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QUANTITATIVE SIGNIFICANCE OF ETHANOL INTAKE, EATING PATTERNS, AND SLEEP DURATION AFFECTING LIPID PROFILES IN MIDDLE-AGED EMPLOYEES

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Abstract

A cross-sectional study was conducted to investigate the associations of ethanol intake, eating patterns, and sleep duration with serum triglycerides, LDL-cholesterol, and HDL-cholesterol levels, along with the contributions of these risk factors to lipids. Study participants (1,582 males and 424 females) who returned questionnaire forms and underwent the mandatory health checkup were enrolled. After adjusting for age, smoking, and exercise, the mean contribution ratio, representing the extent to which each independent variable explained lipid variations in a multiple regression analysis, in the males (and females) was 14% (9%) for body mass index, 2% (3%) for ethanol intake, 0.4% (1.3%) for a total of eating patterns, and 0.06% (0.06%) for sleep duration. Ethanol intake was associated with high triglycerides, high HDL-cholesterol, and low LDL-cholesterol. Breakfast-skipping was associated with high LDL-cholesterol in the males, snacking during work hours was associated with low triglycerides in the females, and dinner time irregularity was associated with low triglycerides in the males. Long sleep duration was associated with high triglycerides in the males. However, there were not significant interactions between drinking and eating patterns in the males or females. In conclusion, preventive measures of dyslipidemia should be taken in consideration of the priority based on the quantitative significance of risk factors. Although moderate drinking appears to reduce risks of hyper-LDL and hypo-HDL cholesterolemia, it may lead to hypertriglyceridemia, in addition to hepatocellular injury and hypertension.

Key words : dyslipidemia, ethanol intake, eating pattern, sleep, risk assessment

Introduction

Dyslipidemia such as high levels of low-density lipoprotein cholesterol (LDL-C) and low levels of high-density lipoprotein cholesterol (HDL-C) elevates the risk of atherosclerotic cardiovascular disease (CVD)[1]. By contrast, moderate ethanol intake is associated with the decreased risk of CVD events such as myocardial infarction and stroke[2,3], whereas excessive ethanol intake leads to the increased risk of cardiac arrhythmia[4], cardiomyopathy[5], and stroke[6]. When analyzing the relationship between daily ethanol intake and cardiometabolic health risks, on the other hand, eating patterns may be associated with the increased risk of such diseases, because breakfast skipping has been suggested to heighten the risks of generalized atherosclerosis[7], diabetes mellitus[8], obesity[9,10], and hypertension[11]. For that reason, it is crucial to examine the interaction between daily ethanol intake and eating patterns, along with the health effects of these factors, inasmuch as heavy drinkers may have a

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specific eating pattern. However, there is little evidence addressing the association between daily ethanol intake and eating patterns in relation to the risk of atherosclerotic CVD.

Sleep duration also is noticed as another factor affecting dyslipidemia inasmuch as a link between sleep duration and CVD events has been suggested[12,13]. Although many studies have been carried out to investigate an association between sleep duration and lipid profiles[14-19], the conclusions remain inconclusive irrespective of the cross-sectional and prospective designs. Nevertheless, since there are a lot of causative factors other than sleep duration, the effects of multifactors including it on lipid profiles should be considered at the same time.

In this study, we focused on subclinical dyslipidemia in middle-aged workers. We examined ethanol intake, eating patterns including breakfast skipping, snacking during work hours, and irregularity of dinner time, and sleep duration possibly affecting it, and calculated to what extent these factors contributed to lipid profiles because we could give priority to the preventive measures. Our hypothesis was that ethanol intake, eating patterns, and sleep duration might affect lipid profiles independently. Since a LDL-C/HDL-C ratio also is reported to be inversely related to alcohol intake[20], we added it in lipid parameters of subclinical dyslipidemia.

