Does Lipoprotein or Hepatic Lipase Activity Explain the Protective Lipoprotein Profile of Premenopausal Women?

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Numerous studies have reported that women have a lipoprotein profile suggestive of a reduced risk of coronary heart disease (CHD). We have therefore tested whether the "protective" lipoprotein profile of women could be explained by differences in hepatic lipase (HL) or lipoprotein lipase (LPL) activities. In the present study, 14 non-obese healthy premenopausal women had higher plasma concentrations of high-density lipoprotein cholesterol (HDL-C), HDL_2-C, HDL_3-C, and HDL–apolipoprotein (apo) AI, and a higher ratio of HDL-C to low-density lipoprotein cholesterol (LDL-C) than 17 non-obese healthy men. Women also had lower plasma triglyceride (TG), HDL-TG, and apo B levels than men. Plasma postheparin LPL (PH-LPL) and HL activities showed no significant sex dimorphism, whereas abdominal and femoral adipose tissue (AT)-LPL activities were significantly higher in women ($P < .005$). In men, PH-LPL activity correlated significantly with plasma HDL_2-C ($r = .52$, $P < .05$), LDL-C ($r = -.47$, $P < .05$), and apo B ($r = -.56$, $P < .01$) levels, as well as with the HDL-C/LDL-C ratio ($r = .67$, $P < .005$). No such relationships were found in women, with the exception of HL activity, which was negatively correlated with HDL–apo AI levels. In both genders, abdominal AT-LPL activity showed no significant association with plasma lipoprotein levels. In contrast, femoral AT-LPL activity in women was positively correlated with plasma HDL-C, HDL_2-C ($r = .53$, $P < .05$ and $r = .69$, $P < .01$, respectively), and HDL–apo AI ($r = .52$, $P < .01$) levels, as well as with the HDL-C/LDL-C ratio ($r = .62$, $P < .01$). These associations were not found in men. Analysis of covariance (ANCOVA) showed that adjustment for HL activity could not explain sex differences in lipoprotein levels. When correction for PH-LPL activity was performed, gender differences observed in plasma lipoprotein levels remained significant. In ANCOVA with inclusion of abdominal AT-LPL activity as a covariate, men still had plasma TG levels significantly higher than women, whereas HDL-C, HDL_2-C, HDL–apo AI, and HDL_3-C concentrations were lower. Finally, femoral AT-LPL activity was the most powerful covariate explaining gender differences in plasma lipoprotein levels. Indeed, adjustment for femoral AT-LPL activity eliminated gender differences in plasma TG, HDL-C, HDL_2-C, HDL–apo AI, and apo B levels and the HDL-C/LDL-C ratio, with the exception being the HDL_3-C level. Although these results do not provide evidence for a cause-and-effect relationship, they suggest that the high femoral AT-LPL activity is a significant correlate of the favorable plasma lipoprotein-lipid profile in women.

IN WESTERN SOCIETIES, women generally live longer than men, and they also show a lower prevalence of coronary heart disease (CHD).[1-2] It has been suggested that this gender dimorphism may result from the differences noted in plasma lipoprotein-lipid levels between men and women.[3] Indeed, women have consistently higher high-density lipoprotein cholesterol (HDL-C) levels,[4-10] especially the HDL_2 subfraction,[10-13] as well as higher HDL–apolipoprotein (apo) AI as compared with men.[14] Women also generally have lower serum triglyceride (TG) levels than men.[5-7,15] Although plasma low-density lipoprotein (LDL-C) levels in women are not consistently lower than in men of similar age,[4,6] women are less likely to show high levels of dense LDL particles, which are believed to be atherogenic.[5] Thus, the overall lipoprotein profile in women is more favorable than in men, especially before menopause.

The physiologic processes that may explain sexual differences in lipoprotein-lipid levels are not fully understood. It has been reported that women have higher adipose tissue (AT) and postheparin (PH) lipoprotein lipase (LPL) activities than men.[16-20] Furthermore, LPL plays a major role in the catabolism of TG-rich lipoproteins and in the production of HDL particles.[21-24] In fact, AT-LPL and PH-LPL activities have been frequently reported to be negatively correlated with TG levels and positively associated with plasma HDL-C concentration.[22-25] However, AT-LPL activity varies according to regions,[25-27] and each site appears to display a specific association with plasma lipoprotein levels.[25]

Another lipolytic enzyme, hepatic lipase (HL), also plays a role in the regulation of lipoprotein levels,[28,29] since its activity has been negatively correlated with plasma HDL-C level.[29,30] Finally, many reports have suggested that LPL activities and particularly HL activity, as well as lipoprotein levels, are regulated by sex steroid hormones.[31-33] Therefore, the aim of the present study was to investigate the potential contribution of HL, PH-LPL, or regional AT-LPL activities to the well-known gender difference found in the plasma lipoprotein-lipid profile.

