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Impact of Adiposity on Incident Hypertension Is Modified by Insulin Resistance in Adults: Longitudinal Observation from the Bogalusa Heart Study

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Abstract

Adiposity and insulin-resistance are closely associated with hypertension. This study aims to investigate whether the association between adiposity and hypertension is modified by insulin resistance. The cohort consisted of 1,624 middle-aged normotensive black and white adults aged 18 to 43 years at baseline who followed for 16 years on average. Overweight/obesity at baseline was defined as BMI ≥ 25 , and insulin resistance was measured using homeostasis model assessment of insulin resistance (HOMA). Prevalence of incident hypertension was compared between the insulin-sensitive adiposity and insulin-resistant adiposity groups. The prevalence of incident hypertension was higher in the insulin-resistant adiposity than in the insulin-sensitive adiposity group (32.1% vs 22.1%, $p < 0.001$). In multivariable logistic analyses, adjusted for baseline age, race, gender, follow-up years, and smoking, baseline insulin-resistant obesity was associated with incident hypertension (odds ratio, OR=1.9, $p = 0.008$). ORs did not differ between blacks and whites ($p = 0.238$). Of note, the ORs of BMI associated with hypertension significantly increased with increasing quartiles of baseline HOMA (OR=1.3, 1.1, 1.5, and 2.5 in quartiles I, II, III, and IV, respectively, $p = 0.006$ for trend). Slopes of increasing follow-up blood pressure (BP) with baseline BMI, measured as regression coefficients (β), were significantly greater in insulin-resistant than in insulin-sensitive individuals ($\beta = 0.60$ vs $\beta = 0.33$ for systolic BP, $p = 0.039$ for

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DISCLOSURE(S) STATEMENT

None

difference; $\beta=0.41$ vs $\beta=0.20$ for diastolic BP, $p=0.019$ for difference). These findings suggest that insulin-resistance has a synergistic effect on the obesity-hypertension association in young adults, indicating that the role of adiposity in the development of hypertension is modified by insulin resistance.

Keywords

blood pressure; insulin sensitive; adiposity; longitudinal study; interaction

INTRODUCTION

The association between adiposity and hypertension has been well established in observational studies,¹⁻³ and intervention studies have also showed that weight loss can lower blood pressure (BP) in obese hypertensives.⁴ In United States, the prevalence of hypertension in obese adults is 40.8%.⁵ The comorbidities of adiposity and hypertension significantly increase the probability of adverse cardiovascular events and represent a serious health hazard nationwide.⁶ Existing evidence suggests that the presence of these comorbidities varies widely in the obese population. A distinct subgroup of obese individuals, known as metabolically healthy obesity, is considered less prone to develop metabolic abnormalities than expected for their adiposity.^{7, 8} Studies have demonstrated that the consistent metabolic characteristics of these metabolically healthy obese individuals was the preserved insulin sensitivity status.^{9, 10}

Insulin resistance or diminished insulin sensitivity, as a core feature of metabolic syndrome, is closely associated with obesity, hypertension, dyslipidemia, and hyperglycemia.¹¹ Although obese individuals are significantly more insulin resistant than their lean counterparts¹², there are also 31.7% of obese adults (about 19.5 million people) being insulin-sensitive.¹³ It has been proposed that the association between obesity and metabolic disorders is more than merely a dose-response relationship.^{7, 14, 15} Insulin resistance is considered a key link for the association of obesity with type 2 diabetes, hypertension and cardiovascular disease. Furthermore, longitudinal studies have shown that insulin-sensitive obese individuals may have relatively lower risk of type 2 diabetes and cardiovascular disease.¹⁶⁻¹⁹ In addition, there is evidence showing that the presence of metabolic disorders varies widely among obese individuals as a function of differences in the degree of insulin sensitivity.^{14, 20}

Compensatory hyperinsulinemia seen in insulin resistance has been suggested to play a causal role in development of hypertension by activating sympathetic nervous system and causing sodium retention.^{21, 22} On the other hand, some human and animal studies suggest that insulin resistance might not be directly involved in the pathogenesis of hypertension.^{21, 23-26} Despite extensive observations on insulin-resistant and sensitive obesity, it is not clear whether the role of adiposity in the development of hypertension is modified by insulin resistance. In the current study, we aimed to assess the hypothesis that insulin-sensitive obesity is associated with a relatively lower risk of hypertension than

insulin-resistant obesity, and the adiposity-hypertension association is modified by insulin resistance.