Methods

Study population

In February-March 2012, a self-reported questionnaire was distributed to approximately 2,900 employees belonging to a health insurance union of motor vehicle dealerships in a prefecture of northeast Japan, including salesmen, mechanics, and office clerks, but excluding the managerial class. Of them, 2,556 consented to our proposal and returned the forms to the occupational health nurse of the union (response rate = 86%). Five hundred and fifty respondents were excluded : those who did not undergo the mandatory health checkup, conducted under the Industrial Safety and Health Law in Japan, in April-July 2012 ; those whose reported questionnaire forms contained imperfect information ; those who took antihyperlipidemic agent ; those whose serological tests for hepatitis B or C infection were positive ; those whose fasting blood could not be taken ; those who had shift work ; and, those who suffered from ischemic heart disease, chronic renal failure, alcoholic dependency diagnosed by a psychiatrist, liver cirrhosis, or cancer. The study population consisted of 1,582 male workers and 424 female workers. Some mechanics in this study had underwent the specific health examination for organic solvent workers under the Industrial Safety and Health Law annually, but such workers had neither symptoms/signs of organic solvent poisoning nor abnormal findings in urinalysis. This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects were approved by the Ethical Review Committee of the Akita University Graduate School of Medicine. Written informed consent was obtained from all participants.

Methods

Eating patterns, as well as sleep duration, smoking and drinking habits, regular exercise, and stress at work or home, were inquired via the questionnaire made for this study. For instance, eating patterns of breakfast-skipping, snacking during work hours, and irregularity of dinner time were scored as "absence"= 0 and "presence"= 1, while Smith *et al*.[21] employed 'late-night eating' instead of 'dinner time irregularity'. Nocturnal sleep duration (min) was computed as the difference between bedtime and wake time on workdays. Smoking habit was scored as "nonsmoker"= 0 and "current smoker"= 1. Concerning drinking habit, the weekly amount of specific type of alcoholic beverage consumed was asked as described previously[22-24] ; *e.g*., "How many 180 ml-cups (or 1,800 ml-bottles) of sake do you drink in a week ?" and "How many 350 ml-cans (500 ml-cans, or 633 ml-bottles) of beer do you drink in a week ?" Types of alcoholic beverages listed were sake, beer, shochu (a Japanese distilled alcoholic beverage primarily made from barley or sweet potatoes), whisky, wine, and others (*e.g*., plum wine, brandy, gin, or vodka). A total of 100% ethanol equivalent dose (g/day) was calculated for each subject. Regular exercise was defined as at least one 30-min session at least once per week. Each subject reported whether the subject felt any stress at work or

home (yes/no). The responses of exercise and work/family stress were scored as "absence"= 0 or "presence"= 1.

Data on lipid parameters, *i.e.*, fasting serum triglycerides (TGs), LDL-C, and HDL-C, along with body mass index (BMI, kg/m^2) and age, were obtained for each subject from the annual health checkup record. These levels were measured by the Akita Foundation for Healthcare, according to the principles recommended by the Japan Society of Clinical Chemistry. LDL-C was computed with the Friedewald equation[25] for only the subjects with TGs below 400 mg/dl. Based on conventional values recommended by the Japan Atherosclerosis Society[26], TGs of 150 mg/dl or more, LDL-C of 140 mg/dl or more, and HDL-C of less than 40 mg/dl were defined as hypertriglyceridemia, hyper-LDL cholesterolemia, and hypo-HDL cholesterolemia, respectively. Atherogenic index (*i.e.*, LDL/HDL ratio) was calculated as LDL-C/HDL-C, and the high LDL/HDL ratio is known to be an important risk factor for cardiovascular disease[27]. The cut-off value was calculated to be 2.40 according to a report by Wakabayashi[20].

Statistical analyses

Sex differences of background characteristics were assessed using Student *t* test or chi-square test. Lipid parameters (*i.e.*, TGs, LDL-C, HDL-C, and LDL/HDL ratio) were logarithmically transformed to achieve near-normal distributions. Comparisons of the lipid parameters among subgroups divided according to three types of eating patterns (breakfast-skipping, snacking during work hours, and irregularity of dinner time) or drinking volumes were made using analysis of covariance with the adjustment for age and BMI, because they are crucial confounders[28]. The relations of daily ethanol intake, three types of eating patterns, and confounders (age, BMI, sleep duration, smoking and drinking habits, work stress, and family stress) to each lipid parameter were analyzed by multiple regression analysis. At the same time, the contribution ratio (CR, %) of each independent variable was calculated from the following equation : $CR = 100 \times (R_{all}^2 - R_i^2)$, where R_{all} and R_i are the multiple correlation coefficients (R) calculated from all independent variables and the remaining independent variables excluding one (ith variable). In addition, interaction terms, *i.e.*, (each eating pattern) × (ethanol intake), were added into the above independent variables, and the analyses were made again. The odds ratio and 95% confidence interval (CI) of ethanol intake (0 g/day, 0.1-20 g/day, 20.1-40 g/day, and > 40.0 g/day), three types of eating patterns, and sleep duration (< 360 min, 360-419 min, 420-479 min, and ≥ 480 min) for dyslipidemia were calculated by multiple logistic regression analysis after adjusting for possible confounders. All analyses with two-side P values were performed using the Statistical Package for the Biosciences (SPBS Ver. 9.68)[29], and the significance level was set at $P < 0.05$.