SUBJECTS AND METHODS

Subjects

A sample of 31 healthy subjects (17 men and 14 premenopausal women) was recruited by solicitation through the media, and each subject signed an informed-consent document as required by the Medical Ethics Committee of Laval University. Each participant was subjected to a complete medical examination performed by a

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physician. Individuals with cardiovascular disease, diabetes, or endocrine disorders, or who were on medication were excluded. Since physical activity and obesity are known correlates of plasma lipoprotein levels and lipase activities, subjects had to be non-obese (body mass index < 25 kg/m^2) and sedentary (no more than one session of 30 minutes of continuous endurance exercise per week) to be included in the study. Body weight of subjects had to be stable for at least 2 months. Moreover, no subject was involved in a weight-loss program or on a diet. Smokers were also excluded.

Body Fatness

The mean of six hydrostatic-weighing measurements was used for estimation of percent body fat from density using Siri's equation.[34] Pulmonary residual volume was determined using the closed-circuit helium-dilution method reported by Meneely and Kaltreider.[35] Fat mass was calculated by multiplying the percentage of body fat by body weight.

Computed Axial Tomography

A Siemens Somatom DRH scanner (Erlangen, Germany) was used to perform computed tomography (CT)-derived measurements of AT areas, using the procedures reported by Sjöström et al[36] as previously described.[37] CT scans were performed, using a radiograph of the skeleton as a reference to establish the position of the scans, at the abdomen (L4-L5) and femoral levels (mid-distance between the iliac crest and the knee joint) to the nearest millimeter. Fat areas were calculated by delineating these areas with a graph pen and computing the AT surfaces with an attenuation range of −190 to −30 HU.

Plasma Lipoprotein-Lipid and Apolipoprotein Analyses

Blood samples were collected in the morning after a 12-hour fast for determination of lipoprotein-lipid and apolipoprotein levels. Venous blood from an antecubital vein was drawn into Vacutainer tubes (Becton Dickinson Vacutainer Systems, Rutherford, NJ) containing EDTA while subjects were in a supine position. Blood samples were obtained while women were in the follicular phase, between days 5 and 12 of the menstrual cycle. TG and cholesterol concentrations in whole plasma and in lipoprotein fractions were measured using automated techniques as previously explained.[31,38] Ultracentrifugation was used to isolate plasma very–low-density lipoproteins (d < 1.006 g/mL).[39] HDL was isolated by precipitation of the infranatant (d > 1.06 g/mL) with heparin and $MnCl_2$.[40] The HDL_3 subfraction was isolated by further precipitation.[41] Apo B concentration was measured in plasma by the rocket immunoelectrophoretic method reported by Laurell,[42] as previously described.[31] Apo AI concentration was also quantified in the isolated HDL fraction using the same method. Lyophilized serum standards used for apolipoprotein measurements were prepared in our laboratory and calibrated with reference standards obtained from the Centers for Disease Control (Atlanta, GA).

Abdominal and Femoral Adipose Cell Size

Under local anesthesia, abdominal (lateral to the umbilicus) and femoral (anterior midthigh) AT was surgically obtained in the morning after a 12-hour fast. Samples were digested with collagenase,[43] and the average size of isolated adipose cells was measured on a microscope equipped with a graduated ocular, as previously described.[44] The transformation of adipose cell volume into fat cell weight was performed using the density of triolein.[45]

AT-LPL and Plasma PH-LPL Activities

Samples of subcutaneous abdominal and femoral AT were immediately frozen at the time of biopsy for later measurement of heparin-releasable LPL activity,[20] as previously described.[46] AT-LPL activity was expressed as micromoles free fatty acid (FFA) per hour per 10^6 cells. Since AT-LPL activity is associated with fat cell size,[46,47] AT-LPL activity was also expressed per unit of cell surface (nanomoles FFA per hour per micrometer squared times 10^8).

Subjects also presented in a 12-hour fasting state for measurement of PH-LPL and HL activities. Ten minutes after injection of heparin (10 IU/kg body weight), a blood sample was obtained. Plasma was separated by low-speed centrifugation at 4°C, and a 0.5-mL aliquot was frozen and lyophilized overnight. Acetone-ether powders were then prepared from these samples, dried under nitrogen, and stored at −20°C for later assays. LPL and HL activities were measured by a modification of the method reported by Nilsson-Ehle and Ekman,[48] as previously described.[30] These assays are in agreement with results obtained by selective inhibition of HL with anti-HL antibodies.[49] The acetone-ether powders were dissolved in 0.9% NaCl and used as an enzyme source for measurements of both LPL and HL activities using two different substrates and selective assay conditions.[30] PH-LPL and HL activities are expressed as nanomoles of oleic acid released per milliliter of plasma per minute. Comparison of HL assays performed with or without the delipidation procedure showed that the delipidation resulted in lower HL activities (results not shown). Indeed, when PH plasma LPL and HL assays performed after the delipidation step were compared with direct measurements on plasma, there was no significant difference in LPL activity, whereas HL activity was systematically lower over a wide range of concentrations, but the two assays were highly correlated (R^2 = .988, y = 1.22× + 19.12, n = 5). Thus, over a wide range of measured HL activities, differences in the two methods (with or without delipidation) were proportional.

