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THE RELATIONSHIP OF HIGH-DENSITY LIPOPROTEIN CHOLESTEROL TO OBESITY, DRINKING AND SMOKING HABITS

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ABSTRACT

Subjects were a total of 726 Japanese male transport service workers between the ages of 35 and 50. They were analyzed for obesity and drinking or smoking habits in relation to their HDL-cholesterol level and total cholesterol concentration. The cases were 100 low HDL-cholesterol (less than 40 mg/dl) and 121 high total cholesterol (greater than 230 mg/dl) subjects. We used a multiple logistic regression analysis. As for abnormally high total cholesterol, it was determined that the odds ratios at 40, 45, and 50 years of age were 1.95, 2.23, and 2.65, respectively, when 35-year-olds were considered the baseline. Abnormally high total cholesterol showed an odds ratio of 0.27 among thin subjects with a Body Mass Index (BMI) less than 21.0, when subjects with a standard BMI were calculated as the baseline. With reference to low HDL-cholesterol, the odds ratio for lean subjects was 0.30 against those who had standard habitus, while subjects with a BMI of more than 25.1 had an odds ratio of more than double. Compared with nondrinkers, low HDL-cholesterol exhibited odds ratios of 0.16 and 0.23, respectively, for moderate and heavy drinkers. In cases of low HDL-cholesterol, the odds ratios for mild and heavy smokers were 1.91 and 2.27, respectively, versus nonsmokers.

Key Words: Lipoproteins, HDL-cholesterol, Obesity, Alcohol consumption, Multiple logistic regression analysis.

INTRODUCTION

Serum total cholesterol level is considered a risk factor in arteriosclerosis and is used as a common clinical diagnostic tool. In addition to total cholesterol, high-density lipoprotein (HDL) cholesterol assays have become common. A low level of HDL-cholesterol relative to total cholesterol is thought to lead to arteriosclerosis.[1] Cigarette smoking and elevations of low-density lipoprotein (LDL) are independent major risk factors for atherosclerosis.[2-4] Cigarette smoking and obesity are associated with increased risk of cardiovascular disease and are known to have a negative impact on lipid and lipoprotein metabolism.[5-9] Aging has long been thought of as a significant factor in the reduction of HDL-cholesterol,[10,11] whereas alcohol consumption has been reported to increase HDL-cholesterol.[12,13] These factors are mutually interrelated, and it is important to know to what degree, if any, they individually affect the total cholesterol and HDL-cholesterol level.

We have therefore investigated the influence of smoking, alcohol consumption, obesity and aging on serum total cholesterol and HDL-cholesterol in Japanese male transport service workers aged 35 to 50 years using multiple logistic regression analysis.

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SUBJECTS AND METHODS

The subjects were 1,050 of the 6,218 municipal transport workers in Nagoya (Japan). They were selected solely on the basis of age: 35, 40, 45 and 50 years old. These workers underwent periodic medical examinations for adult diseases every five years between the ages of 35 and 50. Previously distributed questionnaires concerning drinking and smoking habits and general health were collected at periodic medical examinations for adult diseases (925 male and 11 female respondents, 95.5% response) and analyzed. Due to the small number of participants, the female respondents were excluded from the analyses. Two hundred five respondents currently receiving outpatient treatment for various illnesses were also excluded from the study, because their medications might have some effect on cholesterol level, and their disease might affect their work differently than with healthy workers. After complete screening, only 720 of the initial 1,050 workers were used as subjects for analysis.

Blood samples were collected and immediately isolated and frozen at −20°C at the time of the medical examinations. They were assayed for total cholesterol and HDL-cholesterol levels using an autoanalyzer (Toshiba model TBA−480S). Levels of total cholesterol>230 mg/dl and HDL-cholesterol<40 mg/dl were classified as abnormal values.

