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The Relationship of Waist Circumference to Blood Pressure: The Olivetti Heart Study

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Background: The association between overweight, high blood pressure (BP), and insulin resistance is well established, but the role of body fat distribution in this association has yet to be fully elucidated. The aim of this study was to investigate the role of central adiposity in the association between overweight, high BP, and insulin resistance.

Methods: A total of 1079 men participated in the follow-up of the Olivetti Heart Study from 1994 to 1995. The present analysis includes 768 men, after the exclusion of 184 participants on pharmacological treatment for hypertension. In 65 men fasting blood glucose was >7 mmol/L; in 48, age was below or above 2 standard deviations from the mean of the population ; and in 14 the data set was incomplete. Anthropometric indices of adiposity, metabolic variables (including fasting serum insulin and homeostasis model assessment [HOMA] index of insulin sensitivity), and BP were measured.

Results: In univariate analysis, waist circumference was the anthropometric index that best correlated with BP ($P < .001$). In multiple regression analysis, waist circumference remained the strongest independent predictor of BP after adjustment for confounders. Significant increase of systolic (P value for trend analysis $< .001$) and diastolic ($P < .001$) pressure, heart rate ($P = .003$), fasting and postload serum insulin ($P < .001$), and HOMA index of insulin sensitivity ($P < .001$) were observed across age-adjusted quintiles of waist circumference. Greater degrees of central adiposity were associated with higher prevalence of elevated BP values and insulin resistance (P value $< .001$, χ^2 for linear trend).

Conclusions: In middle-aged men, a central distribution of body fat is associated with increased BP, independently of body mass index and insulin resistance, thus suggesting a key role of central adiposity in the full expression of the "metabolic syndrome." Am J Hypertens 2002;15:780–786 © 2002 American Journal of Hypertension, Ltd.

Key Words: Population study, waist circumference, hypertension, obesity, insulin resistance.

The association of excess body weight with elevated blood pressure (BP) has been demonstrated in several epidemiological studies.[1,2] In addition, body fat distribution is an important contributor to the association between obesity and high BP.[3,4] Central obesity and high BP frequently cluster with metabolic complications such as hyperinsulinemia/insulin resistance and dyslipidemia, a picture often defined as "insulin resistance syndrome" or "metabolic syndrome."[5] In addition, the amount of abdominal fat plays an important role in the relationship between BP and its metabolic correlates.[3,6] Insulin resistance with the attendant hyperinsulinemia may be the intermediate link in the association of central obesity with elevated BP.[7] In support of this hypothesis, both central obesity and hypertension are frequently accompanied by hyperinsulinemia, glucose intolerance, and elevated levels of triglyceride and uric acid.[7,8] However, the mechanisms underlying these associations and, in particular, the role that central obesity plays in relation to insulin resistance and hypertension, are still unclear.

We examined the relationships between BP, body fat distribution, and humoral markers of insulin resistance in a male population undergoing an extensive clinical examination in 1994 to 1995 in the framework of the Olivetti

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Prospective Heart Study. The aim of the present analysis was to determine the relative role of abdominal fat accumulation on the relationship between excess body weight, hyperinsulinemia, and high BP.

Methods

Study Population

The methodology of the study has previously been described in detail.[9,10] Data presented here were collected during the follow-up examination between 1994 and 1995. Between May 1994 and December 1995, a total of 1079 men in the age range 25 to 75 years were examined. In the present analysis, we excluded those participants who were on antihypertensive or antidiabetic drug treatment (n = 184), those with fasting blood glucose concentration above the diagnostic limit for diabetes mellitus (ie, >7 mmol/L; n = 65), and those whose age was below or above two standard deviations from the mean of the study populations (n = 48). Of the remaining 782 men, 768 had a complete data set and were included in the present analysis. The local Ethics Committee approved the study protocol, and participants gave their informed consent to participate.

Procedures

The examinations were performed in the morning, in the medical centers of the Pozzuoli and Marcianise factories, with the participants having fasted for at least 13 hours. The participants were allowed to pursue their normal activities but were asked to abstain from vigorous exercise, smoking, and from drinking alcohol, coffee, tea, and other beverages containing caffeine during the morning of the study. Participants underwent a physical examination, complete anthropometric measures, resting 12-lead electrocardiography, and a blood test, and provided a fasting timed urine collection. A fixed sequence questionnaire was administered including information on job and medical history, working and leisure time physical activity, and dietary, drinking, and smoking habits. Age was recorded as of the last birthday.