MATERIALS AND METHODS

Study cohort

The Bogalusa Heart Study is a series of long-term studies in a semi-rural biracial (65% white and 35% black) community in Bogalusa, Louisiana begun in 1973 by Dr. Gerald Berenson, focusing on the early natural history of cardiovascular disease since childhood²⁷. Ten cross-sectional surveys of adults ages 18 to 52 years who had been previously examined as children were conducted in Bogalusa, Louisiana between 1980 and 2010. Linking these repeated cross-sectional examinations conducted every 2–3 years has resulted in serial observations. The longitudinal cohort of this study consisted of 1,624 middle-aged normotensive adults (1,148 whites and 476 blacks, ages 18.0 to 43.5 years at baseline) enrolled in the Bogalusa Heart Study. These subjects were examined 2 times at baseline and follow-up for BMI, fasting glucose and insulin, and BP during adulthood, with an average follow-up period of 16.0 years (range=5.0~31.2 years).

All subjects in this study gave informed consent at each examination. Study protocols were approved by the Institutional Review Board of the Tulane University Health Sciences Center.

General examinations

Standardized protocols were used by trained examiners across all surveys since 1973.²⁷ Subjects were instructed to fast for 12 hours before screening. Replicate measurements of height and weight were made, and the mean values were used for analysis. Body mass index (BMI, weight in kilograms divided by the square of the height in meters) was used as a measure of overall adiposity. Waist circumference (WC) was measured midway between the lowest border of rib cage and the upper border of iliac crest while the child was standing. Information on smoking status was obtained by questionnaires. Those who smoked 1 cigarette per day during the past 12 months were considered current smokers.

Blood pressure levels were measured between 8:00 AM and 10:00 AM on the right arm of subjects in a relaxed, sitting position by 2 trained observers (3 replicates each). Systolic (SBP) and diastolic (DBP) blood pressure was recorded using a mercury sphygmomanometer. The fifth Korotkoff phase was used for DBP. The mean values of the 6 readings were used for analysis. Hypertension was defined as SBP 140 mmHg or DBP 90 mmHg or taking antihypertensive medications at the time of survey.

A commercial radioimmunoassay kit was used for measuring plasma immunoreactive insulin levels (Phadebas; Pharmacia Diagnostics, Piscataway, NJ). Plasma glucose levels were measured as part of a multiple chemistry profile (SMA20; Laboratory Corporation of America, Burlington, NC) by a glucose oxidase method. Insulin resistance status was assessed using the homeostasis model assessment of insulin-resistance (HOMA) according to the formula described previously: $HOMA = \text{insulin } (\mu\text{U/mL}) \times \text{glucose (mmol/L)} / 22.5$.²⁸

Statistical methods

All statistical analyses were performed with SAS version 9.3 (SAS Institute, Cary, NC). Adiposity at baseline was defined as BMI ≥ 25 and insulin resistance as HOMA $> 55^{\text{th}}$ percentile, with 10% of baseline HOMA in the middle (46th–55th percentile) excluded to make groups more distinct. The remaining cohort was accordingly divided into 4 groups: group I (BMI $\downarrow$ /HOMA $\downarrow$), group II (BMI $\downarrow$ /HOMA $\uparrow$), group III (BMI $\uparrow$ /HOMA $\downarrow$), and group IV (BMI $\uparrow$ /HOMA $\uparrow$). The prevalence of incident hypertension at follow-up was compared between the baseline insulin-sensitive obese (group III, n=149) and insulin-resistant obese groups (group IV, n=383). The 4 groups were also classified by low and high levels of baseline WC defined as below and above gender-specific-64th percentile of WC (86.6 cm for males and 76.3 cm for females), respectively. The reason for choosing this cut-off value was based on the prevalence (36%) of overweight/obesity (BMI ≥ 25) in this study cohort of young adults at baseline. Analyses of covariance were performed using general linear models (GLM) to test differences in study variables between race, gender and adiposity groups. Multivariable logistic regression models were used to examine the association between adiposity groups and hypertension as dichotomous variables, adjusted for baseline age, race, gender, and follow-up years. The modification effect of insulin resistance on the association between BMI and hypertension (or levels of BP) was examined by multivariable logistic (or linear) regression interaction models using the entire sample. Because the wide range of follow-up time might have an impact on odds ratios for the association between adiposity/insulin-resistance and hypertension, logistic regression models were performed by tertile groups of follow-up years to test the heterogeneity of the association parameters among subgroups.