Statistical Analyses

Differences between men and women were tested for significance with Student's *t* test. Univariate associations between variables were quantified using Pearson's product-moment correlation coefficient. Adjustment for concomitant variables was performed by analysis of covariance (ANCOVA).[50] The Statistical Analysis System (SAS Institute, Cary, NC) was used for all analyses performed.

RESULTS

The subjects' characteristics are listed in Table 1. Men were marginally but significantly older than women. In both

Table 1. Physical Characteristics of Non-obese Men and Women

	Men (n = 17)	Women (n = 14)
Age (yr)	36 ± 3	34 ± 3*
Body fat mass (kg)	15 ± 3	16 ± 3
Body mass index (kg/m^2)	23 ± 1	21 ± 2‡
Body fat (%)	21 ± 4	29 ± 5‡
CT-measured fat areas (cm^2)		
Deep abdominal	89 ± 26	50 ± 18‡
Subcutaneous abdominal	158 ± 36	194 ± 66
Femoral	146 ± 30	234 ± 54‡
Adipose cell weight (μg)		
Abdominal	0.46 ± 0.08	0.34 ± 0.14†
Femoral	0.51 ± 0.08	0.52 ± 0.08

NOTE. Values are the mean ± SD.
*P < .05.
†P < .01.
‡P < .001.

genders, age ranged from 30 to 41 years. Although the men had a body fat mass similar to that of the women, they had a higher body mass index and a lower percentage of body fat than women. Deep abdominal fat accumulation, estimated by CT, was significantly greater in men, whereas women had a tendency to have greater levels of subcutaneous abdominal fat. Women had a larger femoral fat depot than men. Men had a larger mean abdominal fat cell weight than women, but no sex difference was found for femoral fat cell weight.

The plasma lipoprotein-lipid profile for both genders is listed in Table 2. As expected, plasma HDL-C, HDL_2-C, and HDL–apo AI levels, and the HDL-C/LDL-C ratio were significantly higher in women than in men. Furthermore, women also had higher plasma HDL_3-C levels. On the other hand, women had lower plasma TG, HDL-TG, and apo B levels than men, but plasma LDL-C levels were similar in both groups.

No significant gender difference was found for plasma PH-LPL activity, whereas HL activity only showed a tendency to be higher in men ($P < .1$). As shown in Fig 1, gender differences were found for AT-LPL activity. Indeed, women had significantly higher AT-LPL than men in both the abdominal and femoral depots. Men showed no difference in abdominal versus femoral AT-LPL activities, whereas women had higher femoral than abdominal AT-LPL activity ($P < .001$). Similar results were obtained when LPL activity was expressed as micromoles FFA per hour per 10^6 cells or as nanomoles FFA per gram AT (results not shown). As presented in Table 3, abdominal AT-LPL activity was positively correlated with femoral AT-LPL activity. No other association was found between the various lipase activities.

Associations between lipoprotein levels and various lipase activities are listed in Table 4. In women, PH-LPL activity did not display any significant correlation with lipoprotein-lipid levels. In contrast, men's PH-LPL activity was positively correlated with HDL_2-C ($P < .05$) and the HDL-C/LDL-C ratio ($P < .005$) but negatively associated

Table 2. Comparison of Plasma Lipoprotein Levels and PH Lipase Activities Between Men and Women

	Men (n = 17)	Women (n = 14)
TG (mmol/L)	1.43 ± 0.65	0.74 ± 0.24¶
HDL-C (mmol/L)	1.03 ± 0.20	1.39 ± 0.27¶
HDL_2-C (mmol/L)	0.39 ± 0.18	0.59 ± 0.20†
HDL_3-C (mmol/L)	0.64 ± 0.10	0.81 ± 0.12¶
HDL-TG (mmol/L)	0.26 ± 0.04	0.20 ± 0.07*
HDL–apo AI (mg/dL)	105 ± 12	120 ± 16‡
LDL-C (mmol/L)	3.42 ± 0.80	3.03 ± 1.00
Apo B (mg/dL)	89 ± 21	70 ± 28*
HDL-C/LDL-C ratio	0.32 ± 0.10	0.53 ± 0.29†
PH-LPL (nmol/mL/min)	8.5 ± 5.6	9.5 ± 5.4
HL (nmol/mL/min)	21 ± 14	16 ± 14

NOTE. Values are the mean ± SD.
*$P < .05$.
†$P < .01$.
‡$P < .005$.
¶$P < .001$.

