Plasma High-Density Lipoprotein Cholesterol But Not Apolipoprotein A-I Is a Good Correlate of the Visceral Obesity–Insulin Resistance Dyslipidemic Syndrome

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Apolipoprotein (apo) A-I is a major component of high-density lipoproteins (HDLs), and it has been suggested that measurement of apo A-I may provide additional information in the assessment of coronary heart disease (CHD) risk. In the present study in a sample of 111 men (age [mean ± SD], 35.3 ± 6.6 years), we determined whether a low apo A-I concentration is associated with the cluster of metabolic abnormalities that characterize the visceral obesity–insulin resistance dyslipidemic syndrome. For this purpose, the first and fourth quartiles of apo A-I and HDL cholesterol (HDL-C) concentrations were compared in relation to body fat distribution, glucose tolerance, and plasma insulin and lipoprotein levels. Men in the first quartile (< the 25th percentile) of HDL-C, as compared with men in the fourth quartile (> the 75th percentile), were characterized by an elevated visceral adipose tissue (AT) accumulation ($P < .05$), as well as by increased plasma levels of triglycerides ([TGs] $P < .0001$), apo B ($P < .0005$), and insulin ($P < .01$). These differences were not found when the first and fourth quartiles of plasma apo A-I concentrations were compared. These results suggest that plasma levels of HDL-C are more closely associated with the various features of the visceral obesity–insulin resistance syndrome than plasma apo A-I.

OBESITY is usually associated with disturbances in lipid metabolism[1] and a dyslipidemic profile including hypertriglyceridemia,[2-5] and hypoalphalipoproteinemia[6-9] is frequently observed among obese subjects. In fact, visceral adipose tissue (AT) accumulation shows stronger associations with various metabolic abnormalities than obesity per se.[10,11] Besides altered lipoprotein-lipid levels, an excess of visceral AT has been associated with an insulin-resistant hyperinsulinemic state in both men and women.[10,11] High plasma triglyceride (TG) and low plasma high-density lipoprotein (HDL) cholesterol (HDL-C) concentrations are often simultaneously observed in insulin-resistant hyperinsulinemic subjects.[12-14] These alterations in the plasma lipid profile and insulin levels in visceral obesity are important risk factors in the etiology of diabetes and coronary heart disease (CHD).[2,8,15-18]

However, some CHD patients show nearly normal plasma lipid profiles. Therefore, the emphasis has been on the determination of plasma nonlipid variables, such as apolipoproteins (apos), for assessment of the CHD risk profile in these subjects. In this regard, cross-sectional and prospective studies[19-26] have reported reduced plasma apo A-I levels in both men and women who are at risk for or who have proven CHD. Thus, measurement of the plasma apo A-I concentration has been suggested to provide additional information to HDL-C in the assessment of CHD risk. Since apo A-I is a major constituent of HDL particles and considering that HDL-C levels are decreased in an insulin-resistant state, we have tested whether low plasma apo A-I concentrations would also be affected as a part of the metabolic cluster found in the visceral obesity–insulin resistance syndrome. For this purpose, we compared the first and fourth quartiles of plasma apo A-I and HDL-C concentrations in a sample of 111 men (age [mean ± SD], 35.3 ± 6.6 years) in relation to body fat distribution, glucose tolerance, plasma insulin levels, and plasma lipoprotein concentrations. Results of this study suggest that decreased plasma apo A-I concentrations, in contrast to HDL-C, are not a common feature of the cluster of metabolic abnormalities found in the visceral obesity–insulin resistance syndrome.

SUBJECTS AND METHODS

Subjects

One hundred eleven men aged 20 to 53 years were recruited through the media to participate in this study, which was approved by the medical ethics committee of Laval University, and an informed-consent document was signed by the participants. A complete physical examination was performed by a physician in charge of the medical supervision of the study, which also included a medical history. All participants were healthy nonsmokers. Exclusion criteria included diabetes, genetic dyslipidemias, or evidence of CHD.

Anthropometric Measurements

Weight, height, and waist and hip circumferences were measured using the procedures recommended at the Airlie Conference,[27] and the waist to hip ratio (WHR) was calculated. Body density was measured by the hydrostatic weighing technique,[28] and the mean of six measurements was used in the calculation of body

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density. Percentage body fat was obtained from body density using the equation of Siri.[29]

Computed Tomography

Computed tomography (CT) was performed on a Siemens Somatom DRH scanner (Erlagen, Germany) using previously described procedures.[30,31] Briefly, the subjects (N = 97) were examined in the supine position with both arms stretched above the head. The CT scan was performed at the abdominal level (between L4 and L5 vertebrae) with a radiograph of the skeleton as a reference to establish the position of the scan to the nearest millimeter. Total AT areas were calculated by delineating these areas with a graph pen and then computing the AT surfaces with an attenuation range of −190 to −30 Hounsfield units.[30-32] Abdominal visceral AT area was measured by drawing a line within the muscle wall surrounding the abdominal cavity. The abdominal subcutaneous AT area was calculated by subtracting visceral AT area from total abdominal AT area.