Anthropometric Measurements

Body weight and height were measured on a standard beam balance scale with an attached ruler. Body weight was measured at the nearest 0.1 kg and height was measured at the nearest centimeter, with subjects wearing only light indoor clothing without shoes. The body mass index was calculated as weight in kilograms divided by the square of the height in meters.

Abdominal circumferences were measured according to standardized methods.[11] The waist circumference was measured at the umbilicus level and the hip circumference was measured at the widest circumference over the trochanters, with the subject standing erect with the abdomen relaxed, arms at the sides, and feet together. The measurements were performed at the nearest 0.1 cm with a flexible inextensible plastic tape. The ratio of waist-to-hip circumference was calculated. Waist circumference was taken as reference measure of abdominal obesity, according to the National Institutes of Health Guidelines on the Identification, Evaluation and Treatment of Overweight and Obesity.[11]

The sagittal (ie, antero-posterior) abdominal diameter was measured with the Holtain-Kahn abdominal caliper (Holtain Ltd., Crosswell, Wales),[12] which allows a direct reading of the distance between the subject's back and the front of his or her abdomen, with the subject in supine position. This distance was read on the centimeter scale of the caliper at the nearest 0.1 cm.

The arm circumference was measured at the mid-point between the acromion and the olecranon with the arm relaxed and hanging just away from the side of the body, after marking the acromion with the arm flexed at a 90° angle.

Subscapular and triceps skinfold thickness was measured using a Lange skinfold caliper (Beta Technology Inc., Santa Cruz, CA). The subscapular fold was picked up just below the inferior angle of the scapula at 45° to the vertical. The triceps fold was measured at the mid-point of the back of the upper arm between the tip of the olecranon and the acromion process of the scapula. The mean of three repeated measurements at each site was used for the calculations.

BP Measurement

Blood pressure was measured between 8 AM and 11 AM after the subject had been sitting upright for at least 10 min. Systolic and diastolic (phase V) BP were taken three times, 2 min apart, with a random zero sphygmomanometer (Gelman Hawksley Ltd., Sussex, England). The first reading was discarded and the average of the last two readings was recorded for systolic and diastolic BP.

Both anthropometric and BP measurements were performed by trained observers who had attended training sessions for standardization of the procedures. The operator code was recorded to check for possible measurement bias.

Blood Sampling and Biochemical Assays

A fasting venous blood sample was taken in the seated position without stasis between 8 AM and 11 AM after the BP measurements for determination of serum lipids, glucose, uric acid, and insulin. A stimulated serum insulin value was available for 339 participants who consented to undergoing a 1-h oral glucose tolerance test (OGTT) on a separate day (within 1 week after the screening examination). In this subgroup, after an overnight fast, venous blood samples were collected at times 0 and 60 min after 75 g of oral glucose for insulin measurement. The blood specimens were immediately centrifuged and stored at −70° until analyzed. Serum cholesterol, triglyceride, glucose, and uric acid levels were measured with automated

Table 1. Characteristics of the study population (n = 768)

Characteristic	Mean	SD	Range
Age (y)	51.3	5.6	36–66
Systolic blood pressure (mm Hg)	127.2	15.2	90–180
Diastolic blood pressure (mm Hg)	82.9	9.1	60–110
Body mass index (kg/m^2)	26.7	3.0	18.8–35.2
Heart rate (beats/min)	61.7	8.9	40–120
Serum glucose (mmol/L)	5.33	0.55	2.50–6.94
Serum cholesterol (mmol/L)	5.70	1.03	1.73–9.96
Serum triglycerides (mmol/L)	1.65	0.93	0.24–10.77
Serum uric acid (μmol/L)	333.4	68.7	95.2–577.0
Serum insulin (fasting) (pmol/L)	60.8	37.6	7.9–653.2
Serum insulin (1 h postload) (pmol/L)*	332.5	210.1	43.8–1353.1
HOMA index†	2.13	1.44	0.24–22.90

* n = 339.

