# Association of sex, adiposity, and diet with HDL subclasses in middle-aged Chinese[1–3]

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**ABSTRACT**

**Background:** There is limited information regarding the associations of lifestyle factors and sex with HDL subclasses containing apolipoprotein (apo) A-I (Lp A-I) and both apo A-I and apo A-II (Lp A-I:A-II).

**Objective:** We sought to examine the relations between 2 major HDL subclasses and sex, menopausal status, nutrient intakes, and adiposity.

**Design:** We conducted interviews and measured blood variables in 409 government employees aged 40–59 y in Taiwan.

**Results:** Women ($n$ = 203) had significantly higher concentrations of HDL cholesterol, Lp A-I, and Lp A-I:A-II than did men ($n$ = 206). Postmenopausal women ($n$ = 72) had higher concentrations of HDL cholesterol, Lp A-I, and Lp A-I:A-II than did premenopausal women ($n$ = 131). Body mass index and waist-to-hip ratio were strong predictors of and exerted an independent additive effect on Lp A-I concentrations in both men and women. However, body adiposity was associated with Lp A-I:A-II concentrations only in men. Waist-to-hip ratio was an independent determinant of Lp A-I but not of Lp A-I:A-II in men and postmenopausal women after adjustment for age, body mass index, smoking, and diet. Although there were relatively weak associations between dietary factors and both HDL subclasses ($r$ = 0.01–0.26) in men and women according to bivariate analyses, multiple regression models showed that total fat, saturated fat, and cholesterol intakes were significantly correlated with HDL cholesterol and both Lp A-I and Lp A-I:A-II in men, but not in women.

**Conclusion:** Our data suggest that body adiposity and dietary fat consumption affect 2 major HDL subclasses differently depending on subject sex and menopausal status. *Am J Clin Nutr* 2001;74:64–71.

**KEY WORDS** Cardiovascular disease, HDL cholesterol, high-density-lipoprotein cholesterol, HDL subclasses, body mass index, BMI, waist-to-hip ratio, adiposity, body fat, diet, dietary fat, sex, menopausal status, Chinese population, Taiwan

## INTRODUCTION

HDL is a specific lipoprotein particle thought to exert a protective effect against the development of atherosclerosis and cardiovascular disease (CVD). In the late 1960s, Glomset (1) formulated the hypothesis that HDL plays a role in reverse cholesterol transport. Since then, heterogeneity among HDL particles has been under investigation. The differential metabolism of these particles with regard to antiatherogenic effects is not yet fully understood. There are many analytic methods for categorizing HDL particles, eg, by density (differential precipitation method: $HDL_2$ = 1.063–1.125 kg/L and $HDL_3$ = 1.125–1.21 kg/L), by particle size (gel electrophoresis method: $HDL_{2a\ and\ 2b}$ and $HDL_{3a,\ 3b,\ and\ 3c}$), and by apolipoprotein composition (2). Two major HDL subclasses have been identified by their apolipoprotein composition: HDL particles containing apolipoprotein (apo) A-I but not apo A-II (Lp A-I) and particles containing both apo A-I and apo A-II (Lp A-I:A-II) (2, 3). The investigation of HDL subclasses is of great interest in the attempt to understand the process by which HDL particles confer their protective effect (2–4).

It was suggested that Lp A-I and Lp A-I:A-II have distinct metabolic roles in cholesterol transport systems (5). In vitro studies found that Lp A-I particles but not Lp A-I:A-II particles increase cholesterol efflux (6, 7). HDL subclass separation systems that use immunoaffinity to separate particles on the basis of the presence of apo A-II were developed (8–10). Puchois et al (11) used this method and reported that the concentrations of Lp A-I but not of Lp A-I:A-II were lower in patients with atherosclerotic coronary heart disease than in control subjects. In contrast, others reported that concentrations of both Lp A-I and Lp A-I:A-II particles were lower in patients with coronary heart disease (12–14). Moreover, a study that compared octogenarians with younger male and female control subjects showed that concentrations of Lp A-I but not of Lp A-I:A-II were significantly higher in the octogenarians (15). Other studies exam-

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Received May 1, 2000.

Accepted for publication November 14, 2000.

ined the particle composition and metabolism of these 2 HDL subclasses by age, sex, and menopausal status. However, the results were of limited use because of the small sample sizes. Also, the studies reported no information about a middle-aged population at high risk of developing CVD (16–21).

Atherosclerosis has long been recognized as a major cause of death in many economically developed societies. However, in newly industrialized societies such as Taiwan, an increase in atherosclerosis-related mortality was noted more recently, after economic development. In 1998, cerebrovascular and heart diseases were the second and third leading causes of death in Taiwan, preceded by malignant neoplasms (22). Little information is available about the associations between lifestyle factors, such as nutrient intakes and body adiposity, and Lp A-I and Lp A-I:A-II particle concentrations. Therefore, we sought to examine the associations of these 2 HDL subclasses with sex, menopausal status, nutrient intakes, and adiposity in a middle-aged Chinese population in Taiwan.

