particles may lead to the development of microalbuminuria. Inflammation has also been implicated in the evolution of albuminuria. Festa et al. [6] recently demonstrated that diabetic patients with microalbuminuria had significantly higher levels of C-reactive protein (CRP) and fibrinogen compared to those with normoalbuminuria. Both CRP and fibrinogen are considered to be inflammatory markers. Stehouwer et al. [7] also documented that increased urinary albumin excretion, endothelial dysfunction, and chronic inflammation are interrelated processes that develop in parallel, progress with time, and are strongly and independently associated with risk of death in type 2 diabetic patients.

Tumor necrosis factor (TNF) is a potent proinflammatory cytokine involved in the pathogenesis of atherosclerosis. TNF is known to induce a cascade of inflammatory reactions involving production of other cytokines, thus participating in the development of atherosclerosis. TNF binds two receptors so far identified referred to as TNF-R1 and TNF-R2. Both of these receptors exist in soluble forms. The two receptors share almost no homology outside the ligand binding domain, suggesting that they signal for different biological functions [8–10]. Elevated soluble TNF-R1 levels have recently been shown to be predictive of cardiovascular mortality in patients with chronic heart failure [11]. However, the studies investigating the relationship between soluble TNF receptors and vascular complications in diabetic patients are limited. Zoppini et al. [12] very recently demonstrated that soluble TNF-R1 level is higher in type 1 diabetic patients with microalbuminuria than those with normoalbuminuria. To the best of our knowledge, however, the relationships between urinary albumin excretion rate and the levels of the two soluble TNF receptors have not yet been examined in type 2 diabetic patients.

In this context, a major problem is that albuminuria itself has been associated with atherosclerotic vascular diseases such as renal failure, cerebral infarction and CHD. Moreover, overweight condition or hyperglycemia *per se* may affect albuminuria, TNF-α, and soluble TNF receptors concentrations in humans [13,14]. We therefore recruited non-obese, well-controlled unique Japanese type 2 diabetic patients without evidence of vascular complications including CHD, cerebral infarction, or renal failure, taking into account of body mass index and fasting glucose level. This is the first finding that albuminuria is independently associated with serum level of soluble TNF receptor in non-obese well-controlled unique Japanese type 2 diabetic patients.

Subjects and Methods

After informed consent was obtained, forty-five diabetic patients with microalbuminuria (twenty-nine men and sixteen women) and forty-three patients with normoalbuminuria (thirty-four men and nine women) were enrolled in the present study. They all were non-obese (BMI < 27 kg/m^2) Japanese type 2 diabetic patients [15]. Type 2 diabetes mellitus was diagnosed based on the WHO criteria [16]. All subjects had ingested at least 150 g of carbohydrate in the three days before the study. Forty-one patients (91%) with microalbuminuria and 37 patients (86%) with normoalbuminuria were taking sulfonylureas, respectively. The rests were treated by diet alone. They all have not received insulin therapy. Blood pressure was measured according to a standard procedure and hypertension was defined as systolic blood pressure ≥ 140 mm Hg and/or diastolic blood pressure ≥ 90 mm Hg or current use of antihypertensive medication. Twenty-two patients (49%) (Ca antagonist 11, ACE-I 8, ARB 3) with microalbuminuria and fifteen patients (35%) (Ca antagonist 5, ACE-I 6, both 2, ARB 2) with normoalbuminuria were treated with antihypertensive drugs, respectively. Fourteen patients (31%) with microalbuminuria and seventeen patients (40%) with normoalbuminuria were treated with lipid lowering agents, respectively. Cigarette smoking was dichotomized into "never" and "ever" (including past and current) using a questionnaire. There was no significant difference in gender, smoking, or medication status between the patients with microalbuminuria and those with normoalbuminuria (Table **1**). They did not consume alcohol or perform heavy exercise for at least one week before the study.

Blood was drawn in the morning after a 12 h fast. Plasma glucose was measured using the glucose oxidase method. Triglycerides, total cholesterol, and HDL cholesterol were also measured. The LDL cholesterol level was calculated using the Friedewald formula [17]. Serum insulin was measured using a two-site immunoradiometric assay (Insulin Riabead II, Dainabot, Japan). Coefficients of variation were 4% for insulin > 25 μU/ml and 7% for insulin < 25 μU/ml, respectively. Serum TNF-α concentrations were measured by enzyme immunoassay kit (Quantikine HS Human TNF-α immunoassay kit, R&D systems. Inc, Minneapolis, MN, USA) and serum concentrations of sTNF-R1 and sTNF-R2 were measured by enzyme-linked immunosorbent assay (ELISA; BIOTRAK, Amersham Life Sciences, Uppsala, Sweden) as described previously [18]. The limits of sensitivity for TNF-α, sTNF-R1 and sTNF-R2 were 0.5 pg/ml, 25 pg/ml and 50 pg/ml, respectively.

Urinary albumin concentration was assessed in a morning spot urine sample using a commercial enzymatic immunoassay. Urinary albumin concentration was measured in duplicate and the mean of the two values was used for the study. Intraassay and interassay coefficients of variation were less than 7% (Orion, Espoo, Finland). Several reports have indicated that early morning spot urine is usually sufficient for detecting the presence of microalbuminuria [19,20]. In the present study, we calculated urinary albumin excretion rate as a ratio of urinary albumin and urinary creatinine that markedly enhances the accuracy of the single spot urine sample in the assessment of microalbuminuria [21]. Microalbumiuria was defined as a urinary albumin concentration greater than 30 mg/g creatinine but less than 300 mg/g creatinine. Normoalbuminuria was defined as urinary albumin concentration less than 30 mg/g creatinine [22].