RESULTS

Mean levels of study variables at baseline and follow-up by race and gender are summarized in Table 1. Baseline BMI, WC, heart rate and glucose showed significant race and gender differences except for race difference in glucose in females and heart rate in males; black females had significantly higher insulin and HOMA than white females. There were significant race differences in follow-up BMI, WC, glucose, insulin and HOMA (blacks>whites) in females. Follow-up BP showed significant gender (males>females) and race differences (blacks>whites); follow-up heart rate had a significant gender difference (females>males). After a 16-year follow-up on average, 320 (19.7%) incident hypertension patients were observed, with prevalence of hypertension at follow-up being higher in blacks than in whites (31.0% vs 15.0%, $p<0.001$). After adjusting for age, race, and gender, baseline heart rate was significantly correlated with baseline insulin ($r=0.053$, $p=0.034$), baseline SBP ($r=0.118$, $p<0.001$) and baseline DBP ($r=0.143$, $p<0.001$). Baseline heart rate was significantly correlated with follow-up HOMA ($r=0.087$, $p=0.001$), follow-up DBP ($r=0.059$, $p=0.017$), marginally correlated with follow-up insulin ($r=0.051$, $p=0.055$), but not correlated with follow-up SBP ($r=0.029$, $p=0.249$), with additional adjustment for follow-up years. Baseline heart rate was not significantly correlated with BMI and WC at both baseline and follow-up.

Figure 1 presents odds ratio (OR) and 95% confidence interval (CI) of baseline BMI, WC, glucose, insulin and HOMA for incident hypertension by race and in total sample, adjusted for age, gender, follow-up years and race (for the total sample). Baseline BMI, WC, glucose, insulin (log-transformed) and HOMA (log-transformed) were significantly associated with incident hypertension at follow-up in the total sample. ORs did not differ significantly between blacks and whites.

Table 2 shows mean levels of study variables in 4 groups classified according to levels of baseline BMI and HOMA, with 10% of baseline HOMA values around the median value excluded. The remaining cohort was divided into four groups as shown in Table 2. Among overweight/obese individuals based on baseline BMI ≥ 25 , the insulin-resistant obese group (group IV) had significantly higher levels of BMI, glucose, insulin, HOMA and BP at follow-up than the insulin-sensitive obese group (group III), adjusted for baseline age, race, gender, and follow-up years. Notably, the prevalence of incident hypertension at follow-up was significantly higher in the insulin-resistant obese group than in the insulin-sensitive obese group (32.1% vs. 22.1%, $p < 0.001$).

Table 3 shows the association between baseline insulin-resistant adiposity (group IV) and hypertension at follow-up, using insulin-sensitive adiposity (group III) as a reference. Individuals with baseline insulin-resistant adiposity were 1.9 times ($p = 0.008$) more likely to have hypertension than those with baseline insulin-sensitive adiposity, after adjustment for baseline age, race, gender, smoking and follow-up years. The ORs did not differ significantly between whites ($OR = 2.50$, $p = 0.008$) and blacks ($OR = 1.41$, $p = 0.335$), with $p = 0.238$ for race difference in ORs. Since the follow-up period of study subjects ranged from 5.0 to 31.2 years, logistic regression models were performed by tertile groups of follow-up years to test the heterogeneity of ORs among 3 subgroups. The follow-up year range was 5.0–11.7 years in tertile I, 11.8–19.7 years in tertile II and 19.8–31.2 years in tertile III. The ORs (95% CIs) were 1.86 (0.80–4.72), 2.18 (1.02–4.88) and 3.44 (1.26–10.46) in tertile I, II and III groups, respectively. The ORs did not differ significantly between groups based on their 95% CIs.