## SUBJECTS AND METHODS

### Study population

A total of 440 subjects were recruited from November 1990 to May 1991 during annual health examinations in the Government Employees' Clinic Center in Taipei, Taiwan. The participants were aged 40–59 y, had no known medical problems, and did not take medications known to affect lipid concentrations, such as β-adrenergic blocking agents, thiazide diuretics, cholesterol-lowering agents, hypoglycemic agents, or hormones. We conducted face-to-face interviews to obtain dietary and lifestyle information, made anthropometric measurements using standard methods, and collected fasting blood samples (23, 24). Smokers were defined as those who smoked regularly on a daily basis during the previous year and nonsmokers were those who did not smoke regularly in the year before the interview. Postmenopausal status was defined as having had no menstrual bleeding for ≥1 y. Details of the study procedures were published previously (23, 24).

The government employees participating in this study had various occupations; they included executives, clerks, teachers, bankers, health professionals, and policemen. Participants were predominantly from the middle socioeconomic class in Taiwan. All participants signed a consent form and the study procedures were approved by the Central Trust of China Government Employee Insurance Department in Taiwan. Volunteers with fasting plasma triacylglycerol concentrations >4.5 mmol/L (400 mg/dL) ($n$ = 5) or with incomplete biochemical, dietary, or lifestyle data ($n$ = 21) were excluded from the analyses. There were 26 subjects with missing values and 5 with either unknown menopausal status or perimenopausal status. Therefore, the study population included a total of 206 men, 131 premenopausal women, and 72 postmenopausal women.

### Dietary and anthropometric assessments

The 24-h dietary recall method was used to determine the dietary intakes of each subject on one typical day. Senior nutrition students were trained to perform the 24-h recalls. Their ability to collect accurate dietary data was evaluated by comparing their interviewing results with 3 standard 24-h recalls. The variation among interviewers was <10% for total energy, protein, and fat. The interviewers used food models and pictures depicting portion sizes and followed a standardized protocol for determining the weight of the food consumed (25). Various sources of Taiwanese food-composition data were used to calculate nutrient intakes (26, 27). The coding procedures for determining the weights of ingredients were standardized for mixed dishes, and substitutes were developed for those food items not listed in the food composition databases.

The subjects' heights and weights were measured by using a calibrated balance scale (Detecto, Webb City, MI) while they were wearing light clothing and no shoes. Body mass index (BMI; in kg/m$^2$) was calculated as a measure of weight relative to height. Body circumferences were measured in duplicate with a tape measure to the nearest 0.1 cm by one of the investigators (L-C L). Waist girth was measured at the smallest girth of the torso at the end of a normal expiration, and hip girth was measured at the maximum extension of the buttocks. The averages of the duplicate measurements for hip and waist girth were used to calculate the waist-to-hip ratio (WHR).

### Lipid profiles and apolipoprotein measurements

After subjects fasted overnight, blood samples for the study were collected concomitantly with the routine samples in the Government Employee's Clinic Center in Taipei. Blood from the antecubital vein was drawn into tubes containing 0.1 g EDTA as an anticoagulant; the samples were immediately placed on ice. Within 4 h, plasma was separated by centrifugation at 1000 × $g$ for 20 min at 4°C. HDL was prepared by precipitating VLDL and LDL in fresh plasma with dextrin sulfate and magnesium chloride (28). Aliquots of plasma and supernatant fluid containing HDL were stored in microtubes at −70°C. Samples from Taipei were packed in dry ice and shipped to Boston, where all lipoprotein cholesterol and apolipoprotein concentrations were measured in the Lipid Metabolism Laboratory of the Jean Mayer US Department of Agriculture Human Nutrition Research Center on Aging at Tufts University. Lipid assays were standardized through the Lipid Standardization Program of the Centers for Disease Control and Prevention in Atlanta. LDL-cholesterol concentrations were estimated by using the Friedewald formula (29) in subjects whose triacylglycerol concentration was <4.5 mmol/L (400 mg/dL).

Noncompetitive enzyme-linked immunosorbent assay with affinity-purified polyclonal antibodies was used to measure the concentrations of apo A-I and apo B in plasma. The CVs for apolipoprotein assays between and within runs were <10% (30, 31). Data that addressed a different study hypothesis were published previously (32).

Lp A-I and Lp A-I:A-II were separated from plasma with a differential electroimmunoassay (Laboratories Sebia, Issyles-Moulineaux, France) that involved the use of an excess of anti-apo A-II antibodies; the Lp A-I:A-II particles were retained close to the wells to form the first peak whereas the Lp A-I particles migrated as a second peak. This method allows a direct measurement of Lp A-I; the reported within- and between-run CVs at high, medium, and low concentrations are <5% (4). Lp A-I:A-II concentrations were estimated by calculating the difference between total apo A-I measured by enzyme-linked immunosorbent assay and apo A-I in Lp A-I.

### Statistical analyses

We used EXCEL97 (Microsoft, Seattle), SAS version 6.12 (SAS Institute Inc, Cary, NC), and SPSS FOR WINDOWS ver-