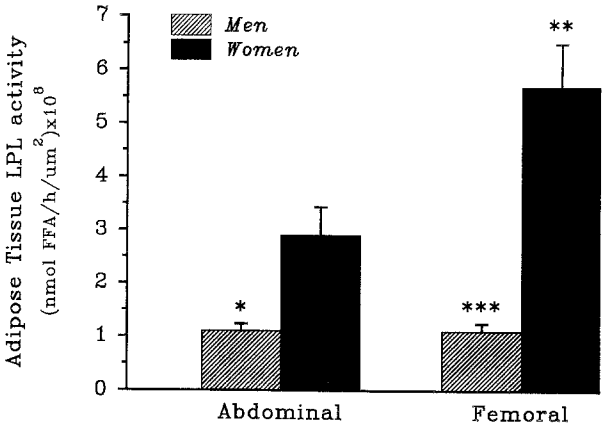


Fig 1. Comparison of abdominal and femoral AT-LPL activities in healthy non-obese men (n = 17) and premenopausal women (n = 14). Values are the mean ± SEM. *$P < .005$, abdominal AT-LPL activity in women *v* men. **$P < .001$, abdominal *v* femoral AT-LPL activity in women. ***$P < .001$, femoral AT-LPL activity in women *v* men.

with plasma LDL-C and with apo B levels. Plasma PH-HL activity was negatively correlated only with HDL–apo AI in women. Abdominal AT-LPL activity did not show any association with plasma lipoprotein-lipid levels in both sexes. Femoral AT-LPL activity showed no relationship with lipoprotein-lipid levels in men. In contrast, femoral AT-LPL activity was positively correlated with HDL-C, HDL_2-C (Fig 2), and HDL–apo AI levels, and the HDL-C/LDL-C ratio in women. Femoral AT-LPL activity in women also tended to be negatively associated with plasma TG level ($P < .08$).

The contribution of each lipase activity to gender differences in the lipoprotein-lipid profile was assessed by ANCOVA; results are presented in Figs 3 to 5. Gender differences in plasma lipoprotein levels were still present despite adjustment for HL or PH-LPL activity. Only the sex difference in plasma apo B level disappeared after adjustment for abdominal AT-LPL activity. However, plasma lipoprotein differences between genders were no longer observed after adjustment for femoral AT-LPL activity, with the exception of plasma HDL_3-C.

Table 3. Interrelationships Among Lipase Activities by Gender

		AT-LPL	
	HL	Femoral	Abdominal
PH-LPL			
Men	−.23	−.17	−.02
Women	.22	.25	.09
HL			
Men	—	−.04	.02
Women	—	−.32	.25
Femoral AT-LPL			
Men	—	—	.65†
Women	—	—	.57*

NOTE. AT-LPL activity is (nmol FFA/h/μm^2) × 10^8.
*$P < .05$.
†$P < .005$.

Table 4. Correlation Coefficients Between PH-LPL and AT-LPL Activities and the Lipoprotein-Lipid Profile in Men and Women

			AT-LPL	
	PH-LPL	HL	Abdominal	Femoral
TG				
Men	−.19	.01	−.15	−.03
Women	−.03	−.32	−.36	−.47
HDL-C				
Men	.36	−.39	−.22	−.10
Women	.11	−.15	.03	.53*
HDL_2-C				
Men	.52*	−.36	−.16	−.10
Women	.31	−.23	.10	.69†
HDL_3-C				
Men	−.20	−.14	−.16	−.01
Women	−.25	.10	−.08	.02
HDL–apo AI				
Men	.23	−.22	−.21	−.23
Women	−.25	−.63*	.12	.52*
LDL-C				
Men	−.47*	−.32	.02	.07
Women	−.38	−.39	−.13	−.38
Apo B				
Men	−.56†	−.18	−.09	.08
Women	−.15	−.20	−.03	−.37
HDL-C/LDL-C ratio				
Men	.67‡	−.08	−.16	−.17
Women	.34	.13	.10	.62†

*$P < .05$.
†$P < .01$.
‡$P < .005$.

