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Effect of obesity on the plasma lipoprotein subclass profile in normoglycemic and normolipidemic men and women

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Abstract

Objective—To determine the effect of obesity without the confounding effect of metabolic complications on the lipoprotein subclass profile in men and women.

Design—Cross-sectional study.

Subjects—40 lean (BMI: 18.5–25 kg/m²) and 40 obese (BMI: 30–45 kg/m²) subjects, with blood pressure <140/90 mm Hg, fasting plasma glucose concentration <100 mg/dl and total triglyceride concentration <150 mg/dl; all obese subjects had normal oral glucose tolerance.

Measurements—Fasting concentrations of very low-, intermediate-, low-, and high-density lipoproteins (VLDL, IDL, LDL, and HDL, respectively) and average VLDL, LDL and HDL particle sizes were evaluated by using proton nuclear magnetic resonance spectroscopy.

Results—Obese compared with lean individuals of both sexes had increased plasma concentrations of VLDL (by ~50%), IDL (by ~100%), LDL (by ~50%), and to some extent HDL (by ~10%) particles ($P<0.05$). The contribution of large VLDL to total VLDL concentration, small LDL to total LDL concentration, and small HDL to total HDL concentration was greater in obese than lean subjects ($P<0.05$), resulting in larger average VLDL size but smaller average LDL and HDL sizes ($P<0.05$). Women, compared with men, had reduced concentrations of total VLDL particles (by ~10%) due to lower concentrations of large and medium VLDL, and a shift towards large at the expense of small HDL particles ($P<0.05$) with no difference in total HDL particle concentration. IDL and total LDL concentrations and LDL subclass distribution were not different between men and women.

Conclusion—Obesity is associated with pro-atherogenic alterations in the lipoprotein subclass profile, which may increase cardiovascular disease risk even in the absence of classical metabolic risk factors. On the other hand, the female cardiovascular disease risk advantage is probably largely related to differences in traditional lipid risk factors (plasma triglyceride and HDL-cholesterol concentrations) because sex differences in the plasma lipoprotein subclass profile are minimal.

Keywords

lipoprotein; subfractions; particle size; sex differences; lipid profile; NMR

Introduction

Alterations in the plasma lipid profile are strong predictors of coronary heart disease (CHD),¹ a leading cause of death and disability.² An increase in plasma triglyceride (TG) and low-density lipoprotein (LDL) cholesterol concentrations and a decrease in high-density lipoprotein (HDL) cholesterol concentration are considered the hallmark of pro-atherogenic dyslipidemia.¹ Besides these traditional risk factors, however, mounting evidence suggests that CHD risk is also influenced by plasma lipoprotein particle concentration itself and the lipoprotein subclass distribution. For example, a predominance of smaller LDL particles is associated with increased CHD risk³ and increased numbers of intermediate-density lipoprotein (IDL) particles, small HDL particles and large very low-density lipoprotein (VLDL) particles are associated with increased incidence and/or progression of angiographically-determined atherosclerosis.^{4,5} Insight into the lipoprotein subclass profile is therefore necessary to better understand the higher CHD risk in obese compared with lean individuals and men compared with women.^{1,6}

It is well established that obesity is often associated with increased plasma TG and decreased HDL-cholesterol concentrations,⁷ whereas women typically have lower plasma TG and higher HDL-cholesterol concentrations than men.⁸ However, the effects of sex and obesity on the plasma lipoprotein subclass distribution are unclear. Existing reports are difficult to interpret because studies in which the effect of obesity on plasma lipoprotein subclass distribution and size was examined included either only men^{9–11} or only women^{12,13} or both sexes but without evaluating potential sex differences;^{14–18} furthermore, more often than not they included subjects with serious metabolic abnormalities such as hypertriglyceridemia (fasting plasma TG concentrations as high as 200–400 mg/dl),^{9–11,15,16,18–20} hyperglycemia (fasting plasma glucose concentrations as high as 110–140 mg/dl),^{9,11,15,18} or glucose intolerance and diabetes,^{14,21} which may affect the distribution and size of plasma lipoproteins independently of adiposity.^{4,13,14,17,21–24} In addition, studies in which the potential impact of sex on the plasma lipoprotein profile was investigated included subjects with various degrees of adiposity and sometimes clinically manifest dyslipidemia.^{19,20,22,25–29}

The purpose of our study was to evaluate the lipoprotein particle profile, by using proton nuclear magnetic resonance (NMR) spectroscopy, in healthy, lean and obese men and women with normal fasting plasma glucose and TG concentrations to determine the effect of obesity on plasma lipoprotein particle concentrations and subclass profile without confounding by clinically significant obesity-associated alterations in substrate metabolism.

