Original Article

Relationship Between Shift Work and Clustering of the Metabolic Syndrome Diagnostic Components

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Aim: To examine the relationship between the type of work and the number of metabolic syndrome diagnostic components (MetS-DC), as well as the risk of MetS, with adjustment for lifestyle habits in Japanese workers.

Methods: We examined the baseline data from 4,427 participants (81.4% male) aged 19 to 69 years old. The physical activity of each participant was classified according to the International Physical Activity Questionnaire (IPAQ). We defined the four MetS-DC in this study as follows: 1) high blood pressure (BP): systolic BP ≥ 130 mmHg, or diastolic BP ≥ 85 mmHg, or the use of antihypertensive drugs; 2) dyslipidemia: high-density lipoprotein-cholesterol concentration < 40 mg/dl or triglyceride concentration ≥ 150 mg/dl, or on medication for dyslipidemia; 3) dysglycemia: fasting blood sugar level ≥ 110 mg/dl, or if less than eight hours after meals ≥ 140 mg/dl, or on medication for diabetes mellitus; 4) overweight: a body mass index ≥ 25 kg/m². We defined MetS as overweight plus two or more of the MetS-DC.

Results: There were 3,094 subjects in the daytime work group, 73 in the fixed nighttime work group, 1,017 in the shift work group and 243 in the day-to-night work group. The Poisson regression analysis revealed that fixed nighttime (regression coefficient [b] = -0.233 , $P=0.028$) and shift work ($b=0.098$, $P=0.034$) independently contributed to the number of MetS-DC, compared to daytime work. The multivariate logistic analysis not including sleep hours in the model showed that shift work was positively related to MetS (odd ratio = 1.47 , $P<0.01$).

Conclusion: Shift work were significantly associated with the number of MetS-DC, and was related to risk of MetS compared to daytime work.

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Key words: Shift work, Metabolic syndrome, Diagnostic components, International Physical Activity Questionnaire, Smoking, Alcohol

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Introduction

The work environment is known to exert both beneficial and negative health effects among the working population¹⁻⁸. Shift work can be defined as employment in any work schedule that is not a regular

daytime schedule (that is, approximately 0900 to 1700)³). The full spectrum of shift work comprises regular evening or night schedules, rotating shifts, split shifts, on-call or casual shifts, 24-hour shifts, irregular schedules and other non-day schedules. A flexible work patterns remain a necessary component for a dynamic, diversified industrial economy⁴). However, shift work has long been known to disrupt circadian rhythm, sleep and work-life balance; a higher incidence of coronary heart disease⁵), metabolic syndrome⁶), as well as mental and behavioral disorders⁷) and sleep disturbances⁸), has also been described among shift workers.

The prevalence of people with metabolic syndrome diagnostic components (MetS-DC) is increasing in Japan, as well as globally. MetS-DC such as high blood pressure (BP), dyslipidemia, dysglycemia and being overweight/obese tend to cluster together and are closely related to insulin resistance⁹⁻¹²). The clustering of MetS-DC is known as metabolic syndrome (MetS), and is thought to be related to lifestyle habits, including nutrient intake, physical activity, smoking and alcohol consumption¹¹⁻¹⁴). Numerous studies have shown that separate components of the MetS-DC are associated with a higher risk of coronary heart disease and stroke, and that an increase in the number of MetS-DC increases the incidence of cardiovascular disease (CVD) events following myocardial infarction¹⁵⁻¹⁷). Therefore, preventing the development of MetS-DC is more important than dichotomizing people into two groups, namely those with and without MetS, in order to prevent the development of MetS. No previous study has examined the associations of shift work with MetS-DC. In addition, there have been very few studies that have examined the relationships between shift work and MetS or MetS-DC that took into consideration the various factors associated with shift work that might lead to MetS.

Aim

The aim of the present study was to cross-sectionally examine the relationship between the type of work and MetS, as well as the number of MetS-DC, with adjustment for lifestyle habits in Japanese workers. Furthermore, we wanted to evaluate the roles of being overweight and having sleep impairment as mediators of the increased development of MetS or MetS-DC by shift workers.