DISCUSSION

Premenopausal women are generally known to have a "better" lipoprotein-lipid profile than men, which may provide them with a greater protection against CHD. In agreement with previous reports,[4-14] non-obese women in the present study showed higher plasma HDL-C, HDL_2-C, and HDL–apo AI levels than non-obese men. Gender differences in HDL-C levels have been generally attributed to variations in HDL_2-C levels.[10,11] Differences between men and women for HDL_3-C are more controversial, with most studies reporting no difference in HDL_3-C concentration or HDL_3 mass.[10-12] However, Anderson et al[13] reported that men had slightly but significantly higher HDL_3 mass than women. In the current study, plasma HDL_3-C levels were higher in women than in men. The HDL-C/LDL-C ratio was also significantly higher in women, whereas plasma TG levels were higher in men, a finding consistent with the available literature.[5-7] On the other hand, plasma

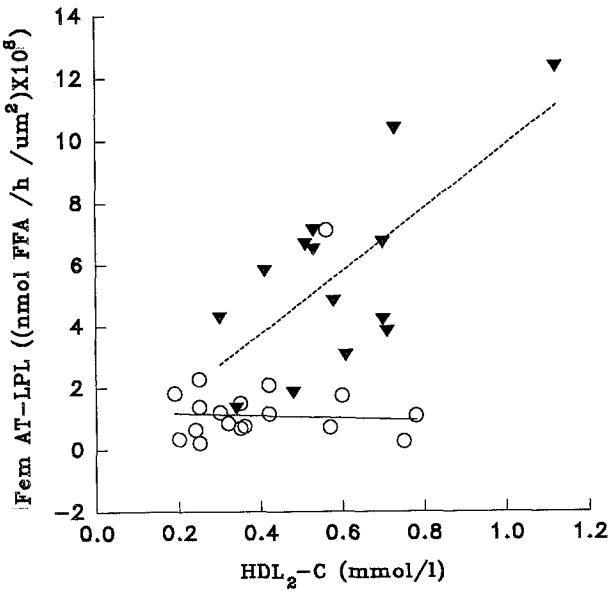
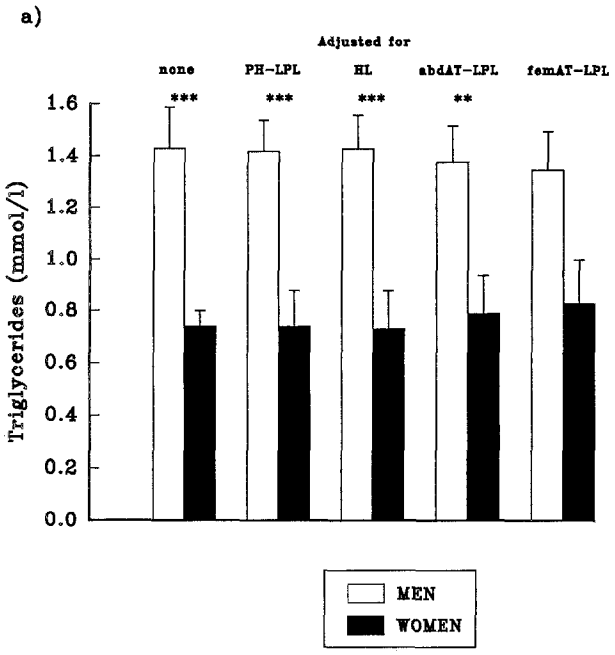


Fig 2. Relationships between femoral AT-LPL activity and plasma HDL_2-C level in non-obese (○) men ($r = -.10$, NS) and (▼) women ($r = .69, P < .01$).



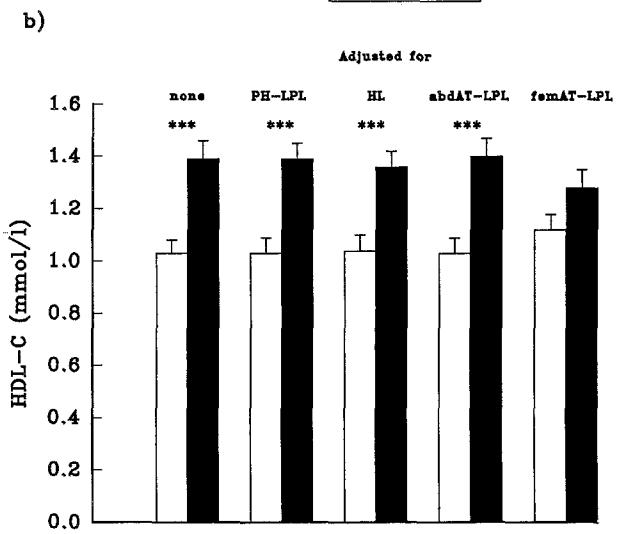


Fig 3. Comparison of plasma (a) TG and (b) HDL-C levels between men and women after adjustment for HL, PH-LPL, abdominal (abd) AT-LPL, and femoral (fem) AT-LPL activities. Values are the mean ± SEM. **$P < .01$, ***$P < .001$.