Oral Glucose Tolerance Test

A 75-g oral glucose tolerance test (OGTT) was performed in the morning after an overnight fast. Blood samples were collected under EDTA and Trasylol (Miles, Rexdale, Ontario, Canada) through a venous catheter from an antecubital vein at −15, 0, 15, 30, 45, 60, 90, 120, 150, and 180 minutes for determination of plasma glucose and insulin. Plasma glucose level was measured enzymatically,[33] and plasma insulin level was measured by radioimmunoassay with polyethylene glycol separation.[34] However, the assay used for plasma insulin showed some cross-reactivity with proinsulin. Since diabetes was an exclusion criteria in our study, we believe that such cross-reactivity did not have a significant impact on the results obtained and their interpretation. The glucose and insulin areas under the curve (AUCs) during the OGTT were determined with the trapezoid method.

Plasma Lipoprotein Analyses

Blood samples were obtained in the morning after a 12-hour fast from an antecubital vein into vacutainer tubes containing EDTA. Cholesterol and TG levels in plasma and in lipoprotein fractions were measured enzymatically on an RA-1000 Autoanalyzer (Technicon, Tarrytown, NY) as previously described.[35] Very-low-density lipoprotein ([VLDL] d < 1.006 g/mL) was isolated by ultracentrifugation, and the HDL fraction was obtained after precipitation of low-density lipoprotein (LDL) in the infranatant (d > 1.006 g/mL) with heparin and $MnCl_2$.[36] The cholesterol content of HDL_2 and HDL_3 subfractions was also determined after further precipitation of HDL_2 with dextran sulfate.[37] Total apo B concentration was measured in plasma, whereas LDL apo B and HDL apo A-I levels were measured in the infranatant (d > 1.006 g/mL) by the rocket immunoelectrophoretic method of Laurell, as previously described.[38] The lyophilized serum standards for apolipoprotein measurements were prepared in our laboratory and calibrated with reference standards obtained from the Centers for Disease Control (Atlanta, GA). The cumulative coefficients of variation for the measurement of HDL-C and apo A-I were 3.3% and 3.4%, respectively.

Statistical Analyses

Student's *t* tests were used to compare the different quartiles of apo A-I and HDL-C concentrations. Pearson's product-moment correlation coefficients were used to quantify associations between means. All statistical analyses were performed with the SAS statistical package (SAS Institute, Cary, NC).

RESULTS

Figure 1 shows the relationship between plasma apo A-I and HDL-C levels. Although a significant correlation was noted, the shared variance only reached 32%, which suggested that apo A-I measurements could not be used to estimate HDL-C levels.

Figure 2 shows that plasma HDL-C levels were significantly correlated with visceral AT accumulation as measured by CT, but apo A-I concentration was not a significant correlate of visceral AT deposition.

Characteristics of men in the four quartiles of plasma apo A-I and HDL-C concentrations are presented in Table 1. Subjects in the first quartile of plasma apo A-I levels did not differ from those in the fourth quartile on body fatness variables. In contrast, comparisons related to HDL-C concentrations showed that subjects in the first quartile had increased body weight, body mass index (BMI), percent body fat, fat mass (FM), waist and hip circumferences, and WHR compared with men in the fourth quartile. Men in the first quartile of HDL-C concentrations also had increased levels of visceral AT compared with men in the fourth quartile, and this difference in visceral AT was not found for apo A-I subgroups.

Table 2 compares plasma lipoprotein-lipid concentrations between subgroups characterized by low and high levels of either plasma apo A-I or HDL-C. Few differences were noted between the first and fourth quartiles of apo A-I distribution, since only plasma HDL-C, HDL_2-C, and HDL_3-C levels were different among the groups. On the other hand, when subjects were subdivided on the basis of HDL-C concentrations, all metabolic variables were significantly different between the first and fourth quartiles, with the exception of plasma cholesterol, LDL-C, and HDL-TG levels.

A comparison of mean lipoprotein ratios showed that subjects with low levels of plasma apo A-I were character-

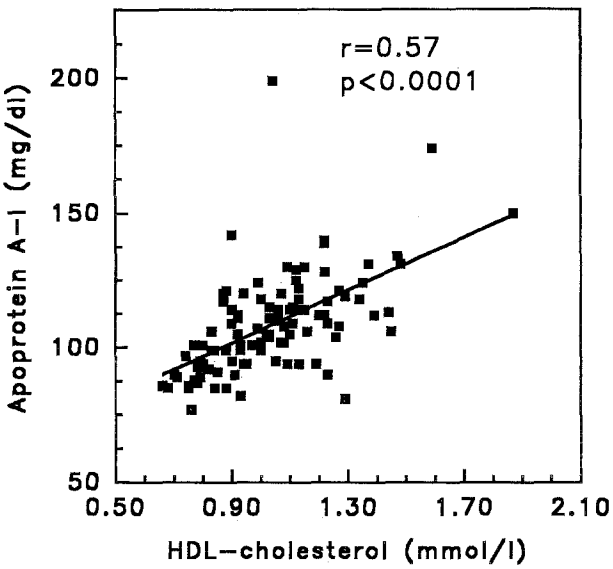

Fig 1. Relationship between plasma HDL-C and apo A-I concentrations in a sample of 111 men.