**TABLE 1**
Anthropometric and biochemical measurements of the study subjects[1]

| | Men ($n$ = 206) | Women ($n$ = 203) | Premenopausal women ($n$ = 131) | Postmenopausal women ($n$ = 72) |
|---|---|---|---|---|
| Age (y) | 49.2 ± 6.3 | 48.0 ± 5.7[2] | 45.1 ± 3.4 | 53.4 ± 5.0[3] |
| Height (cm) | 167.8 ± 4.7 | 156.3 ± 5.1[4] | 156.7 ± 5.1 | 155.5 ± 5.1 |
| Weight (kg) | 68.1 ± 8.4 | 55.3 ± 6.8[4] | 55.5 ± 6.1 | 54.8 ± 7.8 |
| BMI (kg/m$^2$) | 24.2 ± 2.8 | 22.6 ± 2.6[4] | 22.6 ± 2.4 | 22.7 ± 3.0 |
| WC (cm) | 84.3 ± 7.9 | 72.7 ± 6.5[4] | 72.3 ± 6.1 | 73.4 ± 7.3 |
| HC (cm) | 93.7 ± 4.9 | 92.9 ± 5.7 | 93.0 ± 5.3 | 92.7 ± 6.3 |
| WHR | 0.90 ± 0.06 | 0.78 ± 0.05[4] | 0.78 ± 0.05 | 0.79 ± 0.05[5] |
| TC (mmol/L) | 4.99 ± 0.83 | 4.78 ± 0.82[6] | 4.54 ± 0.71 | 5.21 ± 0.85[3] |
| TG (mmol/L) | 1.29 ± 0.66 | 0.89 ± 0.45[4] | 0.86 ± 0.45 | 0.96 ± 0.45 |
| LDL-C (mmol/L) | 3.09 ± 0.08 | 2.73 ± 0.74[4] | 2.55 ± 0.65 | 3.07 ± 0.10[3] |
| HDL-C (mmol/L) | 1.31 ± 0.40 | 1.63 ± 0.38[4] | 1.60 ± 0.38 | 1.70 ± 0.36[5] |
| Lp A-I (g/L) | 0.41 ± 0.14 | 0.53 ± 0.13[4] | 0.52 ± 0.13 | 0.55 ± 0.14 |
| Lp A-I:A-II (g/L) | 0.99 ± 0.22 | 1.10 ± 0.25[4] | 1.06 ± 0.21 | 1.17 ± 0.29[3] |
| Apo A-I (g/L) | 1.40 ± 0.04 | 1.63 ± 0.32[4] | 1.58 ± 0.29 | 1.72 ± 0.35[7] |
| Apo A-II (g/L) | 0.34 ± 0.06 | 0.34 ± 0.05 | 0.33 ± 0.05 | 0.36 ± 0.05[3] |
| Apo B (g/L) | 1.05 ± 0.04 | 0.89 ± 0.29[4] | 0.82 ± 0.26 | 1.02 ± 0.30[3] |

[1] $\bar{x}$ ± SD. WC, waist circumference; HC, hip circumference; WHR, waist-to-hip ratio; TC, total cholesterol; TG, triacylglycerol; HDL-C, HDL cholesterol; LDL-C, LDL cholesterol; apo, apolipoprotein; Lp A-I, HDL particles containing apo A-I; Lp A-I:A-II, HDL particles containing both apo A-I and apo A-II.
[2,4,6] Significantly different from men: [2] $P < 0.05$, [4] $P < 0.001$, [6] $P < 0.01$.
[3,5,7] Significantly different from premenopausal women: [3] $P < 0.001$, [5] $P < 0.05$, [7] $P < 0.01$.

sion 7.5 (SPSS Inc, Chicago) to organize and analyze our data. The dietary variables that we analyzed included daily intakes of energy, carbohydrate, protein, fat, saturated fat, polyunsaturated fat, monounsaturated fat, alcohol, and cholesterol. Results were considered statistically significant if the $P$ value was <0.05. For each variable, we compared men with women and compared premenopausal women with postmenopausal women by using Student's $t$ test for continuous variables (33). Plasma triacylglycerol, alcohol intake, and the ratio of polyunsaturated to saturated fatty acids (P:S) had skewed distributions; therefore, log (n +1) transformation was applied in the analyses. We used both Pearson's product-moment correlation coefficients and Spearman's correlations for the bivariate analyses of associations between blood biochemical measures. We performed multiple regression analyses to estimate the variation in HDL subclasses that was explained by various lifestyle variables. We determined the standardized regression estimates (β) and partial correlation coefficients for WHR and dietary intakes of carbohydrate, protein, fat, saturated fat, monounsaturated fat, polyunsaturated fat, cholesterol, alcohol, and crude fiber and the P:S after adjustment for age, smoking status, BMI, total energy intake, and menopausal status. We performed a two-way analysis of variance (ANOVA) to test for possible interactions between BMI and WHR in their effects on HDL, Lp A-I, and Lp A-I:A-II in men and women (both pre- and postmenopausal). We used the 50th percentile of BMI and WHR as cutoffs to define subjects with high or low values in the analyses.

## RESULTS

The basic characteristics of the study subjects are shown in **Table 1**. The average ages of men and women were 49.2 and 48.0 y, respectively. Men were taller and heavier than were women and had a significantly higher mean BMI (24.2 compared with 22.6) and WHR (0.90 compared with 0.78). Moreover, men had concentrations of total cholesterol, triacylglycerol, LDL cholesterol, and apo B that were significantly higher than those of women, by 4.2%, 30.6%, 11.5%, and 24.4%, respectively. However, men had concentrations of HDL cholesterol, Lp A-I, Lp A-I:A-II, and apo A-I that were significantly lower than those of women, by 24.9%, 28.6%, 11.2%, and 16.3%, respectively. Both systolic and diastolic blood pressures were higher in men than in women (data not shown). In this population, 29.6% ($n$ = 61) of the men and 0.5% ($n$ = 1) of the women were smokers.