Subjects were classified by body mass index (BMI=weight/height^2) rankings in three categories of thin (15.9−21.0), standard (21.1−25.0), and obese (25.1−33.5). Alcohol consumption was categorized by the type of beverage and the amount consumed per sitting: beer (No. of Japanese large bottles: 0.633 liters), "*sake*" (No. of 0.18 liter units), whiskey (No. of single shots), "*shochu*" (a Japanese liquor) (No. of 0.18 liter units). The frequency was broken down into four categories: (1) daily, (2) 3−4 times per week, (3) 1−2 times per week, and (4) seldom or never. The obtained values were converted into four equivalent daily intake quantities of pure ethyl alcohol (g): (1) never, (2) 1−28 g (less than 0.18 liters of "*sake*"), (3) 29−84 g (less than 0.54 liters of "*sake*"), and (4) 85 g or more. Smoking was calculated by the number of cigarettes smoked per day, in three categories: (1) none, (2) 1−20 cigarettes, and (3) 21 or more cigarettes per day.

Statistical analysis was performed using multiple logistic regression analysis.[14] Calculations were made using the SAS statistics software program package of the Nagoya University Computation Center.[15]

RESULTS

Table 1 shows the number of subjects classified acoording to measured total cholesterol, HDL-cholesterol, BMI, and the prevalence of alcohol intake and cigarette smoking. It is clear that the number of subjects with high total cholesterol (>230 mg/dl) tended to increase with advancing age. The number of subjects with low HDL-cholesterol, obese subjects, and prevalence rates of drinking and cigarette smoking were scarcely different in the four age groups (Table 1). The prevalence of drinking and cigarette smoking were 78.8 percent and 57.4 percent, respectively. Mean alcohol consumption per day among drinkers (n=567) was about 52.4 percent, respectively. Mean alcohol consumption per day among drinkers (n=567) was about 52.4 ± 36.1 g (mean ± S.D.), or the equivalent of 0.328 ± 0.226 liters of Japanese "*sake*". The mean number of cigarettes smoked among smokers (n=413) was 24.3 ± 9.7 per person/day.

Table 2 shows the averages of the principal data. The average BMI was 23.1 ± 2.6 (range: 15.9−33.5). The mean total cholesterol and HDL-cholesterol levels were 199.0 ± 34.1 (range:

Table 1. The Number of Subjects Differentiated by Age and the Measured Total Cholesterol, HDL-cholesterol, Obesity and Frequency of Drinking and Smoking

Category	35 yr (n=87)	40 yr (n=144)	45 yr (n=289)	50 yr (n=200)	Total (n=720)
	N (%)	N (%)	N (%)	N (%)	N (%)
High total cholesterol (>230 mg/dl)	7 (8.0)	21 (14.6)	50 (17.3)	43 (21.5)	121 (16.8)
Low HDL-cholesterol (<40 mg/dl)	14 (16.1)	16 (11.1)	38 (13.1)	32 (16.0)	100 (13.9)
Obesity (BMI[1)]>25.0)	19 (21.8)	26 (18.1)	49 (17.0)	63 (31.5)	157 (21.8)
Alcohol drinking	71 (81.6)	114 (79.2)	228 (78.9)	154 (77.0)	567 (78.8)
Cigarette smoking	48 (55.2)	89 (61.8)	160 (55.4)	116 (58.0)	413 (57.4)

1) BMI=Body Mass Index (weight/height^2)

Table 2. The Average of Principal Factors

Factor	Mean ± S.D.	(Minimum, Maximum)
BMI (kg/m^2)	23.1 ± 2.6	(15.9, 33.5)
Total cholesterol (mg/dl)	199.0 ± 34.1	(104, 333)
HDL-cholesterol (mg/dl)	53.6 ± 13.4	(27, 104)

Table 3. Correlation among Factors

Factor	Total cholesterol	HDL-cholesterol
Age[1)] (year)	0.107**	−0.038
BMI[1)] (kg/m^2)	0.244***	−0.300***
Ethanol[2)] (g/day)	−0.058*	0.178**
Tobacco[2)] (/day)	−0.041	−0.142**

1) Pearson product moment coefficient of correlation was calculated on age and BMI.