Figure 2 shows standardized ORs for the association of baseline BMI with incident hypertension by baseline HOMA quartiles in the total sample. After adjusting for covariates mentioned above, the OR values for the association of baseline BMI with hypertension significantly increased across increasing quartiles of baseline HOMA ($OR = 1.28$, 1.12, 1.45, and 2.45 in HOMA quartiles I, II, III, and IV, respectively, $p = 0.006$ for trend).

As shown in Figure 3, slopes of increasing follow-up BP levels with increasing baseline BMI, measured as regression coefficients (β), were significantly greater in the insulin-resistant group than in the insulin-sensitive group ($\beta = 0.74$ vs $\beta = 0.35$ for SBP, $p = 0.011$ for difference in slopes; $\beta = 0.51$ vs $\beta = 0.23$ for DBP, $p = 0.014$ for difference in slopes).

Insulin-sensitive and insulin-resistant adiposity groups were also classified according to levels of baseline WC and HOMA as shown in Supplement Table S1. The prevalence of incident hypertension at follow-up in group IV was significantly higher than in group III (32.7% vs. 21.1%, $p = 0.004$), which was similar to the prevalence in Table 2. The association

parameters using groups III and IV defined by WC in Supplement Table S2 were very close to those as shown in Table 3. Furthermore, the interaction effects of baseline WC with HOMA on hypertension and BP levels at follow-up (data not shown) were substantially similar to the interaction effects as shown in Figures 2 and 3.

DISCUSSION

It is almost indisputable that adiposity is one of the most important risk factors related to the development of hypertension.^{1–4, 29} Although adiposity and insulin resistance are highly correlated, the causal role of insulin resistance in the development of hypertension continues to be debated.^{21, 23–26} The Bogalusa Heart Study has reported that childhood BMI and insulin predict adulthood levels of blood pressure, with BMI being more predictive than insulin.^{30–32} However, previous data did not examine whether insulin resistance modifies the relationship between adiposity and hypertension. In this prospective cohort study, we confirmed the hypothesis that individuals with insulin-resistant adiposity were more likely to develop hypertension than those with insulin-sensitive adiposity. This study provides strong evidence that effect of adiposity on the development of hypertension is modified by insulin resistance in middle-aged adults.

A subset of obese individuals who are characterized by higher insulin sensitivity are often described as metabolically healthy obese, and insulin sensitive adiposity may protect individuals to some extent against obesity-related metabolic complications.^{7, 8} Genellu and colleagues have shown that the risk of developing hypertension, type 2 diabetes, and cardiovascular disease is accentuated in obese individuals with insulin resistance in a population of Brazilians.⁹ A cross-sectional study showed that insulin-sensitive obese children had significantly lower levels of BP compared to their insulin resistant peers.¹⁰ Ikeda et al reported a distinct relation between improvement of insulin sensitivity and a decrease in BP after weight loss in obese hypertensive subjects.³³ Furthermore, Lim et al found that the elevation of BP in high-fat-fed rabbits is moderately mediated by central actions of insulin.³⁴ However, some previous studies did not support the notion that overweight/obesity with insulin sensitivity are benign conditions.³⁵ In the present study, we found that individuals with insulin-resistant obesity at baseline were 1.9 times more likely to have hypertension 16 years later on average than those with insulin-sensitive obesity, and the strength of the association significantly increased across increasing baseline HOMA levels in terms of obesity defined by both BMI and WC. The observations from this study expand previous findings by demonstrating that the relationship between adiposity and hypertension is modified by insulin resistance. The modification effect of insulin resistance on the adiposity-hypertension association noted in this study is to some extent in agreement with observations from the Swedish Obese Subjects (SOS) trial - a prospective controlled intervention study of bariatric surgery. The findings of the SOS study have clearly demonstrated that the beneficial effect of the surgical treatment on future outcomes, including overall mortality, myocardial infarction, stroke, diabetes and cancer, is associated with improvement in baseline insulin resistance but not with baseline BMI.³⁶ The effect of bariatric surgery on diabetes is influenced by the presence or absence of impaired fasting glucose but not by BMI.³⁷

