

Aortic Stiffness Is Associated With Visceral Adiposity in Older Adults Enrolled in the Study of Health, Aging, and Body Composition

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Abstract—The central arteries stiffen with age, causing hemodynamic alterations that have been associated with cardiovascular events. Changes in body fat with age may be related to aortic stiffening. The association between vascular stiffness and body fat was evaluated in 2488 older adults (mean age, 74 years; 52% female; 40% black) enrolled in the Study of Health, Aging, and Body Composition (Health ABC), a prospective study of changes in weight and body composition. Clinical sites were located in Pittsburgh, Pa, and Memphis, Tenn. Aortic pulse wave velocity was used as an indirect measure of aortic stiffness. A faster pulse wave velocity indicates a stiffer aorta. Body fat measures were evaluated with dual energy x-ray absorptiometry and computed tomography. Independent of age and blood pressure, pulse wave velocity was positively associated with weight, abdominal circumference, abdominal subcutaneous fat, abdominal visceral fat, thigh fat area, and total fat ($P < 0.001$ for all). The strongest association was with abdominal visceral fat. Elevated pulse wave velocity was also positively associated with history of diabetes and higher levels of glucose, insulin, and hemoglobin A1c ($P < 0.001$ for all). In multivariate analysis, independent positive associations with pulse wave velocity were found for age, systolic blood pressure, heart rate, abdominal visceral fat, smoking, hemoglobin A1c, and history of hypertension. The association between pulse wave velocity and abdominal visceral fat was consistent across tertiles of body weight. Among older adults, higher levels of visceral fat are associated with greater aortic stiffness as measured by pulse wave velocity. (*Hypertension*. 2001;38:429-433.)

Key Words: vascular stiffness ■ central obesity ■ aging ■ insulin resistance ■ pulse wave velocity

As we age, the arteries stiffen, resulting in higher systolic blood pressure (BP) and widening of the pulse pressure. Structural changes that occur with age include fragmentation and degeneration of elastin, increases in collagen, and thickening of the arterial wall.¹ A progressive dilation of the arteries accompanies this stiffening process. Arterial stiffening occurs at different rates for different individuals and can be viewed as a process of biological aging of the vascular system.

Arterial stiffening can be evaluated indirectly by measurement of the speed of the systolic pressure wave as it travels down the aorta (ie, aortic pulse wave velocity [aPWV]). A faster PWV indicates a stiffer aorta. Elevated aPWV results in an early return of the reflected pressure wave from the periphery, causing amplification of the systolic pressure and a reduction in the diastolic pressure,² the hallmarks of isolated systolic hypertension. The cardiovascular risks associated with systolic hypertension are well documented.^{3,4}

Accelerated arterial stiffness has been linked to diabetes,^{5,6} hyperglycemia, hyperinsulinemia, and impaired glucose tolerance.⁷⁻¹¹ These findings have been confirmed in older adults¹² and suggest that insulin resistance or its products, ie, hyperglycemia and hyperinsulinemia, may promote arterial stiffening independent of age. Although some data suggest that weight and body fat distribution are also related to arterial stiffness,^{7,12} a detailed evaluation of this possibility has not yet been published. The purpose of this report is to evaluate the relationship of weight, body fat distribution, and markers of insulin resistance to aortic stiffness estimated by aPWV.

Methods

Study Population

The Health, Aging, and Body Composition (Health ABC) study is a population-based, prospective study of the impact of changes in weight and body composition on age-related physiological and functional changes. Participants, 70 to 79 years of age, were

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recruited from March 1997 to July 1998 at 2 field centers located in Pittsburgh, Pa, and Memphis, Tenn. Participants were drawn from a random sample of Medicare beneficiaries residing in ZIP codes from the metropolitan areas surrounding Pittsburgh and Memphis. Eligible subjects reported no difficulty walking one quarter of a mile, climbing 10 steps, or performing basic activities of daily living. Participants also had to be free of life-threatening illness and to plan to remain in the area for ≥ 3 years. The cohort consisted of 3075 men (48.4%) and women (51.6%), of whom 41.6% were black. PWV data were missing for 354 participants because of equipment problems and for 233 subjects whose waveforms were of unacceptable quality or out of range (< 300 or > 3000 cm/s). This report is based on the remaining 2488 participants. All participants signed a written informed consent approved by the institutional review boards of the University of Pittsburgh and University of Tennessee.