2) The rank correlation coefficient τ (Kendall's tau) was analyzed for ethanol and tobacco.

*: $p<0.05$, **: $p<0.01$, ***: $p<0.001$

104−333), and 53.6 ± 13.4 (27−104), respectively.

Table 3 shows the simple correlations between total cholesterol, HDL-cholesterol and the original data prior to categorization. These correlations indicate the general trends in the individual factors of age, obesity, drinking and smoking. Although total cholesterol showed a significant positive correlation with both age and obesity, there was no significant connection between total cholesterol and smoking. HDL-cholesterol, on the other hand, was positively linked to drinking, but not with obesity or smoking. Then the categorized data were analyzed by a multiple logistic model to ascertain the influence of the aforesaid four factors on high total cholesterol and low HDL-cholesterol.[16)]

$\log_e px/qx=\beta_0 + \Sigma_i\beta_i \times X\iota$

(px: probability of disease, qx=1-px, px/qx: odds of having disease)

The odds ratio of each factor against the baseline could be determined based on the β of each variable in each category.

The results of the above-mentioned calculations are shown in Table 4. As for abnormally high total cholesterol, it was determined that the odds ratios at 40, 45, and 50 years of age were 1.95, 2.23, and 2.65 ($p<0.05$), respectively, when 35-year-olds were considered the baseline. However, HDL-cholesterol remained virtually unchanged. In examining the influence of obesity, statistically significant differences were found. Abnormally high total cholesterol showed an odds ratio of 0.27 ($p<0.001$) among thin subjects with a BMI less than 21.0, when subjects with a standard BMI (21.1–25.0) were calculated as the baseline. With reference to low HDL-cholesterol, the odds ratio for lean subjects was 0.30 ($p<0.01$) against those who had standard habitus, while subjects with a BMI over 25.1 had an odds ratio of more than double (2.27) ($p<0.01$).

Table 4. Odds Ratios of Independent Variables for Single Binary (0–1) Dependent Variables: Total Cholesterol and HDL-cholesterol

Dependent variables		Total cholesterol>230 mg/dl		HDL-cholesterol<40 mg/dl	
Factor	Category	Odds ratio	(95 % C.I.)	Odds ratio	(95 % C.I.)
Age	35 yr	1.0		1.0	
	40 yr	1.95	(0.79, 4,87)	0.61	(0.27, 1.38)
	45 yr	2.23	(0.96, 5.18)	0.72	(0.35, 1.49)
	50 yr	2.65*	(1.13, 6.23)	0.73	(0.35, 1.55)
BMI	15.9–21.0	0.27***	(0.13, 0.56)	0.30**	(0.14, 0.65)
	21.1–25.0	1.0		1.0	
	25.1–33.5	1.28	(0.81, 2.03)	2.27**	(1.37, 3.76)
Ethanol	never or seldom	1.0		1.0	
(g/day)	1–28 g	0.87	(0.49, 1.52)	0.68	(0.38, 1.17)
	9–84 g	0.70	(0.42, 1.16)	0.16***	(0.09, 0.30)
	85 g or more	0.73	(0.35, 1.49)	0.23**	(0.10, 0.56)
Smoking	none	1.0		1.0	
(cigarettes/day)	1–20	1.07	(0.68, 1.70)	1.91*	(1.12, 3.26)
	21 or more	1.02	(0.61, 1.72)	2.27**	(1.27, 4.05)

1) Although independent variables are mutually interrelated, they are individually estimated odds ratios that affect the levels of total cholesterol and HDL-cholesterol using the multiple logistic regression analysis. Each value represents the odds ratio inherent in abnormal laboratory data when a baseline odds ratio of each independent variable is 1.0. The confidence intervals (95 % C.I.) are given in parentheses under odds ratio.

