Body Fat Distribution, Plasma Lipids, and Lipoproteins

By: Alfred J. Anderson, Kathleen A. Sobocinski, David S. Freedman, Joseph J. Barboriak, Alfred A. Rimm, and Harvey W. Gruchow

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Abstract:

The relation of body fat distribution as measured by the ratio of waist to hip circumferences (WHR) to plasma levels of lipids and lipoproteins was studied In 713 men and 520 women who were employed by two Milwaukee companies. Quetelet Index (kg/m^2), waist girth, hip girth, and WHR were each positively related to levels of total cholesterol, triglycerides, apolipoprotein B, and the ratio of total to high density lipoprotein (HDL) cholesterol. In addition, the anthropometric measures were inversely associated with levels of HDL cholesterol. (Controlling for age, alcohol Intake, exercise level, current smoking status, and oral contraceptive use only slightly reduced the strength of the correlations.) In addition, WHR and Quetelet Index were Independently related to lipid and lipoprotein levels, and the magnitudes of the associations were roughly equivalent For example, the mean (covariate-adjusted) triglyceride level among men in the upper tertile of the Quetelet Index was 37 mg/dl higher than for men in the lower tertile of the Quetelet index; the corresponding difference according to WHR tertiles (upper to lower) was 39 mg/dl ($p < 0.01$ for both effects). These findings indicate that In healthy men and women a less favorable lipid and lipoprotein profile is associated with elevated levels of both Quetelet Index and WHR.

Index Terms: obesity • waist/hip ratio • lipids • lipoproteins • apolipoprotein B • body fat distribution

Article:

Obesity is related to abnormal lipid and carbohydrate metabolism and Is predictive of subsequent cardiovascular disease.[1,2] However, the associations have often been fairly weak or have been observed only over long periods of follow-up,[3,4] and obesity may be a risk factor In only specific subgroups of overweight persons.[5] Much evidence suggests that high risk obese individuals are characterized by their distribution of adipose tissue. Vague[6] was the first to document that the male (android) pattern of upper body obesity, characterized in part by a relatively thick skinfold at the nape of the neck, is more strongly related to increased insulin levels, diabetes, and atherosclerosis than Is the female (gynoid) pattern of lower body obesity.

The adverse effects of upper body obesity have also been studied by using the ratio of waist to hip circumferences (WHR),[7] a relatively simple index that emphasizes abdominal obesity.[8,9,10] WHR Is associated with an Increased prevalence of hypertension and diabetes[11,12] and with levels of triglycerides, glucose, insulin, and blood pressure.[13,14,15] Prospective studies have shown that, even after accounting for Quetelet Index (kg/m^2) or various skinfold thicknesses, the risk of coronary heart disease is greatest in both men[16] and women[17] with an increased WHR.

Although the mechanism by which WHR confers an increased risk of disease is not clear, adipose tissue at different locations exhibits metabolic differences[18] which may influence lipoprotein levels. Although this possibility is supported by reports that WHR is related to adverse levels of lipids and lipoproteins, these studies have examined primarily overweight persons.[13,14,15] We therefore assessed the relation of WHR to levels of lipids and lipoproteins, including apolipoprotein B (apo B), In 1233 apparently healthy men and women. Emphasis was given to the possible confounding effects of relative weight, as measured by Quetelet index.

Methods

Study Population

Participants were primarily white-collar workers who volunteered for plasma cholesterol screenings at their place of employment (two Milwaukee companies) from June 1985 to March 1986. Approximately one-half of all eligible persons participated in the screenings and completed a life quality questionnaire. Informed consent was obtained, and the study protocol was approved by the Human Research Review Committee of the Medical College of Wisconsin.

The current study is restricted to 1233 white 20- to 65year-olds (713 men, 520 women); blacks (n = 38), Orientals (n = 10), and other racial groups represented less than 5% of all participants and were excluded from the current analyses. Persons who had been told by a physician that they were diabetic (n = 10) were also excluded.