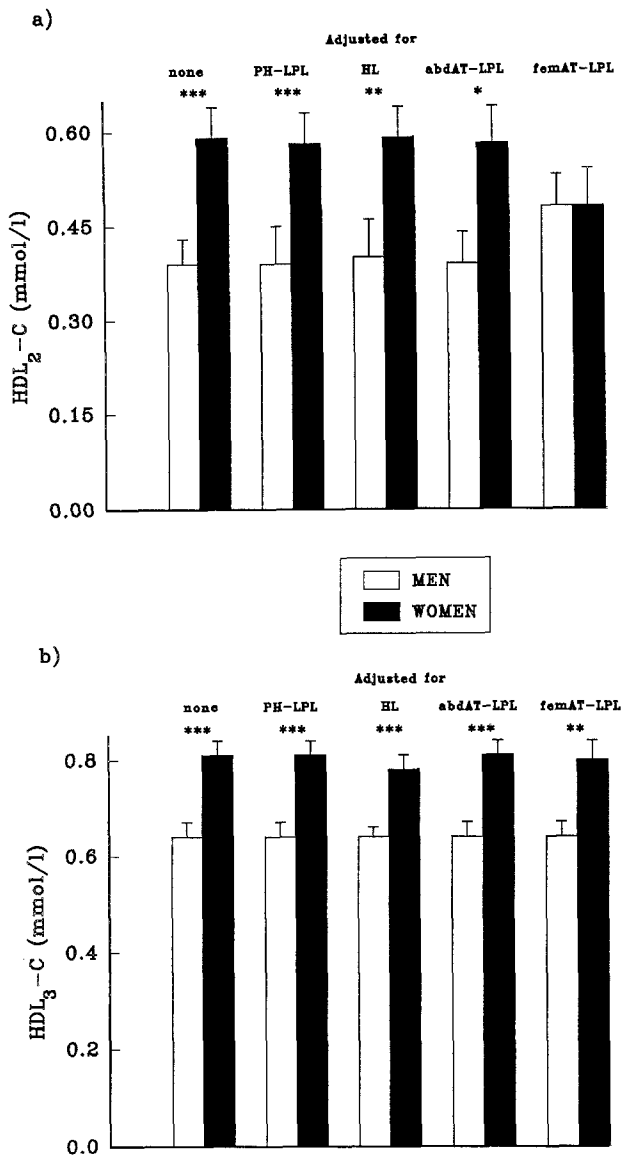


Fig 4. Comparison of plasma (a) HDL_2-C and (b) HDL_3-C levels between men and women after adjustment for various lipase activities. Values are the mean ± SEM. *$P < .05$, **$P < .01$, ***$P < .001$.

LDL-C levels were not significantly different between sexes, although women had significantly lower plasma apo B levels than men. These results suggest that men had more dense atherogenic LDL particles, which is concordant with results reported by McNamara et al.[5]

In the present study, gender differences in body fatness variables were consistent with the well-known gluteal-femoral fat accumulation in women and with a preferential abdominal fat accumulation in men.[51,52] According to Sjöström et al,[53] femoral fat cell weight does not differ between sexes, and femoral fat accumulation in women is due to an increase in adipose cell number. As previously reported,[54] men had greater abdominal fat cell weights than women.

In agreement with results reported by Rebuffé-Scrive et al,[55] men had comparable AT-LPL activity in abdominal and femoral regions. In contrast, premenopausal women had higher AT-LPL activity in the femoral region than in the abdominal region, as previously reported.[25-27] Both abdominal and femoral AT-LPL activities were higher in women than in men. Since it has been reported that gluteal and femoral AT-LPL activities are essentially similar,[26] our results therefore support previous observations of higher gluteal AT-LPL activity in women as compared with men.[16,17] Rebuffé-Scrive et al[54] have reported that there is a nonsignificant trend for lower subcutaneous abdominal AT-LPL activity in premenopausal women as compared with men. In contrast, we report herein a significantly lower subcutaneous abdominal AT-LPL activity in the group of non-obese men, as previously reported by Taskinen et al.[20] These observations may explain why women in the present study tended to have higher subcutaneous abdominal fat accumulation than men. Among the studies in which potential

