Job Strain and Risk of Cardiovascular Events in Treated Hypertensive Japanese Workers: Hypertension Follow-Up Group Study

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Abstract: Job Strain and Risk of Cardiovascular Events in Treated Hypertensive Japanese Workers: Hypertension Follow-Up Group Study: Shuji UCHIYAMA, et al. Hoshizaki Clinic—In Japan, *Karoshi*, which means ‘death from overwork’, has become a focus of social concern. However, no previous study has examined long working hours and job strain simultaneously in relation to incidence of cardiovascular events (CVE) in Japanese workers. We prospectively evaluated the relation between job strain or long working hours and risk of CVE in treated hypertensives during the years 1994–2000. In this study, we followed a sample of 1,615 participants (908 men and 707 women) aged 40–65 yr who were working more than 5 working hours per day. Participants completed questions about work-related conditions and lifestyle variables at baseline, and were free of diagnosed cardiovascular disease, stroke or cancer. Job strain (the combination of job demands and job control) was assessed using a simple questionnaire developed with reference to Karasek’s model. The main outcome measure was incidence of CVE. During the mean follow-up period of 5.6 yr, we documented 38 cases of initial CVE. Analyses were conducted using the Cox proportional hazard model. We found a significant association between incidence of CVE and job strain categories, but not long working hours. Multivariate relative risks for CVE in active jobs and high strain jobs overall were 2.89 (95% CI: 1.33–6.28) and 2.45 (95% CI: 0.87–6.93); for men 2.94 (95% CI: 1.29–6.73) and 1.86 (95% CI: 0.51–6.75), and for women 3.97 (95% CI: 0.34–46.88) and 9.05 (95% CI: 1.17–69.86), respectively. In conclusion, active jobs and high strain jobs were associated with increased risk of CVE for treated hypertensive workers.

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Key words: Job strain, Working hours, *Karoshi*, Hypertension, Cardiovascular events, Prospective study, Treated hypertensive, Worker, Japan

Job stress is associated with a higher risk of cardiovascular disease^{1, 2)}. In Japan, *Karoshi*, which means ‘death from overwork’, has become a focus of social concern since Japan’s speculative ‘bubble’ economy of the 1980s. *Karoshi* is a work-related disease mainly triggered by long working hours³⁾. Extreme overwork might adversely affect hypertension, atherosclerosis, and other illnesses, and contribute to an increased risk of disabling and fatal cardiovascular events. The results of our first hypertension follow-up study conducted in 1984–1990 confirmed that working more than 11 h increased the risk of cardiovascular events (CVE) in treated hypertensive male workers in their fifth decade⁴⁾.

After the collapse of the bubble economy, i.e. the second half of the 1990s, the labor environment in Japan changed. Mean annual working hours have declined, and bankruptcy, unemployment and suicide have increased as a result of the economic recession. Given the various types of job stress during this period, long working hours, based solely on time, may not be a strong risk factor for CVE, although this remains an important element of work stress.

The Karasek job strain model posits that a combination of high psychological demands and low job control is a health risk for employees^{5, 6)}. However, no previous study has examined two categories of stressful components of the work environment, i.e. long working hours and job strain, simultaneously in relation to incidence of CVE in Japanese workers.

In the present study on a cohort of treated hypertensive Japanese, we have tried to prospectively examine the association between long working hours or job strain and incidence of CVE. We hypothesized that job strain, more so than long working hours, would put treated

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hypertensive workers at increased risk of CVE in Japan after the collapse of the bubble economy.

Stressful conditions tend to cause greater increases in blood pressure in hypertensive patients than in normotensive persons^{7,8)}. Since hypertensive patients are also a high-risk group with multiple risk factors⁹⁾, a clearer association might be expected in this cohort between work-related factors and incidence of CVE.

Patients and Methods

Study population

The present study was conducted as a part of the larger Hypertension Follow-up Group Study, which took place between 1994 and 1996 when 3,877 patients aged 40 to 75 yr, who had been receiving antihypertensive drugs regularly for at least one year, were registered for follow-up at 123 hospitals and clinics in 47 prefectures in Japan by members of the Hypertension Follow-up Group of the Japan Federation of Democratic Medical Institutions. Patients with the following conditions were excluded from the study: clear secondary hypertension, idiopathic cardiomyopathy, history of stroke, history of myocardial infarction, renal failure (creatinine of 2.0 mg/dl or above), heart failure (NYHA (1964) class IV), cancer, and those taking hypoglycemic agents, insulin, or steroids. All patients agreed to participate in the study.