Body Fat Measures

Weight was assessed by a balance-beam scale while the participant was wearing lightweight clothing. Standing height was assessed by a stadiometer. Dual energy x-ray absorptiometry (Hologic QDR 4500, software version 8.21) provided measures of total mass, total fat mass, and fat-free (lean) mass.

Abdominal visceral fat was estimated with a 1-cm computed tomography (CT) image obtained during suspended respiration between the fourth and fifth lumbar vertebrae. A GE 9800 Advantage was used in Pittsburgh, and a Siemens Somatom Plus and a Picker PQ2000S were used in Memphis. Central readings were performed at the University of Colorado Health Sciences Center. The adipose tissue density range was determined from a bimodal histogram of adipose and soft tissue intensities. Image pixels with intensity within this range were classified as adipose tissue. The fat area for the entire image was determined by multiplying the number of adipose tissue pixels by the area of a pixel. A region-of-interest line was drawn at the junction of the abdominal wall musculature and the visceral compartment, extending around the body to the back muscles. Adipose tissue within this circle was considered to be abdominal visceral fat. The difference in fat area between the entire image and the visceral fat is equal to the subcutaneous fat area.

Thigh fat was estimated from a CT slice of the mid thigh of the leg used for strength testing, usually the right leg. Intermuscular fat was distinguished from subcutaneous fat by manually drawing a line along the deep facial plane surrounding the thigh muscles. Muscle borders that were not already defined by adipose tissue were outlined manually. As above, areas were calculated by multiplying the number of pixels of classified tissue by the area of a pixel in the image.

Abdominal circumference was measured by use of a metal tape measure at the maximum waist circumference between the lower rib and the iliac crest. Participants were asked to stand with their weight equally distributed on both feet, with arms hanging at their sides and head facing straight ahead, relaxing their abdomen and breathing normally. The abdominal circumference was measured at eye level directly over bare skin, and the measurement was made at the end of a normal expiration to the nearest 0.1 cm. The measurement was taken twice. If the difference between the first 2 measurements was > 1 cm, third and fourth measurements were obtained. The computed abdominal circumference value used was the mean of the 2 or 4 recorded values.

Laboratory Values

HDL, triglycerides, and glucose were assayed with a colorimetric technique on a Johnson and Johnson Vitros 950 analyzer. HDL was assayed after a magnetic precipitation of LDL, VLDL, and chylomicrons. LDL was estimated with the Friedewald equation.¹³ Insulin was assayed with a microparticle enzyme immunoassay (Abbott IMx analyzer), and for hemoglobin A1c, ion-exchange high-performance liquid chromatography (Biorad Variant analyzer) was used.

Medical history was evaluated by questionnaire. A condition was considered present if the participant reported that a physician had told him or her of the condition. History of cardiovascular disease was defined as a history of myocardial infarction, angina, stroke,

transient cerebral ischemia, or any vascular surgery, including endarterectomy or angioplasty.

PWV Methods

aPWV was measured from simultaneous Doppler flow signals obtained from the right carotid and right femoral arteries by use of nondirectional transcutaneous Doppler flow probes (Parks Medical Electronics Inc; model 810A, 9.0- to 10-MHz probes). Digitized data were recorded by custom programming for subsequent analysis. At least 10 beats were averaged for each simultaneous recording site with the QRS used for synchronization. Three separate runs were recorded for each participant, and all usable runs were averaged. The distance between the carotid and femoral sampling sites was measured above the surface of the body with a metal tape measure. Timing between the onset of flow at the carotid and femoral (defined as foot of the velocity signal at each site) sites was divided by the associated distance to produce flow velocity. Stiffer vessels are associated with a faster PWV. The National Institute on Aging, Laboratory of Cardiovascular Science, Gerontology Research Center (Baltimore, Md) trained and certified all study personnel before data collection, read the waveforms, and evaluated data quality. Results from all acceptable runs were averaged for the final PWV measure used in the analyses. Replicate measures of aPWV in 14 subjects revealed intraclass correlations of 0.88 between sonographers and 0.84 between readers.

