

Association between work-related psychological stress and arterial stiffness measured by brachial-ankle pulse-wave velocity in young Japanese males from an information service company

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Objectives This study examined the relationship between work-related psychological stress and arterial stiffness in young Japanese workers.

Methods A cross-sectional study was conducted on 396 Japanese male workers, aged 24 to 39 years, employed in a Japanese information service company. Work-related psychological stress was measured by the Job Content Questionnaire based on the job demand–control model. The job-strain index was defined as the ratio of job demand to job-control scores. The outcome of the study was the degree of arteriosclerosis as assessed by brachial pulse-wave velocity (baPWV). The cardiovascular risk factors analyzed were age, heart rate, blood pressure, body mass index, serum lipid, blood sugar levels, catecholamine levels, ethanol consumption, smoking, and overtime. In addition, psychological responses were assessed by tension–anxiety and anger–hostility scales in the Profile of Mood States (POMS).

Results The baPWV was positively ($P<0.05$) associated with physiological variables including age, heart rate, body mass index, and serum levels of total cholesterol, fasting glucose, and noradrenaline, but negatively ($P<0.01$) associated with the job-strain index. Significant associations were not found on the POMS tension–anxiety and anger–hostility scale scores. The negative correlation between baPWV and the job-strain index was consistent even after control for the effects of significant physiological variables.

Conclusions The association between job stress and baPWV was found to be inconsistent with the results of previous western studies, and it may require further investigation while taking into account occupation, cardiovascular risk factors, and Japanese culture.

Key terms cardiovascular disease; job content questionnaire; work-related psychological stress.

Cardiovascular diseases (CVD) are among the leading causes of illness and death among the working population in industrialized countries. Because of their complex etiologies, only a very small proportion of the cases are officially recognized as occupational diseases. However, recent research indicates that occupational factors account for most of the risk; especially work-related psychological stress greatly contributes to the development of CVD (1).

According to the job demand–control model defined by Karasek (2), workers exposed to high job strain (stressful conditions with high job demand and low job control) have an increased risk of CVD (3–10). A lack

of social support at the workplace (3, 8, 11) and, more importantly, job controllability contribute to a further increase in the risk (11–13).

A significant positive association between psychological stress at work and CVD raises the following important questions for research. First, previous studies (3–14) showing a positive association between job stress indices (ie, job demand, control, strain and support depending on the study) and CVD have been conducted extensively in Europe and the United States, but not in Japan, where the incidence of CVD and culture differ. Second, in these studies, the application of the Job Content Questionnaire with respect to CVD was limited by

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reliance on prevalence data (4, 8, 11, 13). In addition, the diagnosis of CVD was not confirmed by physical examination and laboratory tests (5). Third, most of the previous job stress studies investigated only specific risk factors of interest without adjusting for CVD risk factors. The CVD risk factors considered were serum cholesterol (15, 16), smoking (16), hemoglobin A1c (17), and blood pressure (18, 19). In various models, additional factors for personal characteristics such as type A behavior (20, 21) and hostility (22) have been used to assess work-related stress in CVD-prone workers since stress perception may differ among workers. Elevations in hormones such as catecholamine and cortisol have been reported to be associated with specific work properties, such as time pressure, loud noise, and repetitiveness (23). Furthermore, overtime work has been suggested to increase the burden on the cardiovascular system (24). "Karoshi" (death from excessive work) is said to be one of the major occupational health problems in Japan.

In our study, we investigated the effect of work-related psychological stress on arterial stiffness in young Japanese workers. Increasing arterial stiffness is one of the pathological states of vascular damage, and it is closely associated with atherosclerotic CVD (25). Therefore, measuring the degree of arteriosclerosis with adjustments for the effects of potential CVD risk factors may enable us to understand the mechanism of stress-related CVD in young adults in Japan. Arterial stiffness was measured from the brachial-ankle pulse-wave velocity (baPWV), a reliable predictor of atherosclerotic vascular damage, as confirmed in a Japanese working population of more than 10 000 persons (26–28). It is anticipated that, if stress turns out to be a risk factor for CVD in association with baPWV, early intervention to reduce stress could reduce the risk of CVD. Moreover, the seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure stated that young prehypertensive workers should adopt lifestyle modifications to reduce risk factors (29). As a result of this report, the evaluation of vascular risk factors among young working populations has recently become an urgent concern.