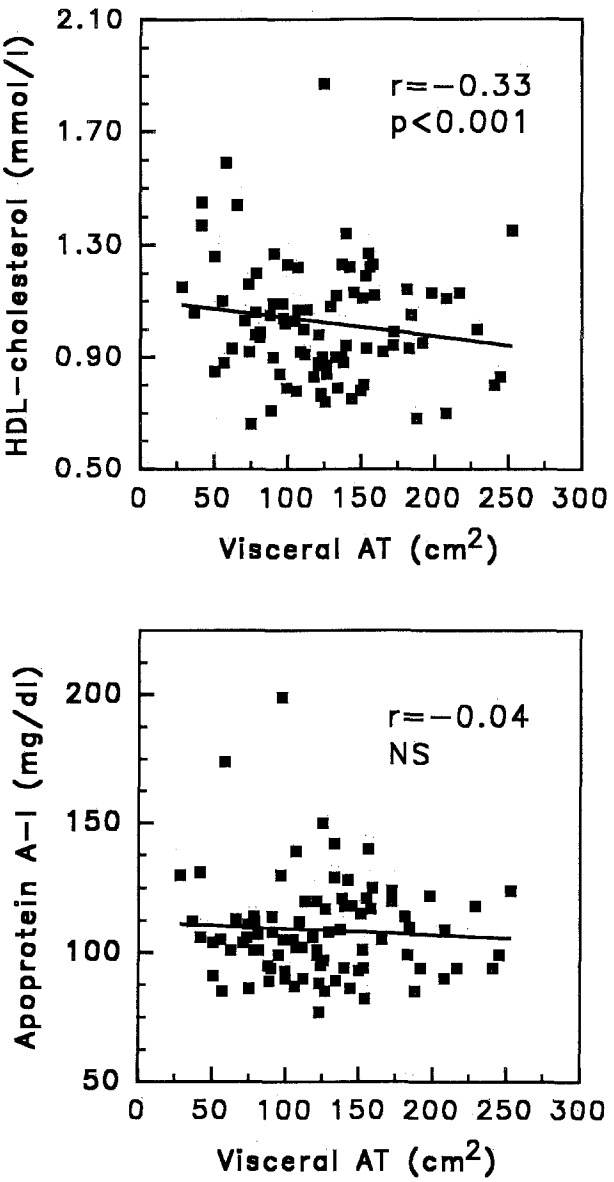

Fig 2. Correlations between visceral AT accumulation and fasting plasma HDL-C and apo A-I concentrations in the sample of men (n = 97).

ized by increased total cholesterol to HDL-C, LDL-C/HDL-C, and HDL-TG/HDL-C ratios, whereas subjects with low HDL-C concentrations were significantly different from subjects with high HDL-C levels on all lipoprotein ratios considered (Table 3).

Figure 3 shows the glycemic and insulinemic responses to the OGTT in subjects in the first and fourth quartiles of apo A-I and HDL-C concentrations. When compared with subjects in the fourth quartile, subjects in the first quartile of apo A-I had identical glucose and insulin responses to the oral glucose challenge. However, although AUCs for glucose levels during the OGTT were not statistically different between the two quartiles, subjects with low plasma HDL-C levels were characterized by significantly higher insulin levels in the fasting state and during the OGTT as compared with men having high HDL-C concentrations. These differences also resulted in a significantly greater insulin AUC for subjects with low HDL-C concentrations.

DISCUSSION

Visceral AT accumulation is an important correlate of the metabolic profile observed in obese men and women.[1] Indeed, increased plasma TG levels[2-5] and decreased HDL-C concentrations[6-9] are frequently observed in subjects with excess visceral AT. Furthermore, the insulin resistance state associated with visceral obesity[10,11] may lead to alterations in lipid metabolism.[12-14] This cluster of metabolic abnormalities increase the risk of CHD.[2,8,15-18]

The relationship between reduced HDL-C levels and CHD is well documented. Since apo A-I is a major component of HDL particles, it has been suggested that measuring plasma apo A-I concentrations could provide information that would complement HDL-C levels in the assessment of CHD risk.[19-26] In fact, plasma apo A-I concentrations, especially in normolipidemic subjects, have been found to be a better predictor of coronary artery disease than plasma lipid levels.[38,39] Furthermore, in case-control studies,[40,41] men with coronary artery disease showed significantly lower plasma apo A-I concentrations as compared with control subjects.

In the present study, although apo A-I concentrations were significantly correlated with HDL-C levels, low levels of apo A-I were not indicative of the alterations in AT distribution and anthropometric variables similar to those associated with reduced levels of HDL-C. Subjects with low plasma HDL-C levels were characterized by increased body weight, BMI, FM, waist girth, and WHR. A relationship between elevated BMI and low plasma apo A-I concentration has been reported,[42] but it was not found in the present study. Furthermore, apo A-I levels were not associated with any measures of body fatness, in contrast to low HDL-C.