General Examinations

Weight, height, waist, and hip measurements were taken In a uniform manner by trained personnel, with participants wearing light clothing. Waist circumference (girth) was measured at the navel; hip circumference at the widest part of the hips and buttocks. (WHR ranged from 0.75 to 1.02 among men, and from 0.59 to 0.93 among women,) Weight and height data were obtained using standard calibrated balance scales with vertical measuring rods. The Quetelet Index (kg/m^2) was calculated as a measure of weight relative to height,[19] The influence of clothing on these anthropometric measurements should have been similar for all participants, and likely introduced little bias into the observed associations.

Information on alcohol intake, smoking, exercise, and oral contraceptive (0C) *use* were obtained from a questionnaire that has been extensively used in patients undergoing coronary arteriography.[20] Alcohol intake was expressed as ounces of absolute alcohol (including beer, wine, and hard liquor) consumed per week. As previously described?[21] exercise was a count of the number of times per month that each person participated in aerobic exercise. Information concerning the use of OC within the last 3 months was also obtained. However, data concerning the specific components of the OC preparations were not collected.

Laboratory Analyses

Employees were requested to fast overnight, and 10 mi of blood was drawn by venipuncture between 8:00 and 9:30 A.M. Plasma levels of total cholesterol and triglycerides were measured using automated procedures[22,23,24] with quality control monitored by the Centers for Disease Control (Atlanta, Georgia). High density lipoprotein (HDL) cholesterol was measured after heparin-manganese precipitation of other lipoproteins, according to procedures developed by the Lipid Research Clinics.[24]

Plasma levels of apo B were measured by our enzyme-linked immunoassay.[25] Apo B levels among men ranged from 34 to 169 mg/dl (mean, 51 mg/dl) and from 22 to 170 mg/dl (mean, 70 mg/dl) among women, agreeing well with values reported In smaller studies using radioimmunoassay procedures.[26] In addition, a previous study[27] examined apo B levels as measured by our assay among 110 male patients undergoing arteriography. Apo B was highly correlated ($r = 0.73$) with the sum of very low and low density lipoprotein cholesterol, and tended to be more strongly related to the extent of coronary artery disease than were levels of total cholesterol, triglycerides, or the sum of very low and low density lipoprotein cholesterol.

Statistical Methods

Because the distributions of several variables were skewed, Spearman rank correlations or log (for triglycerides) and square root transformations (exercise and alcohol intake) were used in several analyses. Statistical significance was assessed at the 0.01 level because of the large number of comparisons. All p values are two-sided.

The mean levels of selected characteristics were contrasted between men, women who were not using 00, and women who were using OC. Analysis of covariance was used in these comparisons to control for age. interrelationships among anthropometric measures (Quetelet Index, waist and hip girths, and WHR) were assessed using correlation coefficients, and their associations (both unadjusted and covariate-adjusted) with levels of lipids and lipoproteins were also examined. Covariates Included age, current smoking status, alcohol intake, exercise, and OC use.

Partial correlation coefficients were used to examine the Independent relation of WHR to levels of lipids *and* lipoproteins after controlling for Quetelet Index and covariates. The relation of WHR to the plasma variables was also examined within strata (tertiles) of Quetelet Index. In addition, two-way analysis of covariance was used to assess linear trends in plasma lipid and lipoprotein levels over Miles of both Quetelet Index and WHR.

Table 1. Selected Characteristics of the Study Population

	Men	Women: Non-OC users	Women: OC users
No.	713	413	107
Age (years)	40 ± 10*	39 ± 11	29 ± 4
Weight (kg)	85 ± 13	67 ± 14	63 (64) ± 11†
Quetelet Index (kg/m²)	25.7 ± 3.4	24.7 ± 4.9‡	22.7 (23.4) ± 3.6‡
Circumferences			
Waist (cm)	92 ± 9	76 ± 12	71 (74) ± 8
Hip (cm)	105 ± 7	101 ± 11‡	97 (98) ± 9‡
WHR	0.88 ± 0.05	0.75 ± 0.07	0.74 (0.75) ± 0.05
Exercise (times/month)	9 ± 9	6 ± 7	9 (7) ± 10
Alcohol intake (oz/week)	4.4 ± 4.6	2.6 ± 2.9	2.8 (2.9) ± 3.1
Smoking			
Current (%)	14%	23%	20%
Past (%)	30%	22%	21%

The mean levels of all variables are significantly different ($p < 0.01$) between men and women after adjusting for differences in age.
*Values are means ± standard deviation.
†Values in parentheses are age-adjusted mean values. The age-adjusted means for men and women who did not use OC were almost identical to the unadjusted levels.
‡The age-adjusted mean levels are significantly different ($p < 0.01$) between women who used OC and those who did not.
OC = oral contraceptive; WHR = ratio of waist to hip circumference.