In the present study, it is found that blacks had higher HOMA than whites in females at both baseline and follow-up. However, the strength of the association of baseline BMI and WC with follow-up hypertension across levels of baseline HOMA did not differ between races. To the best of our knowledge, this is the first longitudinal cohort study to examine the interplay of adiposity and insulin resistance on the development of hypertension in the black and white population. Our data indicated that insulin resistance amplified the association between adiposity and hypertension equally in both races. These observations in black-white race groups need to be confirmed and replicated in other population studies.

There are several putative mechanisms linking adiposity and insulin-resistance to hypertension. Obesity is associated with dietary excess or some diminished capacity for thermogenesis (a low metabolic rate) and results in insulin resistance. Our previous studies have found temporal nature of the relation from obesity to insulin resistance during childhood and adulthood.³⁸ Obesity and insulin resistance may jointly increase sympathetic nervous system activity which is subsequently involved in the pathogenesis of obesity-related hypertension.³⁹ The significant, positive correlations of baseline heart rate, a marker of sympathetic nervous system tone, with insulin and BP at both baseline and follow-up found in this study provided further evidence to support this concept. Second, insulin may enhance sodium retention by directly increasing sodium reabsorption in renal tubules and indirectly through the activation of the renin-angiotensin system and sympathetic nervous system.⁴⁰ Studies have suggested that insulin resistance activates the renin-angiotensin system by increasing expression of angiotensinogen, angiotensin I and II receptor, which may contribute to the development of hypertension in patients with insulin resistance.⁴¹ It has been recently discovered that adipocytes produce aldosterone in response to angiotensin II.⁴² There is also evidence that insulin resistance activates the sympathetic nervous system, increases kidney sodium reabsorption, heart cardiac output and vasoconstriction and finally leads to elevated BP levels.⁴³ Third, obese individuals with insulin-resistance might have additional predisposing factors as compared to insulin-sensitive obese individuals, for example higher lipid deposition in intramyocellular and visceral compartments and lower adiponectin levels.^{44, 45} Under such conditions, insulin resistance may amplify the adverse effect of obesity on the development of hypertension.

This community-based, longitudinal cohort provided a unique opportunity to test the effect of insulin resistance on the obesity-hypertension association in adulthood. The present study has some limitations. First, it seems broad to categorize baseline insulin resistance as top 45th percentile of baseline HOMA. The relatively small sample size with limited statistical power was the primary consideration for the selection of the cut-off value. In sensitivity analyses using a cut-off value of top 25th percentile of HOMA, ORs still remained significant. Second, the follow-up period of the study subjects varied from 5.0 to 31.2 years. The wide range of follow-up time might have an influence on the obesity/insulin resistance-hypertension association. For this reason, the number of follow-up years was included in all logistic models for adjustment in the current analysis. Moreover, we conducted additional association analyses by tertile groups of follow-up year and did not find a significant difference in ORs among 3 subgroups.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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ABBREVIATIONS

BMI	body mass index
WC	waist circumference
HOMA	homeostasis model assessment of insulin resistance
BP	blood pressure
SBP	systolic blood pressure
DBP	diastolic blood pressure
OR	odds ratio
CI	confidence interval
SD	standard deviation

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PERSPECTIVES

The current study demonstrates that insulin-resistant obesity is associated with increased risk of hypertension as compared to insulin-sensitive adiposity, and the obesity-hypertension association is strengthened by the presence of insulin resistance. These results support the notion that that insulin resistance has a synergistic effect on the obesity-hypertension association in middle-aged adults. The findings underscore the importance of controlling both obesity and insulin resistance to prevent the future development of hypertension.

NOVELTY AND SIGNIFICANCE

What Is New?

- Baseline insulin-resistant obesity of young adults is associated with incident hypertension 16 years later in a longitudinal cohort.
- The effect of obesity on hypertension is amplified by insulin resistance measured as homeostasis model assessment.

What Is Relevant?

- Insulin resistance has a synergistic effect on the obesity-hypertension association in middle-aged adults. The findings underscore the importance of controlling both obesity and insulin resistance to prevent the future development of hypertension.