A decreased plasma HDL-C concentration represents a plasma lipid abnormality frequently found in obese subjects. Our analyses showed that subjects with low levels of HDL-C had significant alterations in the plasma lipoprotein-lipid profile as compared with men having high plasma HDL-C concentrations. With the exception of cholesterol and LDL-C, which are poor correlates of visceral obesity and insulin resistance,[15,43] and HDL-TG, all other lipid parameters, including apo B levels, were significantly different between the two quartiles of plasma HDL-C concentrations. On the other hand, subjects with low levels of apo A-I did not show any major differences in the overall lipoprotein-lipid profile when compared with subjects with high plasma apo A-I concentrations.

Measurement of lipoprotein ratios showed that men with low plasma HDL-C levels had lipoprotein ratios predictive of an increased CHD risk versus men with high HDL-C concentrations. However, subjects in the first quartile of apo A-I showed differences when compared with men in the fourth quartile that were not as marked as differences observed when the lowest and highest quartiles of HDL-C were compared. These results suggest that measurement of

Table 1. Physical Characteristics of Men in the 1st, 2nd, 3rd, and 4th Quartiles of Apo A-I and HDL-C Concentrations (mean ± SD)

Characteristic	Apo A-I				HDL-C			
	1st (n = 26)	2nd (n = 28)	3rd (n = 29)	4th (n = 28)	1st (n = 27)	2nd (n = 28)	3rd (n = 27)	4th (n = 29)
Age (yr)	34.6 ± 5.0	34.7 ± 6.2	34.4 ± 7.1	37.3 ± 7.6	35.9 ± 6.5	37.8 ± 6.1	34.6 ± 5.5	32.8 ± 7.4‡
Weight (kg)	83.5 ± 11.1	78.5 ± 12.5	80.4 ± 14.9	81.7 ± 13.9	84.2 ± 13.2	83.9 ± 13.0	82.9 ± 13.2	73.4 ± 10.7†‡§
BMI (kg/m^2)	27.7 ± 3.8	25.9 ± 3.8	26.7 ± 4.6	26.8 ± 4.3	27.9 ± 3.9	28.2 ± 4.2	26.8 ± 3.6	24.3 ± 3.9†‡§
Body fat (%)	25.2 ± 7.5	24.1 ± 7.7	22.7 ± 9.6	23.3 ± 8.3	25.6 ± 7.7	26.5 ± 5.7	25.1 ± 7.7	18.2 ± 9.3†‡§
Fat mass (kg)	21.6 ± 8.2	19.6 ± 8.5	19.4 ± 10.9	20.1 ± 9.5	22.2 ± 9.5	23.0 ± 7.3	21.6 ± 9.0	14.1 ± 8.9†‡§
Waist girth (cm)	95.6 ± 10.8	92.1 ± 13.2	95.0 ± 24.0	95.6 ± 12.8	99.3 ± 22.5	99.1 ± 13.1	94.0 ± 11.8	86.3 ± 11.8†‡
WHR	0.94 ± 0.06	0.91 ± 0.07	0.90 ± 0.08†	0.94 ± 0.06§	0.93 ± 0.07	0.95 ± 0.07	0.92 ± 0.06	0.89 ± 0.08†‡
CT-derived abdominal AT areas (cm^2)*								
Total	389 ± 118	347 ± 145	386 ± 157	394 ± 157	419 ± 132	411 ± 122	370 ± 151	306 ± 155†‡
Visceral	129 ± 47	116 ± 47	131 ± 56	133 ± 57	142 ± 45	140 ± 46	121 ± 56	101 ± 52†‡
Subcutaneous	260 ± 86	232 ± 103	255 ± 114	261 ± 115	277 ± 97	271 ± 83	249 ± 114	205 ± 116†‡

*Apo A-I: 1st, n = 23; 2nd, n = 25; 3rd, n = 23; and 4th, n = 26. HDL-C: 1st, n = 24; 2nd, n = 27; 3rd, n = 24; and 4th, n = 22.
†Significantly different *v* the 1st quartile.
‡Significantly different *v* the 2nd quartile.
§Significantly different *v* the 3rd quartile.

apo A-I alone may be inadequate to appropriately assess CHD risk and the presence of the cluster of metabolic abnormalities (insulin resistance dyslipidemic syndrome) noted in visceral obesity. Indeed, differences in plasma insulin levels were noted between the subgroups of low versus high HDL-C levels. Men with low HDL-C levels had significantly higher fasting insulin levels, as well as post-OGTT insulin levels, compared with men with higher HDL-C levels. These differences in the response may imply that these nondiabetic men with low HDL-C were characterized by a compensatory increase in insulin to a glucose challenge resulting from a state of insulin resistance. No such difference in insulin levels was observed between subjects with low versus high plasma concentrations of apo A-I.