Table 2. Mean Levels of Plasma Lipids and Lipoproteins

	Men	Women: Non-OC users	Women: OC users
No.	713	413	107
Total cholesterol (mg/dl)	203 ± 44*	202 ± 47	196 (211) ± 35
Triglycerides (mg/dl)†‡	120 ± 98	80 ± 43	87 (98) ± 34
HDL cholesterol (mg/dl)†	48 ± 13	63 ± 16	63 (64) ± 15
Total/HDL cholesterol†	4.6 ± 1.7	3.4 ± 1.1	3.3 (3.5) ± 0.9
Apo B (mg/dl)†‡	81 ± 23	70 ± 21	70 (76) ± 16

*Values are means ± standard deviation. Values in parentheses are age-adjusted mean levels. Statistical comparisons were made after using analysis of covariance to adjust for differences in age.
†Men vs. women: $p < 0.01$; ‡non-OC users vs. OC users: $p < 0.01$.
OC = oral contraceptive.

Results

Except for height and HDL cholesterol levels, all anthropometric and plasma variables were related to age, with correlations reaching 0.42 for WHR in men and 0.37 for total cholesterol in women. Tables 1 and 2 show the mean levels of selected characteristics, adjusted by analysis of covariance for the younger age of OC users. As compared with women, men weighed more and had higher mean values of Quetelet Index, waist girth, hip girth, and WHR. Men also exercised more frequently and consumed more alcohol, but were less likely to currently smoke cigarettes than were women. Although women who were not using OC had higher mean Quetelet Index and a larger hip circumference than did OC users, all male-female differences existed Irrespective of OC use.

With the exception of total cholesterol, levels of all lipids and lipoproteins differed significantly between men and women (Table 2). Women had a higher mean level of HDL cholesterol (+16 mg/dl), but lower levels of triglycerides (— 30 mg/d1) and apo B (— 8 mg/dl). In addition, OC use was associated with increased (age-adjusted) levels of triglycerides and apo B.

Interrelations among the anthropometric measures are shown in Table 3 for men (upper right) and women (lower left). Although Quetelet Index was strongly related *(r* > 0.8) to waist and hip circumferences, this index showed a weaker correlation with WHR: r = 0.39 In women, r = 0.53 in men. Waist and hip girths were also strongly correlated *(r* > 0.8), but WHR was more strongly associated with waist circumference. In men, correlations with WEIR were 0.76 (waist girth) and 0.34 (hip girth); corresponding correlations in women were 0.71 and 0.20, respectively.

Table 3. Interrelationships among the Anthropometric Variables

	Weight	Height	Quetelet Index	Waist girth	Hip girth	WHR
Weight	—	0.47	0.85	0.87	0.89	0.49
Height	0.32	—	−0.05	0.25	0.34	0.03
Quetelet Index	0.93	−0.04	—	0.84	0.81	0.53
Waist girth	0.86	0.11	0.87	—	0.87	0.76
Hip girth	0.91	0.17	0.89	0.83	—	0.34
WHR	0.37	−0.01	0.39	0.71	0.20	—

Partial (Pearson) correlations are used to control for age. The upper right matrix contains the values for the 713 men. Correlations among the 520 women are presented in the lower left.
WHR = ratio of waist to hip circumference.

The relation of anthropometric measures to plasma lipid and lipoprotein levels Is shown In Table 4. Before adjustment for covariates, all measures showed highly significant ($p<0.001$) associations with levels of plasma lipids and lipoproteins, particularly with triglycerides and total/HDL cholesterol. Although lipid and lipoprotein levels showed roughly similar associations with each anthropometric measure, correlations with waist circumference were, In general, slightly larger than those with Quetelet Index, hip circumference, or WHR. Adjustment for covariates reduced (he magnitude of the associations very little.