Statistical analysis

The statistical analysis was performed using the StatView 5 system (Statview, Berkeley, CA). The differences of mean were determined by the Mann-Whitney U-test. Data were expressed as the mean ± SEM. Simple (Spearman's rank) correlation coefficients between urinary albumin concentration and measures of variables were calculated, and a stepwise multiple regression analysis was then used to evaluate the independent association of these variables with urinary albumin concentration. Values of $p < 0.05$ were considered significant. In multivariate analysis, $F \geq 4$ was considered significant.

Table 1 Characteristics of patients with type 2 diabetes stratified by albuminuria status

	Microalbuminuria	*Normoalbuminuria*	*p*
Urinary albumin (mg/gCr)	90 ± 8	10 ± 1	0.001
Number of subjects	45	43	
M/F	29/16	34/9	0.159
Age (yrs)	65.6 ± 1.2	59.8 ± 1.3	0.001
Systolic blood pressure (mm Hg)	140 ± 3	133 ± 3	0.940
Diastolic blood pressure (mm Hg)	81 ± 2	83 ± 2	0.570
Smoking (yes/no)	9/36	13/30	0.328
Duration of diabetes (yrs)	11.7 ± 1.1	10.2 ± 1.1	0.314
BMI (kg/m^2)	22.6 ± 0.3	23.1 ± 0.3	0.301
Fasting glucose (mg/dl)	144 ± 3	138 ± 4	0.256
HbA_{1c} (%)	7.1 ± 0.1	7.0 ± 0.2	0.654
Fasting insulin (μU/ml)	6.6 ± 0.6	6.5 ± 0.4	0.540
Triglycerides (mg/dl)	119 ± 8	124 ± 9	0.705
Total cholesterol (mg/dl)	204 ± 6	204 ± 5	0.929
HDL cholesterol (mg/dl)	58 ± 2	59 ± 2	0.715
LDL cholesterol (mg/dl)	126 ± 5	126 ± 5	0.984
Serum creatinine (mg/dl)	0.77 ± 0.03	0.75 ± 0.02	0.537
TNF-α (ng/l)	3.5 ± 0.4	3.2 ± 0.2	0.479
sTNF-R1 (ng/l)	1272 ± 71	1084 ± 33	0.018
sTNF-R2 (ng/ml)	2172 ± 91	1933 ± 49	0.022
SU/diet	40/5	35/8	0.094
HMG-CoA reductase inhibitor	7/38	5/38	0.284
Bezafibrate	7/38	12/31	0.090
Ca antagonist	11/34	7/36	0.147
ACE inhibitor or ARB	8/37	8/35	0.500

Results

The clinical characteristics and clinical profile between the patients with microalbuminuria (n = 45) and normoalbuminuria (n = 43) were compared (Table 1). Urinary albumin concentrations in patients with microalbuminuria and normoalbuminuria were 90 ± 8 (range, 35 – 282) and 10 ± 1 (range, 0.6 – 24.9) mg/g creatinine, respectively. There was no overlap in the urinary concentration of albumin between the two groups. While age was significantly greater in the patients with microalbuminuria than those with normoalbuminuria, no significant difference was observed in systolic and diastolic blood pressure, smoking, diabetes duration, BMI, fasting glucose, hemoglobin A_{1c}, or fasting insulin levels between the two groups. The two groups did not differ with respect to concentrations of serum triglycerides, total, HDL, or LDL cholesterol. Although there was no significant difference in the levels of serum creatinine and TNF-α, soluble TNF-R1 (1,272 ± 71 *vs.* 1,084 ± 33 pg/ml, p = 0.018), and soluble TNF-R2 (2172 ± 91 *vs.* 1933 ± 49 pg/ml, p = 0.022) were significantly higher in patients with microalbuminuria compared to those with normoalbuminuria.

Spearman's rank correlations of urinary albumin concentration with measures of variables were calculated for all our diabetic patients (Table 2). Urinary albumin concentration was positively correlated with soluble TNF-R1 (r = 0.364, p < 0.001), soluble TNF-R2 (r = 0.342, p < 0.005), age (r = 0.380, p < 0.001), and serum creatinine (r = 0.214, p < 0.05). Other variables including systolic and diastolic blood pressure, TNF-α, and serum lipid profile including triglycerides were not associated with urinary albumin level. Multiple regression analyses were carried out using the stepwise procedure.

The analysis included urinary albumin level as a dependent variable and candidate risk factors (soluble TNF-R1, soluble TNF-R2, age, serum creatinine) as independent variables (Table 2). The concentration of urinary albumin was independently predicted by serum concentration of soluble TNF-R1, which explained 26.3 % of the variability of urinary albumin concentration in our patients. Other variables including age, serum creatinine, and soluble TNF-R2 were not independently associated with urinary albumin concentration in our non-obese Japanese type 2 diabetic patients. On the other hand, in a model incorporating BMI and systolic blood pressure, soluble TNF-R1 was also independently associated with urinary albumin concentration in our patients (Table 3).

Discussion and Conclusions

This is the first published observation that soluble TNF-R1 is independently associated with urinary albumin concentration in non-obese Japanese type 2 diabetic patients.