From the participants of the above study, 1,659 persons (942 men and 717 women) aged 40–65 yr who were working more than 5 working hours per day (i.e. portal-to-portal hours) were enrolled in the present study. Of them, 44 persons (34 men and 10 women) were excluded from the database because they were not followed at all. The final database comprised of 1,615 persons (908 men and 707 women). The mean (SD) age of the population was 53.8 (6.5) yr for men and 54.0 (6.0) yr for women.

The participants worked in various occupations, and included both full-time and part-time employees of mainly small and medium-sized enterprises, as well as those who were self-employed. Follow-up was conducted until the end of 2000, at which time the follow-up rate was 75%.

For the year before registration, the participants' blood pressure, laboratory values, electrocardiographic findings, and the types of antihypertensives they were taking were obtained from their medical records. At the time of entry, each participant completed a self-administered questionnaire on family and hypertension histories, lifestyle variables and work-related conditions. Each patient was checked each year for cardiovascular event, development of cancer, and survival during the follow-up period. The background and basis for diagnosis for any patient who sustained a cardiovascular event were recorded on the survey sheet. For patients who did not present for examination, this information was obtained by telephone and the patient was urged to come in for examination. Cardiovascular events (CVE) were defined

as initial cerebral hemorrhage, cerebral infarction, subarachnoidal hemorrhage, myocardial infarction, heart failure, aortic aneurysmal rupture, or sudden death during the follow-up period.

Assessment of working hours and job strain

Long working hours were defined as working more than 10 h (i.e. portal-to-portal hours) per day. The respective rates for working hours of 5, 6, 7, 8, 9, 10, 11 and 12 h or more were 2%, 3%, 7%, 36%, 18%, 21%, 3% and 10% for men, and 12%, 17%, 19%, 32%, 8%, 8%, 1% and 3% for women, respectively.

Using a simple questionnaire to measure the components of job strain with reference to Karasek's model, job demand was calculated as the sum of the scores ("rarely" (0 points), "sometimes" (1 point) and "always" (2 points)) for the following 3 items: 1) Heavy burden ("Do you consider work a burden?"), 2) Intense competition ("Do you need to compete with others in your work place?"), 3) Time urgency ("Do you work under time pressure?").

The scores were used to divide job demand into tertiles (low demand of lower third, intermediate demand of middle third, or high demand of upper third). To classify the job strain quadrant, job demand was also dichotomized by the scores into low job demand (low or intermediate demand) or high job demand (high demand).

Internal consistency in the three items of job demands was assessed by Cronbach's alpha value.

Job control was rated in three groups by "low" response (0 points), "moderately low" response (1 point) or "high" response (2 points) for the question: "Do you have a choice in deciding how you do your work?" For the classification of job strain quadrant, job control was also dichotomized by the scores into low job control (lower third) or high job control (middle third or upper third).

In the analyses of job strain, subjects were classified into four groups according to the combination of job demands and job control. The four groups were low strain jobs (low job demands and high job control), passive jobs (low job demands and low job control), active jobs (high job demands and high job control) and high strain jobs (high job demands and low job control).

The respective rates for job demands scores of 0, 1, 2, 3 and 4 points or more were 27%, 22%, 18%, 16% and 17% for men, and 40%, 27%, 18%, 9% and 7% for women, respectively.

Zero points of job demands scores were classified as low job demands, one or two points were classified as intermediate job demands, and three or more points were classified as high job demands. For the classification of job strain quadrant, job demands were dichotomized into low job demands (two or fewer points) or high job demands (three or more points).

Cronbach's alpha of the internal consistency of the

three items of job demands was 0.62. If items of heavy burden, intense competition, or time urgency were deleted, the alpha was 0.66, 0.47 and 0.39, respectively. The standardized item alpha was 0.62, which was deemed consistent.

The respective rates for job control responses of "low", "moderately low" or "high" were 5%, 21% and 74% for men, and 15%, 30% and 55% for women, respectively. Therefore, job control was dichotomized into low job control ("low" or "moderately low" response) or high job control ("high" response) for the classification of job strain quadrant.