† Homeostasis model assessment (HOMA) index calculated as: fasting serum insulin (μIU/mL) × fasting serum glucose (mmol/L)/22.5.

methods (Cobas-Mira, Roche, Milan, Italy). Serum insulin concentration was measured by radioimmunoassay (Insulina Lisophase, Technogenetics, Milan, Italy). Insulin resistance was estimated by homeostasis model assessment (HOMA) using the formula: fasting serum insulin (μU/mL) × fasting serum glucose (mmol/L)/22.5, as described by Matthews et al.[13]

Statistical Analysis

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS version 8.0; SPSS Inc., Chicago, IL). The distributions of serum glucose and triglyceride, serum insulin, and HOMA index were normalized by log transformation, and log-transformed values were used in the analysis. Pearson linear correlation and partial correlation analyses were used to test the bivariate associations between different variables. Stepwise multiple regression equations were calculated to adjust further for confounders using either systolic or diastolic BP as the dependent variables. To analyze the effect of waist circumference on BP and metabolic variables, the population sample was divided into quintiles of waist circumference. The presence of a linear trend in mean values of the considered variables was tested across the age-adjusted quintiles of waist circumference. The prevalence of both high BP and insulin resistance across quintiles of waist circumference was tested by χ^2 for linear trend. Results are expressed as means and SD or 95% confidence intervals as indicated. Two-sided P values $< .05$ were considered statistically significant unless otherwise indicated.

Results

Characteristics of the study population are described in Table 1. There were 223 participants with systolic pressure ≥140 mm Hg or diastolic pressure ≥90 mm Hg.

Blood pressure was positively and significantly associated with age, body mass index, and all of the anthropometric measures indicating prevalent central fat deposition, ie, waist circumference, waist/hip ratio, sagittal abdominal diameter, and subscapular skinfold thickness (Table 2). In addition, BP was positively associated with fasting and post-OGTT insulin levels and HOMA index. The simple correlation coefficient of waist circumference (marker of central adiposity) with both systolic and diastolic BP tended to be higher than that of body mass index (index of total adiposity) with BP. In fact, in a partial correlation analysis, the relationship between waist circumference and BP was unaffected by the adjustment for body mass index (partial correlation analysis: SBP, r = 0.191, $P < .001$; DBP, r = 0.166, $P < .001$). By contrast, the correlation between body mass index and BP was no longer significant when controlling for waist circumference (partial correlation analysis: SBP, r = −0.068, P = .055; DBP, r = 0.003, P = .994).

As high collinearity was apparent at univariate analysis, multiple stepwise regression models were computed to assess the relative influence of age and both metabolic and anthropometric variables on BP. Based on the results of univariate analysis, age, body mass index, waist circumference, and HOMA index were chosen as independent variables with the alternative inclusion of systolic or diastolic pressure as the dependent variable. As shown in Table 3, models 1 and 2, age and waist circumference were independently associated with either systolic or diastolic BP, whereas no additional independent contribution was found for either the body mass index or the HOMA index, which in fact did not pass the tolerance criterion to be entered in the equation. The inclusion of other indices of insulin resistance (ie, fasting serum insulin or glucose) in place of the HOMA index did not modify the results. The inclusion in the equation of other parameters of body fat distribution (waist/hip ratio or subscapular skinfold) did not alter the independent value of waist circumference as a predictor of BP (equations not shown). Finally, when multiple regression analysis was performed on the subgroup of participants undergoing the oral glucose tolerance test, the inclusion of post-OGTT serum insulin did

Table 2. Univariate correlations, age, blood pressure, metabolic, and anthropometric variables

Variable	SBP	DBP	S-INS (Fasting)	S-INS (1 h postload)*	HOMA Index	BMI	Waist	SAD	WHR	Subscapular skinfold
Age	0.226†	0.111†	−0.027	0.148†	−0.008	−0.007	0.110†	0.090‡	0.152†	0.008
SBP		0.779†	0.095†	0.142†	0.111†	0.142†	0.230†	0.204†	0.216†	0.187†
DBP			0.225†	0.196†	0.123†	0.213†	0.271†	0.258†	0.204†	0.249†
S-INS (fasting)*				0.145†	0.985†	0.243†	0.227†	0.227†	0.128†	0.190†
S-INS (1-h post-load)*§					0.164†	0.258†	0.343†	0.306†	0.309‡	0.251†
HOMA index*						0.262†	0.247†	0.246†	0.155†	0.209†
BMI							0.793†	0.776†	0.488†	0.542†
Waist								0.842†	0.734†	0.354†
SAD									0.577†	0.533†
WHR										0.556†

SBP = systolic blood pressure (mm Hg); DBP = diastolic blood pressure (mm Hg); S-INS = serum insulin (pmol/L); BMI = body mass index (kg/m^2); SAD = sagittal abdominal diameter (cm); WHR = waist to hip ratio; other abbreviation as in Table 1.