Results

Background characteristics are shown in Table 1. All characteristics except for sleep duration and proportions of subjects with regular exercise and work stress showed significant sex differences. Of them, the proportion of subjects with family stress was significantly higher in the females than in the males, but the others were higher in the males than in the females. Daily ethanol intake was significantly higher in the male workers (mean 21.4 g/day, range 0-243 g/day) than in the female workers (8.5 g/day, 0-125 g/day). TGs, LDL-C, and LDL/HDL ratio of the male workers were significantly higher than those of the female workers, but the male HDL-C was significantly lower than the female one. Proportions of dyslipidemia among the male and female workers were 17.3% and 3.3% for hypertriglyceridemia, 18.9% and 9.7% for hyper-LDL cholesterolemia, 4.7% and 0.9% for hypo-HDL choelsterolemia, and 30.5% and 9.4% for high LDL/HDL ratio, respectively.

As shown in Table 2, TGs were low in the male and female workers with snacking during work hours when compared to those without it. Likewise, TGs in the males with irregularity of dinner time were lower than those without it. LDL-C and LDL/HDL ratio were higher in the male workers with breakfast-skipping than in those without it. By contrast, HDL-C was lower in the males with it. As ethanol intake increased in the male workers (Table 3), TGs and HDL-C were increased and LDL-C and LDL/HDL ratio were decreased ; simi-

Table 1. Background characteristics of Japanese workers

	1,582 male workers		424 female workers		*P*
	Mean ± SD (% or median, 5th and 95th percentiles)		Mean, SD (% or median, 5th - 95th percentiles)		
Age (years)	36	± 10	33	± 8	< 0.001
Body mass index (kg/m^2)	23.3	± 3.7	20.9	± 3.2	< 0.001
Sleep duration (min)	420	± 55	414	± 55	0.089
Breakfast-skipping	25.2		18.4		0.003
Snacking during work hours	45.7		81.8		< 0.001
Irregularity of dinner time	59.2		31.4		< 0.001
Smoking habit	59.3		21.9		< 0.001
Drinking habit					< 0.001
Nondrinker	31.6		54.7		
Drinker, 0.1-20.0 g/day	35.2		31.4		
Drinker, 20.1-40.0 g/day	14.7		8.0		
Drinker, ≥ 40.0 g/day	18.5		5.9		
Regular exercise	17.0		15.3		0.426
Work stress	64.3		62.0		0.395
Family stress	18.3		25.2		0.002
Lipid parameters					
Triglycerides (mg/dl)	83,	36 - 269.5	53,	40 - 74	< 0.001
LDL-cholesterol (mg/dl)	113,	69 - 168.5	99,	85.5 - 120	< 0.001
HDL-cholesterol (mg/dl)	57,	40 - 84.5	66,	59 - 76	< 0.001
LDL/HDL ratio [c]	1.95,	1.00 - 3.56	1.50,	0.82 - 2.70	< 0.001

LDL/HDL ratio, LDL-cholesterol/HDL-cholesterol ratio.
P value by Student *t* test, Mann-Whitney *U* test or χ^2 test.

larly, LDL-C and LDL/HDL ratio in the female workers were decreased in relation to ethanol intake.

As shown in Table 4, all regression coefficients of age and BMI on the lipid parameters, except for that of age on HDL-C, were statistically significant in the male and female workers. Similarly, ethanol intake was significantly connected with these lipid parameters in both sexes, excluding TGs in the female workers. In the male workers, TGs were related positively to sleep duration and negatively to irregularity of dinner time ; LDL-C and LDL/HDL ratio were related positively to breakfast-skipping ; and, HDL-C was negatively related to smoking. Among the female workers, TGs were related positively to smoking and negatively to snacking ; HDL-C was related positively to work stress and negatively to smoking ; and, the LDL/HDL ratio was positively to breakfast-skipping and negatively to work stress. When adding three interaction terms of eating patterns and ethanol intake in the independent variables of Table 4, only one interaction term, *i.e.*, (dinner time irregularity) × (ethanol intake), was significantly related to HDL-C in the male workers ($\beta = 0.074$, $P < 0.048$), but significance levels ($P < 0.05$) of other independent variables remained unchanged in both sexes.