Since HDL-C concentrations have been reported to be decreased in the visceral obesity–insulin resistance syndrome,[44,45] the lack of a concomitant variation in apo A-I may reflect alterations in the composition of HDL. The estimation of the relative cholesterol content of HDL particles, as crudely assessed by the HDL-C/apo A-I ratio, was not different between the first and fourth quartiles of plasma apo A-I concentrations. Thus, low levels of apo A-I, believed to be indicative of a reduced number of HDL particles, were not associated with major changes in HDL composition. However, the complexity of HDL composition requires that more studies assessing HDL particle number and composition need to be conducted before a firm conclusion can be reached on this issue. Furthermore, comparison of the first and fourth quartiles of plasma HDL-C showed that both plasma apo A-I and the relative cholesterol content of HDL particles (as estimated by the HDL-C/apo A-I ratio) were significantly different between the two HDL-C subgroups. In this regard, it has been reported that obese women show a reduced HDL-C concentration per mole of HDL protein as compared with leaner subjects.[42] In the present study, men in the first quartile of HDL-C levels had an increased level of body fat and a

Table 2. Mean Plasma Lipoprotein-Lipid Concentrations of Men in the 1st, 2nd, 3rd, and 4th Quartiles of Apo A-I and HDL-C Concentrations (mean ± SD)

Parameter	Apo A-I				HDL-C			
	1st (n = 26)	2nd (n = 28)	3rd (n = 29)	4th (n = 28)	1st (n = 27)	2nd (n = 28)	3rd (n = 27)	4th (n = 29)
Cholesterol	4.83 ± 0.88	4.86 ± 1.04	4.88 ± 0.97	5.11 ± 0.67	4.91 ± 0.81	5.15 ± 0.90	4.95 ± 0.91	4.68 ± 0.94
TG	1.76 ± 0.88	1.66 ± 0.90	1.29 ± 1.02	1.52 ± 0.75	2.19 ± 1.08	1.77 ± 0.76*	1.44 ± 0.67*	0.84 ± 0.39*†‡
VLDL-C	0.65 ± 0.40	0.62 ± 0.43	0.45 ± 0.48	0.53 ± 0.31	0.86 ± 0.52	0.65 ± 0.37*	0.50 ± 0.25*	0.24 ± 0.15*†‡
VLDL-TG	1.22 ± 0.74	1.16 ± 0.76	0.86 ± 0.97	1.01 ± 0.64	1.63 ± 1.00	1.23 ± 0.67*	0.97 ± 0.53*	0.43 ± 0.30*†‡
LDL-C	3.30 ± 0.78	3.26 ± 0.98	3.38 ± 1.01	3.39 ± 0.63	3.31 ± 0.84	3.56 ± 0.87	3.37 ± 0.78	3.11 ± 0.91
LDL-TG	0.23 ± 0.13	0.22 ± 0.15	0.19 ± 0.10	0.24 ± 0.14	0.26 ± 0.14	0.26 ± 0.13	0.19 ± 0.14	0.17 ± 0.10*†
HDL-C	0.88 ± 0.17	0.97 ± 0.16	1.09 ± 0.18*†	1.19 ± 0.26*†	0.77 ± 0.06	0.93 ± 0.04*	1.08 ± 0.04*†	1.33 ± 0.17*†‡
HDL-TG	0.31 ± 0.10	0.28 ± 0.09	0.24 ± 0.05*†	0.27 ± 0.07	0.30 ± 0.09	0.28 ± 0.07	0.28 ± 0.10	0.25 ± 0.06
HDL_2-C	0.29 ± 0.11	0.34 ± 0.12	0.40 ± 0.15*	0.43 ± 0.18*†	0.22 ± 0.05	0.29 ± 0.07*	0.39 ± 0.09*†	0.55 ± 0.12*†‡
HDL_3-C	0.58 ± 0.10	0.64 ± 0.09	0.69 ± 0.08*	0.76 ± 0.14*†‡	0.55 ± 0.06	0.64 ± 0.06*	0.70 ± 0.10*†	0.77 ± 0.13*†‡
Apo A-I	88.8 ± 4.7	101.7 ± 3.5*	113.1 ± 3.3*†	135.8 ± 18.6*†‡	94.5 ± 9.4	109.0 ± 15.7	115.0 ± 19.8*	121.7 ± 21.3*†
Apo B	95.3 ± 22.0	91.0 ± 24.9	85.9 ± 23.1	95.0 ± 23.0	100.6 ± 16.9	101.0 ± 23.0	88.0 ± 22.5*†	77.7 ± 22.5*†

NOTE. Concentrations are mmol/L, except for apo A-I and apo B, which are mg/dL.
*Significantly different *v* the 1st quartile.
†Significantly different *v* the 2nd quartile.
‡Significantly different *v* the 3rd quartile.

Table 3. Lipoprotein Ratios of Men in the 1st, 2nd, 3rd, and 4th Quartiles of Apo A-I and HDL-C Concentrations (mean ± SD)