Diabetic nephropathy has rapidly become an important public health problem since it is the leading cause of dialysis in Japan. Early detection of risk factors causing diabetic nephropathy before advanced renal damage occurs is therefore an urgent prior-

Table 2 Correlation of urinary albumin concentration to measures for variables in diabetic patients

	Univariate		*Multivariate*
	r	*p*	*F*
TNF-α	0.127	0.236	–
sTNF-R1	0.364	< 0.001	32.1
sTNF-R2	0.342	< 0.005	0.2
Age	0.380	< 0.001	1.9
Serum creatinine	0.214	0.046	0.1
Gender	– 0.083	0.440	–
Diabetes duration	0.202	0.060	–
BMI	– 0.191	0.076	–
Systolic blood pressure	0.189	0.097	–
Diastolic blood pressure	– 0.079	0.488	–
Fasting glucose	0.104	0.334	–
$HbA1_c$	0.136	0.203	–
Triglycerides	– 0.081	0.452	–
Total cholesterol	– 0.077	0.471	–
HDL cholesterol	– 0.109	0.310	–
LDL cholesterol	– 0.094	0.383	–

Table 3 Determinants of urinary albumin concentration by multivariate analysis

	Model 1 (F)	*Model 2 (F)*
sTNF-R1	32.1	31.0
sTNF-R2	0.2	0.2
Age	1.9	0.7
Serum creatinine	0.1	0.2
BMI	–	0.1
Systolic blood pressure	–	1.8
R2	0.263	0.280

ity. Microalbuminuria has been shown to be not only an indicator of incipient nephropathy but also an independent risk factor for cardiovascular disease [5]. The mechanisms underlying the evolution of microalbuminuria in diabetic patients are not fully clarified. Genetic factors, insulin resistance, glycemic control, blood pressure, smoking, and lipid abnormalities have been implicated in albuminuria development in diabetic patients [23].

Inflammation seems to be associated with urinary albumin excretion in diabetic patients. Gabazza et al. [24] showed high concentrations of serum fibrinogen in type 2 diabetic patients with albuminuria compared to those without albuminuria. Microalbuminuria has been shown to be associated with fibronectin and sialic acid in type 2 diabetic patients [25,26]. Furthermore, Festa et al. [6] have reported an association of CRP and fibrinogens with urinary albumin excretion in the microalbuminuric range of type 2 diabetic individuals. Stehouwer et al. [7] confirmed that increased urinary albumin excretion, endothelial dysfunction, and chronic inflammation are interrelated processes associated with risk of death in type 2 diabetic patients.

In the present study, we investigated the relationship between albuminuria and TNF-α system after carefully matching the participants for smoking, BMI, blood pressure, glycemic control, and lipid profile. We used serum TNF-α, soluble TNF-R1, and soluble TNF-R2 as the index of TNF-α system activity and found, for the first time, that soluble TNF-R1 was independently associated with albuminuria in type 2 diabetic patients. However, we could not find the relationship between albuminuria and TNF-α. The reason is not known, but may be due to circulating TNF receptor levels remaining elevated for a longer time than TNF-α itself and reflecting the degree of TNF-α activation more accurately than the measurement of TNF-α itself. TNF receptor levels might be considered to be a more valuable factor for monitoring the degree of TNF-α system activity. Thus, the TNF-α system could predispose to the development of microalbuminuria in type 2 diabetic patients. Baud and Ardaillou [27] have shown that TNF-α induces glomerular infiltration by leukocytes. Klein et al. [28] have demonstrated that TNF-α influences the metabolism of glycosaminoglycans, which are components of the vascular endothelium and the glomerular basement membrane and are involved in the etiology of microalbuminuria.

The mechanisms for the increased activity of TNF-α system in type 2 diabetic patients with microalbuminuria are unknown; however, elevated synthesis, reduced catabolism, or both must be present. *In vitro* investigations have shown increased TNF-α messenger RNA expression in glomeruli from diabetic rats [29]. Recent studies have demonstrated that advanced glycation end products binding to specific cell-surface receptor molecules expressed on kidney cells may induce local cytokine and initiate local inflammatory reaction [30]. Angiotensin II, a substance associated with development of renal injury in diabetic patients, has been shown to upregulate TNF-α expression [31].

Interestingly, soluble TNF-R1, but not soluble TNF-R2, was associated with albuminuria in our diabetic patients. The reasons for the discrepancy between the TNF-R1 or TNF-R2 relationship to albuminuria in our diabetic patients are not clear. These two receptors seem to differ in terms of signaling and functional properties [8–10]. Several studies have demonstrated that obese subjects overexpress TNF-alpha and TNF-R2 in adipose tissue and have higher concentrations of serum TNF-R2 levels in relation to lean controls [32,33]. TNF-α can upregulate TNF-R2 expression in humans [34]. In contrast, the majority of biological responses classically attributed to TNF-α such as cytotoxicity and nuclear kappa B activation are mediated by TNF-R1 [35]. Pichler et al. [36] have shown that sTNF-R1 may play an important role in the onset of the acute stage of Graves' disease.

Nevertheless, the present study that TNF-R1, but not TNF-R2, is associated with albuminuria in diabetic patients suggests that TNF-R1 may play a role in the evolution of vascular complications in our non-obese type 2 diabetic patients. This idea is supported by the recent study by Rauchhaus et al. [11] demonstrating that elevated soluble TNF-R1 levels are predictive of cardiovascular mortality in patients with chronic heart failure. Furthermore, Zoppini et al. [12] have reported that TNF-R1 is associated with the progression of microalbuminuria and retinopathy in type 1 diabetic patients.