The contribution ratios of individual independent variables also are presented in Table 4. In both sexes, the highest contribution to lipid parameters was BMI. The contribution ratio of a total of eating patterns was 0.46% for the male TGs (1.17% for the female TGs), 0.45% (1.25%) for LDL-C, 0.20% (1.08%) for HDL-C, and 0.49% (1.64%) for LDL/HDL ratio, and it was higher in the females than in the males ($P < 0.05$ by paired *t* test).

Since the prevalence rates of dyslipidemia and the proportion of ethanol intake of 40.1 g/day and over in the fe-

Table 2. Log-transformed lipid parameters (mean ± SD) after adjustment for age and body mass index between subgroups with and without each eating pattern

	Eating pattern		*P*
	Absence	Presence	
Male workers with			
Breakfast-skipping	(*n* = 1183)	(*n* = 399)	
Triglycerides	1.944 ± 0.247	1.964 ± 0.254	0.169
LDL-cholesterol	2.037 ± 0.119	2.052 ± 0.109	0.022
HDL-cholesterol	1.761 ± 0.093	1.746 ± 0.088	0.006
LDL/HDL ratio	0.276 ± 0.154	0.306 ± 0.148	< 0.001
Snacking during work hours	(*n* = 858)	(*n* = 724)	
Triglycerides	1.965 ± 0.251	1.930 ± 0.245	0.005
LDL-cholesterol	2.036 ± 0.116	2.047 ± 0.117	0.075
HDL-cholesterol	1.758 ± 0.093	1.756 ± 0.091	0.753
LDL/HDL ratio	0.278 ± 0.153	0.290 ± 0.153	0.122
Irregularity of dinner time	(*n* = 645)	(*n* = 937)	
Triglycerides	1.967 ± 0.247	1.937 ± 0.249	0.016
LDL-cholesterol	2.040 ± 0.114	2.041 ± 0.119	0.863
HDL-cholesterol	1.760 ± 0.094	1.755 ± 0.091	0.383
LDL/HDL ratio	0.281 ± 0.159	0.286 ± 0.149	0.511
Female workers with			
Breakfast-skipping	(*n* = 346)	(*n* = 78)	
Triglycerides	1.749 ± 0.184	1.748 ± 0.188	0.971
LDL-cholesterol	1.995 ± 0.110	2.012 ± 0.115	0.233
HDL-cholesterol	1.826 ± 0.085	1.803 ± 0.093	0.030
LDL/HDL ratio	0.169 ± 0.142	0.209 ± 0.157	0.027
Snacking during work hours	(*n* = 77)	(*n* = 347)	
Triglycerides	1.796 ± 0.161	1.738 ± 0.188	0.013
LDL-cholesterol	2.008 ± 0.125	1.996 ± 0.108	0.404
HDL-cholesterol	1.806 ± 0.081	1.826 ± 0.087	0.068
LDL/HDL ratio	0.202 ± 0.154	0.170 ± 0.143	0.085
Irregularity of dinner time	(*n* = 291)	(*n* = 133)	
Triglycerides	1.755 ± 0.179	1.735 ± 0.196	0.307
LDL-cholesterol	2.004 ± 0.107	1.985 ± 0.117	0.088
HDL-cholesterol	1.823 ± 0.087	1.819 ± 0.087	0.621
LDL/HDL ratio	0.181 ± 0.142	0.166 ± 0.153	0.314

LDL/HDL ratio, LDL-cholesterol/HDL-cholesterol ratio.
P value by analysis of covariance.

male workers were too small to calculate odds ratios of ethanol intake, Table 5 represents odds ratios of dietary lifestyles and ethanol intake for abnormal lipids in the male workers and all workers (*i.e.*, male plus female workers). Among the male workers and all workers, ethanol intake of 40.1 g/day and over was associated with hypertriglyceridemia, and that of 20.1 g/day and over was associated with hyper-LDL cholesterolemia and elevated LDL/HDL ratio ; in addition, ethanol intake of 40.1 g/day and over was associated with hypo-HDL cholesterolemia