Materials and Methods

Subjects

Eighty subjects between the ages of 18 and 50 years participated in the study: 40 were lean with a body mass index (BMI) between 18.5 and 25 kg/m² and 40 were obese with a BMI between 30 and 45 kg/m² (Table 1). All subjects were considered to be in good health after completing a medical evaluation, which included a history and physical examination and standard blood tests. Subjects were included if they were free of hypertension (blood pressure < 140/90 mm Hg) and had normal fasting plasma glucose (< 100 mg/dl) and total TG (< 150 mg/dl) concentrations; in addition, all obese subjects had normal oral glucose tolerance (plasma glucose concentration 2 h after a 75 g oral glucose challenge < 140 mg/dl) and 36 of them had HDL-cholesterol concentrations below those adopted by the NCEP for the metabolic syndrome (i.e., 40 mg/dl for men and 50 mg/dl for women). None of the subjects were smoking or taking medications known to affect glucose or lipid metabolism. Body composition (fat mass and fat-free mass) was assessed by dual-energy X-ray absorptiometry (Delphi-W densitometer, Hologic, Waltham, MA). Written informed consent was obtained from all subjects before their

participation in the study, which was approved by the Human Studies Committee and the General Clinical Research Center (GCRC) Advisory Committee at Washington University School of Medicine in St. Louis, MO.

Experimental protocol

Fasting blood samples were obtained from each subject after an overnight controlled fast in the GCRC. Subjects were instructed to adhere to their regular diet and to refrain from physical activity for a minimum of three days before being admitted to the GCRC the afternoon before the day of blood sampling. At ~1930 h, they consumed a standard meal, containing ~12 kcal per kg of body weight for lean persons and per kg of adjusted body weight for obese persons (55% of total energy from carbohydrate, 30% from fat, and 15% from protein) and then fasted (except for water) and rested in bed until blood samples were obtained the next day. Adjusted body weight was calculated as ideal body weight (i.e., the midpoint of the medium frame of the 1983 Metropolitan Life Insurance Company Table)³⁰ + 0.25 × (actual body weight – ideal body weight).³¹ The following morning, between 0700 and 0800 h, four fasting venous blood samples (total volume ~20 ml) were collected in chilled tubes containing sodium EDTA. Serial blood samples were obtained to reduce the variability of plasma lipid measurements.³² Plasma was separated by centrifugation (3000 rpm for 15 min at 4°C), pooled and stored at –80°C until final analyses were performed. It has previously been demonstrated that freezing does not affect the NMR spectra of lipoproteins in blood samples obtained from normotriglyceridemic subjects in the fasted state.^{33,34} To determine glucose concentration, blood was collected in tubes containing heparin; plasma was separated by centrifugation and analyzed immediately.

Sample analyses

Plasma glucose concentration was determined by using an automated glucose analyzer (YSI 2300 STAT plus, Yellow Spring Instrument Co., Yellow Springs, OH). Plasma insulin concentration was measured by radioimmunoassay (Linco Research, St. Louis, MO). The homeostasis model assessment insulin resistance (HOMA-IR) index, reflecting whole-body insulin resistance,³⁵ was calculated as the product of plasma insulin (in mU/l) and glucose (in mmol/l) concentrations divided by 22.5. Plasma TG and HDL-cholesterol concentrations were determined by NMR; the NMR-derived values are highly correlated ($r > 0.9$) with the respective measurements from conventional lipid analysis.³⁶