In summary, although our present study was performed among the limited patients that were well-controlled in terms of BMI, HbA_{1c}, blood pressure, LDL cholesterol, triglycerides, total and HDL cholesterol, serum soluble TNF-R1 seems to be associated with albuminuria in non-obese Japanese type 2 diabetic patients. Further study should be undertaken to clarify whether or not serum soluble TNF-R1 is reflective of early stage of atherosclerosis in non-obese Japanese type 2 diabetic patients.

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New "Pre-diabetes" Category and the Metabolic Syndrome in Japanese

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Abstract

Background: Recently, impaired fasting glucose (IFG) was redefined as fasting plasma glucose of 100–125 mg/dl, and individuals with IFG and/or impaired glucose tolerance (IGT) were referred to as having "pre-diabetes". However, there is a lack of data using the new definition of IFG and "pre-diabetes". **Objective:** The aim of this study was to examine associations of the metabolic syndrome components with the new "pre-diabetes" category in relatively lean Japanese. **Methods:** Six hundred and sixty-one Japanese study participants underwent a 75 g oral glucose tolerance test. They were classified into three groups-normal (n = 225), pre-diabetes (n = 308), and diabetes (n = 128). The metabolic syndrome was defined according to the National Cholesterol Education Program Adult Treatment Panel III, as modified for waist circumference criteria by the Regional Office for the Western Pacific Region of WHO. **Results:** Prevalence of the metabolic syndrome in each group was 10.7%, 27.9%, and 53.9%, respectively. Of the metabolic syndrome components, the OR for prevalent pre-diabetes was 2.00 (95% CI, 1.73–2.31, $p < 0.001$) for fasting glucose, 1.93 (95% CI, 1.54–2.42, $p < 0.001$) for waist circumference, and 1.36 (95% CI, 1.10–1.68, $p = 0.005$) for triglycerides. Similar associations were found in prevalent diabetes. Insulin resistance assessed using Stumvoll's index was significantly associated with both pre-diabetes and diabetes. **Conclusion:** Pre-diabetes and the metabolic syndrome frequently coexist in relatively lean Japanese. This association seems to link with abdominal adiposity and insulin resistance.

Key words
Impaired fasting glucose · Insulin resistance · Metabolic syndrome · Prediabetes

Introduction

Recently, a modification was made regarding the criteria of impaired fasting glucose (IFG) by the 2003 Expert Committee's report [1]. In the recommendation, individuals with a fasting plasma glucose (FPG) ≥ 100 mg/dl but < 126 mg/dl are considered to have "newly defined IFG" [1]. Furthermore, individuals with IFG and/or impaired glucose tolerance (IGT) are referred to as belonging to the new "pre-diabetes" category [2]. "Pre-diabetes" indicates the relatively high risk for development of type 2 diabetes and cardiovascular disease. To our knowledge, there is a lack of data using this definition of IFG. The aim of this study was to examine associations between the metabolic syndrome components and the new "pre-diabetes" category in relatively lean Japanese.

Subjects and Methods

Subjects

This report covers a total of 661 study participants aged 20 to 79 years selected from 924 patients that had undergone a 75 g oral

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Original Article

Five-year Stability of Job Characteristics Scale Scores among a Japanese Working Population

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BACKGROUND: The job characteristics scale of job strain, which combines high job demands and low decision latitude based on Karasek's model, has been applied to studies on health care and cardiovascular disease. However, little is known about the long-term stability of this scale with exposure of workers to job. We investigated the 5-year intraindividual variation in job characteristics scores among healthy community workers.
METHODS: Subjects of the study were 458 community dwelling persons forming part of the Jichi Medical School Cohort Study at Yamato (currently, Minami-Uonuma city), Niigata prefecture. The Japanese version of the World Health Organization Multinational Monitoring of Trends and Determinants in Cardiovascular Disease (WHO-MONICA) Psychosocial Study Questionnaire was implemented twice (from 1992 through 1995, and in 1999) to measure job demands and decision latitude levels. Intraclass correlation coefficients were computed to evaluate stability of scores of the questionnaire.
RESULTS: Intraclass correlation coefficient of the decision latitude scores was 0.629 (95% confidence interval: 0.564 - 0.686) and that of the job demands scores was 0.551 (0.476 - 0.617). Subgroup analyses by age, sex, education level, years since first employment, number of co-workers, and job category and status at baseline revealed similar results. In contrast, subjects who experienced position changes within the same enterprise or changed jobs showed lower correlation coefficients of both decision latitude and job demands scores compared to those who experienced no change in job contents.
CONCLUSION: The Japanese version of the WHO-MONICA Psychosocial Study Questionnaire showed statistically significant long-term stability and could be to some extent responsive to change in job strain levels.
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Key words: job strain, Karasek's model, WHO-MONICA Psychosocial Study Questionnaire, long-term stability, population study.