Study population and methods

Study population

The investigation was carried out in the morning between 0830 and 1130 in June and July 2003 during periodic health check-ups in a Japanese information service company. The company is located in the central area of Tokyo and offers consultation in information technology (IT), system integration solutions, IT-based

science solutions, and data management. The company employs computer software engineers and technicians, sales workers, and computer equipment operators. Among 1000 employees, 526 workers aged ≤ 40 years received annual medical check-ups at the company. These check-ups were mandatory according to the Industrial Safety and Health Law in Japan, and thus the attendance rate was 100%. Those older than 40 years of age were referred to an independent health examination center outside the company for closer examinations. The study was approved by the Committee of Health and Safety in the company. All of the 526 workers were recruited for our study, but two men refused because they were unwilling to share their psychological information. The remaining 524 persons signed a written informed consent. The female workers were excluded because of their small sample size (17%), and therefore 437 men participated in the analysis. Of the 437, 41 with less than 0.9 of the ankle-brachial pressure index recorded on one side of a leg were excluded because the range of the ankle-brachial pressure index indicated a possibility of arteriosclerosis obliterans, which would decrease pulse-wave velocity (27, 30). Thus the data of 396 men (mean age of 30 years) were analyzed in the study. The study population included 5 men with a past history of angina pectoris (without myocardial infarction) and 14 with a past history of hypertension, hyperlipidemia, or diabetes mellitus, all of whom had not received any medication in the past year. All of the participants were instructed to refrain from breakfast, coffee, and smoking on the morning of the health examination.

Brachial-ankle pulse-wave velocity

The baPWV, ankle-brachial pressure index, and blood pressure were measured simultaneously using an automatic waveform analyzer (VaSera VS-1000, Fukuda, Japan). The measurements were taken with the participants lying in the supine position after they had rested for at least 5 minutes. The occlusion and monitoring cuffs were placed around both sides of the participants' upper and lower extremities. Pressure waveforms of the brachial and tibial arteries were recorded simultaneously with the use of an oscillometric method. The time interval between the wave front of the brachial and ankle waveform was defined as the time interval between the brachium and the ankle (ΔT_{ba}). The distance between the sampling points of the baPWV was calculated automatically according to the body height of the participant. The path lengths from the heart to the brachium and to the ankle are designated as L_b and L_a , respectively. The $L_a - L_b$ was estimated according to the following equation: $L_a - L_b = 0.59 \times \text{body height (cm)} + 14.2$, and the baPWV was then calculated as follows: baPWV

$= (L_a - L_b) / \Delta T_{ba}$ (31). The normal range of the baPWV is between 9.84 and 10.35 m/s (31), and the reliability and validity have been reported to be excellent (28). A higher baPWV indicates more severe arterial stiffness. A mean of the right- and left-sided baPWV in the second measurement was used for our analyses.

Cardiovascular risk factors

Using previous baPWV studies (26, 32) as a guide, we assessed the following CVD risk factors: age, heart rate, blood pressure, body mass index, serum total cholesterol, serum triglyceride, fasting glucose and catecholamine levels, ethanol consumption (grams/week), cigarettes smoked/day, and overtime work (hours/month). Body weight and height were obtained by anthropometric measurements and used to calculate the body mass index (kg/m^2). The biochemical markers were measured by standard laboratory techniques, and the plasma catecholamine levels (adrenaline, noradrenaline, and dopamine) were measured by routine high-performance liquid chromatography (33). Alcohol consumption was determined according to the quantity and frequency and converted into weekly ethanol consumption (grams/week). Overtime work was defined as any extra hours worked that exceeded the normal daily workhours. The data on overtime work were obtained from each participant's computerized work records for the 4 months prior to our study.