	Apo A-I				HDL-C			
Ratio	1st (n = 26)	2nd (n = 28)	3rd (n = 29)	4th (n = 28)	1st (n = 27)	2nd (n = 28)	3rd (n = 27)	4th (n = 29)
Cholesterol/ HDL-C	5.70 ± 1.38	5.15 ± 1.45	4.66 ± 1.37*	4.50 ± 1.16*	6.36 ± 1.08	5.52 ± 0.98*	4.59 ± 0.87*†	3.57 ± 0.82*†‡
LDL-C/HDL-C	3.88 ± 1.05	3.47 ± 1.21	3.21 ± 1.14*	3.00 ± 0.89*	4.26 ± 0.98	3.82 ± 0.92	3.12 ± 0.74*†	2.38 ± 0.79*†‡
LDL apo B/LDL-C	26.4 ± 3.0	25.3 ± 3.3	23.9 ± 3.27*	25.5 ± 3.5	27.7 ± 3.6	25.5 ± 3.0*	24.3 ± 2.25*	23.8 ± 3.1*†
HDL_2-C/HDL_3-C	0.51 ± 0.16	0.54 ± 0.20	0.58 ± 0.23	0.58 ± 0.29	0.42 ± 0.13	0.46 ± 0.14	0.58 ± 0.21*†	0.75 ± 0.24*†‡
HDL-TG/HDL-C	0.37 ± 0.13	0.30 ± 0.10	0.23 ± 0.08*†	0.24 ± 0.09*†	0.38 ± 0.13	0.31 ± 0.08*	0.25 ± 0.09*†	0.19 ± 0.05*†‡
HDL-C/apo A-I	0.010 ± 0.002	0.010 ± 0.001	0.010 ± 0.002	0.009 ± 0.002	0.008 ± 0.001	0.009 ± 0.001	0.010 ± 0.001*†	0.011 ± 0.002*†‡

*Significantly different *v* the 1st quartile.
†Significantly different *v* the 2nd quartile.
‡Significantly different *v* the 3rd quartile.

decreased HDL-C/apo A-I ratio, a finding that is concordant with these previous results. Furthermore, results from the Atherosclerosis Risk in Communities Study[46] also support this notion, since it was reported that the reduction of HDL-C concentration observed with obesity was primarily due to its associations with the plasma TG level, whereas changes in HDL-C concentrations attributable to a change in plasma apo A-I levels were more closely mediated by smoking and alcohol consumption. The elevated visceral AT accumulation commonly observed in the insulin resistance syndrome is associated with increased plasma TG levels, thereby providing substrate for lipid exchange with HDL by the action of lipid transfer proteins (ie, cholesteryl ester transfer protein). This process leads to changes in the core composition of HDL particles, such as TG enrichment, rather than alterations in HDL protein composition. In our subjects, increased visceral AT accumulation and increased TG levels were observed in the first quartile of HDL-C compared with the fourth. These metabolic characteristics are in concordance with those reported in the Atherosclerosis Risk in Communities Study. It is therefore proposed that the decreased plasma HDL-C concentrations found in subjects with features of the visceral obesity–insulin resistance syndrome may be due to reductions in both HDL particle number and cholesterol content.

In summary, we have attempted to compare how low levels of apo A-I and HDL-C could identify individuals showing the features of the insulin resistance–dyslipidemic syndrome found in viscerally obese men. In this regard, it appears that low levels of apo A-I provide less information

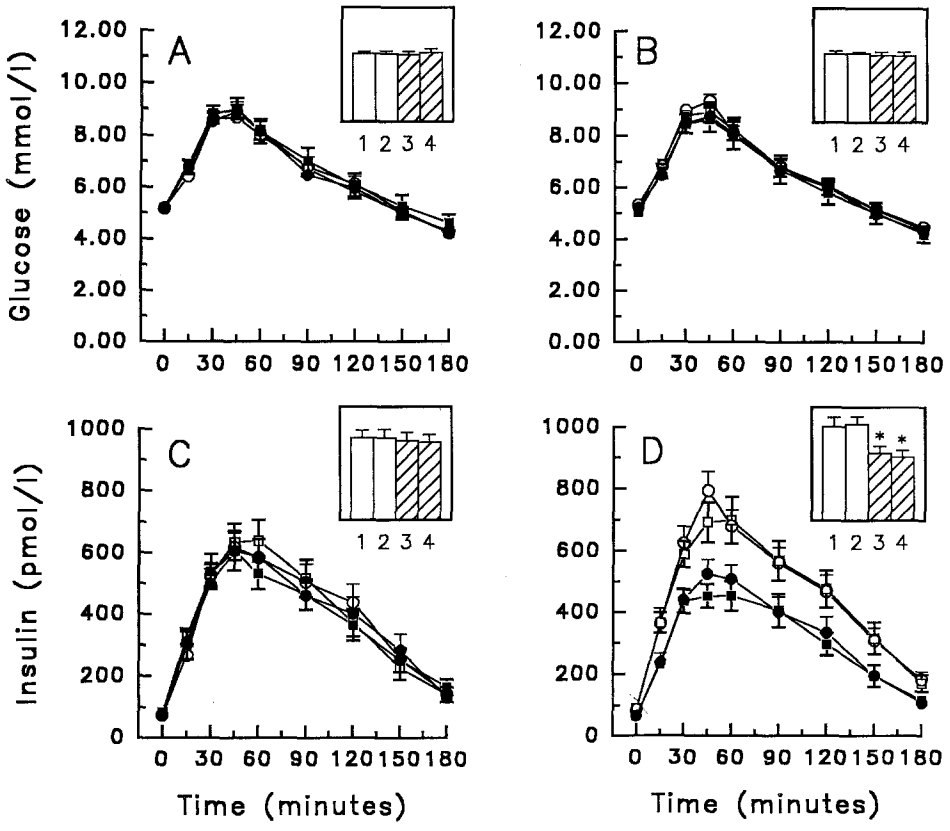

Fig 3. Plasma glucose and insulin responses following a 75-g OGTT among men in the first (□), second (○), third (●), and fourth (■) quartiles of plasma apo A-I (A and C) and HDL-C (B and D) concentrations. *AUC significantly different *v* quartiles 1 and 2 ($P < .01$). Third quartile of HDL-C: insulin levels significantly different *v* the first and second quartiles at 0, 15, 30, 45, 60, and 90 minutes and *v* the second quartile at 180 minutes. Fourth quartile of HDL-C: insulin levels significantly different *v* the first and second quartiles at 0, 15, 30, 45, 60, 90, and 120 minutes and *v* the second quartile at 180 minutes.