The job characteristics scale of job strain, which combines high job demands and low decision latitude based on Karasek's model,[1] has been applied to studies on health care and cardiovascular disease in North America, Europe and East Asian countries.[2,3,4] Moreover, a number of studies[5,6,7,8,9] have reported acceptable levels of reliability based on internal consistency using data at only one time point. The Japanese version[10] of the World Health Organization Multinational Monitoring of Trends and Determinants in Cardiovascular Disease (WHO-MONICA) Psychosocial Study Questionnaire[11] is one of the representative scales used for the Karasek's model in Japan. An acceptable level of internal consistency has also been reported for this.[12]

In prospective studies, job strain levels at baseline have been regarded as representative of chronic levels and consequently used as long-term risk indicators. Although it is plausible that job characteristics change even within a job title and that employees develop coping skills against stressful situations deriving from such changes, few studies have reported the long-term stability of

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the job characteristics scale with exposure to job strain. We therefore investigated the 5-year intraindividual variation in job characteristics scores among healthy community workers in Japan.

METHODS

This study formed part of the Jichi Medical School Cohort Study, a large-scale population-based prospective study designed to explore the risk factors for cerebro-cardiovascular disease in 12 Japanese communities. Local governments in all areas approved the study and informed consent was obtained from all participants. Details of the study design were published previously.[13]

The cohort study population in the present analyses comprised residents from a community in Yamato (currently, part of Minami-Uonuma city), Niigata prefecture. Baseline data were collected from 1993 through 1995 with mass screening for cerebro-cardiovascular diseases conducted in accordance with the health and medical service law for the aged. Invitations to participate were sent to eligible individuals by the local government office of Yamato in accordance with the law; all residents aged 19 to 69 years were included. Those undergoing treatment or care for cardiovascular diseases was excluded from the cohort. A total of 2404 participants agreed to participate in the cohort study. For the present analyses, retired persons (154), full-time housewives (846), and subjects without job category data (27) were excluded from the participants. Full-time farmers (372) were also excluded from the analyses because little is known about validity and reliability of the job characteristics scale for Japanese farmers. Thus, 987 full- and part-time workers were eligible for potential subjects for the analyses; 95% worked for small-size enterprises employing ≤50 members of staff. All were followed-up annually, after collection of baseline data, by home visits, phone calls, mail, and interviews during annual health examinations. Of the 987 participants at baseline examination, 17 died and 47 dropped out because of moving. Four hundred and fifty eight (46.4 percent), 199 men and 259 women, attended the follow-up examination in 1999. The mean follow-up period was 5 years. The subject selection process for the present analyses is shown in Figure 1.

Sociodemographic and behavioral variables were investigated with a standardized questionnaire that was completed independently; answers were checked by a trained interviewer. The questionnaire consisted of the following items: occupation, status in the work place, years since first employment, number of co-workers, and changes in job content during the follow-up period. The following categories were included under the occupation item: security guard (n=3), service (104), transport (5), construction (77), production (132), merchant (60), clerk (28), and professional (49). The first five and last three categories were designated blue- and white-collar occupations, respectively.

The Japanese version of the WHO-MONICA Psychosocial

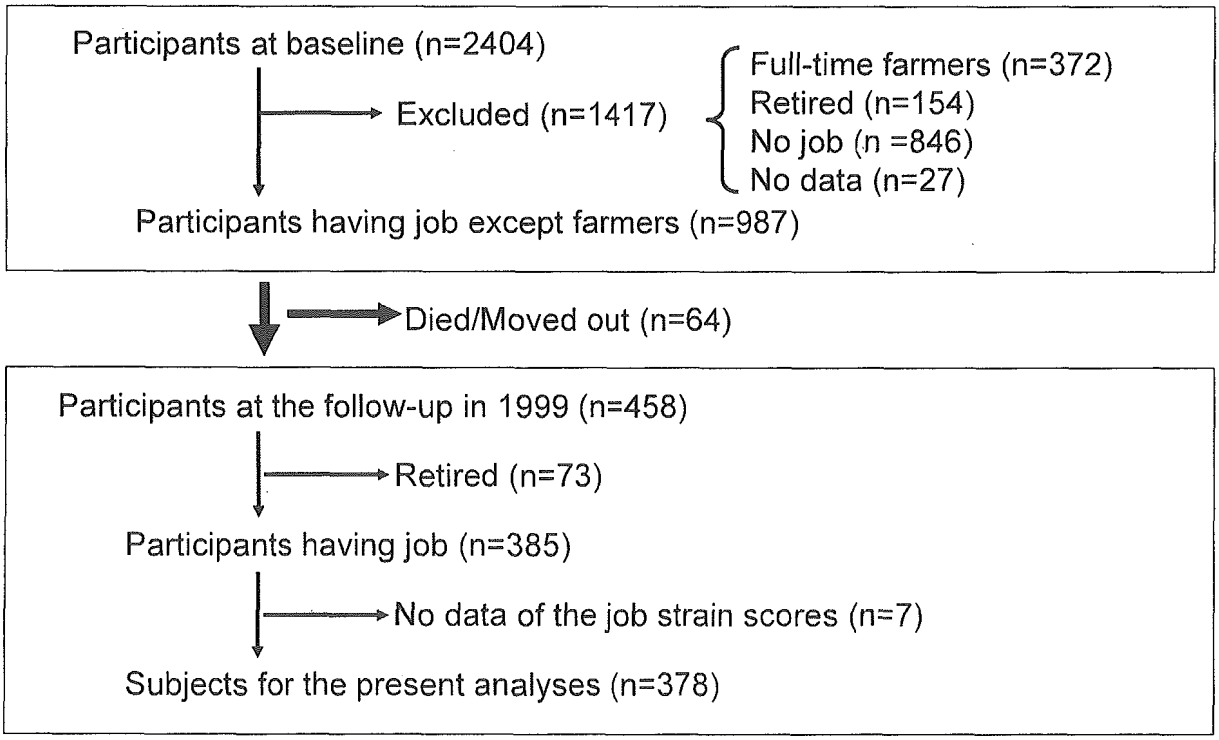

Figure 1. Outline of the subjects selection in the present analyses.