Statistical Analysis

The distribution of aPWV values was not normal; thus, median values were compared across subgroups. A Wilcoxon test was used to determine differences across groups. The PWV distribution was normalized through a natural log transformation, and its association with other continuous variables was evaluated by use of Pearson correlation coefficients. Other variables that were log transformed to obtain normality were triglycerides, glucose, insulin, hemoglobin A1c, and thigh fat area. Age- and systolic BP-adjusted associations were performed with partial correlations.

Linear regression was used to model the natural log of aPWV. Several variables were forced into the model, including age and systolic BP, which were positively correlated with aPWV; height and weight to control for body size; and clinical site to control for potential variations in protocol implementation and/or study population between sites. Through a stepwise approach, all other variables significantly associated with PWV in univariate analysis were considered candidates to enter the model. The final model was then run by race and gender subgroups to determine whether associations differed by race and gender. The presentation of the multivariate model included the standardized coefficient, which was calculated as the parameter estimate divided by the ratio of the sample standard deviation of the dependent variable to the sample standard deviation of the regressor.¹⁴ This allowed comparison of the strength of the coefficient across the variables in the model.¹⁵

Results

aPWV was available for 2488 of the 3075 Health ABC participants. The average age of these individuals was 74 years; 52% were female, and 40% were black. Values of aPWV ranged from 312 to 2998 cm/s, with a mean of 903 cm/s and a median of 808 cm/s. Ninety percent of the PWV values were between 525 and 1399 cm/s. This distribution of PWV values is similar to that found in other population studies.^{12,16,17}

Significantly higher values of aPWV were found among blacks compared with whites, men compared with women, and smokers compared with those who never smoked (Table 1). Higher values of aPWV were also seen among those with a history of cardiovascular disease, diabetes, or hypertension.

TABLE 1. Median PWV by Sociodemographic and Disease History Variables

Variable	n	Median PWV, cm/s	P
Race			
White	1486	796	
Black	1002	835	<0.001
Gender			
Male	1186	841	
Female	1302	787	<0.001
Site			
Pittsburgh	1455	763	
Tennessee	1033	866	<0.001
Smoking			
Never	1095	782	
Former	1135	832	
Current	254	829	0.005
History of cardiovascular disease			
No	1804	795	
Yes	684	851	0.008
History of diabetes			
No	2127	793	
Yes	358	908	<0.001
History of hypertension			
No	1216	756	
Yes	1251	865	<0.001

Participants from Tennessee had consistently higher aPWV values than Pittsburgh participants.

Systolic BP showed the strongest association with aPWV (Table 2). Age was significantly but weakly related to aPWV, most likely because of the narrow age range represented here. Other risk factors positively associated with aPWV were triglycerides, glucose, insulin, and hemoglobin A1c. A significant negative association was seen between HDL cholesterol and aPWV. In addition, all body fat measures were positively associated with aPWV, even after age and systolic BP were controlled for (Table 2). The strongest association was with abdominal visceral fat.