Table 3. Log-transformed lipid parameters (mean ± SD) after adjustment for age and body mass index among different ethanol intake subgroups

	Ethanol intake			*P*
	0 g/day	0.1-20 g/day	> 20 g/day	
Male workers	(*n* = 501)	(*n* = 557)	(*n* = 524)	
Triglycerides	1.936 ± 0.228	1.932 ± 0.239	1.980 ± 0.274*	0.002
LDL-cholesterol	2.053 ± 0.118	2.046 ± 0.113	2.023 ± 0.117*	< 0.001
HDL-cholesterol	1.733 ± 0.087	1.755 ± 0.091*	1.782 ± 0.092*	< 0.001
LDL/HDL ratio	0.320 ± 0.146	0.291 ± 0.148*	0.241 ± 0.154*	< 0.001
Female workers with :	(*n* = 232)	(*n* = 133)	(*n* = 59)	
Triglycerides	1.735 ± 0.185	1.762 ± 0.184	1.773 ± 0.181	0.232
LDL-cholesterol	2.011 ± 0.107	1.995 ± 0.107	1.957 ± 0.125*	0.003
HDL-cholesterol	1.817 ± 0.086	1.825 ± 0.081	1.837 ± 0.099	0.250
LDL/HDL ratio	0.194 ± 0.131	0.170 ± 0.148	0.119 ± 0.176*	0.002

P value by one-way analysis of variance (*F* test).
* $P < 0.05$ v.s. nondrinker (0 g/day) group by Scheffe multiple comparison.

in all workers. With regard to eating patterns, snacking during work hours in the male workers and breakfast-skipping in all workers were associated with hyper-LDL cholesterolemia. Likewise, sleep duration of 480 min and over was associated with hypertriglyceridemia in the male workers ($P = 0.09$) and in all workers ($P = 0.04$).

Discussion

In this study, ethanol intake, eating patterns, and sleep duration, as well as age and BMI, were significantly related to some lipid parameters ; especially, heavy ethanol intake and long sleep duration were associated with high TGs, and heavy ethanol intake also was associated with high HDL-C, and low LDL/HDL ratio. Next, the contribution of each lifestyle-related factor to lipid profiles was calculated : The contribution of BMI to lipid profiles was the strongest among all lifestyle-related factors (mean, 14% for males and 9% for females), that of ethanol intake was approximately 2% for males and 3% for females, and that of a total of eating patterns was around 0.4% for males and 1.3% for females. Taken together, obesity, drinking habit, and eating patterns were indicated to be more important for the prevention of dyslipidemia and the consequent CVD and/or cerebrovascular disease than the other lifestyle-related factors. To our knowledge, this is the first report to point out the quantitative significance of risk factors for dyslipidemia.

According to results of multiple regression analyses in the present study, BMI explained mean 14.2% (standard deviation, 4.5%) of the variation of each lipid parameter among the males and 9.3% (3.4%) among the females, and were thought to be the strongest modifier for dyslipidemia[28]. The second contributor was ethanol intake, and the third was age for males and a total of eating patterns for females. A total of eating patterns explained 0.40% (0.13%) for males and 1.29% (0.25%) for females, whereas the values were considerably small as compared with those of BMI. Given a human study on lipid profiles, ethanol intake and eating patterns, together with age and BMI[28], are inevitable confounders, and also the analyses should be made in males and females separately to avoid the effects of sex hormones.

We observed significant differences of lipid profiles between two subgroups with and without each eating pattern of breakfast skipping, snacking during work hours, and irregularity of dinner time (Table 2). As ethanol intake increased, TGs and HDL-C tended to increase and LDL-C and LDL/HDL ratio tended to decrease (Table 3). Nevertheless, significant interactions of eating patterns and ethanol intake to lipid parameters were hardly found, though ethanol intake seemed to have a relation to irreg-

Table 4. Relations of lifestyle-related factors and stress to triglycerides, LDL-cholesterol, HDL-cholesterol, and LDL-cholesterol/HDL-cholesterol ratio and the contribution ratios in Japanese workers : results of multiple regression analysis