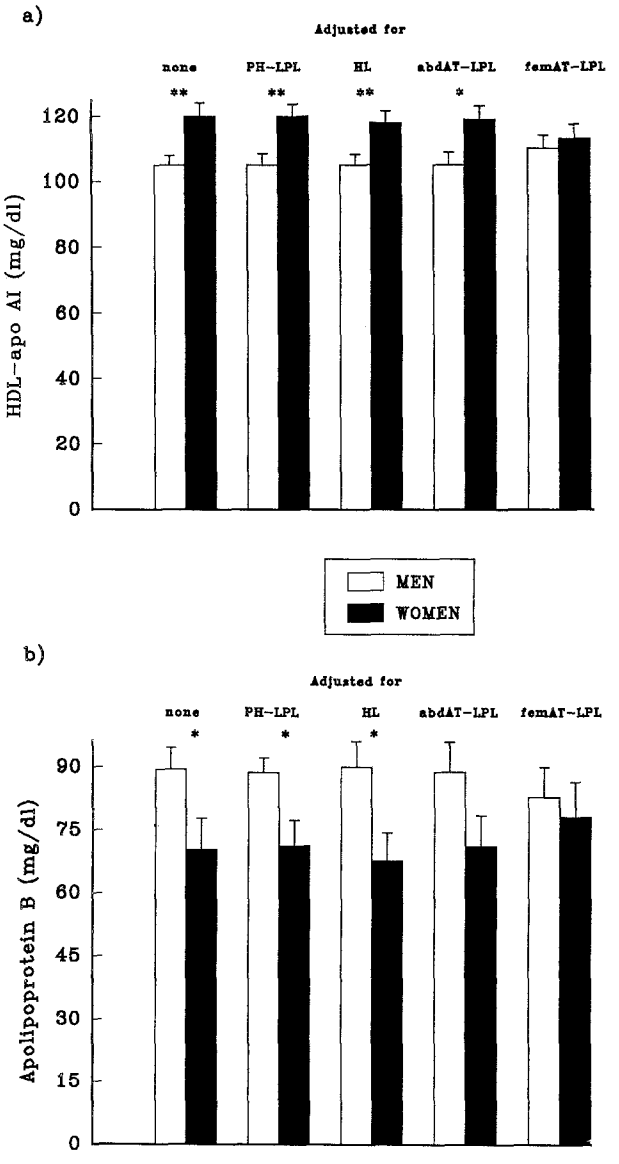


Fig 5. Plasma (a) HDL-apo AI and (b) apo B levels of men and women after adjustment for various lipase activities. Values are the mean ± SEM. *$P < .05$, **$P < .01$.

gender differences in PH-LPL activity were investigated,[10,18,19,56,57] only two have observed a significant sex difference.[18,19] In both cases, higher doses of heparin (100 IU/kg body weight) were injected than in the other studies, including ours (10 IU/kg). Furthermore, Taskinen et al[20] have observed no sex difference in LPL activity in skeletal muscle biopsies. The previous observations are in agreement with the present results, since Brunzell et al[58] have suggested that blood withdrawn shortly after heparin injection mostly included LPL derived from tissues other than AT, especially muscle tissue.

Previous investigations have observed that HL activity is higher in men than in women,[10,18,56,57] although this is not a unanimous finding.[59] Only a tendency for a higher mean HL activity in men was noted in the present study. In the current study, HL activity in men was not significantly correlated with lipoprotein levels. However, Kuusi et al[29] have reported a significant negative correlation of HL activity with HDL-C and HDL_2-C levels in men. However, it is important to point out that there are major differences between the current study and that of Kuusi et al.[29] In the present study, subjects were sedentary and self-selected with an undetermined and possibly highly variable diet, whereas Kuusi et al[29] studied physically well-conditioned young men from the Military Academy of Helsinki who were therefore on a rather uniform dietary and physical-activity regimen. These factors may contribute to explain the differences between the two studies. In women, only the concentration of HDL–apo AI was associated with HL activity in the present study, whereas we had previously reported a significant relation with HDL-C and HDL_2-C levels in obese women.[30] The fact that our subjects were non-obese may explain the weak association between HL and HDL-C concentration reported herein.

On the other hand, in women, PH-LPL activity showed no significant association with the lipoprotein profile, as reported by Applebaum-Bowden et al.[10] In men, PH-LPL activity was the best correlate of lipoprotein levels. Thus, in contrast to women, skeletal muscle LPL activity may be an important regulator of the lipoprotein profile of men. In contrast to some previous studies[18,19] but in agreement with others,[10] PH-LPL activity was not correlated with TG level in both sexes. In women, femoral AT-LPL activity appeared to be the most important correlate of plasma lipoprotein levels. Nikkilä et al[17] also reported significant associations between plasma HDL-C level and gluteal AT-LPL activity in women, but they also reported that this association was significant in men. Other reports[23,24] have shown that gluteal AT-LPL activity was significantly correlated with plasma HDL-C level, but no control over potential gender differences was performed in these studies.