HOMA index calculated as: fasting serum insulin (μIU/mL) × fasting serum glucose (mmol/L) / 22.5.

* log-transformed values.

† $P < .01$.

‡ $P < .05$.

§ $n = 339$.

not modify the results, with age and waist circumference being the only significant independent predictors of BP (Table 3, models 3 and 4). Also, in this case, neither BMI nor post-OGTT serum insulin met the tolerance criterion for being entered into the equation.

To analyze further the relative influence of central adiposity on BP, the entire population was classified by quintiles of waist circumference. The small age difference among quintiles was accounted for by entering age as covariate. A graded and statistically significant increase of both systolic and diastolic BP, as well as of resting heart rate, was observed across quintiles of waist circumference (Table 4). A statistically significant increase in the values of all metabolic and anthropometric factors was also observed in association with increase in central adiposity. In particular, placement in the highest quintile of waist circumference was associated with higher values of fasting blood glucose, serum triglyceride, uric acid, fasting and postload serum insulin, and HOMA index (Table 4). Because higher values of serum insulin (or HOMA index) were associated with higher values of waist circumference, we repeated the analysis of BP across quintiles of waist circumference by entering also fasting serum insulin as a covariate. The inclusion of insulin in the model did not affect the analysis, the effect of this covariate being not statistically significant.

Finally, the prevalence of both elevated BP values (BP >140 or >90 mm Hg, corresponding to the 80th percentile for our population) and insulin resistance (HOMA index >2.74, ie, the 80th percentile for our population) increased gradually and significantly across quintiles of waist circumference (Fig. 1). The values adopted to define high BP in our population match the 1999 World Health Organization–International Society of Hypertension cut-off levels for the diagnosis of hypertension.[14]

Discussion

Excess body weight and obesity are well recognized risk factors for high BP.[1,2] In particular, central body fat accumulation is associated with both hypertension[3,4] and insulin resistance.[3,6] The latter condition is more frequent in overweight than in lean individuals,[15] and also more common in hypertensive individuals than in matched normotensive controls.[16,17] Thus the case has been made for a possible pathogenetic role of insulin resistance and the attendant chronic hyperinsulinemia in the development of hypertension.[5,7]

An important confounder in the insulin-BP relationship is the amount and distribution of body fat.[18,19] Although in some studies the positive association between insulin resistance and high BP seemed to be independent of overweight,[7,20] other studies suggested that obesity and, in particular, central obesity may be in the causal pathway of this association.[6,19,21,22]

We evaluated the relative role of central fat accumulation on the relationship between excess body weight, in-

Table 3. Stepwise multivariate regression analyses with systolic and diastolic blood pressure as dependent variables

Variable	B	95% CI of B	t	*P* Value	Change in R^2
Model 1. Dependent variable: SBP (mm Hg); independent variables: age (y), waist (cm), BMI (kg/m^2), HOMA*					
Age	0.599	0.410–0.788	6.24	<.001	0.084
Waist	0.352	0.222–0.482	5.30	<.001	0.040
Model 2. Dependent variable: DBP (mm Hg); independent variables: age (y), waist (cm), BMI (kg/m^2), HOMA*					
Waist	0.280	0.200–0.359	6.90	<.001	0.086
Age	0.173	0.057–0.289	2.90	.003	0.013
Model 3. Dependent variable: SBP (mm Hg); independent variables: age (y), waist (cm), BMI (kg/m^2), 1-h postload serum insulin (pmol/L) (*n* = 339)					
Age	0.640	0.388–0.891	6.30	<.001	0.082
Waist	0.333	0.150–0.539	3.42	.001	0.035
Model 4. Dependent variable: DBP (mm Hg); independent variables: age (y), waist (cm), BMI (kg/m^2), 1-h postload serum insulin (pmol/L) (*n* = 339)					
Waist	0.328	0.211–0.446	5.51	<.001	0.095
Age	0.168	0.01–0.322	2.15	.04	0.010