Methods

Participants

We analyzed the baseline data from the high-risk and population strategy for occupational health promotion (HIPOP-OHP) study¹⁸⁻²¹). In brief, the HIPOP-OHP was an interventional survey to establish a methodology for reducing CVD risk factors in the workplace. This study population consisted of full-time workers at 12 large companies throughout Japan. Each company had 500-1000 employees. Researchers collected data regarding CVD risk factors and lifestyle habits¹⁸⁻²¹). This study was carried out as part of the management of safety and health, with the approval of the Safety Hygiene Committee at each company. Approval for the study was obtained from the Institutional Review Board of Shiga University of Medical Science for Ethical Issues (No. 10-16). From 1999 to 2000, baseline data were collected from 7,346 male and female workers aged 19-69 years old. The present study examined the baseline data from 4,427 participants (3,604 males and 823 females), aged 19-69 years old (mean $\pm$ SD, 41.9 $\pm$ 9.4 years) who underwent a physical examination, a lifestyle survey and a blood chemical examination.

Data Collection and Standardization

Physical and laboratory data were standardized according to the manual of the HIPOP-OHP research group¹⁸). Briefly, after 5 min of silent rest measured by an hourglass, the blood pressure (BP) was measured twice for each participant using an automatic sphygmomanometer (BP-103iII; Omron Colin, Tokyo, Japan) at each company, and the mean value was recorded. To measure the lipid levels in each participant, the company established a contract with a clinical laboratory; the blood testing was standardized through the US Cholesterol Reference Method Laboratory Network (CRMLN)²²). The non-HDL-cholesterol (non-HDL) level was calculated by subtracting HDL from the total cholesterol concentration²³). The BMI was calculated as the weight (in kg) divided by the height squared (m^2). Information on the shift work schedule at the baseline (daytime work, fixed nighttime, [rotating] shift or day-to-night work) and the average overtime work hours per day in the previous one month (seldom, <1 h, 1 to <2 h, $\geq$ 2 h) was obtained from a questionnaire. The sleep duration was investigated using the question, 'How many hours of sleep do you get on an average weekday per night?' in the lifestyle survey. The physical activity of each participant was converted into MET-minutes per week (=MET level $\times$ minutes of activity/day $\times$ days per

week) according to the International Physical Activity Questionnaire (IPAQ)²⁴, and participants were classified into four classes of physical activity; high (≥ 3000 MET-minutes per week), moderate (< 3000 but ≥ 1500 MET-minutes per week), some activity (< 1500 but ≥ 600 MET-minutes per week) or sedentary (< 600 MET-minutes per week). The drinking habits for each subject were assessed by a questionnaire common to all companies¹⁹. Drinkers were defined as those consuming more than 1 g of ethanol per day. The average alcohol intake (ml) per day was obtained for each participant¹⁹.

We defined four MetS-DC in this study as follows: 1) high BP: systolic BP (SBP) ≥ 130 mmHg, or diastolic BP (DBP) ≥ 85 mmHg or the use of an anti-hypertensive drug; we defined dyslipidemia in two ways: 2a) high-density lipoprotein cholesterol (HDL) < 40 mg/dl for males, or HDL < 50 mg/dl for females, or triglycerides (TG) ≥ 150 mg/dl for both sexes, or on medication for dyslipidemia; or 2b) non-HDL ≥ 160 mg/dl for both sexes, or on medication for dyslipidemia (the cutoff level was chosen to be when the prevalence of 2a and 2b were similar)²³; 3) dysglycemia: a fasting plasma glucose concentration ≥ 110 mg/dl, or if less than eight hours after meals ≥ 140 mg/dl, or on medication for diabetes mellitus^{17, 25, 26}; 4) overweight: defined as a BMI ≥ 25 kg/m²^{27, 28}. We defined MetS as overweight plus two or more of the high BP, dyslipidemia or dysglycemia. Although the recent WHO guidelines suggests that a BMI < 23.0 kg/m² is healthy for Asians²⁹, we found that the risk of total mortality was lowest in participants with a BMI 23.0–24.9 kg/m² in Japan²⁸. Thus, we used a cutoff for overweight as a BMI ≥ 25 kg/m².

Statistical Analyses

The chi-square test was used to compare dichotomous variables to see whether there were significant differences among the groups stratified by work type, followed by a post-hoc application of Bonferroni's method comparing the data to those of the daytime work group. A one-way analysis of variance was used to compare the means among the groups, followed by a post-hoc application of Dunnett's test, which compared the data to those of the daytime work group when the F values showed a significant difference at $P < 0.05$.