Psychological responses

The Profile of Mood States (POMS) (34), completed before the physician's interview, identifies and assesses transient, fluctuating affective mood states of tension-anxiety, depression-dejection, anger-hostility, vigor-activity, fatigue-inertia, and confusion-bewilderment. The reliability and validity of the Japanese version of the POMS was reported to be excellent (35). In our study, the POMS tension-anxiety and anger-hostility scales were used according to a previous report on the effect of psychosocial stress on CVD (22).

Work-related psychological stress

Work-related psychological stress was measured by the Japanese version of the Job Content Questionnaire, whose reliability and validity has been reported to be excellent for assessing job stressors among Japanese employees (36). The questionnaire consists of scales for job demand, control, and social support (2, 37). The scale for job demand is defined by the speed in completing work, the degree of difficulty of the work, the amount of work, the time allowed to complete the work, and conflicting demands. Job control was defined by the

possibility to learn new things, the repetitious nature of the work, the requirement for creativity, the level of skill required, the ability to make decisions over how to perform the work, the right to make one's own decisions, and the ability to take part in group decisions. The social support scale consists of support from supervisors and colleagues.

The subjects completed the questionnaire in a quiet room before the physical examination. The mean scores of the study population were 33.0 (SD 5.5) for job demand, 67.1 (SD 11.0) for job control, and 30 (SD 3.3) for social support.

According to the literature on the Japanese version of the questionnaire (36), a "high job-demand" group was defined as having a job-demand score of ≥ 30 , and for the "low job-demand" group the score was < 30 . A "high job-control" group was defined as having a job-control score of ≥ 65 , and "low job control" was used for scores of < 65 (36). Job strain was calculated as job demand divided by job control. According to Landsbergis et al (38), since the top 20% predicts job-related psychological stress, the percentile score formed a high job-strain group with the remaining participants allocated to a low job-strain group (35).

Differences in the cardiovascular risk factors and the psychological responses between the high and low job-strain groups

Table 1 shows the distributions of the CVD risk factors and the POMS scores in the high and low job-strain groups. The participants in the high job-strain group tended to be younger and have higher POMS tension-anxiety and anger-hostility scores than those in the low job-strain group. Those in the high job-demand group tended to work for a longer time and have higher POMS tension-anxiety and anger-hostility scores than those in the low job-demand group (data not shown). Those in the high job-control group tended to be older than those in the low job-control group (data not shown).

Statistical methods

The data analyses were conducted using SAS version 8.12 for Windows (32). All of the tests were two-sided with a significance level of 5%.

The generalized linear model (GLM) (32) of the SAS program was used to estimate the impacts of the job-stress variables, CVD risk factors, and the POMS scores on baPWV. In this model, the questionnaire parameters were treated as continuous variables. First, linearity was assessed between each explanatory variable and baPWV, and, in the linear regression model, an outlier in fasting glucose was excluded. The corresponding regression coefficient reflects either an increase or

Table 1. Distribution of risk factors for cardiovascular disease and psychological responses in the high and low job-strain groups. ^a