2) *: $p<0.05$, **: $p<0.01$, ***: $p<0.001$

Total cholesterol did not change significantly between drinkers and nondrinkers. Compared with nondrinkers, low HDL-cholesterol exhibited the odds ratios of 0.16 ($p<0.001$) and 0.23 ($p<0.01$), respectively, for subjects who drank equivalent to 29–84 g, and 85 g or more of pure

ethyl alcohol. In cases of low HDL-cholesterol, the odds ratios for those who smoked 1−20 cigarettes per day, and more than 21 were 1.91 ($p<0.05$) and 2.27 ($p<0.01$), respectively, versus nonsmokers. Total cholesterol did not change significantly between smokers and nonsmokers.

DISCUSSION

The negative correlation of HDL-cholesterol with obesity and smoking, and the positive correlation between HDL-cholesterol and alcohol consumption are well-known facts. The HDL-cholesterol trend shown in Table 3 confirms the previously reported findings. Results obtained from these simple correlations, however, do not include the individual influence of each factor. We examined the factors of normal lifestyle that related to the change of HDL-cholesterol level in a group of Japanese middle-aged male transport workers, while adjusting as far as possible any interactive influences among factors, and to that end we used multiple logistic regression analysis. The three factors of obesity, alcohol, and cigarette smoking are clearly related to the change of HDL-cholesterol level, as shown in Table 4. Salomaa et al. suggested that five-year aging caused an increase of serum HDL-lipoprotein cholesterol in the Finnish population aged 25−64 years.[17] However, the effect age has on HDL-cholesterol has proven to be less than the close connections found between HDL-cholesterol level and the above three factors in the present study. An obese smoker ranking above the BMI of 25.1 who smokes more than 21 cigarettes per day has an odds ratio of $2.27 \times 2.27=5.15$ greater than the nonsmoker with standard BMI. Conversely, an obese drinker ranking above the BMI of 25.1 who consumes the equivalent of 85 g or more pure ethyl alcohol daily has an odds ratio of $2.27 \times 0.23=0.52$ times less than the nondrinker with standard BMI. Thus, obesity, alcohol consumption and smoking must be considered individually when examining HDL-cholesterol, rather than making an evaluation based simply on the magnitude of the numerical values of HDL-cholesterol. Each of these factors exerts a significant influence on the HDL-cholesterol level. Haarbo et al. showed that cigarette smoking and central fat distribution had a significant, independent, negative influence on lipids, lipoproteins, and apolipoproteins, whereas moderate alcohol consumption had a positive effect on these parameters in early postmenopausal women.[12]

In a population at high coronary risk, Patterson et al. analyzed factors influencing total cholesterol and HDL-cholesterol using multiple regression analysis.[17] They found that total cholesterol increased with age, while HDL-cholesterol showed little variation with age in both sexes. They also found lower HDL-cholesterol levels among men and women who abstained from alcohol, and indicated that cigarette smoking was associated with significant increases in total cholesterol values and decreases in HDL-cholesterol values. Our findings are coincident with these results. Elevated HDL-cholesterol level in drinkers indicates an undesirable change inasmuch as alcohol is known to retard the HDL-cholesterol metabolism.[14] This factor is important when evaluating HDL-cholesterol levels in habitual drinkers. A drinking pattern, such as moderate daily drinkers adopting a weekend binge drinking pattern, was suggested to affect plasma lipoproteins and body weight in squirrel monkeys.[19] A binge cycle caused unfavorable alterations in lipoprotein composition (↑ LDL cholesterol, ↑ apolipoprotein B) and metabolism (↓ lecithin: cholesterol acyltransferase (LCAT) activity), and weight loss and depletion of body fat. Drinking patterns could not be analyzed in the present study. Reavent et al. studied the relationship between leisure time exercise and lipid and lipoprotein levels in an older population. They concluded that exercise levels attainable by older adults might significantly improve HDL-cholesterol levels and could theoretically reduce the risk of ischemic heart disease.[20] In the present

study, we did not use a variable of exercise. Multivariate estimations of total cholesterol and HDL-cholesterol including the factor of exercise should be investigated further.

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