Besides the significant difference in mean age between postmenopausal and premenopausal women, postmenopausal women had significantly higher concentrations of total cholesterol, LDL cholesterol, HDL cholesterol, Lp A-I:A-II, apo A-I, apo A-II, and apo B; the mean values were higher by 14.9%, 20.4%, 6.8%, 10.5%, 9.0%, 9.1%, and 23.9%, respectively. Postmenopausal women also had triacylglycerol and Lp A-I concentrations that were higher than those of premenopausal women (by 11.4% and 6.4%, respectively), but not significantly so. Even though the mean BMI of postmenopausal women was not significantly different from that of premenopausal women, the WHR was significantly higher in postmenopausal than in premenopausal women. These data show that in this population of nonobese postmenopausal women, concentrations of HDL cholesterol and both subclasses were not lower than those of nonobese premenopausal women.

The dietary intakes of men and women and of the premenopausal and postmenopausal subgroups are shown in **Table 2**. Men had significantly higher intakes of energy, carbohydrate, protein, fat, alcohol, cholesterol, and crude fiber than did women. Compared with women, men had a higher percentage of energy from carbohydrate and a lower percentage of energy from fat. The percentage of energy from protein was ≈16% and the P:S was 1.4 for both men and women. Premenopausal women had significantly higher intakes of carbohydrate and protein than did postmenopausal women. However, the relative amounts of

**TABLE 2**
Dietary intakes of the study subjects[1]

| | Men ($n$ = 206) | Women ($n$ = 203) | Premenopausal women ($n$ = 131) | Postmenopausal women ($n$ = 72) |
|---|---|---|---|---|
| Total energy | | | | |
| (MJ) | 8.99 ± 2.33 | 6.72 ± 1.69[2] | 7.01 ± 1.81 | 6.19 ± 1.31[3] |
| (k/cal) | 2147.6 ± 557.4 | 1605.0 ± 404.5[2] | 1674.6 ± 432.3 | 1478.3 ± 313.5[3] |
| Carbohydrate | | | | |
| (g) | 269.3 ± 85.8 | 190.7 ± 57.3[2] | 199.3 ± 59.6 | 174.9 ± 49.6[4] |
| (% of energy) | 50.2 ± 8.6 | 47.8 ± 9.9[5] | 47.9 ± 9.4 | 47.8 ± 1.8 |
| Protein | | | | |
| (g) | 85.1 ± 3.5 | 63.5 ± 2.2[2] | 65.8 ± 2.0 | 59.2 ± 2.1[6] |
| (% of energy) | 15.9 ± 3.9 | 16.0 ± 4.3[2] | 16.0 ± 3.9 | 16.0 ± 5.0 |
| Fat | | | | |
| (g) | 82.4 ± 28.5 | 67.4 ± 25.2[2] | 70.1 ± 26.7 | 62.4 ± 21.6 |
| (% of energy) | 34.4 ± 7.6 | 37.5 ± 8.7[2] | 37.4 ± 8.9 | 37.5 ± 8.6 |
| Alcohol (g) | 7.9 ± 19.4 | 1.1 ± 3.4[2] | 1.1 ± 3.5 | 1.2 ± 3.3 |
| MUFA (g) | 29.7 ± 12.1 | 23.8 ± 1.5[2] | 25.0 ± 1.9 | 21.7 ± 9.3 |
| PUFA (g) | 25.9 ± 8.3 | 21.3 ± 8.2[2] | 22.2 ± 8.5 | 19.6 ± 7.2 |
| SFA (g) | 20.6 ± 8.5 | 16.9 ± 7.8[2] | 17.4 ± 7.8 | 16.1 ± 7.8 |
| P:S | 1.4 ± 0.5 | 1.4 ± 0.6 | 1.4 ± 0.5 | 1.4 ± 0.7 |
| Cholesterol (mg) | 340.0 ± 211.3 | 258.3 ± 196.4[2] | 264.9 ± 185.8 | 246.3 ± 215.3 |
| Crude fiber (g) | 5.5 ± 4.5 | 4.8 ± 4.2[7] | 5.1 ± 4.7 | 4.2 ± 3.0 |

[1] $\bar{x}$ ± SD. MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids; SFA, saturated fatty acids; P:S, ratio of polyunsaturated to saturated fatty acids.
[2,5,7] Significantly different from men: [2] $P < 0.001$, [5] $P < 0.01$, [7] $P < 0.05$.
[3,4,6] Significantly different from premenopausal women: [3] $P < 0.001$, [4] $P < 0.01$, [6] $P < 0.05$.

energy provided by carbohydrate, fat, protein, and alcohol were similar in these 2 subgroups.

Spearman's correlation coefficients between various lipoprotein variables in men and women are shown in **Table 3**. For both men and women, HDL cholesterol, Lp A-I, Lp A-I:A-II, and apo A concentrations were highly correlated with each other and were positively correlated with the total cholesterol concentration. The Lp A-I:AII concentration was significantly correlated with the total cholesterol concentration in men and women. For men, triacylglycerol concentrations were negatively correlated with concentrations of HDL cholesterol, Lp A-I, Lp A-I:A-II, and apo A. However, for women, triacylglycerol concentrations were negatively correlated with HDL cholesterol and Lp A-I but not with Lp A-I:A:II and apo A-I. Bivariate associations between HDL subclasses and selected variables including age, body fatness, and dietary intakes of men and women and of the pre- and postmenopausal subgroups were also determined (data not shown). There were strong associations between age and concentrations of HDL cholesterol, apo A-I, Lp A-I, and Lp A-I:AII in women but not in men. Body fatness indexes including BMI and WHR were negatively associated with concentrations of HDL cholesterol, apo A-I, Lp A-I, and Lp A-I:AII in men and with concentrations of HDL cholesterol, apo A-I, and Lp A-I in women. In both pre- and postmenopausal women, body adiposity was associated with concentrations of Lp A-I but not with those of Lp A-I:AII (data not shown).