Variable	Job strain				Total (N=396)	
	Low (N=314)		High (N=82)			
	Median	Interquarter range	Median	Interquarter range	Median	Interquarter range
Cardiovascular disease risk factors						
Age	31	27–35	29	25–34	30	26–34
Heart rate (beats/min)	63	58–70	64	57–73	63	57–71
Blood pressure (mm Hg)						
Systolic blood pressure	110	110–128	118	110–126	120	110–126
Diastolic blood pressure	79	68–80	70	68–78	70	68–78
Body mass index (kg/m ²)	22.5	20.5–24.4	21.9	20.5–24.5	22.4	20.5–24.4
Serum lipid and sugar						
Total cholesterol (mg/dl)	182	157–208	175	148–209	181	155–208
Triglyceride (mg/dl)	90	62–134	87	59–142	90	61–134
Fasting glucose (mg/dl)	89	84–94	87	83–92	89	84–93
Serum catecholamines						
Adrenaline	0.04	0.03–0.05	0.04	0.03–0.05	0.04	0.03–0.05
Noradrenaline	0.36	0.28–0.46	0.35	0.28–0.48	0.36	0.28–0.46
Dopamine	0.01	0.01–0.01	0.01	0.01–0.01	0.01	0.01–0.01
Ethanol consumption ^b (g/week)	80	40–140	46	20–120	70	30–140
Overtime work ^c (hours/month)	32	14–54	35	12–60	32	13–56
Profile of mood states (POMS)						
Tension–anxiety	8	5–13	10	7–16	8	5–13
Anger–hostility	4	1–8	5	2–12	4	1–9

^a Smokers (current and past) versus nonsmokers (never smokers): total number of 179 (46%), 135 (44%) having low job strain and 44 (54%) having high job strain. There were 11 missing values.

^b There were 109 missing values.

^c There were 121 with overtime work.

decrease in baPWV per unit increase in this variable. Then the significant variables at $P < 0.1$ in the univariate GLM were selected for entry into the next GLM step (31). Since job strain could operate through higher blood pressure giving rise to higher baPWV (26–28), it has been suggested that blood pressure may play a role as an intermediary between job strain and baPWV. Thus blood pressure was excluded from the model, since it could have overadjusted the results. Alcohol consumption and overtime work were also excluded in the final model because of the large number of missing data. In these multivariate analyses the questionnaire scores were represented by job demand and control (model I) or by the job-strain index (model II). Variance inflation, tolerance, and co-linearity were examined to determine the existence of multi co-linearity problems (39). A more sophisticated diagnosis was achieved via a principal components analysis of the standardized predictor variables. Detailed explanations and the recommended values for each co-linearity diagnostic testing have been reported elsewhere (40). The model fitness by residuals was assessed to determine a set of significant covariates for the final GLM.

To examine the specific interactive effects of the CVD risk factors and psychological responses between job strain and baPWV, the statistical interaction was also assessed including an “interaction term” between each

risk factor and the POMS score and job-strain variable in the analysis.

Results

Table 2 shows the effects of job stress at work, the CVD risk factors, and the psychological responses on baPWV. The univariate analyses showed that the significant predictors of baPWV were the job stress variables of job control and strain, age, heart rate, body mass index, and the serum lipid, fasting glucose and serum noradrenaline levels. Social support, smoking, and the two POMS scores were not significantly associated with baPWV. Co-linearity problems existed between the total cholesterol and triglyceride levels. A representative variable of total cholesterol was selected for the final GLM with the other variables selected at the significant level of 0.1 in the univariate analyses. Residual analyses revealed no obvious curvilinearity. The multivariate analyses showed that the independent significant predictors of baPWV were job strain, age, heart rate, and serum noradrenaline levels. While these CVD risk factors were positively associated with baPWV, only job strain predicted baPWV inversely.

Table 2. Effects of job stress at work, risk factors for cardiovascular disease, and psychological responses on brachial-ankle pulse-wave velocity (N=396).