Results of the multivariate analysis (Table 3) indicate that in addition to age and systolic BP, factors independently associated with aPWV were heart rate, abdominal visceral fat, smoking, hemoglobin A1c, and history of hypertension. Black race was borderline significant ($P=0.07$). Height and weight were forced into the model to control for body size and to determine whether the association with visceral fat was independent of obesity in general. Neither height nor weight was significant after controlling for the other factors in the model. When height and weight were not included in the model, the associations remained the same with the exception of male gender, which became significantly and positively associated with aPWV. In the final multivariate model, after hemoglobin A1c was controlled for, glucose, insulin, and history of diabetes were not associated with aPWV. When either glucose or history of diabetes was placed in the model

TABLE 2. Correlations Between (Log) Aortic PWV and Age, Hemodynamic, Biochemical, and Body Composition Measures

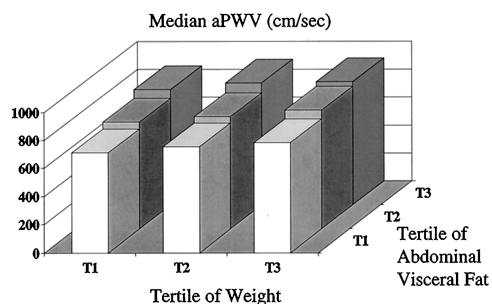
Variable	Unadjusted	P	Age and Systolic BP Adjusted	P
Age	0.069	<0.001
Hemodynamic				
Systolic BP	0.212	<0.001
Diastolic BP	0.075	<0.001	-0.032	0.137
Pulse pressure	0.203	<0.001	0.032	0.137
Heart rate	0.155	<0.001	0.151	<0.001
Laboratory values				
Cholesterol	-0.004	0.832	-0.010	0.658
HDL	-0.067	<0.001	-0.070	0.001
LDL	0.003	0.888	0.005	0.832
(Log) triglycerides	0.067	0.001	0.081	<0.001
(Log) glucose	0.133	<0.001	0.118	<0.001
(Log) insulin	0.112	<0.001	0.112	<0.001
(Log) hemoglobin A1c	0.128	<0.001	0.103	<0.001
Body composition				
Height	0.062	<0.002	0.093	<0.001
Weight	0.125	<0.001	0.126	<0.001
Abdominal circulation	0.103	<0.001	0.104	<0.001
Subcutaneous fat	0.059	0.004	0.049	0.026
Visceral fat	0.179	<0.001	0.187	<0.001
(Log) thigh fat area	0.142	<0.001	0.128	<0.001
Total fat	0.082	<0.001	0.078	<0.001

in place of hemoglobin A1c, each remained independently associated with aPWV. Insulin was also associated with aPWV independent of age, gender, race, systolic BP, visceral fat, smoking, history of hypertension, and height. However, when heart rate, weight, or hemoglobin A1c was entered, insulin added no further predictive value to the model. Forcing insulin into the model did not affect the strength of the association between abdominal visceral fat and aPWV. When the subgroup of 358 participants with a history of diabetes were excluded from the analysis, results were unchanged.

TABLE 3. Independent Associations With the Log of PWV Linear Regression

Covariate	Coefficient	Standardized Coefficient	P
Age (y)	0.010	0.071	<0.001
Male (vs female)	0.028	0.036	0.212
Black (vs white)	0.031	0.039	0.073
Systolic BP (mm Hg)	0.004	0.203	<0.001
Heart rate (bpm)	0.004	0.122	<0.001
Log (visceral fat)	0.110	0.142	<0.001
Ever smoked (vs never)	0.030	0.050	0.011
Hemoglobin A1c (%)	0.027	0.077	<0.001
History of hypertension (yes vs no)	0.062	0.079	<0.001

Model also includes clinical site, height, and weight. Model $R^2=0.1438$.



aPWV by tertile of weight and tertile of abdominal visceral fat.

The association between abdominal visceral fat and aPWV was clearly independent of body weight. In the Figure, median aPWV is plotted by tertiles of both weight and abdominal visceral fat. The positive association between abdominal visceral fat and aPWV was consistently strong in each tertile of body weight. In comparison, the association between body weight and aPWV was relatively weak within each tertile of abdominal visceral fat.