Table 4. Relation of Anthropometric Measures to Plasma Lipids and Lipoproteins

		Correlation with				
Group	Anthropometric variable	Total cholesterol	Triglycerides	HDL-C	Total/HDL cholesterol	Apo B
Men	Quetelet Index	0.28 (0.22)*	0.36 (0.30)	−0.20 (−0.20)	0.35 (0.31)	0.30 (0.24)
	Waist girth	0.31 (0.23)	0.42 (0.34)	−0.23 (−0.23)	0.40 (0.34)	0.34 (0.27)
	Hip girth	0.25 (0.21)	0.31 (0.28)	−0.15 (−0.16)	0.30 (0.28)	0.25 (0.22)
	WHR	0.28 (0.14)	0.37 (0.27)	−0.22 (−0.21)	0.36 (0.27)	0.32 (0.22)
Women	Quetelet Index	0.22 (0.15)	0.25 (0.23)	−0.20 (−0.19)	0.34 (0.29)	0.27 (0.22)
	Waist girth	0.28 (0.21)	0.34 (0.32)	−0.20 (−0.21)	0.39 (0.34)	0.31 (0.26)
	Hip girth	0.17 (0.10)†	0.24 (0.22)	−0.19 (−0.20)	0.30 (0.25)	0.19 (0.14)‡
	WHR	0.27 (0.21)	0.30 (0.28)	−0.14 (−0.14)‡	0.33 (0.28)	0.33 (0.29)

Spearman correlation coefficients in 713 men and 520 women. Unless specified, all correlations are statistically significant at the 0.001 level.
*The values in parentheses are partial correlations adjusted for age, smoking, alcohol intake, exercise, and oral contraceptive use in women.
†$p > 0.01$; ‡$0.001 < p < 0.01$.
WHR = ratio of waist to hip circumference.

Partial correlations were then used to assess the relation of body fat distribution to levels of lipids and lipoproteins, independently of relative weight (Table 5). Controlling for Quetelet Index eliminated the associations with hip girth, but both waist circumference and WHR remained related to adverse lipid and lipoprotein levels, (Almost all waist girth and WHR associations were statistically significant at the 0.01 level.) In addition, with the exception of apo B levels In women, associations with waist girth and WHR were of similar magnitude. Stratified analyses (data not shown) indicated that the association between levels of ape B and WHR was strongest (r = 0,30) in women who were relatively heavy (upper tertile of Quetelet Index, >25.1 kg/m^2), The corresponding association between apo B levels and waist girth among these women was only 0.13.

Table 5. Independent Relation of Waist and Hip Girths to Plasma Lipids and Lipoproteins

			Spearman correlation with				
Group	No.		Total cholesterol	Triglycerides	HDL cholesterol	Total/HDL cholesterol	Apo B
Men	713	Waist	0.08	0.16*	−0.12†	0.16*	0.13*
		Hip	0.06	0.07	−0.01	0.06	0.05
		WHR	0.03	0.12†	−0.13*	0.13*	0.10†
Women	520	Waist	0.14†	0.24*	−0.08	0.19*	0.14†
		Hip	−0.06	0.04	−0.06	0.02	−0.09
		WHR	0.17*	0.22*	−0.07	0.20*	0.22*

Partial correlations are used to control for Quetelet Index, age, smoking, alcohol intake, exercise, and oral contraceptive use.
*$p < 0.001$; †$p < 0.01$.
WHR = ratio of waist to hip circumference.

Mean plasma levels of lipids and lipoproteins were then calculated according to tertiles of Quetelet Index and WHR, and the results are shown in Tables 8 (men) and 7 (women). (Analysis of covariance was used to adjust for possible confounders.) The middle tertile of Quetelet Index ranged from 24.1 to 26.4 kg/m^2 for men, and from 21.8 to 25.1 kg/rn^2 for women; corresponding cutpoints for the middle WHR tertile were 0.86 and 0.90 for men, and 0.72 and 0.76 for women.