than low HDL-C levels, and that a reduced apo A-I concentration does not appear to be a component of the prevalent metabolic cluster associated with the insulin resistance syndrome. Moreover, studies have shown that plasma apo A-I concentrations did not add to the predictive value of HDL-C and other conventional CHD risk factors.[20,47,48] Thus, results of the present study do not support the measurement of apo A-I levels in addition to conventional lipoprotein-lipid levels for a more precise assessment of CHD risk.

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REFERENCES

1. Larsson B, Björntorp P, Tibblin G: The health consequences of moderate obesity. Int J Obes 5:97-116, 1988
2. Kissebah AH, Vydelingum N, Murray R, et al: Relation of body fat distribution to metabolic complications of obesity. J Clin Endocrinol Metab 54:254-260, 1982
3. Krotkiewski M, Björntorp P, Sjöström L, et al: Impact of obesity on metabolism in men and women: Importance of adipose tissue distribution. J Clin Invest 72:1150-1162, 1983
4. Kalkhoff RK, Hartz AH, Rupley D, et al: Relationship of body fat distribution to blood pressure, carbohydrate tolerance, and plasma lipids in healthy obese women. J Lab Clin Med 102:621-627, 1983
5. Evans DJ, Hoffman RG, Kalkhoff RK, et al: Relationship of body fat topography to insulin sensitivity and metabolic profiles in premenopausal obese women. Metabolism 33:68-75, 1984
6. Després JP, Allard C, Tremblay A, et al: Evidence for a regional component of body fatness in the association with serum lipids in men and women. Metabolism 34:967-973, 1985
7. Haffner SM, Stern MP, Hazuda HP, et al: Do upper-body and centralized adiposity measure different aspects of regional body-fat distribution? Relationship to non insulin-dependent diabetes mellitus, lipids, and lipoproteins. Diabetes 36:43-51, 1987
8. Després JP, Tremblay A, Pérusse L, et al: Abdominal adipose tissue and serum HDL-cholesterol: Association independent from obesity and serum triglyceride concentration. Int J Obes 12:1-13, 1988
9. Anderson AJ, Sobocinski KA, Freedman DS, et al: Body fat distribution, plasma lipids and lipoproteins. Arteriosclerosis 8:88-94, 1988
10. Després JP, Ferland M, Moorjani S, et al: Role of hepatic-triglyceride lipase activity in the association between intraabdominal fat and plasma HDL-cholesterol in obese women. Arteriosclerosis 9:485-492, 1989
11. Pouliot MC, Després JP, Nadeau A, et al: Visceral obesity in men—Associations with glucose tolerance, plasma insulin, and lipoprotein levels. Diabetes 41:826-834, 1992
12. Zavaroni I, Bonini L, Fantuzzi M, et al: Hyperinsulinemia, obesity and syndrome X. J Intern Med 235:51-56, 1994
13. Zavaroni I, Bonora E, Pagliara M, et al: Risk factors for coronary artery disease in healthy persons with hyperinsulinemia and normal glucose tolerance. N Engl J Med 320:702-706, 1989
14. Zavaroni I, Dall'Aglio E, Bonora E, et al: Evidence that multiple risk factors for coronary artery disease exist in persons with abnormal glucose tolerance. Am J Med 83:609-612, 1987
15. Després JP: Obesity and lipid metabolism: Relevance of body fat distribution. Curr Opin Lipidol 2:5-15, 1991
16. Després JP: Lipoprotein metabolism in visceral obesity. Int J Obes 15:45-52, 1991
17. Björntorp P: Hazards in subgroups of human obesity. Eur J Clin Invest 14:239-241, 1984
18. Després JP, Tremblay A, Thériault G, et al: Relationship between body fatness, adipose tissue distribution and blood pressure in men and women. J Clin Epidemiol 41:889-897, 1988
19. Buring JE, O'Connor GT, Goldhaber SZ, et al: Decreased HDL_2 and HDL_3 cholesterol, apo A-I and apo A-II, and the risk of myocardial infarction. Circulation 85:22-29, 1992
20. Stampfer MJ, Sacks FM, Salvini S, et al: A prospective study of cholesterol, apolipoproteins and the risk of myocardial infarction. N Engl J Med 325:373-381, 1991
21. Miller NE: Associations of high-density lipoprotein subclasses and apolipoproteins with ischemic heart disease and coronary atherosclerosis. Am Heart J 113:589-597, 1987
22. Kwiterovich PO, Sniderman AD: Atherosclerosis and apoproteins B and A-I. Prev Med 12:815-834, 1983
23. Maciejko JJ, Holmes DR, Kottke BA, et al: Apolipoprotein A-I as a marker of angiographically assessed coronary artery disease. N Engl J Med 309:385-389, 1983
24. DeBacker G, Rosseneu M, Deslypere JP: Discriminative value of lipids and apoproteins in coronary heart disease. Atherosclerosis 42:197-203, 1982
25. Reisen WF, Mordasini R, Salzmann C, et al: Apoproteins and lipids as discriminators of severity of coronary heart disease. Atherosclerosis 37:157-162, 1980
26. Puchois P, Kandoussi A, Fieret P, et al: Apolipoprotein A-I lipoproteins in coronary artery disease. Atherosclerosis 68:35-40, 1987
27. Lohman T, Roche A, Martorel R (eds): The Airlie (VA) Consensus Conference, in Standardization of Anthropometric Measurements. Champaign, IL, Human Kinetics, 1988, pp 39-80
28. Behnke AR, Wilmore JH: Evaluation and regulation of body build and composition. Engelwood Cliffs, CA, Prentice-Hall, 1974, pp 20-37
29. Siri WE: The gross composition of the body. Adv Biol Med Phys 4:239-280, 1956
30. Ferland M, Després JP, Tremblay A, et al: Assessment of adipose tissue distribution by computed tomography in obese women: Association with body density and anthropometric measurements. Br J Nutr 61:139-148, 1986
31. Després JP, Prud'homme D, Pouliot MC, et al: Estimation of deep abdominal adipose-tissue accumulation from simple anthropometric measurements in men. Am J Clin Nutr 54:471-477, 1991
32. Kvist H, Tylen U, Sjöström L: Adipose tissue volume determinations in women by computed tomography: Technical considerations. Int J Obes 10:53-67, 1986
33. Richterich R, Dauwalder H: Zur bestimmung der plasmaglukosekonzentration mit der hexokinase-glucose-6-phosphat-dehydrogenase-methode. Schweiz Med Wochenschr 101:615-618, 1971
34. Desbuquois B, Aurbach GD: Use of polyethylene glycol to separate free and antibody-bound peptide hormones in radioimmunoassays. J Clin Endocrinol Metab 37:732-738, 1971
35. Moorjani S, Dupont A, Labrie F, et al: Increase in plasma high-density lipoprotein concentration following complete androgen blockage in men with prostatic carcinoma. Metabolism 36:244-250, 1987
36. Burstein M, Samaille J: Sur un dosage rapide du cholestérol lié aux β-lipoprotéines du sérum. Clin Chim Acta 5:609-610, 1960