Each of the other body fat measures was tested in the final multivariate model in place of abdominal visceral fat. Each variable was tested twice, once without weight in the model and once with weight included. When weight was not included in the model, each body fat measure was independently associated with aPWV. Visceral fat showed the strongest association, followed closely by percent body fat. With weight in the model, only visceral fat, total body fat, and percent body fat remained independently associated with aPWV. When weight and visceral fat were in the model, total and percent body fat added no further predictive value.

To determine whether the association between abdominal visceral fat and aPWV was consistent across race and gender subgroups, the final multivariate model was stratified by race and gender. Abdominal visceral fat was independently and significantly associated with aPWV in each of the 4 race and gender subgroups.

Discussion

This study presents new data demonstrating a specific association between aortic stiffening and abdominal visceral fat. Although all body fat measures were related to aortic stiffening in univariate analysis, it was clear from the multivariate analysis that the visceral fat depot was the most important. Thus, body weight and body fat measures may be risk factors for aortic stiffness primarily because they are correlated with the degree of visceral adipose tissue. However, even in those participants who were not obese, a more central distribution of body fat was associated with higher aPWV.

These findings have broad implications for the health of older individuals and suggest that factors that promote weight gain in older adults may accelerate vascular stiffening. The causes of a shift to greater central adiposity with age are unknown but are thought to be due in part to decreasing activity levels.¹⁸⁻²⁰ If the shift to central adiposity can be slowed (possibly through exercise), then the process of vascular stiffening might also be slowed. A slowing of the vascular stiffening process would probably reduce the likeli-

hood of systolic hypertension and the associated risk of cardiovascular events.

Visceral adipose tissue is the main fat store responsible for insulin resistance²¹; thus, elements of the insulin resistance syndrome may serve as part of the link between increased visceral adipose tissue and stiffening of the aorta. The literature consistently reports increased aortic stiffening with diabetes,^{5,6} as well as less extreme alterations in glucose metabolism.^{8,9,11} Our data support this finding, with glycosylated hemoglobin being a strong independent predictor of higher aPWV. Hyperglycemia can cause vascular damage by stimulating collagen synthesis and causing glycation of proteins in the arterial wall, which leads to cross linking between protein fibers.²²

Insulin stimulates the sympathetic nervous system, resulting in increases in heart rate and BP,²³ both of which add to the mechanical strain on the vascular system. In fact, a higher heart rate was one of the stronger associations with increased aPWV in this analysis, and in multivariate analysis, the association between insulin and PWV was markedly reduced when heart rate was added to the model. In addition, insulin may cause hypertrophy of the vascular wall, resulting in an increase in the number and size of monocytes, increases in collagen, and proliferation of smooth muscle cells.^{23,24}

Although exposure to insulin may contribute to vascular stiffness, we did not find it to be an independent predictor of vascular stiffness, indicating that other factors associated with the insulin resistance syndrome are more important. One possibility is an increase in nonesterified fatty acids, which have been found to be associated with central obesity.²⁵ Nonesterified fatty acids may contribute to vascular stiffness by increasing α -adrenergic reactivity, vascular tone, and BP.²⁵ Increases in the expression of proinflammatory cytokines have also been associated with abdominal obesity. Both interleukin-6 and tumor necrosis factor- α are expressed in adipose tissue and have been linked specifically to central obesity.²⁶ These proinflammatory cytokines have been hypothesized to induce a low-grade systemic inflammation in persons with excess body fat and central fat specifically.²⁷ Measures of inflammation have been found to be positively associated with aPWV in a recent evaluation of women with lupus.²⁸

Age was a significant predictor of aPWV in this population, although the correlation was lower than in studies with a wider age range.^{17,29} The distribution of aPWV found in Health ABC is remarkably consistent with that found in other studies of older adults. The median aPWV for Health ABC was 808 cm/s (mean age, 74 years) compared with 821 cm/s in the Cardiovascular Health Study¹² (mean age, 78 years) and 810 cm/s among 75-year-old men in the Baltimore Longitudinal Study of Aging.¹⁷ A somewhat younger population (mean age, 51 years) with low activity levels studied as part of the Activity Counseling Trial had a median aPWV of 778 cm/s.¹⁶