Study Questionnaire[10] was used to evaluate job strain levels at baseline examination (from 1992 through 1995) and follow-up in 1999. The questionnaire consists of two scales, decision latitude and psychological job demands. Decision latitude is defined as the sum of two subscales given equal weight: (a) skill discretion, measured by four elements (the continuous need to acquire new knowledge, skill requirements, creativity requirements, and repetitiveness [reversed score]), and (b) decision authority, measured by two elements (freedom to make decisions and choice in the approach to work). Higher scores indicate a higher level of decision latitude. Psychological job demands are defined by five elements (the need to work fast, the need to work hard, demands for extra work, insufficient time to do work, and conflicting demands). Higher scores indicate higher demand status. All questions were scored on a Likert scale of 1 to 4. The psychometric properties of the Japanese version of the demand-control questionnaire were reported previously.[14,15] Cronbach's coefficient alpha for the decision latitude and psychological demands scores were 0.80 and 0.79, respectively, with the baseline data obtained from the present subjects.

Descriptive parameters are shown as arithmetic means with standard deviations and percentage. The unpaired student's t-test and chi-square test were used to compare the baseline characteristics of participants and those of non-participants at the follow-up examination. The stability of the job characteristics scale measurements at baseline and follow-up was evaluated by calculating intraclass correlation coefficients and their 95% confidence intervals (CIs) using the two-way mixed effects model with absolute agreement. Differences in scores between baseline and follow-up were tested using a paired t-test. A general linear model was used for comparisons between the no job change group and other groups. Significance was defined as $p<0.05$. All statistical analyses were performed using the SPSS® statistical package 11.5j for Windows (SPSS, Chicago, Illinois, USA) with default settings.

RESULTS

The baseline characteristics of individuals who participated in the 1999 follow-up and those who did not are shown in Table 1. Compared to the non-participants, participants were more likely

Table 1. Baseline characteristics of the study population according to those who participated in the follow-up examination and those who did not.

	Follow-up examination:				
	Participants		Non-participants		p-value
No.	458*		529		
Sex, females (%)	259	(56.6)	261	(49.3)	<0.05
Age (years)**	46.7	11.4	45.2	12.9	n.s.
Education status (%)					n.s.
Elementary and junior high school	248	(54.4)	288	(55.2)	
High school	154	(33.8)	167	(32.0)	
University or other	54	(11.8)	67	(12.8)	
Years since first employment (%)					n.s.
Quartile 1 (12-15 years)	95	(20.9)	103	(19.6)	
Quartile 2 (16-17 years)	117	(25.7)	121	(23.0)	
Quartile 3 (18-19 years)	141	(31.0)	168	(31.9)	
Quartile 4 (≥20 years)	102	(22.4)	134	(25.5)	
No. of co-workers (%)					
Quartile1(1-2)	136	(30.6)	123	(24.8)	n.s.
Quartile2(3-5)	122	(27.4)	141	(28.4)	
Quartile3(6-10)	103	(23.1)	120	(24.2)	
Quartile4(≥11)	84	(18.9)	112	(22.6)	
Job category (%)					n.s.
White-collar occupations	137	(29.9)	176	(33.3)	
Blue-collar occupations	321	(70.1)	353	(66.7)	
Status at work (%)					n.s.
Administrative	70	(15.5)	91	(17.5)	
Non-administrative	383	(84.5)	430	(82.5)	
Job strain scores**					
Decision latitude†	15.6	±3.2	15.7	±3.4	n.s.
Psychological job demands‡	11.8	±2.7	11.4	±2.8	<0.05

* : This includes a number of subjects retired.

**: Values represent the mean ± standard deviation.

† : Higher scores indicate higher levels of decision latitude.

‡ : Higher scores indicate higher levels of demand.

n.s. not significant

to be women (56.6 vs. 49.3%, $p<0.05$) and to have a slightly higher job demands score (11.8±2.7 vs. 11.4±2.8, $p<0.05$). No statistically significant differences were observed with regard to age, education level, job-related variables, and decision latitude score.

Of the 458 participants of the follow-up in 1999, 73 retired during the follow-up period. A further 7 were excluded because of missing job strain score values at follow-up examination. Data of a total of 378 workers were therefore analyzed.

Intraclass correlation coefficient of the decision latitude scores was 0.629 (95% CI: 0.564 to 0.686) and that of the job demands scores was 0.551 (95% CI: 0.476 to 0.617) (Table 2 and Figure 2). Subgroup analyses according to age, sex, education level, years since first employment, number of co-workers, and job category and status at baseline revealed similar results (Table 2). A high correlation coefficient for decision latitude score was observed for workers with a higher education level (0.894, 95% CI: 0.818 to 0.939). Correlation coefficients for scores at baseline and follow-up examinations of decision latitude scale and of job demands scale among the 63 subjects who experienced position changes within the same enterprise or changed jobs were lower than those for subjects who experienced no changes (Table 2).