Associations between the type of work, lifestyle and the number of MetS-DC (defining dyslipidemia as 2a or 2b as above) were analyzed by Poisson regression models, including the age, sex, type of work (nighttime, shift, day-to-night vs. daytime), alcohol consumption (ml/day), IPAQ classification (IPAQ2 to

IPAQ4 vs. IPAQ1), sleep hours, average overtime work hours per day (< 1 h, 1 to < 2 h, ≥ 2 h vs. seldom), smoking status (ex-smoker, current smoker (1–9, 10–19, ≥ 20 cigarettes per day vs never-smoker); data not shown), and work site (site 1 to 12, site 1 as a reference). To examine the contribution of being overweight to the associations of the type of work with the number of MetS-DC, the above analysis was performed after stratification by the presence of overweight (BMI ≥ 25 kg/m²), excluding the overweight component from MetS-DC. The relationships between lifestyle traits, including the type of work and MetS, were analyzed by logistic regression models. In the logistic regression, we included potential confounders in the model. First, we defined dyslipidemia as abnormal HDL and triglyceride levels, as stated above. In model 1, we included the sex, age, type of work (nighttime, shift, day-to-night vs. daytime), and site (site 1 to 12, site 1 as a reference).

In model 2, in addition to the model 1 covariates, we included the alcohol intake (ml/day), smoking status (ex-smoker, current smoker (1–9, 10–19, ≥ 20 cigarettes per day) vs. never-smoker), average overtime work hours per day (< 1 h, 1 to < 2 h, ≥ 2 h vs. seldom) and IPAQ classification (IPAQ2 to IPAQ4 vs. IPAQ1). In model 3, in addition to the model 2 covariates, we included the sleep hours. In model 4, the model 3 analysis was performed by defining dyslipidemia as a non-HDL level ≥ 160 mg/dl or on medication for dyslipidemia. A Poisson regression analysis and model 4 logistic regression analysis were also performed after stratifying by sex. All statistical tests were two-sided, and a value of $P < 0.05$ was considered to be statistically significant. All analyses were carried out using the SAS version 9.4 software program for Windows (SAS Institute, Cary, NC, USA).

Results

Among the 4,427 participants, 3,094 were in the daytime work group, 73 were in the fixed nighttime work group, 1,017 were in the shift work group and 243 were in the day-to-night work group. Among these participants, those who had 0 to 4 MetS-DC accounted for 2,184, 1,255, 674, 262 and 52 people, respectively, in the Poisson distribution. The characteristics of the participants by group according to the type of work are shown in **Table 1**. There were fewer females among the non-daytime work groups. The mean age, SBP, DBP, alcohol consumption per day and the percentages of subjects with a high BP, dyslipidemia, dysglycemia and IPAQ4 were higher in the fixed nighttime work group compared to the daytime

Table 1. The Characteristics of the Participants Divided into Groups According to the Type of Work

Type of Work	Daytime	Fixed nighttime	Shift	Day-to-night	<i>P</i>	Total	Range
Characteristics							
Number of people	3,094	73	1,017	243		4,427	
Age (years)	42.6 ± 8.9	50.8 ± 6.8*	37.9 ± 10.1**	40.1 ± 9.7**	<0.001	41.6 ± 9.58	19-69
Female (%)	23.0	1.4*	7.5**	13.1**	<0.001	18.6	
SBP (mmHg)	116.7 ± 16.6	128.2 ± 17.4*	120.0 ± 16.2**	120.2 ± 17.5**	<0.001	117.8 ± 16.8	74.5-19705
DBP (mmHg)	72.2 ± 11.9	78.5 ± 11.1*	72.6 ± 11.3	73.4 ± 12.6	<0.001	72.5 ± 11.8	43.0-118.5
High BP (%)	23.5	43.8*	26.9	29.2	<0.001	25.0	
Dyslipidemia (%)	24.9	56.2*	29.0*	30.5	<0.001	26.7	
High non-HDL (%)	27.4	42.5	26.8	30.0	0.742	27.7	
Dysglycemia (%)	8.0	16.4*	6.9	7.9	0.032	7.8	
Overweight (%)	20.1	20.6	26.2**	24.7	<0.001	21.8	
IPAQ1 (%)	35.1	46.6	45.7*	40.7	<0.001	38.1	
IPAQ4 (%)	1.1	4.2*	2.3*	2.5	<0.001	1.5	
Current smoking	39.6	50.7	60.3**	49.4*	<0.001	45.1	
MetS (%)	5.7	9.6	8.0*	6.2	0.049	6.3	
Sleep (h)	6.40 ± 0.85	6.47 ± 1.09	6.46 ± 1.07	6.15 ± 1.06**	<0.001	6.41 ± 0.95	3-15
Overwork ≥ 2 h/d (%)	34.0	9.6**	21.3**	47.7**	<0.001	31.5	
BMI (kg/m ²)	22.7 ± 3.06	22.8 ± 2.91	23.3 ± 3.37**	23.4 ± 3.30**	<0.001	22.9 ± 3.17	14.5-47.6
Alcohol (ml/d)	20.7 ± 29.9	29 ± 40.2	22.4 ± 35.2	17.1 ± 26	0.003	21.0 ± 31.3	0-250