Variables	Univariate analyses		Multivariate analysis ^a			
	Regression coefficient	Standard error	Model I ^b		Model II ^c	
			Regression coefficient	Standard error	Regression coefficient	Standard error
Scales of the job content questionnaire						
Demand	−0.009	0.012	−0.022 ^a	0.010	.	.
Control	0.023 ^f	0.006	0.016 ^f	0.005	.	.
Social support	0.002	0.020	.	.	.	.
Job strain	−1.860 ^f	0.520	.	.	−1.382 ^f	0.448
Cardiovascular disease risk factors						
Age	0.103 ^g	0.012	0.076 ^g	0.012	0.077 ^g	0.012
Heart rate (beats/min)	0.034 ^g	0.006	0.022 ^g	0.006	0.022 ^g	0.006
Body mass index (kg/m ²)	0.068 ^f	0.021	0.004	0.020	0.002	0.020
Serum lipid and sugar						
Total cholesterol (mg/dl)	0.008 ^g	0.002	0.003	0.002	0.003	0.002
Triglyceride ^d (mg/dl)	0.004 ^g	0.001	.	.	.	.
Fasting glucose (mg/dl)	0.020 ^a	0.008	0.010	0.005	0.010	0.005
Serum catecholamines						
Adrenaline	2.529	1.758	.	.	.	.
Noradrenaline	1.334 ^f	0.438	0.855 ^a	0.395	0.835 ^a	0.394
Dopamine	16.649	12.076	.	.	.	.
Cigarettes smoked a day	0.007	0.007	.	.	.	.
Profile of mood states						
Tension–anxiety	0.004	0.011	.	.	.	.
Anger–hostility	0.012	0.010	.	.	.	.

^a Adjusted for age, heart rate, body mass index, total cholesterol, fasting glucose, and serum noradrenaline.

^b Demand and control were analyzed simultaneously, R-square 0.26.

^c Job strain was analyzed by excluding demand and control, R-square 0.25.

^d Because of collinearity, triglyceride was excluded from the multivariate analysis.

^e P<0.05.

^f P<0.01.

^g P<0.001.

Table 3. Interaction effect of age, body mass index, and total cholesterol in the multivariate model of brachial pulse-wave velocity (baPWV).

Variables	Parameter estimate of baPWV ^a		P-value of statistical interaction
	Upper-half group ^b	Lower-half group ^b	
Age (years)	-2.93	-0.549	0.043
Body mass index (kg/m ²)	-1.974	-1.022	0.044
Total cholesterol (mg/dl)	-2.446	-0.722	0.011

^a Adjusted for job strain, age, heart rate, and total cholesterol, glucose and noradrenaline levels.

^b The upper- and lower-half groups were based on the medians of the three variables studied.

Statistical interaction was assessed between the job-stress variables and baPWV with other independent variables selected at P<0.1 by a univariate model. An inverse association between job strain and baPWV was found to vary depending on age, body mass index, and total cholesterol (data not shown). In addition, table 3 shows the parameter estimate of baPWV when age, body mass index, and total cholesterol were tentatively

divided into binary variables at the cut-off point of the median. The negativity of the parameter estimate of baPWV was stronger in the groups with the older age, larger body mass index, and higher total cholesterol levels than in those with the younger age, smaller body mass index, and lower total cholesterol level, respectively.

Discussion

In our study, the effect of the work-related stress parameters on baPWV did not agree with the results of previous studies investigating the effects of job stress on CVD in western countries. In fact, the effects were the opposite of what was expected from the job-strain hypothesis, stating that workers with high job strain have an increased risk for CVD (11). Job strain was found to be negatively associated with baPWV even after control for significant CVD risk factors such as age, heart rate, and serum noradrenaline levels. This inverse association became stronger as age, body mass index, and total cholesterol increased.

Although a relationship between job strain and CVD has been widely researched in western countries (3–5, 8), the job-strain hypothesis remains to be established in other countries (15, 17–18, 20, 41–43). The results of the CARDIA study (18) were compatible with our findings, showing inverse associations with risk factors for high job demand, low control, and job strain among young adults. Several possible reasons for the inconsistent effects for job stress with respect to the job-strain hypothesis on baPWV as observed in our study follow. First, the characteristics of the study groups (ie, high and low job-strain groups) appeared to differ; the participants in the low job-strain group tended to have higher diastolic blood pressure, body mass index, total cholesterol, triglyceride, fasting glucose, and ethanol consumption than those in the high job-strain group. Although it was inconclusive, this finding may indicate that the adverse effects of unhealthy lifestyles on baPWV were more severe in the low job-strain group than in the high job-strain group and contributed to the statistical interaction finding that the inverse association between job strain and baPWV was stronger as body mass index and total cholesterol increased.