Summary

- Insulin-resistant obesity is associated with increased risk of hypertension as compared with insulin-sensitive adiposity.
- The obesity-hypertension association is strengthened by the presence of insulin resistance.

Figure 1.

Odds ratio (OR) and 95% confidence interval (CI) of baseline BMI, WC, glucose, insulin and HOMA for incident hypertension by race

BMI=body mass index; WC=waist circumference; HOMA=homeostasis model assessment of insulin resistance; OR=odds ratio; CI=confidence interval

Figure 2.

Standardized odds ratio (OR) and 95% confidence intervals (CI) of baseline BMI for incident hypertension by baseline HOMA quartile groups

BMI=body mass index; HOMA=homeostasis model assessment of insulin resistance;

OR=odds ratio; CI=confidence interval

Figure 3.
 Relationship between baseline BMI and follow-up blood pressure by low and high HOMA groups
 BMI=body mass index; HOMA=homeostasis model assessment of insulin resistance

Table 1

Descriptive data of study variables in baseline and follow-up by race and gender

Variable	Whites (n=1148)		Blacks (n=476)		P-values*	
	Males	Females	Males	Females	Males	Females
N	497	651	192	284		
Baseline						
Age (year)	23.8 (5.2) ‡	22.9 (4.2)	23.4 (5.2)	22.6 (4.4)	0.561	0.236
HR (beats/min)	71.1 (9.1) ‡	77.2 (10.7)	70.7 (8.8) ‡	75.4 (9.0)	0.490	0.004
BMI (kg/m ²)	25.4 (5.0) ‡	23.6 (5.6)	24.2 (4.7) ‡	25.7 (7.0)	0.007	<0.001
WC (cm)	87.1 (12.7) ‡	74.7 (12.3)	81.7 (10.6) ‡	78.1 (15.3)	<0.001	<0.001
Glucose (mg/dL)	85.3 (10.9) ‡	80.7 (8.8)	83.3 (8.5) ‡	81.1 (13.6)	0.027	0.632
Insulin (μU/mL)	10.8 (6.5)	10.8 (5.9)	11.0 (7.5) ‡	13.6 (10.3)	0.866	<0.001
HOMA	2.3 (1.7)	2.2 (1.5)	2.3 (1.7) ‡	2.8 (2.4)	0.833	<0.001
Follow-up						
Age (year)	39.8 (6.5)	39.2 (6.7)	38.7 (7.5)	38.8 (7.0)	0.079	0.464
Follow-up years	16.0 (7.3)	16.2 (7.2)	15.3 (7.2)	16.2 (7.3)	0.249	0.950
HR (beats/min)	69.4 (11.2) ‡	71.6 (9.0)	69.7 (9.2) ‡	72.0 (9.2)	0.712	0.681
Smokers, n (%)	144 (29.0)	201 (30.9)	79 (41.1) ‡	77 (27.1)	0.003	0.221
BMI (kg/m ²)	29.5 (5.8) ‡	28.1 (7.4)	28.9 (7.3) ‡	31.7 (9.1)	0.419	<0.001
WC (cm)	100.9 (15.1) ‡	88.6 (16.6)	96.3 (18.4)	95.0 (18.6)	0.003	<0.001
Glucose (mg/dL) §	90.6 (17.1) ‡	85.5 (13.4)	91.4 (23.8)	88.7 (19.4)	0.539	0.002
Insulin (μU/mL) §	12.6 (9.9) ‡	10.5 (8.3)	12.4 (9.4)	13.2 (9.5)	0.844	<0.001
HOMA ^b	3.0 (2.8) ‡	2.3 (2.2)	3.0 (2.8)	3.1 (2.6)	0.823	<0.001
Systolic BP(mmHg) §	117.3 (11.1) ‡	110.0 (11.0)	123.6 (16.1) ‡	115.5 (14.3)	<0.001	<0.001
Diastolic BP(mmHg) §	74.5 (9.1) ‡	69.2 (8.2)	75.6 (12.0) ‡	71.5 (10.7)	0.025	<0.001
Hypertension, n (%)	94 (18.9) ‡	78 (12.0)	59 (30.7)	89 (31.3)	<0.001	<0.001

Continuous variables are presents as means (SD).