	$\log_{10}$[TGs]		$\log_{10}$[LDL-C]		$\log_{10}$[HDL-C]		$\log_{10}$[LDL/HDL]	
	β	CR, %	β	CR, %	β	CR, %	β	CR, %
1,582 male workers								
Age	0.145*	1.92	0.151*	2.11	0.005	0.00	0.106*	1.03
Body mass index	0.384*	14.25	0.289*	8.08	−0.399*	15.40	0.442*	18.89
Sleep duration	0.049*	0.22	0.014	0.02	0.009	0.01	0.005	0.00
Breakfast-skipping	0.026	0.06	0.063*	0.38	−0.044	0.18	0.071*	0.48
Snacking during work hours	−0.040	0.15	0.028	0.07	0.013	0.02	0.012	0.01
Irregularity of dinner time	−0.053*	0.25	0.001	0.00	−0.006	0.00	0.004	0.00
Smoking habit	0.024	0.08	−0.034	0.11	−0.110*	1.17	0.041	0.16
Daily ethanol intake	0.108*	1.23	−0.080*	0.59	0.175*	2.73	−0.160*	2.32
Regular exercise	−0.016	0.02	0.001	0.00	0.008	0.01	−0.004	0.00
Work stress	0.022	0.04	0.036	0.12	−0.013	0.02	0.034	0.10
Family stress	−0.024	0.05	−0.025	0.06	−0.013	0.02	−0.010	0.01
R	0.448*		0.347*		0.445*		0.484*	
424 female workers								
Age	0.126*	1.48	0.196*	3.58	0.091	0.77	0.095*	0.83
Body mass index	0.363*	12.71	0.236*	5.36	−0.282*	7.66	0.342*	11.27
Sleep duration	0.046	0.19	−0.014	0.02	−0.021	0.04	0.002	0.00
Breakfast-skipping	−0.037	0.13	0.088	0.72	−0.078	0.56	0.112*	1.15
Snacking during work hours	−0.099*	0.94	−0.032	0.10	0.068	0.44	−0.064	0.39
Irregularity of dinner time	−0.034	0.10	−0.069	0.43	−0.031	0.08	−0.034	0.10
Smoking habit	0.120*	1.34	−0.039	0.14	−0.158*	2.26	0.063	0.35
Daily ethanol intake	0.016	0.03	−0.187*	3.29	0.162*	2.48	−0.236*	5.22
Regular exercise	0.031	0.10	−0.049	0.24	0.003	0.00	−0.038	0.15
Work stress	−0.031	0.08	−0.060	0.33	0.111*	1.11	−0.110*	1.09
Family stress	0.005	0.00	−0.019	0.03	−0.021	0.04	0.002	0.00
R	0.425*		0.385*		0.388*		0.450*	

TGs, triglycerides ; LDL-C, LDL-cholesterol ; HDL-C, HDL-cholesterol ; LDL/HDL, LDL-cholesterol/HDL-cholesterol ; CR, contribution ratio ; β, standardized regression coefficient ; *R*, multiple correlation coefficient.
* $P < 0.05$.

ularity of dinner time in assessing the effect on HDL-C in the males. These findings imply that eating patterns and drinking habit may affect dyslipidemia independently.

Breakfast-skipping was associated with high LDL-C and LDL/HDL ratio in the male and female workers, as shown in Table 4. A similar finding was observed in a study reported by Smith *et al*.[21], in which ethanol intake was not considered. Apart from lipid parameters, Cahill *et al*.[30] reported that men who skipped breakfast had a higher risk of coronary heart disease (CHD) compared with men who did not (relative risk 1.27, 95% CI 1.06-1.53) and that men who ate late at night had a higher CHD risk as compared with men who did not (1.55, 1.05-2.29). Also, breakfast-skipping increased the risk of type 2 diabetes mellitus, BMI, and fasting blood glucose[8] ; it was associated with stress-independent over-activity in the hypothalmic-pituitary-adrenal axis[11] ; and, the prevalence rate of obesity decreased as

Table 5. Odds ratios of eating patterns, daily ethanol intake, and sleep duration for abnormal lipids in Japanese workers : results of multiple logistic regression analysis