The results of the multiple regression analyses of associations between HDL subclasses and lifestyle variables are shown in **Table 4** for all subjects stratified by sex and menopausal status. The significant negative association remained between WHR and the Lp A-I concentration in men, all women, and postmenopausal women. However, Lp A-I:A-II was not significantly associated with WHR after adjustment for BMI in men, all women, premenopausal women, or postmenopausal women. Total fat and saturated fat intakes were positively associated with Lp A-I concentrations in men and

**TABLE 3**
Spearman's correlation coefficients between blood lipoprotein variables in men (top right triangular area) and women (bottom left triangular area)[1]

| | TC | TG | LDL-C | HDL-C | Lp A-I | LpA-I:A-II | Apo A-I | Apo B |
|---|---|---|---|---|---|---|---|---|
| TC | | 0.2654[2] | 0.8699[2] | 0.1693[2] | 0.1160 | 0.3193[2] | 0.2721[2] | 0.7442[2] |
| TG | 0.2974[2] | | 0.1790[2] | −0.4870[2] | −0.3352[2] | −0.1428[2] | −0.2600[2] | 0.3590[2] |
| LDL-C | 0.8818[2] | 0.2566[2] | | −0.1709[2] | −0.1766[2] | 0.0878 | −0.0293 | 0.7853[2] |
| HDL-C | 0.2473[2] | −0.4093[2] | −0.1359 | | 0.7282[2] | 0.6001[2] | 0.7636[2] | −0.1870[2] |
| Lp A-I | 0.1898[2] | −0.3128[2] | −0.0686 | 0.7227[2] | | 0.4504[2] | 0.7779[2] | −0.2237[2] |
| Lp A-I:A-II | 0.3281[2] | 0.0347 | 0.0889 | 0.4932[2] | 0.3840[2] | | 0.9063[2] | 0.0582 |
| Apo A-I | 0.3245[2] | −0.1099 | 0.0307 | 0.6844[2] | 0.7249[2] | 0.9124[2] | | −0.0731 |
| Apo B | 0.8311[2] | 0.3872[2] | 0.8361[2] | −0.0336 | −0.0854 | 0.1605[2] | 0.0833 | |

[1] TC, total cholesterol; TG, triacylglycerol; LDL-C, LDL cholesterol; HDL-C, HDL cholesterol; apo, apolipoprotein; Lp A-I, HDL particles containing apo A-I; Lp A-I:A-II, HDL particles containing both apo A-I and apo A-II.
[2] $P < 0.05$.

**TABLE 4**
Multiple regression models for associations between HDL subclasses and lifestyle variables (WHR and dietary intakes)[1]

| (*n* = 72) | Men (*n* = 206) | | | | Women (*n* = 203) | | | | Premenopausal women (*n* = 131) | | | | Postmenopausal wom | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Lp A-I ($R^2$ = 0.215) | | Lp A-I:A-II ($R^2$ = 0.127) | | Lp A-I ($R^2$ = 0.261) | | Lp A-I:A-II ($R^2$ = 0.215) | | Lp A-I ($R^2$ = 0.222) | | Lp A-I:A-II ($R^2$ = 0.212) | | Lp A-I ($R^2$ = 0.417) | | Lp A-I:A-II ($R^2$ = 0.265) | |
| | β | Partial *r* | β | Partial *r* | β | Partial *r* | β | Partial *r* | β | Partial *r* | β | Partial *r* | β | Partial *r* | β | Partial *r* |
| WHR | −0.243[2] | −0.194 | 0.021 | 0 .017 | −0.218[2] | −0.201 | −0.127 | −0.113 | −0.166 | −0.149 | −0.160 | −0.136 | −0.304[3] | −0.287 | −0.092 | −0.083 |
| Carbohydrate | −0.268[3] | −0.162 | −0.269[3] | −0.160 | −0.086 | −0.064 | 0.010 | 0.007 | 0.011 | 0.008 | 0.054 | 0.036 | −0.259 | −0.221 | −0.020 | −0.017 |
| Protein | 0.180 | 0.135 | 0.097 | 0.072 | 0.085 | 0.072 | 0.067 | 0.054 | 0.067 | 0.052 | 0.193 | 0.142 | 0.104 | 0.096 | −0.022 | −0.019 |
| Fat | 0.237[3] | 0.164 | 0.271[2] | 0.185 | 0.163 | 0.112 | −0.051 | −0.034 | 0.016 | 0.011 | −0.189 | −0.120 | 0.454[3] | 0.320 | 0.195 | 0.131 |
| MUFA | 0.129 | 0.100 | 0.203[3] | 0.155 | 0.114 | 0.084 | 0.000 | 0.000 | −0.008 | −0.006 | −0.183 | −0.121 | 0.310[3] | 0.242 | 0.267 | 0.199 |
| PUFA | 0.098 | 0.076 | 0.116 | 0.089 | 0.060 | 0.051 | 0.035 | 0.029 | −0.020 | −0.016 | −0.010 | −0.007 | 0.165 | 0.160 | 0.087 | 0.081 |
| SFA | 0.244[3] | 0.195 | 0.216[3] | 0.169 | 0.140 | 0.107 | 0.037 | 0.027 | 0.019 | 0.014 | −0.098 | −0.067 | 0.344[3] | 0.276 | 0.239 | 0.183 |
| P:S | −0.117 | −0.122 | −0.087 | −0.089 | −0.034 | −0.036 | −0.007 | −0.007 | −0.016 | −0.017 | 0.061 | 0.061 | −0.063 | −0.066 | −0.108 | −0.110 |
| Alcohol | 0.047 | 0.050 | 0.025 | 0.026 | 0.110 | 0.117 | 0.020 | 0.020 | 0.140 | 0.147 | −0.021 | −0.021 | 0.065 | 0.069 | 0.085 | 0.086 |
| Cholesterol | 0.156[3] | 0.149 | 0.160[3] | 0.150 | 0.119 | 0.120 | 0.042 | 0.040 | 0.098 | 0.101 | 0.071 | 0.069 | 0.169 | 0.155 | 0.019 | 0.016 |
| Crude fiber | −0.158[3] | −0.157 | −0.042 | −0.041 | 0.041 | 0.044 | 0.078 | 0.081 | 0.070 | 0.074 | 0.089 | 0.089 | −0.041 | −0.044 | 0.088 | 0.091 |