Decision latitude scores tended to increase after position (mean difference: 1.6, 95% CI: -0.1 to 3.3) and job changes (0.9, 95%CI: -0.1 to 1.9), although these results were not statistically significant. No meaningful interpretations were found with regard to changes in job demands scores.

Table 2. Intraclass correlation coefficients (ICC) of decision latitude and job demands scores between baseline and 5-year follow-up.

	Decision latitude			Job demands		
	N*	ICC	95% confidence interval	N	ICC	95% confidence interval
Whole subjects	377	0.629	0.564 - 0.686	378	0.551	0.476 - 0.617
Age(year)						
19-29	32	0.503	0.186 - 0.723	32	0.415	0.076 - 0.666
30-39	92	0.678	0.546 - 0.777	92	0.608	0.461 - 0.722
40-49	130	0.674	0.568 - 0.758	129	0.531	0.394 - 0.644
50-59	76	0.556	0.378 - 0.694	76	0.595	0.429 - 0.722
60-69	47	0.567	0.335 - 0.734	49	0.532	0.298 - 0.706
Sex						
Men	181	0.582	0.476 - 0.670	182	0.612	0.513 - 0.696
Women	196	0.587	0.487 - 0.671	196	0.410	0.286 - 0.520
Education status						
Elementary or Junior High school	191	0.593	0.492 - 0.677	192	0.572	0.469 - 0.660
High school	137	0.561	0.434 - 0.665	137	0.457	0.314 - 0.579
University or other school	48	0.894	0.818 - 0.939	48	0.661	0.466 - 0.794
Years since first employment (year)						
Quartile1 (12-15)	79	0.600	0.438 - 0.724	79	0.525	0.344 - 0.669
Quartile2 (16-17)	100	0.619	0.482 - 0.727	99	0.625	0.488 - 0.731
Quartile2 (18-19)	123	0.580	0.450 - 0.686	123	0.425	0.268 - 0.560
Quartile4 (20-)	74	0.736	0.611 - 0.825	76	0.629	0.470 - 0.748
Number of co-worker						
Quartile1(1-2)	120	0.478	0.327 - 0.605	119	0.575	0.441 - 0.684
Quartile2(3-5)	103	0.586	0.443 - 0.699	103	0.571	0.425 - 0.688
Quartile3(6-10)	85	0.704	0.579 - 0.797	86	0.651	0.510 - 0.757
Quartile4(≥11)	59	0.646	0.468 - 0.774	59	0.349	0.104 - 0.554
Job category						
White-collar occupations	118	0.632	0.510 - 0.729	117	0.549	0.409 - 0.664
Blue-collar occupations	259	0.622	0.542 - 0.691	261	0.543	0.451 - 0.623
Job status						
Administrative	63	0.553	0.356 - 0.703	64	0.574	0.384 - 0.717
Non-administrative	310	0.595	0.517 - 0.663	310	0.513	0.426 - 0.590
Change of job contents						
No change	315	0.678	0.613 - 0.733	316	0.620	0.548 - 0.684
Position change	22	0.195	-0.182 - 0.545	23	0.170	-0.210 - 0.523
Job change	40	0.431	0.151 - 0.649	39	0.302	-0.021 - 0.561

* : For some variables, the numbers do not total 378 because of missing values.

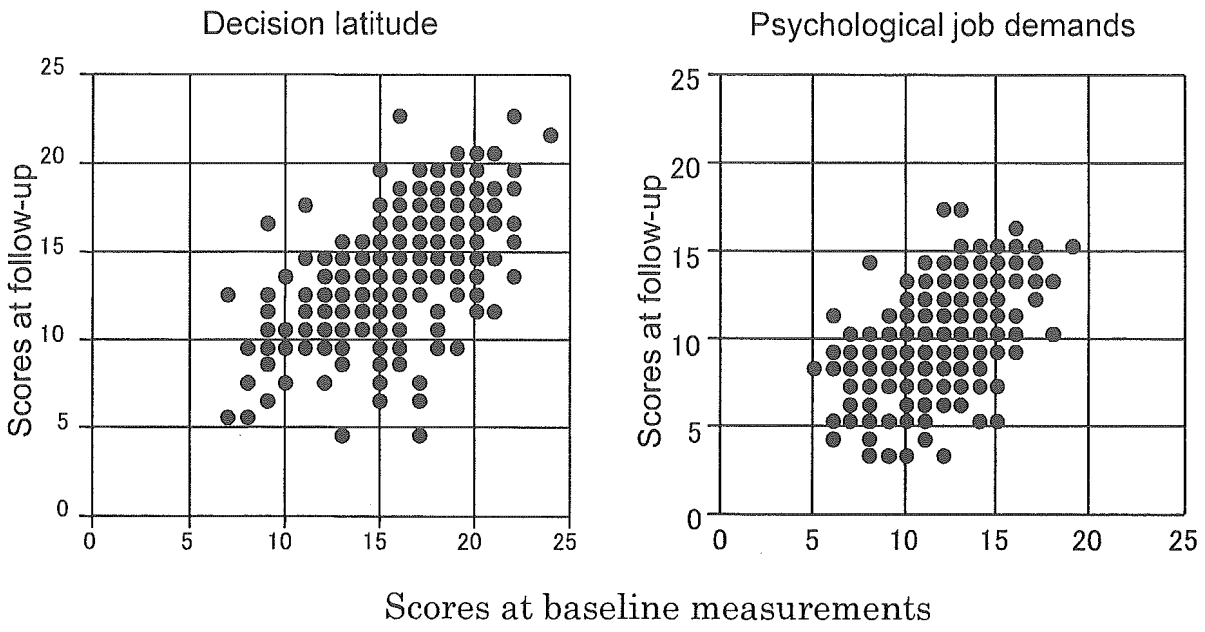

Figure 2. Correlation of decision latitude and job demand scores between baseline and follow-up. Whole subjects.