	Hyper-triglyceridemia		Hyper-LDL cholesterolemia		Hypo-HDL cholesterolemia		LDL/HDL ratio ≥ 2.40	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
1,582 male workers								
Breakfast-skipping	1.34	0.97-1.86	1.26	0.92-1.71	0.95	0.54-1.67	1.20	0.91-1.58
Snacking	0.79	0.59-1.06	1.34	1.02-1.75	1.14	0.70-1.85	1.11	0.87-1.42
Irregularity of dinner time	0.88	0.66-1.18	1.04	0.79-1.38	0.82	0.50-1.36	1.04	0.81-1.34
Sleep duration (min)								
< 360	1.19	0.72-1.97	1.10	0.68-1.76	0.72	0.29-1.81	0.98	0.62-1.54
360-419	0.82	0.58-1.16	0.99	0.72-1.35	1.04	0.60-1.82	1.21	0.91-1.61
420-479	1.00		1.00		1.00		1.00	
≥ 480	1.39	0.95-2.05	0.98	0.67-1.44	0.91	0.44-1.87	1.27	0.90-1.78
Ethanol intake (g/day)								
0 (nondrinker)	1.00		1.00		1.00		1.00	
0.1-20	1.06	0.74-1.53	1.11	0.81-1.52	1.06	0.61-1.85	0.77	0.58-1.02
20.1-40	1.12	0.71-1.78	0.59	0.37-0.93	0.56	0.24-1.35	0.49	0.33-0.73
> 40	1.61	1.07-2.42	0.64	0.42-0.98	0.45	0.19-1.04	0.37	0.25-0.54
1,582 male and 424 female workers [c]								
Breakfast-skipping	1.34	0.97-1.84	1.39	1.04-1.85	0.96	0.55-1.66	1.26	0.97-1.65
Snacking	0.78	0.58-1.03	1.24	0.95-1.60	1.17	0.72-1.90	1.04	0.82-1.32
Irregularity of dinner time	0.85	0.64-1.13	1.01	0.78-1.31	0.80	0.49-1.31	1.01	0.80-1.29
Sleep duration (min)								
< 360	1.21	0.75-1.96	1.17	0.76-1.80	0.65	0.26-1.62	1.05	0.69-1.59
360-419	0.79	0.56-1.11	1.03	0.77-1.38	0.99	0.58-1.70	1.16	0.88-1.51
420-479	1.00		1.00		1.00		1.00	
≥ 480	1.46	1.01-2.11	1.01	0.70-1.44	0.78	0.38-1.59	1.20	0.87-1.66
Ethanol intake (g/day)								
0 (nondrinker)	1.00		1.00		1.00		1.00	
0.1-20	1.03	0.72-1.46	1.06	0.80-1.42	1.03	0.61-1.77	0.81	0.62-1.06
20.1-40	1.05	0.67-1.64	0.59	0.38-0.91	0.55	0.23-1.29	0.52	0.35-0.75
> 40	1.52	1.02-2.27	0.63	0.42-0.94	0.44	0.19-1.02	0.38	0.26-0.55
Female sex	0.32	0.17-0.59	0.59	0.39-0.87	0.29	0.10-0.86	0.38	0.26-0.57

LDL/HDL, LDL-cholesterol/HDL-cholesterol ; OR, odds ratio after adjusting for age, body mass index, smoking habit, regular exercise, work stress, and family stress in Table 4 ; 95% CI, 95% confidence interval.

the frequency of breakfast consumption increased, and the odds of developing obesity for breakfast skippers was 1.34 (95% CI 1.15-1.56)[9]. By contrast, although we observed an association of snacking during work hours with reduced TGs in the female workers (Table 4), this relation remains unclear according to meal frequency regimens without calorie restriction by the American Heart Association[31]. Thus, breakfast-skipping can lead to the high CHD/CVD risk by elevating LDL-C, diabetic risk, and body weight. Additional study is needed to clarify a pathogenetic mechanism connecting such eating patterns and cardiometabolic risks.