Although the body fat measures were significantly correlated with aPWV in the Health ABC population, the strength of the correlations was somewhat weak, and the final model explained only 14% of the total variance in aPWV. It is possible that aPWV is not a precise measure of vascular

stiffness or that there are major risk factors that have yet to be identified. One important point is that the strongest predictor of aPWV—age—is muted in this analysis because of the limited age range. Avolio et al²⁹ published data on aPWV for subjects ranging in age from 2 months to 94 years who were living in urban and rural areas of China. In this analysis, the correlation between aPWV and age was 0.55 for the rural Chinese and 0.67 for the urban Chinese. Thus, the variance explained by our model is limited to some extent by the truncated age range.

In studies of older adults, the issue of selective survival must always be considered. It is likely that subjects who were genetically or environmentally prone to diabetes or insulin resistance either may not have survived to be included in this study or may not have met the eligibility criteria. Thus, we may be left with a population that is less susceptible to either insulin resistance or the adverse effects of components of the insulin resistance syndrome on the vascular system. Thus, in a middle-aged population with increased insulin resistance, the associations observed here may be much stronger.

In conclusion, we have found that among healthy older individuals, measures of body weight and degree of fat are correlated with greater vascular stiffness. The strongest association was with visceral adipose tissue. The association between visceral adipose tissue and aortic stiffening may be mediated through elements of the insulin resistance syndrome.