The values are shown as the means ± SD, or %. The characteristics of participants divided by group according to the type of work in 4,427 Japanese males and females evaluated in 1999-2000 are shown. The chi-square test was used to compare dichotomous variables to see whether there were significant differences among the groups stratified by the type of work, followed by a post-hoc application of Bonferroni's method. A one-way analysis of variance was used to compare the means among the groups, followed by a post-hoc application of Dunnett's test when the *F* value showed a significant difference at *p* < 0.05. We defined four MetS-DC in this study as follows: 1) high blood pressure (BP): systolic BP (SBP) ≥ 130 mmHg, or DBP ≥ 85 mmHg, or the use of an antihypertensive drug; 2) dyslipidemia: HDL < 40 mg/dl for men, or HDL < 50 mg/dl for women, or TG ≥ 150 mg/dl for both genders, or on medication for dyslipidemia; 3) dysglycemia: fasting blood sugar concentration ≥ 110 mg/dl, or if less than eight hours after meals ≥ 140 mg/dl, or on medication for diabetes mellitus; 4) overweight: defined as a BMI ≥ 25 kg/m². We defined metabolic syndrome as being overweight plus two or more of high BP, dyslipidemia or dysglycemia. The non-HDL-cholesterol (non-HDL) level was calculated by subtracting the HDL from the total cholesterol concentration. A high non-HDL level was defined as non-HDL ≥ 160 mg/dl for both genders.

P* < 0.05, *P* < 0.01 compared to daytime work. SBP=systolic blood pressure, DBP=diastolic blood pressure, MetS=metabolic syndrome, BMI=body mass index, IPAQ=International Physical Activity Questionnaire classification.

work group. Compared to the daytime work group, the mean age in the shift work group was lower; the mean SBP, BMI and the percentages of dyslipidemia, being overweight, the IPAQ1, IPAQ4, current smoking and MetS were higher. Compared to the daytime work group, the mean age in the day-to-night work group was lower; the mean SBP, BMI and the percentages of subjects who were overweight and current smokers were higher. The mean sleep hours in the day-to-night work group was less than that in the daytime work group.

The results of the Poisson regression analysis are shown in **Table 2**. When we defined dyslipidemia as a lower HDL or a higher triglycerides, the independent factors that positively contributed to the number of MetS-DC were the age (regression coefficient [*b*₁] = 0.025, *P* < 0.001), being male (*b*₁ = 0.446, *P* < 0.001), shift work vs daytime work (*b*₁ = 0.098, *P* = 0.034) and alcohol consumption (ml/d)

(*b*₁ = 0.002, *P* = 0.003). Fixed nighttime vs. daytime work (*b*₁ = -0.233, *P* = 0.028), IPAQ4 vs IPAQ1 (*b*₁ = -0.366, *P* = 0.032) and sleep (h) (*b*₁ = -0.078, *P* < 0.001) significantly inversely contributed to the number of MetS-DC. When dyslipidemia was defined as a higher non-HDL, the positive association of shift work vs. daytime work, and the positive association with alcohol, and the inverse association of the IPAQ4 vs IPAQ1 with the number of MetS-DC (*b*₂ and *P*₂) lost their statistical significance. The analysis in just males yielded similar results, but not the analysis focused on women, probably due to the smaller number of female participants (data not shown).