[1] All models were adjusted for age, smoking, total energy intake, BMI, and menopausal status (for women only). WHR, waist-to-hip ratio; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids; SFA, saturated fatty acids; P:S, ratio of polyunsaturated to saturated fatty acids.
[2] $P < 0.01$.
[3] $P < 0.05$.

postmenopausal women, but not in premenopausal women. Weak associations (low magnitude of *r* values) between intakes of other dietary variables and concentrations of HDL subclasses were found in bivariate and multiple regression analyses. Taken together, these data suggest that variables related to fat consumption, such as total fat, saturated fat, and dietary cholesterol, were associated with both HDL subclasses in men and with Lp A-I in postmenopausal women, but not with either HDL subclass in premenopausal women.

For men, the model explained 21.5% of the variation in Lp A-I; the factors that made significant contributions to the variation were body adiposity (WHR) and dietary intakes of carbohydrate, fat, saturated fat, cholesterol, and crude fiber (Table 4). For Lp A-I:A-II, the model explained 12.7% of the variation in men; dietary intakes of carbohydrate, fat, monounsaturated fat, saturated fat, and cholesterol were significant contributors. In premenopausal women, no dietary predictors were significant for either Lp A-I or Lp A-I:A-II. However, in postmenopausal women, WHR, total fat, monounsaturated fat, and saturated fat were significant predictors of Lp A-I, but not of Lp A-I:A-II; the models explained 41.7% and 26.5% of the variation, respectively.

The two-way ANOVA indicated that there was no significant interaction between BMI and WHR in their effects on HDL cholesterol, Lp A-I, or Lp A-I:A-II concentrations. Mean (±SD) HDL cholesterol, Lp A-I, and Lp A-I:A-II concentrations for both men and women are shown in **Figure 1**; subjects were divided into 4 subgroups on the basis of a high or low BMI and a high or low WHR. The main effects of BMI and WHR were significant for HDL cholesterol and Lp A-I but not for Lp A-I:A:II in both men and women. These results indicate significant, independent, additive effects of BMI and WHR on Lp A-I but not on Lp A-I:A-II in both men and women.

## DISCUSSION

This study examined the associations of 2 HDL subclasses, Lp A-I and Lp A-I:A-II, with sex, menopausal status, nutrient intakes, and adiposity by analyzing data from a population of middle-aged Chinese men and women living in Taiwan. HDL subclasses that differ in terms of apolipoprotein composition may have different metabolic functions in reverse cholesterol transport. Currently available evidence indicates that Lp A-I seems to be a better intermediate biomarker for lifestyle modifications, such as diet and obesity control, than is Lp A-I:A-II. Nonmodifiable factors such as sex and menopausal status appeared to influence both HDL subclasses.

Previously reported Lp A-I and Lp A-I:A-II concentrations from 5 population studies with sample sizes >50 adults (4, 10–12, 34) are shown in **Table 5** in comparison with results from the present study. The Chinese population in the present study seemed to have lower Lp A-I but higher Lp A-I:A-II concentrations than several Western populations, even though the subjects in all of the studies had comparable HDL-cholesterol concentrations. There are many possible explanations for this observation. Chinese in Taiwan consume a relatively high-fat diet (34% and 38% of energy as fat for men and women, respectively) with a P:S as high as 1.4. A clinical study by Fumeron et al (35) showed reductions in Lp A-I and $HDL_2$-cholesterol concentrations when the dietary P:S was increased from 0.2 to 1.1. The question of whether high polyunsaturated fat intakes reduce HDL-cholesterol concentrations was the focus of attention and debate in the past (36). Our data suggest that the HDL subclass distribution is affected by the quantity and quality of dietary fat; therefore, this issue should be investigated further. A high intake of polyunsaturated fat coupled with a high total fat intake may decrease Lp A-I concentrations without lowering HDL-cholesterol concentrations.