Second, age-related cultural factors may have resulted in an atypical phenomenon with respect to the relationship between job strain and baPWV observed in our study. Iwata and his colleagues (44–47) indicated that self-reported psychological distress is affected among Japanese workers by traditional Japanese culture in relation to age in that older workers are more likely to suppress their expressions of positive feelings than younger workers. For instance, in the Honolulu heart program study, the participants from the Japanese ancestry cohort in Hawaii showed that high job strain appeared to be inversely associated with arteriosclerosis (41). Inconsistent results of other studies (48, 49) also suggest that the application of the Job Content Questionnaire among Japanese workers is of concern and needs to be further evaluated with cultural influences and worker's age taken into consideration.

Some methodological problems were encountered in our study. First, the reliability and validity of measurement for baPWV should be discussed. baPWV is reported to be a valid, noninvasive method for monitoring arteriosclerotic vascular changes in large population studies (32, 49). A higher baPWV has been found to be associated with an increased risk of myocardial infarction (27, 28). In our study, the baPWV reproducibility was 97.1%, and baPWV was associated positively with the CVD risk factors of age, heart rate, blood pressure, and serum noradrenaline levels, as in a previous study (26). These results support the possibility that baPWV is a reliable predictor of arteriosclerosis even for young workers. In relation to the measurement using an automatic waveform analyzer, the number of participants

with an ankle-brachial pressure index of <0.9 ($N=41$) seemed to be somewhat large. An ankle-brachial pressure index of <0.9 indicates the possibility of arteriosclerosis obliterans, and, accordingly, these persons were excluded from our study. It was not sure whether such a relatively large number may be due to measurement error (22 out of the 41 persons with an ankle-brachial pressure index of <0.9 were recorded on one side of one of their legs). Nevertheless, our previous study (30) showed that people with an ankle-brachial pressure index of <0.9 accounted for 10% of the total study population, a finding compatible with the present study. We performed additional analyses that included the 41 persons with an ankle-brachial pressure index of <0.9 and confirmed that the results did not significantly differ (data not shown). Future studies should include a modality for measuring arteriosclerosis obliterans as objectively as possible.

Second, although overtime work and lifestyle factors such as drinking and smoking are known predictors of arteriosclerosis (24), overtime work and ethanol consumption were not included in our multivariate analyses due to the large number of missing data. With regard to smoking effect, although unhealthy lifestyles were suggested to be linked with low job strain, as discussed earlier, the proportion of smokers was lower in the low job-strain group. However, smoking status did not take into account the duration of smoking, and, accordingly, more precise information is needed. Hence the effects of overtime work and lifestyle factors on baPWV require further investigation in future studies.

Third, with regard to the generalizability of the results of our study, the types of work need to be assessed in a comparison with those in relevant studies. They include computer software engineers and technicians, sales workers, and computer equipment operators. The results of the Job Content Questionnaire [31.9 (SD 5) for job demand and 66.1 (SD 11) for job control] of our study were comparable with the findings of another study (36) investigating job-related psychological stress in the information technology industry as measured by the Japanese version of the Job Content Questionnaire.

Finally, since our study was cross-sectional, a definite inference is difficult with respect to a causal relationship between work-related psychological stress and baPWV, as well as between psychological stress and cardiovascular and psychological responses. Additional studies are needed that employ a more sophisticated study design.

In summary, we evaluated baPWV as a CVD proxy after simultaneously adjusting for CVD risk factors and psychological responses. Although baPWV was consistently related to the traditional CVD factors of age and heart rate, our study did not support the job-strain hypothesis stating that high job strain increases the risk of

CVD. Areas needing additional research are the applicability of the Job Content Questionnaire to a Japanese cohort and the need for a more delicate conceptualization of work-related stress on CVD with occupation, CVD risk factors, and traditional Japanese culture taken into account.

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