Other covariates

Mean blood pressure was measured at each season in the year before registration. Hypercholesterolemia and obesity were defined as total cholesterol ≥ 240 mg/dl (6.24 mmol/l) and body mass index (BMI) ≥ 25 kg/m², respectively.

Statistical analysis

The major focus of the present data analysis was the relationship between incidence of CVE and the two job stress categories of long working hours and job strain.

We used the Cox proportional hazards model to assess the impact of long working hours or job strain on CVE. For each participant, the observation years were the period from entry until the initial cardiovascular event or final survey. The relative risk (RR) of CVE was defined as the hazard ratio of the model. RR was adjusted for sex and age (yr) for all subjects, or age for men or women, and the 95% confidence interval (CI) was calculated. The following risk factors were added by the forced entry method to adjust multivariate RR: mean SBP (mmHg), BMI (kg/m²), total cholesterol (mg/dl), HDL-cholesterol (mg/dl), proteinuria (yes/no), family history of stroke (yes/no), left ventricular hypertrophy (yes/no), ischemic ST-T change (yes/no), atrial fibrillation (yes/no), and current smoking (yes/no).

The attributable fraction was calculated with use of the following formula: $(P1-P0)/P1 \times 100$. The population attributable fraction was then calculated as follows: $((P1 \times L1 + P0 \times L0) - P0) / (P1 \times L1 + P0 \times L0) \times 100$. (P0: incidence of reference group, P1: incidence of risk group, N0: n of reference group, N1: n of risk group, L0: N0/(N0+N1), L1: N1/(N0+N1)). The statistical significance of age in groups was tested using Student's t-test or one-way analysis of variance. The differences in the categorical variables were assessed by Pearson's chi-square test for non-ranking categories using cross-tabulation analyses. All analyses were conducted with the SPSS statistical program (SPSS Japan, Inc.).

Results

During the mean follow up of 5.6 yr, involving 9,087

patient-years, 38 (6 deaths) CVEs (29 (4 deaths) in men and 9 (2 deaths) in women) occurred among the 1,615 participants (908 men and 707 women). These included 6 (1 death) cerebral hemorrhages, 3 subarachnoid hemorrhages, 13 cerebral infarctions, 14 (4 deaths) myocardial infarctions, 1 heart failure, and 1 sudden death. Incidence rates of CVE per 1,000 patient-years were 4.18 in all, 5.70 in men and 2.25 in women.

Among 22 cases of stroke, all cases were diagnosed using computed tomography, except for 3 cases in which the diagnostic measures were unknown. Among 14 cases of acute myocardial infarction, 9 cases were confirmed by cardiac catheterization, 3 cases were diagnosed by diagnostic electrocardiographic changes or elevated cardiac-enzyme levels, and in 2 cases the diagnostic measures were unknown.

Table 1 shows the distribution of work-related factors and risk factors for cardiovascular disease in the long working hours (more than 10 h) group and all others by sex. The proportion of men with long working hours was higher than that of women (34% of men against 12% of women). Although the mean age of women was similar in the two groups, men with long working hours were younger than the other group ($p=0.000$). The long working hours group was more likely to have overwork-related factors including midnight work and fewer days off than the other group, though, the distribution of risk factors for cardiovascular disease was similar in both groups in both sexes.

Table 2 shows the relative risks of CVE according to long working hours. Long working hours for all participants slightly increased the risk of CVE (RR=1.24, 95% CI: 0.60–2.55 and multivariate RR=1.18, 95% CI: 0.57–2.43).

When limited to men, long working hours further increased the risk of CVE, but the risk was still not significant (RR=1.54, 95% CI: 0.70–3.32 and multivariate RR=1.45, 95% CI: 0.67–3.14). No women in the long working hours group had CVE.

Table 3 shows the relative risks of CVE according to job demands and job control by sex. Overall, the risk of CVE was the lowest in the intermediate job demands group (RR=0.45, 95% CI: 0.18–1.13 and multivariate RR=0.44, 95% CI: 0.18–1.12), and the highest in the high job demands group (RR=1.88, 95% CI: 0.89–3.96 and multivariate RR=1.81, 95% CI: 0.86–3.82). The risks for CVE in the intermediate and high demands groups were similar in men and women.

Table 4 shows the relative risks of CVE according to job demands and job control dichotomized for classification of the job strain quadrant.