CI = confidence interval; other abbreviations as in Tables 1 and 2.
* HOMA index calculated as: fasting serum insulin (μIU/mL) $\times$ fasting serum glucose (mmol/L) / 22.5.

sulin resistance/hyperinsulinemia, and high BP in a sample of middle-aged men that included normotensive and untreated hypertensive individuals. A novel aspect of the present study is the simultaneous measurement of a number of anthropometric indices of total adiposity and body fat distribution and of biochemical indicators of insulin resistance. In previous studies, body mass index and waist-to-hip ratio have been the two anthropometric measures often used as expressions of overweight and of the pattern of body fat distribution, respectively. However, waist circumference has been found to be a better marker of abdominal fat content than is waist-to-hip ratio and the use of waist circumference for the assessment of abdominal fat content has been recently recommended by the National Institutes of Health Guidelines on the Identification, Evaluation and Treatment of Overweight and Obesity.[11]

In our population, the waist circumference represented a better correlate of BP than body mass index itself. Indeed, the association between body mass index and BP was no longer statistically significant when controlling for waist circumference. The graded increase of BP across quintiles of waist circumference, the strength of the relationship, and its independence from other recognized predictors of BP such as age and body mass index suggest that our findings are unlikely to be due to chance.

An important novel finding of this study is that the predictive role of central adiposity on BP is independent of indices of insulin resistance such as fasting insulin, insulin response to OGTT, and HOMA index of insulin resistance. The HOMA index, an indirect estimate of insulin resistance, has been validated by Bonora et al[23] against euglycemic hyperinsulinemic clamp, the gold standard measure of insulin resistance. The Pearson's correlation between insulin sensitivity as measured by insulin clamp and as estimated by HOMA was 0.792.[23] According to this result, the HOMA index may be considered a reliable index of individual's insulin sensitivity for the purpose of large-scale population studies.

Thus, the inexpensive and easy-to-perform measurement of waist circumference may be of practical relevance in the assessment of the risk associated with the different components of the metabolic syndrome, as recently confirmed by Lemieux et al.[24].

The results of our study need to be interpreted in the context of two other recent studies in which insulin sensitivity was measured by the euglycemic hyperinsulinemic clamp. The European Group for the Study of Insulin Resistance multicenter study by Ferrannini et al[20] on 333 normotensive nondiabetic subjects (66% women) detected a significant inverse association between insulin sensitivity and BP and a direct association between BP and fasting serum insulin in either sex, independently of age and body mass index. In this study, however, the role of body fat distribution was not evaluated and the number of male participants was rather small.

The same issue was investigated by Toft et al[25] in a case-control study comparing 60 hypertensive patients and

Table 4. Analysis of covariance: age-adjusted blood pressure and metabolic variables by quintiles of waist circumference

	Waist Circumference (cm) (quintile) (mean, range)					F (*P* for Trend)
	I (82.6, 70–87)	II (89.7, 88–91)	III (93.4, 92–95)	IV (97.5, 96–99)	V (104.8, 100–127)	
Age (y)	49.8 (48.6–51.0)	49.9 (48.8–51.0)	51.2 (50.6–52.2)	51.9 (50.7–53.0)	52.0 (50.8–53.2)	
SBP (mm Hg)	121.7 (119.3–124.0)	127.6 (125.1–130.0)	127.0 (124.8–129.1)	128.1 (125.7–130.4)	131.3 (129.0–133.5)	8.9 (<.001)
DBP (mm Hg)	78.8 (77.5–80.2)	82.4 (80.9–83.8)	82.5 (81.2–83.8)	83.8 (82.4–85.2)	86.2 (84.9–87.6)	14.9 (<.001)
Heart rate (beats/min)	60.6 (59.2–62.0)	60.1 (58.6–61.5)	62.4 (61.1–63.6)	62.3 (60.1–63.7)	62.9 (61.6–64.2)	3.0 (.02)
FBG (mmol/L)	5.16 (5.07–5.24)	5.26 (5.17–5.35)	5.34 (5.26–5.42)	5.40 (5.31–5.48)	5.43 (5.35–5.51)	7.2 (<.001)
S-TG (mmol/L)	1.45 (1.31–1.59)	1.63 (1.48–1.78)	1.60 (1.47–1.74)	1.70 (1.56–1.85)	1.84 (1.70–1.98)	3.9 (.004)
S-UA (μmol/mL)	309 (299–320)	315 (304–326)	338 (329–348)	343 (332–353)	361 (351–371)	15.7 (<.001)
S-INS$^{(fasting)}$ (pmol/L)	49.4 (43.2–55.6)	56.3 (49.8–62.9)	59.0 (53.2–64.8)	68.5 (62.2–74.9)	71.7 (65.8–77.7)	8.4 (<.001)
S-INS$^{(1\text{-h post load})}$ (pmol/L)	249.1 (197.7–300.5)	263.6 (207.1–320.2)	331.7 (286.2–377.2)	371.1 (323.3–419.0)	426.5 (379.1–474.0)	8.3 (<.001)
HOMA index	1.65 (1.43–1.87)	1.91 (1.68–2.14)	2.03 (1.83–2.23)	2.39 (2.17–2.62)	2.52 (2.31–2.73)	10.3 (<.001)