37. Gidez LI, Miller GJ, Burstein M, et al: Separation and quantitation of subclasses of human plasma high density lipoproteins by a simple precipitation procedure. J Lipid Res 23:1206-1223, 1982

38. Avogaro P, Bittolo Bon G, Cazzolato G, et al: Are apolipoproteins better discriminators than lipids for atherosclerosis? Lancet 1:901-903, 1979

39. Bittolo Bon G, Cazzolato G, Sccardi M, et al: Total plasma apo E and high density lipoprotein apo E in survivors of myocardial infarction. Atherosclerosis 53:69-75, 1984

40. Kwiterovich PO, Coresh J, Smith HH, et al: Comparison of the plasma levels of apolipoprotein B and apo A-I and other risk factors in men and women with premature coronary artery disease. Am J Cardiol 69:1015-1021, 1992

41. Genest JJ, Bard JM, Fruchart JC, et al: Plasma apolipoprotein A-I, A-II, B, E and C-III containing particles in men with premature coronary artery disease. Atherosclerosis 90:149-157, 1991

42. Meilhan EN, Kuller LH, Stein EA, et al: Characteristics associated with apoprotein and lipoprotein lipid levels in middle aged women. Arterioscler Thromb 8:515-520, 1988

43. Després JP, Moorjani S, Lupien PJ, et al: Regional distribution of body fat, plasma lipoproteins, and cardiovascular disease. Arteriosclerosis 10:497-511, 1990

44. Laws A, Reaven GM: Evidence for an independent relationship between insulin resistance and fasting plasma HDL-cholesterol, triglyceride and insulin concentrations. J Intern Med 231:25-30, 1992

45. Laakso M, Sarlund H, Mykkanen L: Insulin resistance is associated with lipid and lipoprotein abnormalities in subjects with varying degrees of glucose tolerance. Arterioscler Thromb 10:223-231, 1990

46. Patsch W, Sharett AR, Sorlic PD, et al: The relation of high density lipoprotein cholesterol and its subfractions to apolipoprotein A-I and fasting triglycerides: The role of environmental factors. The Atherosclerosis Risk in Communities (ARIC) Study. Am J Epidemiol 136:546-557, 1992

47. Cremer P, Elster H, Labrot B, et al: Incidence ratio of fatal and unfatal myocardial infarction in relation to the lipoprotein profile: First prospective results from the Gottingen Risk, Incidence, and Prevalence Study (GRIPS). Klin Wochenschr 66:42-49, 1988 (suppl 11)

48. Salonen JT, Salonen R, Penttila I, et al: Serum fatty acids, apolipoproteins, selenium and vitamin antioxidants and the risk of death from coronary artery disease. Am J Cardiol 56:226-231, 1985