Abdominal AT-LPL activity was not correlated with any lipoprotein-lipid variables in both sexes, and this may be attributed to the fact that abdominal AT-LPL activity was low. However, we have only measured subcutaneous abdominal AT-LPL activity, not the activity of AT-LPL in intraabdominal fat depots, which has been reported to show a significant sex dimorphism.[54] Furthermore, we have previously reported that the amount of abdominal visceral AT shows a closer association with lipoprotein levels than the amount of subcutaneous fat.[60] On the other hand, it is also possible that abdominal AT-LPL activity may be less important for the regulation of lipoprotein metabolism in non-obese than in obese individuals. Indeed, we have already reported that a certain amount of abdominal fat must be present before alterations in lipoprotein levels can be found.[61]

Although sex differences in lipoprotein levels are well documented, the factors involved are not well understood. Consequently, the contribution of LPL and HL activities to gender differences in plasma lipoprotein levels was investigated by ANCOVA. Adjustment for HL or PH-LPL activity did not eliminate sex differences in lipoprotein levels. However, in view of the small number of subjects and the homogeneous nature of our sample, we need to be cautious in not overgeneralizing these conclusions. Indeed, the possibility that HL activity may play a minor role in gender differences in the lipoprotein-lipid profile, especially for HDL-C levels, cannot be excluded. When differences in abdominal AT-LPL activity were controlled for, only the gender difference in apo B level disappeared. This finding is not surprising, since no significant correlation was found between abdominal AT-LPL activity and lipoprotein levels. However, ANCOVA showed a powerful "effect" of adjusting for femoral AT-LPL activity on gender differences in plasma lipoprotein-lipid levels. Indeed, after controlling for femoral AT-LPL activity, men and women presented an essentially similar plasma lipoprotein profile with the exception of HDL_3-C, suggesting that femoral AT-LPL activity was the critical covariate of the well-known sex dimorphism reported in the plasma lipoprotein-lipid profile.

The present results emphasize the importance of femoral AT-LPL activity as a correlate of gender-based lipoprotein differences and are in agreement with results reported by Nikkilä and Kekki,[15] who suggested that the gender difference in plasma TG levels could be attributed to a more efficient TG-removal system in women and not to a lower endogenous TG production rate. Results of the present study are also concordant with a report from Rebuffé-Scrive et al,[27] who showed that menopause in women seemed to be associated with a reduction in femoral AT-LPL activity. In this regard, the Lipid Research Clinics Program Prevalence Study has shown an overall deterioration of the lipoprotein profile in postmenopausal women.[6] Furthermore, postmenopausal women have an increased CHD risk in comparison to premenopausal women.[1]

Our results are also concordant with previous studies reporting that the well-known preferential accumulation of gluteal-femoral regional fat in women is associated with a favorable lipoprotein profile,[62] a finding consistent with the fact that a high femoral AT-LPL activity in women is also associated with a predominantly femoral fat accumulation. Moreover, femoral AT-LPL activity could be partially responsible for the association between body fat distribution and lipoprotein levels, since gluteal AT-LPL has been reported to have a strong inverse association with the waist to hip ratio.[63]

Populations with low CHD rates and a low fat intake do not present major sex differences in lipoprotein levels,[11] as opposed to men and women of Western societies who

display substantial differences in lipoprotein-lipid levels.[4-14] Furthermore, Ononogbu[64] has reported that European women had HDL-C levels similar to those of Nigerian women, whereas European men had significantly lower HDL-C levels than Nigerian men. Thus, it is possible that premenopausal women, who have a higher femoral AT-LPL activity than men, may be better protected against a high-fat diet than men, as reflected by gender differences in plasma HDL-C, TG, and apo B levels. This notion is also in agreement with a previous study reporting a greater elevation of postprandial HDL_2 concentration in women than in men.[65] Moreover, in this previous study, postprandial HDL_2 concentration in women correlated significantly ($r = .96$, $P < .05$) with gluteal AT-LPL activity.

The high activity of femoral AT-LPL in women may contribute to a more efficient TG clearance than in men. Therefore, transfer of TG from TG-rich lipoproteins to HDL may be decreased, as well as the reciprocal transfer of cholesterol ester from HDL to TG-rich lipoproteins.[66] Consequently, a higher proportion of cholesterol ester may remain associated with HDL, the protective lipoprotein fraction against CHD.[8,9] Moreover, a higher femoral AT-LPL activity may also lead to a higher HDL production.[21,23] However, further studies will be needed to verify whether the association reported in the present study truly reflects a cause-and-effect association or is only an epiphenomenon.

In conclusion, this study suggests that the favorable lipoprotein profile observed in women in comparison to men appears to be largely explained by gender differences in femoral AT-LPL activity. Prospective studies evaluating various lipase activities as independent risk factors for CHD will be needed to establish the validity of the present cross-sectional observations.

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