Table 3. Age-adjusted scores of the decision latitude and the job demands scale at the baseline examination by the job status changes.

Job change status	N	Adjusted mean*	SE	Estimated difference*	95% confidence interval	
				Decision latitude score		p<0.0001
No change	316	16.2	3.1	Reference		
Position change	23	14.4	2.5	-2.0	-3.3 - -0.7	
Job change	40	14.5	3.1	-1.9	-2.9 - -0.9	
Retired	72	13.8	3.0	-2.2	-3.0 - -1.3	
				Job demands score		p=0.064
No change	317	12.0	2.5	Reference		
Position change	24	10.8	3.0	-1.1	-2.2 - 0.0	
Job change	39	11.4	2.9	-0.6	-1.4 - 0.3	
Retired	71	11.5	3.0	-0.7	-1.4 - 0.1	

* : Estimated with multivariate generalized linear model.
SE: standard error of the mean

To explore bias due to the healthy worker effect, decision latitude and job demands scores at baseline were compared according to job change status, including retirement, using a multivariate generalized linear model. After adjusting for age, the no job change group showed a statistically significant higher decision latitude score at baseline than other groups (Table 3).

DISCUSSION

Of the workers who participated in both baseline and follow-up examination, 84% did not change their job or job status during the study period, and their job strain scores showed moderate correlation coefficient levels. Results varied with age, sex, education status, years since first employment, and number of co-workers, and job category and status at baseline. Subgroups that experienced changes showed lower coefficients and the decision latitude

scores at follow-up examination tended to be higher than those at baseline.

To the best of our knowledge, this is the first study to evaluate the long-term reproducibility of the job characteristics scale in a large-scale population-based study in Japan. Two US studies previously reported the reproducibility of this scale. As part of the Work Site Blood Pressure Study in New York City, the 3-year test-retest correlation coefficient was shown to be 0.64 for job decision latitude and psychological job demands.[6] A four-year follow-up study of female nurses showed a moderate degree of stability with correlation coefficients for job control and job demands of 0.60 and 0.54, respectively.[16] These results are similar to those obtained here.

When compared with other behavioral factors, the coefficients for leisure-time physical activity in a Finnish study ranged from 0.41 to 0.43.[17] Regarding biomedical factors in the present population, we previously reported[18] that the coefficients for job strain scores were lower than those for body mass index (0.93), total and high-density lipoprotein cholesterols (0.73 and 0.75, respectively), and blood pressure (0.65). The job characteristics scores in our study seemed to have similar reproducibility compared with other behavioral and biomedical factors in the population-based studies.

Education is known as an important determinant of workers' health.[19] Higher correlation coefficients were observed for those with higher educational attainment. This is probably because they would have achieved a more stable job position than those with lower education levels.

Workers who experienced changes in their job or job status showed a weaker correlation between baseline and follow-up job strain scores and their decision latitude levels tended to increase. Although the small number of subjects who experienced job changes limits interpretation of the results, the job characteristics scales adopted seem responsive to change.

While some studies in Europe and North America have shown a significant relationship between high job strain and ischemic heart disease,[1] considerable numbers of studies, including a study of Japanese immigrants in Hawaii, have failed to show a significant positive association.[20] One reason is suggested to be misclassification of job characteristics due to the lack of information on cumulative exposure to high job strain.[2,21] Instability of job strain levels during study periods could also result in underestimations of the association between job characteristics and health problems. Our results estimating the responsiveness of the job characteristics scale to changes in job strain levels could support this partly.

In previous studies examining the relationship between behavioral work characteristics and health, subjects have mainly included workers from large enterprises with a narrow job category range. Studies on employees in small-sized firms, who tend to have diverse job categories, are scarce.[2] Moreover, the annual statistics of the Japanese labor force survey[22] reported that 97% of enterprises employ ≤50 members of staff, and 62% of the total work force work for small enterprises with ≤50 employees. In this study, 95% of the subjects worked for small-size enterprises (≤50 employees), and 69% were categorized as blue-collar workers. Our findings are unique in that they were derived from workers with diverse occupations, and therefore they are valuable with regard to Japanese workers' health.

This study has some limitations that need to be addressed in future research. First, most subjects in the present analysis were middle aged with relatively high levels of job security. The results displayed in Table 3 suggest that most subjects developed job adaptation skills prior to the baseline examination. This healthy workers effect could have biased our results. Secondly, the small number of subjects who experienced changes in their job circumstances lowered the power to detect the responsiveness of score changes. Thirdly, categorization of workers into job groups defined on the basis of self-administered questionnaire scores could induce misclassification. This study probably underestimated differences of stability of the job strain scores between job categories. Finally, the results of this study were restricted to information from workers living in a local municipality and therefore we should be cautious in generalizing the study findings to other municipal urban populations.

Despite these limitations, however, the findings of this study have important implications. The Japanese version of the WHO-MONICA Psychosocial Study Questionnaire showed statistically significant long-term stability and was supposed to be to some extent responsive to change in job strain levels.

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