Plasma concentrations of VLDL, IDL, LDL, and HDL particles and subgroups were determined (LipoScience, Raleigh, NC) by using an AVANCE INCA NMR Chemical Analyzer equipped with a Bruker BioSpin UltraShield super-conducting magnet (Bruker BioSpin, Billerica, MA). Plasma samples were diluted 2-fold, and 600 µl of the diluted sample were introduced into the NMR spectrometer (400 MHz, 47°C). Each sample was run once, multiple scans were obtained and the data were averaged. Lipoprotein particle concentrations and sizes were calculated by using described standard NMR lipoprotein analysis method.^{22, 36} With this method the coefficient of variation (CV) of the individual subpopulation signals is < 10%. Concentrations of the following nine lipoprotein subclass categories were measured: large VLDL (> 60 nm), medium VLDL (35–60 nm), small VLDL (27–35 nm), IDL (23–27 nm), large LDL (21.2–23 nm), small LDL (18–21.2 nm), large HDL (8.8–13 nm), medium HDL (8.2–8.8 nm), and small HDL (7.3–8.2 nm). Average VLDL, LDL and HDL particle sizes (diameter in nm) were computed as the sum of the diameter of each subclass multiplied by its relative mass percentage. Reproducibility of NMR determinations, expressed as the CV of replicate analyses of plasma samples, was < 4% for total VLDL, LDL, and HDL particle concentrations, < 2% for VLDL size, < 0.5% for LDL and HDL size, < 10% for large, medium, and small VLDL subclasses, < 8% for large and small LDL subclasses, and < 5% for large and

small HDL subclasses. Higher CVs were obtained for IDL (< 20%) and medium HDL (< 35%) subclasses, due to their typically low concentrations in plasma.

Statistical analysis

All data sets were normally distributed according to Kolmogorov-Smirnov. Results for lean and obese men and women were compared by using two-way analysis of variance with interaction, including BMI group (lean or obese) and sex (male or female) as main effects. All data are presented as means $\pm$ standard error (s.e.). A P -value ≤ 0.05 was considered statistically significant. Analyses were carried out with SPSS 16.0.0 (SPSS Inc, Chicago, IL).

Because increased body fat has a major impact on the plasma lipid profile and women typically have much more body fat than men, we carried out a secondary analysis to determine whether sex differences are present independent of differences in body composition between men and women. We thus compared the lipoprotein profile in a subgroup of men and women from our cohort who had $\geq 20\%$ but $\leq 50\%$ body fat. Data from men and women who were matched on percent body fat were compared by using the Levene's test to assess equality of group variances and the Student's t -test for independent samples.

Results

Age, body composition and basic metabolic characteristics of lean and obese men and women (Table 1)

Lean and obese men and women were of similar age. Obese men and women weighed more, and had greater fat and fat-free masses than lean subjects. Compared with men, women were shorter, weighed less, and had greater fat mass but less fat-free mass; BMI was not different between sexes.

Obese, compared with lean subjects of both sexes had significantly greater plasma glucose and insulin concentrations and were more insulin resistant (HOMA-IR index); they also had greater plasma TG and lower HDL-cholesterol concentrations than lean subjects. Women, compared with men, had significantly lower plasma glucose concentrations and higher HDL-cholesterol concentrations and tended to have lower plasma TG concentration.

Lipoprotein particle concentrations and size in lean and obese men and women (Table 2)

There were no significant interactions between BMI group and sex for any of the NMR-derived variables (Table 2). Irrespective of sex, obesity was associated with increased concentrations of VLDL (by $\sim 50\%$), IDL (by $\sim 110\%$), LDL (by $\sim 55\%$), and HDL (by $\sim 10\%$) particles in plasma. The greater VLDL particle concentration in obese compared with lean subjects was due to greater concentrations of large ($\sim 220\%$), medium ($\sim 40\%$) and small ($\sim 50\%$) VLDL particles, whereas the greater concentration of LDL particles was entirely due to an increase (by $\sim 100\%$) in small LDL particles with no difference between lean and obese in the concentration of large LDL particles. The greater concentration of HDL particles in obese compared with lean subjects was due to a $\sim 30\%$ greater concentration of small HDL particles which was accompanied by $\sim 50\%$ reduced concentration of large HDL particles. Thus, average VLDL particle size was $\sim 8\%$ greater, average LDL particle size was $\sim 3\%$ smaller, and average HDL particle size was $\sim 7\%$ smaller in obese than lean subjects.

Compared with men (irrespective of BMI group), the concentration of VLDL particles was $\sim 10\%$ less in women, due to lower concentrations of both large and medium (by 23% and 16%, respectively) but not small VLDL particles. Men and women did not differ with respect to total HDL particle concentration, but the concentrations of large and medium HDL particles were greater and the concentration of small HDL particles was $\sim 15\%$ less in women than in men.