HR=Heart rate; WC= Waist circumference; BMI=body mass index; HOMA=homeostasis model assessment of insulin resistance; BP=blood pressure.

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* P-values for race difference in continuous variables were adjusted for age.

Gender difference:

$p < 0.05$; $p < 0.01$

§ Individuals who took medications were excluded.

Table 2

Descriptive data of study variables in groups by baseline BMI and HOMA

Variable	Groups by levels of baseline BMI and HOMA *				P-Value [†]	P-Value [‡]
	Group I: BMI↓/HOMA↓	Group II: BMI↓/HOMA↑	Group III: BMI↑/HOMA↓	Group IV: BMI↑/HOMA↑		
N	582	348	149	383		
Whites/Blacks	411/171	264/84	96/53	267/116	0.058	0.284
Males/Females	223/359	137/211	76/73	179/204	0.005	0.430
Baseline						
Age (year)	23.0 (4.3)	21.3 (3.6)	25.5 (5.1)	24.4 (5.5)	<0.001	0.030
BMI (kg/m ²)	21.0 (2.1)	21.7 (2.0)	27.8 (2.6)	31.5 (5.7)	<0.001	<0.001
Glucose (mg/dL)	78.6 (7.2)	85.2 (8.3)	79.4 (8.5)	87.2 (15.1)	<0.001	<0.001
Insulin (μU/mL)	6.5 (1.9)	14.3 (5.6)	6.9 (1.8)	18.3 (9.4)	<0.001	<0.001
HOMA	1.3 (0.4)	3.1 (1.6)	1.4 (0.3)	4.0 (2.3)	<0.001	<0.001
Follow-up						
Age (year)	39.1 (6.8)	39.3 (7.5)	39.5 (5.7)	39.2 (6.5)	0.825	0.601
Follow-up years	16.2 (7.1)	18.0 (7.5)	14.0 (5.9)	14.8 (7.1)	<0.001	0.217
Smokers, n (%)	200 (34.4)	100 (28.7)	59 (39.6)	96 (25.1)	<0.001	0.001
BMI (kg/m ²)	25.5 (4.8)	26.9 (5.2)	32.3 (5.7)	36.2 (7.5)	<0.001	<0.001
Glucose (mg/dL) [§]	86.2 (15.6)	89.1 (15.4)	88.7 (15.8)	103.1 (38.3)	<0.001	<0.001
Insulin (μU/mL) [§]	8.8 (5.7)	11.8 (7.9)	11.8 (9.7)	18.9 (13.2)	<0.001	<0.001
HOMA [§]	2.0 (1.5)	2.8 (2.1)	2.8 (2.8)	5.1 (4.8)	<0.001	<0.001
Systolic BP(mmHg) [§]	114.1 (13.4)	113.9 (11.8)	118.8 (15.6)	121.2 (16.1)	<0.001	0.024
Diastolic BP(mmHg) [§]	72.1 (9.7)	71.1 (9.8)	74.6 (9.7)	76.4 (11.2)	<0.001	0.014
Hypertension, n (%)	84 (14.4)	51 (14.7)	33 (22.1)	123 (32.1)	<0.001	<0.001

Continuous variables are presented as means (SD).

BMI=body mass index; HOMA=homeostasis model assessment of insulin resistance; BP=blood pressure.

* Low and high levels of baseline BMI were defined as BMI below and above 25, respectively, and low and high levels of baseline HOMA were defined as below 45th and above 55th percentiles, respectively.

† P-values for difference in continuous variables among 4 groups were adjusted for age, race, and gender.

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† P-values for difference in continuous variables between groups III and IV were adjusted for age, race, and gender.

§ Individuals who took medications were excluded.

Association between follow-up hypertension and baseline insulin-resistant adiposity defined by BMI and HOMA, adjusting for covariates in logistic regression models

OR=odds ratio; CI=confidence interval

* Baseline overweight/obesity was defined as BMI ≥ 25 , and baseline insulin resistance was defined as HOMA above 55th percentiles.