In male workers and all workers at around 35 years of age of this study, ethanol intake of more than 40 g/day

was associated with hypertriglyceridemia. By contrast, ethanol intake of more than 20 g/day seemed to reduce the incidence of hyper-LDL cholesterolemia and high atherogenic index. These are consistent with previous findings[32,33], whereas the critical dose (g/day) of ethanol, at which the significant effect appears initially, differed among them. For instance, Kojima *et al*.[34] reported in 21,493 men and women at 52.9 years of mean age that the critical doses of ethanol were more than 20 g/day for hypertriglyceridemia, less than 10 g/day for hyper-LDL cholesterolemia, and less than 10 g/day for hypo-HDL cholesterolemia ; in 22,349 men (mean 48.6 years)[35], they were less than 20 g/day for hypo-HDL cholesterolemia and more than 20 g/day for hypertriglyceridemia ; and, less than 66 g/day for LDL/HDL ratio ≥ 2.4 in 7,570 men (mean 46.8 years)[36] and less than 22 g/day for hypo-LDL cholesterolemia in 1,440 Japanese non-diabetic men (mean 54.2 years)[37]. Yet, a part of the above reports did not consider any effects of crucial confounders such as BMI, smoking habit, or stress. In this way, although critical doses of ethanol differ by the average age of each population or human race[32,33], drinking habit appears to suppress the incidence of CVD through the low LDL-C and high HDL-C levels. Still, it should be noted that a similar volume of ethanol leads to not only hyper-triglyceridemia but also hepatocellular injury[22,38] and hypertension[23,38].

As shown in Tables 4 and 5, long sleep duration was associated with high TGs, nevertheless the contribution ratio for the variation of TGs was around 0.2% and extremely small. This relation to TGs agrees with some preceding reports[17,19]. However, some reported that long sleep durations decreased the risk of high TGs[15,18], and others showed a *U*-shaped relationship between sleep duration and TGs[16]. Three possible reasons for the inconsistency are as follows : First, usual sleep durations, different from smoking and drinking habits, are changeable according to daily workload and aging ; in other words, misclassification of the exposure can readily occur even though researchers used objectively measured sleep duration. Given the time lag between the exposure and outcomes involved in dyslipidemia, the short study period of two to four months may be favorable rather than the long period of several years. Secondly, although inconsistency of the results may have resulted from different study designs, it is also plausible that participants employed in each study may have differed in the characteristics undescribed in the Subjects and Methods. Some characteristics, such as shift work, inoccupation, solvent exposure, or postmenopausal women, might affect lipid profiles. Finally, the definition of high TGs differed among the above reports ; *e.g*., TG level ≥ 150 mg/dl[16,17], TG level ≥ 200 mg/dl[18], and TG level ≥ 177 mg/dl (2 mmol/l)[14]. Before scrutinizing a relationship between sleep duration and lipid profiles, it is necessary to determine the definition of dyslipidemia, characteristics of study population, and the study design.

The strength of this study is that all participants belonging to a health insurance union of motor vehicle dealerships were day workers in a socioeconomically homogenous condition ; for this reason, their sleep durations were not affected by shift work. Although a self-reported questionnaire might introduce bias, alcohol data in this study showed a consistency with our past study[22,23], and other items of the questionnaire, about which approximately 5% of the subjects were directly asked by the occupational health nurse 5 months after the mandatory health checkups in 2012, remained unchanged. In addition, we obtained detailed information about weekly amount of each type of alcoholic beverage, different from the conventional data examined by medical examination institutions[28].

Our study was a cross-sectional design, whereas the questionnaire survey was conducted two to four months before the mandatory health checkups began ; for this reason, the directions of associations should be interpreted carefully. Nonetheless, the associations of eating patterns and daily ethanol intake with dsylipidemia in the present study are in accordance with those of previous studies. Potential confounders such as age, regular exercise, smoking habit, and stress were considered in the data analysis. Thus, it is suggested that our data were not heavily influenced by measurement bias or confounders ; whereas, the target population may be limited in those with similar job categories.

Conclusions

The prevention of dyslipidemia attenuates potential risks of cardiovascular and cerebrovascular diseases. The strongest contributor to dynamics of serum lipid profiles was suggested to be BMI, followed by ethanol intake and eating patterns including breakfast-skipping. Ethanol intake appeared to reduce risks of hyper-LDL and hypo-HDL cholesterolemias but elevated the risk of hypertriglyceridemia. On the other hand, long sleep duration was associated with high TGs, but its contribution was smaller than those of ethanol intake and eating patterns. Since these risk factors were associated with lipid profiles independently, preventive measures of dyslipidemia should be taken in consideration of the above priority.

Conflicts of interest

The authors declare no conflict of interest.

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