(Table 2). There were no sex differences in IDL and LDL subclass concentrations. Average VLDL and LDL particle sizes were not different between sexes but average HDL particle size was ~4% greater in women than in men.

Lipoprotein subclass distribution in lean and obese men and women (Figure 1)

The relative subclass distributions of VLDL, LDL, and HDL in lean and obese men and women are shown in Figure 1. In obese, compared with lean individuals (both men and women), the contribution of large VLDL to total VLDL concentration was increased ($P < 0.001$), although only to a minor extent, at the relative expense of both medium and small VLDL particles; the contribution of small LDL to total LDL particle concentration was increased at the relative expense of large LDL particles ($P < 0.001$); the HDL subclass profile was shifted towards more small at the relative expense of large HDL particles ($P < 0.001$).

In women, compared with men (both lean and obese), the contribution of large VLDL to total VLDL concentration was reduced at the relative expense of both medium and small VLDL ($P = 0.012$), but actual sex differences in VLDL subclass distribution were very small (i.e., ~3% of all VLDL were large in men vs ~2.5% in women). There was no difference between men and women in the relative contribution of large and small LDL to total LDL concentration. The HDL subclass profile was shifted towards fewer small but more medium and large HDL in women than in men ($P < 0.01$; both lean and obese).

Age, body composition and basic metabolic characteristics of men and women who are matched on percent body fat (Table 3)

Women were shorter, weighed less and had less fat mass and fat-free mass than men. There were no differences in plasma glucose and insulin concentrations and HOMA-IR index between men and women. However, men had greater concentrations of total plasma TG and less HDL-cholesterol than women.

Lipoprotein particle concentrations and size in men and women who are matched on percent body fat (Table 4)

The total concentration of VLDL particles was ~30% less in women than in men whereas the total concentrations of IDL, LDL, and HDL were the same in men and women. The lower VLDL particle concentration in women than men was due to lower concentrations of large (~55%), medium (~35%) and small (~25%) VLDL particles. There was no difference in the subclass distribution of LDL in men and women, but women had ~170% more large and ~25% fewer small HDL particles. Average VLDL and LDL particle sizes were the same in men and women but the average HDL size was ~8% greater in women than in men.

The relative subclass distributions of VLDL, LDL, and HDL in men and women who are matched on percent body fat are shown in Figure 2.

Discussion

In this study we evaluated the effect of obesity on plasma lipoprotein concentrations and the lipoprotein subclass distribution. We studied men and women who were free of clinically significant alterations in substrate metabolism to avoid potential confounding due to marked dyslipidemia and insulin resistance, which are often present in obese individuals.⁷ We found that obesity, even in the absence of clinically significant imbalances in glucose and lipid homeostasis, was associated with a 50% to 100% increase in the concentrations of the pro-atherogenic lipoproteins VLDL, IDL, and LDL, as well as a small, and biologically probably insignificant, increase (by ~10%) in HDL particle concentration. Furthermore, we found that obesity was associated with a shift towards a pro-atherogenic subclass distribution, the most

marked of which was the change towards predominately small LDL; in addition, there was a shift, although less marked, towards small HDL and an even less pronounced shift towards large VLDL. These changes in lipoprotein profile likely increase CHD risk^{3–5} in obese subjects who are considered healthy on the basis of their blood biochemistries and plasma glucose and lipid concentrations. On the other hand, the female CHD risk advantage is probably largely related to differences in traditional lipid risk factors (e.g., plasma TG and HDL-cholesterol concentrations) because there were no sex differences in the concentrations of circulating IDL, LDL (total and subclasses) and HDL (total) particles and the differences between men and women in VLDL (total and large) particle concentration and HDL subclass profile, although statistically significant, were relatively minor.