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References

- Lakatta EG, Mitchell JH, Pomerance A, Rowe GG. Human aging: changes in structure and function. *J Am Coll Cardiol*. 1987;10(suppl A):42A–47A. Review.
- Nichols WW, Nicolini FA, Pepine CJ. Determinants of isolated systolic hypertension in the elderly. *J Hypertens*. 1992;10(suppl):S73–S77.
- SHEP Cooperative Research Group. Prevention of stroke by antihypertensive drug treatment in older persons with isolated systolic hypertension: final results of the Systolic Hypertension in the Elderly Program (SHEP). *JAMA*. 1991;265:3255–3264.
- Wilkinson I, Cockcroft J. Mind the gap: pulse pressure, cardiovascular risk, and isolated systolic hypertension. *Am J Hypertens*. 2000;13:1315–1317.
- Stella A, Gessaroli M, Cifello BI, Salardi S, Reggiani, Cacciari E, D'Addato M. Elastic modulus in young diabetic patients (ultrasound measurements of pulse wave velocity). *Angiology*. 1984;35:729–734.
- Airaksinen KE, Salmela PI, Linnaluoto MK, Ikaheimo MJ, Ahola K, Ryhanen LJ. Diminished arterial elasticity in diabetes: association with fluorescent advanced glycosylation end products in collagen. *Cardiovasc Res*. 1993;27:942–945.
- Toto-Moukouo JJ, Achimastos A, Asmar RG, Hugues CJ, Safar ME. Pulse wave velocity in patients with obesity and hypertension. *Am Heart J*. 1986;112:136–140.
- Taquet A, Bonithon-Kopp C, Simon A, Levenson J, Scarabin, Malmejac A, Ducimetiere P, Guize L. Relations of cardiovascular risk factors to aortic pulse wave velocity in asymptomatic middle-aged women. *Eur J Epidemiol*. 1993;9:298–306.
- Amar J, Chamontin B, Pelissier M, Garelli I, Salvador M. Influence of glucose metabolism on nocturnal blood pressure variability in hypertensives with an elevated waist-hip ratio: a link with arterial distensibility. *Am J Hypertens*. 1995;8(pt 1):426–428.
- Salomaa V, Riley W, Kark JD, Nardo C, Folsom AR. Non-insulin-dependent diabetes mellitus and fasting glucose and insulin concentrations are associated with arterial stiffness indexes: the Atherosclerosis Risk in Communities Study. *Circulation*. 1995;91:1432–1443.
- Kupari M, Hekali P, Keto P, Poutanen VP, Tikkanen MJ, Standerstjöld-Nordenstam CG. Relation of aortic stiffness to factors modifying the risk of atherosclerosis in healthy people. *Arterioscler Thromb*. 1994;14:386–394.
- Mackey R. Correlates of aortic stiffness by carotid-femoral pulse wave velocity in a subgroup of the cardiovascular health study. *Circulation*. 1998;97:828. Abstract.
- Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem*. 1972;18:499–502.
- SAS Institute Inc. The REG procedure. In: *SAS/STAT User's Guide, Version 6*. 4th ed. Cary, NC: SAS Institute Inc; 1989;2:1351–1456.
- Snedecor GW, Cochran WG. Multiple linear regression. In: Snedecor GW, Cochran WG, eds. *Statistical Methods*. 7th ed. Ames, Iowa: Iowa State University Press; 1980;334–364.
- Havlik R, Brock D, Lohman K, Haskell W, Snell P, O'Toole M, Ribisl P, Vaitkevicius P, Spurgeon H, Lakatta E. High density lipoprotein cholesterol and vascular stiffness at baseline in the Activity Counseling Trial. *Am J Cardiol*. 2001;87:104–107.
- Vaitkevicius PV, Fleg JL, Engel JH, O'Connor FC, Wright JG, Lakatta LE, Yin FC, Lakatta EG. Effects of age and aerobic capacity on arterial stiffness in healthy adults. *Circulation*. 1993;88(pt 1):1456–1462.
- Weinsier RL. Genes and obesity: is there reason to change our behaviors? *Ann Intern Med*. 1999;130:938–939. Editorial comment.
- Schwartz R, Shuman W, Larson V, Cain K, Fellingham G, Beard J, Kahn S, Stratton J, Cerqueira M, Abrass I. The effect of intensive endurance exercise training on body fat distribution in young and older men. *Metabolism*. 1991;40:545–551.
- Samaras K, Kelly P, Chiano M, Spector T, Campbell L. Genetic and environmental influences on total-body and central abdominal fat: the effect of physical activity in female twins. *Ann Intern Med*. 1999;130:873–882.
- Brunzell JD, Hokanson JE. Dyslipidemia of central obesity and insulin resistance. *Diabetes Care*. 1999;22(suppl 3):C10–C13. Review.
- Feener EP, King GL. Vascular dysfunction in diabetes mellitus. *Lancet*. 1997;350(suppl 1):S19–S13. Review.
- DeFronzo RA, Ferrannini E. Insulin resistance: a multifaceted syndrome responsible for NIDDM, obesity, hypertension, dyslipidemia, and atherosclerotic cardiovascular disease. *Diabetes Care*. 1991;14:173–194. Review.
- King GL, Wakasaki H. Theoretical mechanisms by which hyperglycemia and insulin resistance could cause cardiovascular diseases in diabetes. *Diabetes Care*. 1999;22(suppl 3):C31–C37.
- Egan BM, Lu G, Greene EL. Vascular effects of non-esterified fatty acids: implications for the cardiovascular risk factor cluster. *Prostaglandins Leukot Essent Fatty Acids*. 1999;60:411–420. Review.
- Yudkin JS. Abnormalities of coagulation and fibrinolysis in insulin resistance. *Diabetes Care*. 1999;22(suppl 3):C25–C30.
- Visser M, Bouter L, McQuillan G, Wener M, Harris T. Elevated C-reactive protein levels in overweight and obese adults. *JAMA*. 1999;282:2131–2171.
- Selzer F, Sutton-Tyrrell K, Fitzgerald S, Tracy RP, Kuller LH, Manzi S. Vascular stiffness in women with systemic lupus erythematosus. *Hypertension*. 2001;37:1075–1082.
- Avolio AP, Deng FQ, Li WQ, Luo YF, Huang ZD, Xing LF, O'Rourke MF. Effects of aging on arterial distensibility in populations with high and low prevalence of hypertension: comparison between urban and rural communities in China. *Circulation*. 1985;71:202–210.