Our data show that variables related to fat consumption, such as total fat, saturated fat, and dietary cholesterol, were associated with both HDL subclasses in men and with Lp A-I in postmenopausal women, but consistent associations were not found in premenopausal women. The analyses also suggest that HDL subclass profiles are influenced by diet more profoundly in men than in women; this is particularly apparent in comparisons of men with premenopausal women. These results agree with the finding of Sonnenberg et al (37) in 695 premenopausal and 727 postmenopausal women in the Framingham nutrition studies of a direct relation between dietary fat and HDL cholesterol in the postmenopausal subgroup only. The results of a meta-analysis by Cobb et al (38) to investigate sex differences in lipopro-

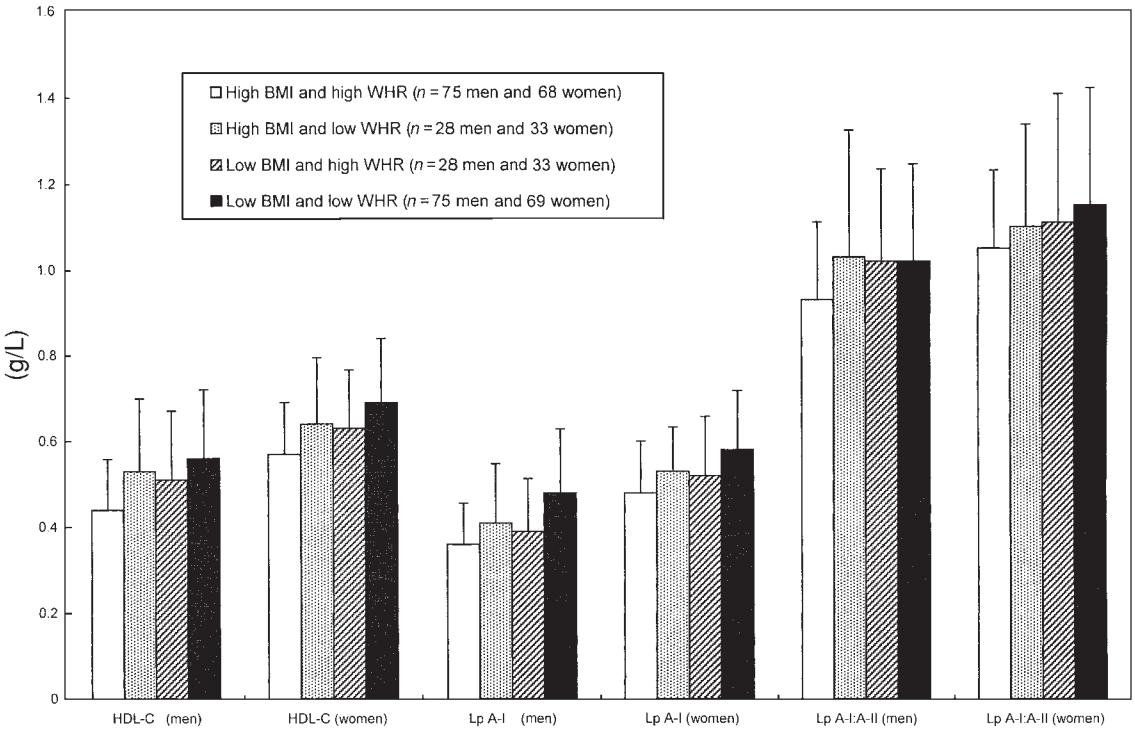


**FIGURE 1.** Mean (±SD) concentrations of HDL cholesterol (HDL-C) and the HDL subclasses containing apolipoprotein (apo) A-I (Lp A-I) and both apo A-I and apo A-II (Lp A-I:A-II) particles categorized by body mass index (BMI) and waist-to-hip ratio (WHR) in men and women. There were no significant interactions between BMI and WHR in their effects on any of the HDL variables. BMI and WHR had significant ($P < 0.05$) main effects on HDL cholesterol and Lp A-I concentrations in both men and women. There were no significant main effects of either BMI or WHR on Lp A-I:A-II in either men or women. The 50th percentiles for BMI were 23.8 and 22.1 and for WHR were 0.90 and 0.78 in men and women, respectively. To convert HDL-C from g/L to mmol/L, multiply by 2.586.

tein responses to diet suggest that the LDL-cholesterol response is sex-independent whereas the HDL-cholesterol response is sex-specific. Therefore, it is likely that the metabolic responses of the 2 HDL subclasses to dietary variables differ by sex and menopausal status. Our data suggest that Lp AI:A:II particles seem to be affected more by hormonal factors than by lifestyle factors, compared with Lp A:I particles.