Our findings regarding the effect of obesity on plasma lipoprotein subclass concentrations confirm and extend the observations made earlier by other investigators. In agreement with our results, obesity is almost uniformly reported to be associated with increased total plasma apolipoprotein (apo) B-100 concentration due to increased concentrations of all three apoB-100 containing lipoprotein classes (i.e., VLDL, IDL and LDL).³⁷ In addition, obesity has previously been found to be associated with increased concentrations of small, dense LDL particles and smaller average LDL particle size^{9,10,15,18,20,25} as well as smaller average HDL particle size due to reciprocal changes in the concentrations of small (increased) and large (decreased) HDL particles.^{16,18,19,38} However, in all of these earlier studies it was not clear whether these changes were largely the result of obesity (as in our study) or due to obesity-related metabolic comorbidities, because most studies included individuals with clinically significant dyslipidemia (e.g., fasting plasma TG concentrations as high as 200–400 mg/dl)^{9–11,15,16,18–20} and fasting hyperglycemia (plasma glucose concentrations as high as 110–130 mg/dl),^{9,11,15,18} while others included individuals with variable drinking and smoking habits and subjects who used medications.^{20,25,38}

Existing data regarding the effect of obesity on VLDL subclass distribution is inconclusive. By using cumulative flotation ultracentrifugation, Bioletto *et al.*¹⁷ observed no differences in the concentrations of three VLDL subfractions in lean and obese subjects (both men and women). However, by using NMR spectroscopy, MacLean *et al.*¹² found no differences in VLDL subclass concentrations and average VLDL size between some lean and obese subject groups but not others and other investigators, also relying on NMR spectroscopy measurements, reported positive associations between adiposity measures and average VLDL particle size^{14,21} and particularly with large VLDL subfraction concentrations.^{13,18,21} The discrepancy in results is probably due to differences in the metabolic characteristics of subjects because fasting glucose, insulin and TG concentrations, glucose intolerance, and insulin resistance have all been shown to influence the distribution and size of VLDL.^{13,14,21–24} In fact, the strength of the relationship between these metabolic parameters and VLDL subclass profile is stronger than that for LDL and HDL,^{14,21,23,39} indicating that VLDL subclass distribution and size might be particularly susceptible to these influences.

The pro-atherogenic effect of obesity on the plasma lipoprotein profile was present in both sexes and was of similar magnitude in men and women. However, independent of obesity, we discovered differences between the sexes in the concentration of VLDL particles (all subclasses), which was reduced in women, and the subclass distribution of HDL, which was shifted towards larger particles at the expense of smaller ones in women. The concentrations of IDL, LDL (all subclasses) and total HDL particles were not different between the sexes. As is the case with the traditional CHD risk factors (e.g., plasma TG and HDL-cholesterol concentrations), differences between sexes in the lipoprotein subclass profile are not due to differences in body composition between men and women because women have more body fat than men and yet a less pro-atherogenic plasma lipoprotein profile. In addition, the observed sex differences were small and it remains unclear whether they significantly contribute to the

reduced CHD risk in women, beyond the differences in traditional lipid risk factors. For instance, women typically have 20–40% lower plasma TG and higher HDL-cholesterol concentrations than men,^{22,27,40–43} whereas sex differences in VLDL particle concentrations and HDL subclass distribution profile in our study were generally around 10% or less.

The differences in HDL subclass distribution between our men and women are in agreement with previous population-based studies using NMR spectroscopy, in which total HDL particle number was found to be the same in men and women but the HDL subfraction distribution was shifted towards larger particles and average HDL size was greater in women than in men.^{22,26,27,44} In addition, our finding regarding lower VLDL particle concentrations in women than in men is in agreement with previous reports.^{22,26,27} However, we and other small cohort studies²⁶ found no difference between the sexes in VLDL particle size, whereas population-based studies reported smaller average VLDL size in women than in men, the difference being around 7–8%.^{22,27,28} Our inability to detect a statistically significant difference of smaller magnitude (2–6% in our subjects) is therefore likely due to the relatively small sample size. Part of the discrepancy in outcomes between studies may also rest on differences in subject characteristics, such as subjects' BMI, plasma TG and HDL-cholesterol and insulin concentrations, which have been shown to influence the magnitude of sex differences in VLDL particle size.^{22,39,44}