In almost all cases, Quetelet Index and WHIR were independently related to the levels of lipids and lipoproteins. For example, among men in the lower tertile of Quetelet Index (<24.1 kg/m^2), mean levels of triglycerides Increased from 90 to 114 mg/dl as WHR Increased. Similarly, among men with WHR levels below 0.86, mean triglyceride levels increased from 90 to 109 mg/dl with increasing Quetelet Index. Overall, levels of triglycerides increased by 37 mg/d1 from the lowest to highest tertile of Quetelet Index; the corresponding increase according to WHR tertiles was 39 mg/dl. (No significant Quetelet Index x WHIR Interactions were observed for any of the lipids and lipoproteins.) As previously observed (Table 4), except for levels of total cholesterol In men and HDL cholesterol in women, WHR was independently related to all lipids and lipoproteins. Along with the covariates, Quetelet Index and WHIR °explained° from 10% (HDL cholesterol In men) to 24% (total cholesterol in women) of the variability in lipid and lipoprotein levels.

To assess the relative Importance of waist circumference (vs. WHR) as a measure of body fat distribution, comparable cross-tabulations of Quetelet Index and waist girth were formed (data not shown). However, because of the very strong correlation between waist girth and Quetelet Index, neither was a significant predictor of lipid and lipoprotein levels in women. Among men, however, waist circumference generally showed an independent association with lipid and lipoprotein levels.

Table 6. Mean Lipid and Lipoprotein Levels by Tertiles of Quetelet Index and WHR in Men

	Quetelet Index tertile	WHR tertile			Changes* in lipid levels associated with		
		Low	Middle	High	Quetelet Index	WHR	R^2
No.	Low	156	61	20			
	Middle	69	103	66	—	—	—
	High	18	69	151			
Total cholesterol (mg/dl)	Low	189†	198	210			
	Middle	197	206	205	+12	+13	0.14
	High	203	214	214			
Triglycerides (mg/dl)	Low	90	104	114			
	Middle	88	117	122	+37‡	+39‡	0.12
	High	109	139	169			
HDL cholesterol (mg/dl)	Low	51	48	48			
	Middle	51	50	44	−4‡	−4‡	0.10
	High	47	46	44			
Total/HDL cholesterol	Low	3.9	4.5	4.6			
	Middle	4.1	4.4	5.0	+0.7§	+0.7§	0.17
	High	4.7	5.0	5.3			
Apo B (mg/dl)	Low	73	80	80			
	Middle	76	83	82	+6	+9‡	0.13
	High	75	88	89			

*Adjusted level in upper tertile − adjusted level in lower tertile. Changes represent independent effects of Quetelet Index and WHR.

†Values are mean levels of plasma lipids and lipoproteins. Analysis of covariance was used to control for age, current smoking status, and alcohol intake.

‡$p < 0.01$; §$p < 0.001$.

WHR = ratio of waist to hip circumference.

Discussion

Current findings Indicate that the distribution of adipose tissue as assessed by the ratio of waist to hip circumferences is related to plasma levels of total and HDL cholesterol, triglycerides, and apo B in apparently healthy men and women. These associations exist independently of age, smoking, alcohol intake, exercise, OC use, and most Importantly, Quetelet Index. Although earlier studies[28,29] have yielded inconsistent results concerning the relation of relative weight to levels of apo W. results from this larger study indicate that Quetelet Index and WHIR are each independently associated with levels of apo B.

In the current study, lipid and lipoprotein levels showed comparable associations with both waist girth and WHR, whereas associations with hip girth were generally weaker. In agreement with these findings, Krotkiewski et al.[8] also reported that triglyceride levels were more strongly related to waist, as compared with hip, circumference. However, the current multivariable results (Tables 6 and 7) Indicate that although lipid and lipoprotein levels remain related to WHR even after controlling for Quetelet Index, independent associations with waist girth are less consistent. These differences probably reflect the very strong correlation between Quotelet Index and waist girth. However, further studies are needed to assess the value of waist girth (vs. WHR) as an index of body fat distribution In populations with varying degrees of obesity. The stronger relation between apo B levels and WHIR in relatively heavy women agrees with the findings of Hartz et al,[11,12] based on women enrolled In a weight reduction organization.