Age adjusted at 50.98 years; FBG = fasting serum glucose (mmol/L); S-TG = serum triglyceride (mmol/L); S-UA = serum uric acid (μmol/mL); other abbreviations as in Tables 1–3.
Values are mean (95% confidence intervals).
HOMA index calculated as: fasting serum insulin (μIU/mL) × fasting serum glucose (mmol/L) / 22.5.

FIG. 1. Prevalence of high blood pressure (ie, >140 or >90 mm Hg, corresponding to the 80th percentile of the distribution of the population) (**left panel**) and insulin resistance (homeostasis model assessment index >2.74, corresponding to the 80th percentile of the distribution of the population) (**right panel**) across quintiles of waist circumference (χ^2 for linear trend: hypertension 29.5, $P <$ .001; insulin resistance 46.6, $P <$ .001).

60 matched normotensive control subjects. The two groups did not differ in fasting glucose and insulin levels and in the insulin sensitivity index. Moreover, a number of metabolic differences between hypertensive and normotensive subjects, such as serum triglyceride, C-peptide, and 2-h postload levels of glucose and insulin, were no longer statistically significant after adjustment for body fat distribution (measured as waist-to-hip ratio). These investigators suggested that even small differences in central adiposity might have a strong impact on variables associated with insulin resistance.

The comparative evaluation of the available evidence suggests an independent role of central adiposity in the association between insulin resistance and high BP. This view is supported by our findings in addition to those of others,[6,25,26] as well as by the consideration that studies that could not demonstrate a significant influence of fat distribution on BP either did not rely on accurate measures of abdominal fat or did not include hypertensive individuals.[7,17,20]

Several pathogenetic models have been proposed to explain the association between central adiposity and BP, including neuroendocrine abnormalities identified in abdominally obese subjects[26] and enhanced sympathetic nervous system activity.[27] In the present study, we observed a significant trend toward faster resting pulse rate across quintiles of waist circumference, a clue suggestive of higher sympathetic tone.[28] Enhanced sympathetic activity induces vasoconstriction and increases cardiac output. It may also promote renal tubular sodium reabsorption, particularly at proximal sites.[29] In fact, we recently showed that altered proximal sodium handling may be a possible mechanistic link between central adiposity and hypertension in men.[10]

Some limitations of the present work are inherent to the nature of the Olivetti study population, which comprised white male participants only and thus may not be regarded as representative of the general population. For this reason, the results of this study can only be generalized to a comparable

white male population. The relationship between body fat distribution, insulin sensitivity, and BP deserves further studies in specific subgroups of the population, such as those with frank obesity and type 2 diabetes.

In conclusion, the simple measure of waist circumference as an index of central adiposity is a key feature of the metabolic and haemodynamic abnormalities clustered under the definition of "metabolic syndrome."[30] This observation has important implications for the prevention of the excess cardiovascular risk associated with central adiposity and its related metabolic and hemodynamic abnormalities. These results provide supportive evidence for the need to reduce overweight and ameliorate insulin sensitivity, both by caloric restriction and by increased physical activity.

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