In contrast to the results from our study, in which there is no indication for sex differences in either total LDL particle concentration or subclass distribution and average particle size, LDL subclass profile was shifted towards larger particles and LDL size was greater in women than in men in all^{19,20,22,26,27,29,45–54} but two^{28,55} reports on this issue that we are aware of. However, the reported sex differences in LDL particle size are typically in the range of 1–2%^{19,20,22,26,27,29,48–50,52} and may therefore only be detected in much larger samples than ours.^{22,50,52} Moreover, most of these studies included lean, overweight, and obese individuals combined, with plasma TG concentrations as high as 200–400 mg/dl,^{19,20,22,26,27,29,48–50,52} which complicates the interpretation of these earlier reports. Indeed, studies that stratified their cohort according to plasma TG concentration found that the sex difference in LDL particle size was only present in subjects with hypertriglyceridemia (plasma TG concentration > 200 mg/dl)⁴⁸ but not among normotriglyceridemic men and women (plasma TG concentration < 150 mg/dl).^{48,55} Our men and women were matched for BMI and insulin resistance (as indicated by the HOMA-IR) within the lean and obese groups, and plasma TG concentrations in both lean and obese men and women were within the normal range (< 150 mg/dl). Thus, we conclude that when men and women are healthy and well-matched, there is no sex difference in LDL size or subclass distribution.

The mechanisms underlying the observed effects of obesity and sex on plasma lipoprotein concentrations and subclass distribution are not well understood. Obesity is characterized by hepatic overproduction of VLDL-apoB-100 (i.e., VLDL particles), decreased catabolism of apoB-100 containing lipoprotein particles (VLDL, IDL, and LDL) and increased turnover of apoA-I containing HDL particles,^{37,56} which is consistent with higher VLDL, IDL, and LDL particle concentrations and a shift towards smaller HDL particles in obese compared with lean subjects. The size of circulating apoB-100 containing lipoprotein particles is largely determined by their TG content, and studies examining the effect of obesity on VLDL-TG kinetics reported an increase in VLDL-TG secretion in obese men and impaired plasma VLDL-TG clearance in obese women,³¹ which may underlie the larger circulating VLDL particles in obese than lean subjects. The alterations in the relevant mechanisms determining IDL and LDL particle sizes in obesity are not clear, but they are related to the metabolism of their precursor, i.e., VLDL (both VLDL-TG and VLDL-apoB-100), as well as the catabolism of the IDL/LDL-TG and IDL/LDL-apoB-100.^{57–59} Sex differences in VLDL-apoB-100 (i.e., VLDL particle) metabolism are small and have been examined mainly among lean, overweight and obese

individuals combined;⁶⁰ still, lean women secrete fewer VLDL particles (i.e., VLDL-apoB-100) than lean men⁶¹ consistent with their lower total VLDL particle concentration. Similarly, there is no difference between normotriglyceridemic (plasma TG concentration < 185 mg/dl) men and women in IDL-apoB-100 and LDL-apoB-100 kinetics,^{62,63} consistent with the absence of sex differences in IDL and LDL subfraction concentrations and LDL subclass distribution and particle size. Studies evaluating HDL-apoA-I and apoA-II kinetics generally report some^{64–66} or no^{62,67,68} differences between men and women, indicating relatively small effects on HDL metabolism. Clearly, more kinetic studies are needed to better understand the mechanisms responsible for the observed effects of obesity and sex on plasma lipoprotein profile.

In summary, we found that obesity is not only associated with a significant increase in circulating pro-atherogenic lipoprotein particles (i.e., VLDL, IDL, LDL) but also leads to unfavorable, pro-atherogenic alterations in VLDL, LDL, and HDL subclass distributions, namely a disproportionate increase in the concentration of large VLDL and small LDL, and an increase in the concentration of small HDL at the expense of large HDL. Importantly, the effect of obesity on the lipoprotein subclass profile is evident in the absence of clinically significant imbalances in plasma glucose and lipid homeostasis, and is qualitatively the same in men and women, although women have overall fewer circulating VLDL (all subclasses) and fewer small but more large HDL. These alterations in obese subjects likely increase their risk for CHD^{3–5} even in the absence of clinically manifest dyslipidemia and hyperglycemia; the female CHD risk advantage is largely related to the traditional lipid risk factors (e.g., plasma TG and HDL-cholesterol concentrations) because the differences between men and women in lipoprotein particle concentration and subclass profile are comparably minor.

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Figure 1. Subclass distribution (% of total) of very low-, low-, and high-density lipoproteins (VLDL, LDL, and HDL, respectively) in lean and obese men and women. Values are means $\pm$ s.e. There were no significant interactions between obesity and sex. * Significantly different from corresponding value in lean subjects of the same sex ($P < 0.05$). † Significantly different from corresponding value in men of the same body mass index group ($P < 0.05$).