The results of the analysis stratified by the presence of overweight (BMI ≥ 25 kg/m²) by Poisson regression models on the associations between the type of work, lifestyle traits and the number of MetS-DC (excluding overweight) are shown in **Table 3**. Significant positive associations were found for day-to-night

Table 2. The Independent Factors That Contributed to the Number of Metabolic Syndrome Diagnostic Components: Results of Poisson Regression Analysis

Variable	b1	P1	b2	P2
Age	0.025	<0.001	0.032	<0.001
Male	0.446	<0.001	0.469	<0.001
Fixed nighttime vs. Daytime	-0.233	0.028	-0.331	0.010
Shift vs. Daytime	0.098	0.034	0.072	0.010
Day-to-night vs. Daytime	0.131	0.070	0.071	0.121
Alcohol intake (ml/d)	0.002	0.003	0.001	0.272
IPAQ2 vs IPAQ1	0.017	0.706	0.032	0.482
IPAQ3 vs IPAQ1	-0.050	0.498	0.004	0.959
IPAQ4 vs IPAQ1	-0.366	0.032	-0.184	0.240
Sleep (h)	-0.078	<0.001	-0.075	<0.001

The results of analysis by Poisson regression models on associations between the type of work, lifestyle traits and the number of MetS-DC are shown. The covariates included were age, sex, work site (site 2 to 12, vs site 1), work type (nighttime, shift, day-to-night vs. daytime), alcohol consumption (ml/day), IPAQ classification (IPAQ2 to IPAQ4 vs. IPAQ1), sleep hours, average overtime work hours per day (<1 h, 1 to <2 h, ≥2 h vs. seldom) and smoking status (ex-smoker, current smoker (1-9, 10-19, ≥20 cigarettes per day) vs. never-smoker; data not shown). b1 and P1 are the regression coefficients and *P* values when dyslipidemia was defined as high-density lipoprotein cholesterol (HDL) <40 mg/dl for men, or HDL <50 mg/dl for women, or triglycerides (TG) ≥150 mg/dl for both genders, or on medication for dyslipidemia; b2 and P2 are the regression coefficients and *P* values when dyslipidemia was defined as non-HDL ≥160 mg/dl for both genders, or on medication for dyslipidemia. IPAQ=International Physical Activity, MetS-DC=metabolic syndrome diagnostic components.

Table 3. Independent Factors that Contributed to the Number of Metabolic Syndrome Diagnostic Components Stratified by Overweight: Results of the Poisson Regression Analysis

Variable	BMI < 25 kg/m ² (N=3,454)		BMI ≥ 25 kg/m ² (N=973)	
	b1	P1	b1	P1
Age	0.040	<0.001	0.011	0.005
Male	0.428	<0.001	0.245	0.042
Fixed nighttime vs. Daytime	-0.082	0.626	0.037	0.881
Shift vs. Daytime	0.062	0.382	0.097	0.256
Day-to-night vs. Daytime	0.242	0.025	0.021	0.880

The results of the analysis stratified by the presence of overweight (BMI ≥ 25 kg/m²) by Poisson the regression models on the associations between the type of work, lifestyle traits and the number of MetS-DC (excluding overweight) are shown. The covariates included were the same as in Table 2. Here, we defined dyslipidemia as high-density lipoprotein cholesterol (HDL) <40 mg/dl for men, or HDL <50 mg/dl for women, or triglycerides (TG) ≥150 mg/dl for genders, or on medication for dyslipidemia. BMI=body mass index, MetS-DC=metabolic syndrome diagnostic components.

vs. daytime work with the number of MetS-DC in participants who were not overweight (b1=0.242, *P*1=0.025). No associations were found between any type of work and the number of MetS-DC in participants who were overweight, probably due to the smaller number of participants who were overweight.