In the present study of middle-aged Chinese men and women, the postmenopausal women had higher blood concentrations of HDL cholesterol and the HDL subclasses Lp A-I and Lp A-I:A-II than did the premenopausal women. Independent of age, men had lower HDL cholesterol, apo A-I, Lp A-I, and Lp A-I:A-II concentrations than did women. In contrast with our findings, Ohta et al (17, 18), Koren et al (10), Bakaert et al (20), Duverger et al (16), and Li et al (34) reported differences in Lp A-I concentrations but not in Lp A-I:A-II concentrations between men and women. An analysis of our data from the subgroups of postmenopausal and premenopausal women suggested that the discrepancy among different studies was related to the menopausal status of the women (16, 18, 20). In the current study, premeno-

**TABLE 5**
Concentrations of Lp A-I and Lp A-I:A-II in subjects from previous studies and the present study[1]

| | Puchois et al (11), 1987, France, men ($n$ = 50)[2] | Koren et al (10), 1987, United States | | Parra et al (4), 1990, France | | Parra et al (12), 1992 | | Li et al (34), 1996, Framingham, MA | | This study, Taipei, Taiwan | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Men ($n$ = 50) | Women ($n$ = 50) | Men ($n$ = 40) | Women ($n$ = 45) | Ireland, men ($n$ = 180)[2] | France, men ($n$ = 432)[2] | Men ($n$ = 146) | Women ($n$ = 139) | Men ($n$ = 206) | Women ($n$ = 203) |
| Age (y) | 51.0 ± 8.0 | NA | NA | 29.8 ± 7.7 | 29.0 ± 8.2 | 54.1 ± 7.8 | 53.3 ± 8.6 | 48.8 ± 10.7 | 48.7 ± 10.1 | 49.2 ± 6.3 | 48.0 ± 5.7 |
| HDL (mmol/L) | 1.5 ± 0.6 | NA | NA | 1.5 ± 0.4 | 1.7 ± 0.4 | 1.3 ± 0.4 | 1.4 ± 0.4 | 1.2 ± 0.3 | 1.5 ± 0.3 | 1.31 ± 0.4 | 1.6 ± 0.4 |
| Lp A-I (g/L) | 0.5 ± 0.2 | 0.6 ± 0.2 | 0.6 ± 0.2 | 0.5 ± 0.1 | 0.6 ± 0.1 | 0.4 ± 0.1 | 0.5 ± 0.2 | 0.4 ± 0.1 | 0.6 ± 0.2 | 0.4 ± 0.1 | 0.5 ± 0.1 |
| Lp A-I:A-II (g/L) | 0.8 ± 0.1 | 0.8 ± 0.1 | 0.8 ± 0.1 | NA | NA | 0.8 ± 0.2 | 0.8 ± 0.2 | 0.9 ± 0.2 | 0.88 ± 0.2 | 0.99 ± 0.2 | 1.1 ± 0.3 |
| Apo A-I (g/L) | 1.3 ± 0.3 | 1.4 ± 26.1 | 1.4 ± 0.3 | 1.2 ± 0.2 | 1.3 ± 0.2 | 1.46 ± 0.3 | 1.49 ± 0.3 | 1.4 ± 0.4 | 1.6 ± 0.4 | 1.4 ± 0.4 | 1.6 ± 0.3 |
| Lp A-I/apo A-I (%) | 38.0 | 42.3 | 44.9 | 40.8 | 45.1 | 35.2 | 33.9 | 31.3 | 37.8 | 29.4 | 32.5 |

[1] NA, not available; apo, apolipoprotein; Lp A-I, HDL particles containing apo A-I; Lp A-I:A-II, HDL particles containing both apo A-I and apo A-II.
[2] Case-control study of men; data are from control subjects only.

pausal women had concentrations of Lp A-I:A-II that were similar to those of men, whereas postmenopausal women had higher concentrations than men. A study by Tilly-Kiesi et al (19) that compared the apo A-I kinetics in Lp A-I and Lp A-I:A-II particles from postmenopausal women and older men showed that the catabolic rates of apo A-I in both HDL subclasses were similar in the 2 groups; however, the synthesis rate of apo A-I was higher in postmenopausal women than in older men. Thus, it is likely that after menopause the synthesis of apo A-I for Lp A-I:A-II particles increases more than that for Lp A-I particles.

The present study also provided evidence that body adiposity, including general body fatness and body fat distribution, might exert different effects on the 2 HDL subclasses. Measures of general body fatness (ie, BMI) and body fat distribution (ie, WHR) had an independent additive effect on Lp A-I concentrations but not on Lp A-I:A-II concentrations. General obesity showed a strong association with both HDL subclasses; however, central fat distribution affected Lp A-I but not Lp A-I:A-II concentrations. Furthermore, our analyses showed no interaction between BMI and WHR in their effects on HDL cholesterol, Lp A-I, or Lp A-I:A-II concentrations in men and women. There is no information in the literature that is relevant to these findings. Many other studies showed that abdominal obesity is a clinical marker for a metabolic syndrome that involves elevated triacylglycerol and blood glucose concentrations, insulin resistance, and high blood pressure and decreased HDL-cholesterol concentrations (23, 36, 39). The results of this investigation suggest that central body fat has distinctly different effects from those of general obesity on Lp A-I concentrations.

The influence of diet and obesity on Lp A-I and Lp A-I:A-II particle concentrations was discernible in men and in premenopausal and postmenopausal women. It is apparent from the present analyses that sex and menopausal status were major factors contributing to the variability in HDL subclass distribution and that body adiposity and dietary factors were also significant predictor variables. In conclusion, for Lp A-I particle concentration, general body fatness and central body fat have an additive influence and diet has a minor but significant influence in men and postmenopausal women; for Lp A-I:A-II particle concentration, the associations with lifestyle factors are less profound than with the Lp A-I subclass. Therefore, when individuals make lifestyle modifications to lower their risk of developing CVD, the Lp A-I concentration may serve as a better biomarker of risk than the Lp A-I:A-II concentration.

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