Figure 2. Subclass distribution (% of total) of very low-, low-, and high-density lipoproteins (VLDL, LDL, and HDL, respectively) in men and women who are matched on percent body fat. Values are means $\pm$ s.e. * Significantly different from corresponding value in men ($P < 0.05$).

Table 1
Age, body composition and basic metabolic characteristics of lean and obese men and women

	Lean (N = 40)		Obese (N = 40)		obesity	Two-way ANOVA P-values	
	Men	Women	Men	Women		sex	interaction
N	18	22	13	27			
Age (years)	30.9 ± 1.6	30.9 ± 1.9	33.5 ± 2.4	35.5 ± 1.7	0.069	0.604	0.615
Weight (kg)	73.3 ± 1.8	62.2 ± 1.5	106.6 ± 4.5	96.9 ± 2.4	< 0.001	< 0.001	0.776
Height (cm)	180 ± 1	166 ± 2	176 ± 3	166 ± 1	0.109	< 0.001	0.196
Body mass index (kg/m ²)	22.6 ± 0.4	22.4 ± 0.3	34.5 ± 1.2	35.1 ± 0.7	< 0.001	0.793	0.547
Fat mass (%)	14.1 ± 1.3	28.2 ± 0.8	33.9 ± 2.2	48.2 ± 1.1	< 0.001	< 0.001	0.929
Fat mass (kg)	10.4 ± 1.1	17.6 ± 0.7	36.7 ± 3.6	47.2 ± 2.0	< 0.001	< 0.001	0.401
Fat-free mass (%)	85.9 ± 1.3	71.8 ± 0.8	66.1 ± 2.2	51.8 ± 1.1	< 0.001	< 0.001	0.929
Fat-free mass (kg)	62.8 ± 1.5	44.6 ± 1.1	69.8 ± 2.7	49.8 ± 1.0	< 0.001	< 0.001	0.532
Glucose (mmol/l)	5.0 ± 0.1	4.9 ± 0.1	5.3 ± 0.1	5.0 ± 0.1	0.012	0.003	0.202
Insulin (pmol/l)	29 ± 3	30 ± 4	66 ± 13	71 ± 7	< 0.001	0.625	0.758
HOMA-IR	1.10 ± 0.09	1.10 ± 0.14	2.61 ± 0.24	2.63 ± 0.26	< 0.001	0.910	0.945
Plasma triglyceride (mg/dl)	71 ± 3	60 ± 4	107 ± 6	101 ± 5	< 0.001	0.072	0.596
HDL-cholesterol (mg/dl)	35 ± 2	45 ± 2	31 ± 2	35 ± 2	< 0.001	0.001	0.198

Values are means ± s.e. Abbreviations: HOMA-IR, homeostasis model assessment of insulin resistance; HDL, high-density lipoprotein.

Table 2
Lipoprotein particle concentrations and size in lean and obese men and women

	Lean		Obese		Two-way ANOVA <i>P</i> -values	
	Men	Women	Men	Women	obesity	sex interaction
VLDL particles, total (nmol/l)	48.6 ± 2.3	37.7 ± 3.0	67.3 ± 4.4	62.3 ± 3.1	< 0.001	0.019
Large	0.9 ± 0.2	0.6 ± 0.1	2.9 ± 0.3	2.0 ± 0.2	< 0.001	0.006
Medium	15.2 ± 1.2	11.3 ± 1.4	20.4 ± 2.6	17.2 ± 1.4	0.001	0.033
Small	32.5 ± 1.6	25.8 ± 2.4	44.0 ± 2.8	43.1 ± 2.2	< 0.001	0.120
Average VLDL size (nm)	48.4 ± 1.2	45.8 ± 0.9	51.5 ± 1.5	50.5 ± 1.0	0.001	0.123
LDL particles (nmol/l)	18.4 ± 4.0	22.7 ± 5.1	36.5 ± 6.4	47.7 ± 6.5	0.001	0.207
LDL particles, total (nmol/l)	728 ± 34	640 ± 43	1020 ± 50	1082 ± 60	< 0.001	0.818
Large	337 ± 23	298 ± 23	333 ± 24	333 ± 28	0.568	0.477
Small	391 ± 35	342 ± 43	687 ± 58	750 ± 59	< 0.001	0.900
Average LDL size (nm)	21.4 ± 0.1	21.5 ± 0.2	20.9 ± 0.1	20.9 ± 0.1	< 0.001	0.797
HDL particles, total (μmol/l)	23.4 ± 0.8	24.1 ± 0.6	26.1 ± 1.3	25.9 ± 0.8	0.013	0.759
Large	4.9 ± 0.6	6.7 ± 0.5	1.7 ± 0.2	3.5 ± 0.5	< 0.001	0.002
Medium	1.4 ± 0.3	3.4 ± 0.6	2.9 ± 0.8	3.6 ± 0.5	0.128	0.019
Small	17.1 ± 0.8	14.0 ± 0.7	21.4 ± 0.7	18.7 ± 0.7	< 0.001	< 0.001
Average HDL size (nm)	9.0 ± 0.1	9.5 ± 0.1	8.4 ± 0.1	8.7 ± 0.1	< 0.001	< 0.001