The results of a logistic regression analysis of the relationship between the type of work, lifestyle and MetS are shown in **Table 4**. In model 1, the independent factors that were significantly and positively related to MetS were age (odds ratio [OR]=1.02 [95% confidence intervals [1.01-1.04], *P*<0.01), being male (OR=2.35 [1.56-3.55], *P*<0.01) and shift vs. daytime work (OR=1.47 [1.05-2.05], *P*<0.01). In

model 2, the independent factors that were significantly positively related to MetS were age (OR=1.02 [1.01-1.04], *P*<0.01), being male (OR=2.45 [1.59-4.00], *P*<0.01) and shift vs. daytime work (OR=1.42 [1.01-1.99], *P*<0.05). The addition of the sleep duration to model 2 covariates resulted in a marginal disappearance of the statistical significance of shift vs. daytime work in model 3. When we defined dyslipidemia as non-HDL ≥160 mg/dl, or as subjects who were on medication for dyslipidemia in model 4, the independent factors that were significantly positively related to MetS were age (OR=1.04 [1.03-1.06], *P*<0.01), being male (OR=2.56 [1.66-3.95], *P*<0.01) and shift vs. daytime work (OR=1.47 [1.06-2.04], *P*

Table 4. Independent Factors Associated with Metabolic Syndrome: Results of the Logistic Regression Analysis

Variables	Model 1		Model 2		Model 3		Model 4	
	OR	95% CL	OR	95% CL	OR	95% CL	OR	95% CL
Age (years)	1.02**	1.01-1.04	1.02**	1.01-1.04	1.02**	1.01-1.04	1.04**	1.03-1.06
Male	2.35**	1.56-3.55	2.45**	1.55-3.88	2.52**	1.59-4.00	2.56**	1.66-3.95
Fixed nighttime vs. Daytime	0.46	0.18-1.14	0.44	0.18-1.11	0.42	0.17-1.07	0.63	0.27-1.47
Shift vs. Daytime	1.47**	1.05-2.05	1.42*	1.01-1.99	1.51	0.998-1.97	1.47*	1.06-2.04
Day-to-night vs. Daytime	1.06	0.62-1.85	1.07	0.62-1.86	1.04	0.60-1.80	1.20	0.71-2.02
Alcohol (ml/d)			1.00	0.99-1.01	1.00	0.997-1.01	1.00	0.996-1.04
Ex-smoker vs. Never smoker			0.93	0.64-1.37	0.94	0.64-1.38	1.17	0.81-1.70
Current smoker (1-9 cig/d) vs. Never			1.03	0.43-2.56	1.04	0.44-2.50	1.09	0.45-2.63
Current smoker (10-19 cig/d) vs. Never			0.80	0.51-1.25	0.81	0.51-1.27	1.02	0.66-1.58
Current smoker (≥ 20 cig/d) vs. Never			1.04	0.75-1.45	1.04	0.75-1.46	1.09	0.78-1.53
IPAQ2 vs IPAQ1			1.08	0.78-1.50	1.09	0.78-1.51	1.06	0.77-1.47
IPAQ3 vs IPAQ1			0.92	0.53-1.60	0.93	0.54-1.62	0.92	0.54-1.59
IPAQ4 vs IPAQ1			1.36	0.53-3.47	1.38	0.54-3.59	0.98	0.34-2.78
Sleep (h)					0.89	0.78-1.02	0.85**	0.74-0.97

The odds ratios (OR) and 95% confidence intervals (95% CI) of the analyses by logistic regression models on the relationships between the type of work, lifestyle traits and metabolic syndrome are shown. First, we defined dyslipidemia as high-density lipoprotein cholesterol (HDL) < 40 mg/dl for men, or HDL < 50 mg/dl for women, or triglycerides (TG) ≥ 150 mg/dl for both genders, or on medication for dyslipidemia. In model 1, we included sex, age, the type of work (nighttime, shift, day-to-night vs. daytime), and site (site 1 to 12, site 1 as a reference). In model 2, in addition to the model 1 covariates, we included the alcohol intake (ml/day), smoking status (ex-smoker, current smoker (1-9, 10-19, ≥ 20 cigarettes per day) vs. never-smoker), the average overtime work hours per day (< 1 h, 1 to < 2 h, ≥ 2 h vs. seldom) and the IPAQ classification (IPAQ2 to IPAQ4 vs IPAQ1). In model 3, in addition to the model 2 covariates, we included the sleep hours. In model 4, the model 3 analysis was performed by defining dyslipidemia as non-HDL ≥ 160 mg/dl, or on medication for dyslipidemia for both genders. * $P < 0.05$, ** $P < 0.01$. IPAQ=International Physical Activity Questionnaire classification.

< 0.01). The sleep duration was inversely associated with MetS (OR=0.85 [0.74-0.97], $P < 0.01$). The model 4 analysis of only male subjects yielded similar results, but not in only women (data not shown).

