in Japanese men. This association is independent of ASFA and insulin resistance. The mechanism by which visceral fat may increase the odds of high blood pressure remains to be determined. Further prospective research is warranted to explore the relationship of visceral fat accumulation to the risk of incident high blood pressure in Japanese.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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