Values are means ± s.e. Abbreviations: VLDL, very low-density lipoprotein; LDL, intermediate-density lipoprotein; HDL, high-density lipoprotein.

Table 3

Age, body composition and basic metabolic characteristics of men and women who are matched on percent body fat

	Men	Women	P-value
<i>N</i>	15	15	
Age (years)	34.6 ± 2.2	33.9 ± 2.4	0.841
Weight (kg)	103.5 ± 4.4	71.7 ± 3.5	< 0.001
Height (cm)	177 ± 2	166 ± 2	0.001
Body mass index (kg/m ²)	33.2 ± 1.4	26.0 ± 1.4	0.001
Fat mass (%)	32.5 ± 2.1	33.0 ± 2.3	0.874
Fat mass (kg)	34.5 ± 3.4	24.7 ± 2.9	0.038
Fat-free mass (%)	67.5 ± 2.1	67.0 ± 2.3	0.874
Fat-free mass (kg)	69.0 ± 2.4	47.0 ± 1.2	< 0.001
Glucose (mmol/l)	5.2 ± 0.1	5.1 ± 0.1	0.359
Insulin (pmol/l)	59 ± 12	51 ± 12	0.646
HOMA-IR	2.31 ± 0.50	1.98 ± 0.48	0.640
Plasma triglyceride (mg/dl)	102 ± 6	75 ± 9	0.016
HDL-cholesterol (mg/dl)	30 ± 2	40 ± 3	0.002

Values are means ± s.e. Abbreviations: HOMA-IR, homeostasis model assessment of insulin resistance; HDL, high-density lipoprotein.

Table 4

Lipoprotein particle concentrations and size in men and women who are matched on percent body fat

	Men	Women	P-value
VLDL particles, total (nmol/l)	65.3 ± 4.1	46.4 ± 5.8	0.013
Large	2.6 ± 0.4	1.2 ± 0.4	0.009
Medium	19.3 ± 2.4	13.2 ± 1.8	0.049
Small	43.4 ± 2.5	32.1 ± 4.5	0.038
Average VLDL size (nm)	51.1 ± 1.4	47.8 ± 1.4	0.102
IDL particles (nmol/l)	37.8 ± 5.6	43.3 ± 10.1	0.636
LDL particles, total (nmol/l)	999 ± 46	812 ± 98	0.101
Large	327 ± 24	296 ± 44	0.543
Small	672 ± 51	516 ± 90	0.145
Average LDL size (nm)	20.9 ± 0.1	21.2 ± 0.2	0.254
HDL particles, total (μmol/l)	25.3 ± 1.2	24.8 ± 0.7	0.749
Large	1.9 ± 0.2	5.2 ± 0.8	0.001
Medium	2.6 ± 0.7	3.3 ± 0.7	0.433
Small	20.8 ± 0.8	16.3 ± 1.0	0.002
Average HDL size (nm)	8.5 ± 0.1	9.2 ± 0.2	0.001

Values are means ± s.e. Abbreviations: VLDL, very low-density lipoprotein; IDL, intermediate-density lipoprotein; LDL, low-density lipoprotein; HDL, high-density lipoprotein.