Discussion

In the present study, when we defined dyslipidemia as having a lower HDL and a higher triglyceride level, we found that shift work was significantly and positively associated with, and fixed nighttime work was significantly and inversely associated with, the number of MetS-DC compared to daytime work, independent of confounding factors, using a Poisson regression analysis. When we defined dyslipidemia as having a higher non-HDL level, the inverse association of fixed nighttime vs. daytime work with the number of MetS-DC remained significant, but the positive association of shift vs. daytime work lost its statistical significance. By a logistic regression analysis, we found that shift work was significantly and positively related to the risk of MetS compared to daytime work when we defined dyslipidemia as having a higher non-HDL level.

Our findings regarding shift work are consistent with those of previous studies³⁰⁻³⁴. A higher risk of having more MetS-DC was observed through a range of different occupations, such as police officers, road builders, factory workers and nurses in different countries and areas in cross-sectional studies³⁰⁻³², as well as in cohort studies^{33, 34}. However, there have been conflicting reports on the association of shift work with cardiovascular disease morbidity and mortality in cohort studies^{5, 35-38}. A recent meta-analysis by Vyas *et al.* including 34 studies and more than 2 million people confirmed that shift work was associated with an increased risk of myocardial infarction and stroke³⁹.

A higher prevalence of MetS-DC, such as hypertension, dyslipidemia, dysglycemia, or MetS would account for the association of shift work with increased risk cardiovascular morbidity and mortality. Gaining weight, disruption of the circadian rhythm and impairment of sleep associated with shift work have been shown to generate more MetS-DC^{5-8, 40-42}. Scheer *et al.* showed adverse cardiometabolic effects of the circadian misalignment produced by shifting the eating and sleeping time 12 hours out of phase from habitual times, which resulted in systematically

decreased leptin, increased glucose despite increased insulin, a completely reversed daily cortisol rhythm, an increased mean arterial pressure and reduced sleep efficiency⁴³). The fact that the addition of sleep hours to model covariates in the logistic analysis resulted in the disappearance of the statistical significance of shift vs. daytime work in the present study confirms the importance of sleep impairment as a mediator of the relationship. However, the statistical significance of shift work on the risk of MetS remained even after the inclusion of the sleep hours in the logistic analysis when we defined dyslipidemia as having a higher non-HDL level in the present study. This may imply that other factors besides the sleep hours affected the relationship. The significant positive association of day-to-night vs. daytime work with the number of MetS-DC in participants who were not overweight may also imply that factors other than being overweight affect this relationship.

We found that fixed nighttime work was significantly and inversely associated with the number of MetS-DC compared to daytime work using a multivariate Poisson regression analysis. There have been few studies that have examined the effects of fixed nighttime work on health. In their prospective cohort study, Fujino et al. found that fixed nighttime work was not associated with ischemic heart disease compared to daytime work⁵). Some studies have indicated that adaptation of the circadian rhythm by fixed night workers can be achieved, while this is not possible for rotating-shift workers^{44, 45}). However, there have been no studies that have shown any favorable effect of fixed night work on the cardiometabolic risk factors, and an inverse relationship was not noted between fixed night work and MetS by the logistic analysis in the present study. Further studies are needed to re-evaluate the relationship.

We found that day-to-night work was significantly associated with the number of MetS-DC using a multivariate Poisson regression analysis in participants who were not overweight. Kobayashi et al. found that longer working hours were significantly associated with the risk of MetS⁴⁶). We partially confirmed their results.

Our findings of a significant direct association of alcohol consumption, and the inverse associations of physical activity and sleep duration with MetS-DC, are consistent with previous studies by others and our group^{2, 8, 46-48}).

This is the first study to examine the effect of incorporating a higher non-HDL level as a dyslipidemia component of MetS-DC. When we set the cut-off value of the non-HDL so that the prevalence of

dyslipidemia became similar to that derived from the usual criteria, we found that the results of the Poisson and logistic regression analyses using the two different definitions of dyslipidemia were comparable.

In conclusion, shift work was significantly and positively associated with the number of MetS-DC compared to daytime work, independent of confounding factors. Shift work, compared to daytime work, was also significantly related to the risk of MetS.

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The investigators and members of the research group are listed in the appendix of Reference 19.

Conflicts of Interest

None.

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