Table 7. Mean Lipid and Lipoprotein Levels by Tertiles of Quetelet Index and WHR in Women

	Quetelet Index tertile	WHR tertile: Low	WHR tertile: Middle	WHR tertile: High	Changes* in lipid levels associated with: Quetelet Index	Changes* in lipid levels associated with: WHR	R^2
No.	Low	75	65	31			
	Middle	67	61	48	—	—	—
	High	26	52	95			
Total cholesterol (mg/dl)	Low	185†	198	203			
	Middle	194	194	218	+10	+18§	0.24
	High	200	204	211			
Triglycerides (mg/dl)	Low	69	74	73			
	Middle	68	75	96	+15‡	+23§	0.20
	High	69	85	105			
HDL cholesterol (mg/dl)	Low	65	67	64			
	Middle	63	68	61	−6‡	−3	0.13
	High	62	59	56			
Total/HDL cholesterol	Low	3.0	3.1	3.3			
	Middle	3.3	3.0	3.7	+0.5§	+0.5§	0.19
	High	3.3	3.6	3.9			
Apo B (mg/dl)	Low	64	66	67			
	Middle	66	66	78	+7‡	+9§	0.22
	High	68	71	79			

*Adjusted level in upper tertile − adjusted level in lower tertile. Changes represent independent effects of Quetelet Index and WHR.

†Values are mean levels of plasma lipids and lipoproteins. Analysis of covariance was used to control for age, current smoking status, alcohol intake, and oral contraceptive use.

‡$p < 0.01$; §$p < 0.001$.

WHR = ratio of waist to hip circumference.

Although the relation of various weigh/height Indices to cardiovascular disease has been extensively studied, only markedly overweight persons have been consistently shown to be al increased risk.[30] However, over sufficiently long follow-up periods, even moderate overweight confers excess risk for disease.[3,4] In addition, although indices of relative weight do not distinguish between muscle and adipose tissue,[19,31] more direct measures of obesity have not markedly Increased the association between obesity and cardiovascular disease.[32] Because of these discrepancies, Bjeirntorp[5] has suggested that only specific subgroups of obese persons may be at increased risk for cardiovascular disease.

Vague[6] first documented that the distribution of adipose tissue (upper vs. lower body) is related to diabetes and atherosclerosis, and even at comparable weights, men have higher levels of insulin and triglycerides than do women.° The adverse impact of upper body obesity has been more recently studied by using WHR,[7, 10-17] an Index that emphasizes the importance of abdominal fate.% [10] An increased WHR in women has been related to an Increased prevalence of diabetes and hypertension,[7].[11, 12] and both men and women with a high WHR are at Increased risk for coronary heart disease.[18,17] Although WHR has also been related to adverse levels of lipids and lipoprotelns,[13]. [14, 15] these studies have consisted primarily of overweight subjects. Current analyses document a similar association in healthy men and women who were not selected because of obesity.

The importance of other body fat patterns has also been assessed, typically by skinfold thickness measurements. A truncal (vs. peripheral) localization of adipose tissue has been related to increased triglyceride levels,[33,34] elevated glucose levels following an oral glucose load, [35] and an Increased prevalence of diabetes. [38, 37]

Independently of total cholesterol and blood pressure levels, subscapular skinfold thickness is also predictive of subsequent cardiovascular disease? e.[38,39] Even In children, a central distribution of body fat Is associated with Increased insulin levels.[40] *As* determined by 13 different skinfold measurements, a truncal fat pattern (mainly abdominal) was the fat-distribution parameter most predictive of coronary heart disease in the Paris Prospective Study.[41]

Metabolic characteristics of adipocytes depend, in part, upon their location. Enlarged abdominal adipocytes obtained from women with upper body obesity are very responsive to stimuli promoting triglyceride release.[42] This easily mobilized fat draining directly into the portal vein could lead to Increased synthesis of very low density lipoproteins in the liver.[43] High portal concentrations of free fatty acids may also lead to peripheral hyperinsulinemia, which could result in relative insulin resistance.[44] Kissebah et al.[10] have suggested that upper body obesity could also lead to decreased hepatic removal of Insulin and subsequent hyperinsulinemia. Evidence from the present study Indicates that body fat distribution, irrespective of the overall level of relative weight, is associated with lipid and lipoprotein levels. Men and women with an elevated WHR, which probably reflects an Increased amount of abdominal fat, are more* apt to have increased levels of total cholesterol, triglycerides, and ape B, along with decreased levels of HDL cholesterol. Although additional research is needed to determine the relative importance of various patterns of body fat,[45] the current observations document the relation of adipose tissue distribution to lipid and lipoprotein levels in an unselected, healthy population.

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