There was an inverse association in the proportion of these categories between men and women. The proportion of high demands was two times higher in men than in women (304/908 (33%) versus 112/707 (16%),

Table 1. The distribution of work-related factors and risk factors of cardiovascular disease in the long working hours group (LWH group) and all others by sex, in the treated hypertensive workers aged 40–65 yr follow-up study, 1994–2000, Japan

Characteristic	Men			Women		
	All others	LWH group		All others	LWH group	
No. (%)	601 (66%)	307 (34%)		624 (88%)	83 (12%)	
Mean age $\pm$ SD (p^a value)	54.8 $\pm$ 6.5	51.8 $\pm$ 6.2 (0.000)		53.9 $\pm$ 6.0	53.9 $\pm$ 5.9 (0.934)	
	%	%	p^b value	%	%	p^b value
Work status: Part-time employee	6	1	0.012	47	9	0.000
Full-time employee	66	65		32	30	
Self-employed	26	31		10	37	
Others	2	2		11	25	
Type of work: Hard physical work	24	19	0.006	16	19	0.854
Mild physical work	40	36		56	47	
Clerical or intellectual work	36	46		28	33	
Midnight work (≥ 4 times per month)	7	17	0.000	4	25	0.000
Few days off (< 4 d per 4 wk)	9	22	0.000	14	35	0.000
Alcohol intake (≥ 2 go ^c per d)	30	32	0.447	3	4	0.579
Current smoker	41	42	0.913	9	15	0.102
High SBP (≥ 140 mmHg)	65	61	0.239	63	64	0.855
Electrocardiograph findings ^d	22	24	0.721	17	13	0.764
Hypercholesterolemia	22	22	0.997	34	29	0.424
Obesity	37	39	0.673	42	47	0.493

^a p value by assessed Student's t -test between 2 groups; ^b p value by assessed Pearson's chi-square test among distribution of categories compared with all others group; ^c1 go is equivalent to ethanol 29 ml; ^dEither left ventricular hypertrophy, ischemic ST-T changes, or atrial fibrillation.

Table 2. Relative risks (RR) of cardiovascular events (CVE) according to long working hours, in the treated hypertensive workers aged 40–65 yr follow-up study, 1994–2000, Japan

Sex	Working hours	No.	Cases ^a	RR ^b	Multivariate RR ^c
ALL:	Less than 10 h	1225	27	1.00	1.00
	10 h or more	390	11	1.24 (0.60–2.55)	1.18 (0.57–2.43)
Men:	Less than 10 h	601	18	1.00	1.00
	10 h or more	307	11	1.54 (0.70–3.32)	1.45 (0.67–3.14)
Women:	Less than 10 h	624	9	1.00	1.00
	10 h or more	83	0	1.8E–06 (0.00–.)	1.7E–06 (0.00–.)

^aIncident cases of CVE; ^bAge- and sex-adjusted RR for all participants and age-adjusted for men or women; ^cAdjusted for age, sex (if for all participants), mean SBP, BMI, total cholesterol, HDL-cholesterol, proteinuria, family history of stroke, left ventricular hypertrophy, ischemic ST-T change, atrial fibrillation and current smoking; 95% CI are shown in parentheses.

$p=0.000$). In contrast, the proportion of low control was 1.8 times higher in women than in men (321/707(45%) versus 234/908 (26%), $p=0.000$).

Among all participants, compared with low job demands, those with high job demands had a significant RR of CVE of 2.74 (95% CI: 1.42–5.27) and a significant multivariate RR of CVE of 2.63 (95% CI: 1.36–5.11).

The risks for CVE in the high demands group were similar in men and women. On the other hand, there was an inverse association in the risks for CVE in the low job control group between men and women. That is, the RR in men was low (RR=0.62, 95% CI: 0.24–1.63 and multivariate RR=0.68, 95% CI: 0.25–1.80), and the RR in women was high (RR=2.70, 95% CI: 0.66–10.94 and

Table 3. Relative risks (RR) of cardiovascular events (CVE) according to job demands and job control by sex, in the treated hypertensive workers aged 40–65 yr follow-up study, 1994–2000, Japan

Group		No.	Cases ^a	RR ^b	Multivariate RR ^c
Job demands:					
All:	Low	524	13	1.00	1.00
	Intermediate	675	7	0.45 (0.18–1.13)	0.44 (0.18–1.12)
	High	416	18	1.88 (0.89–3.96)	1.81 (0.86–3.82)
Men:	Low	243	9	1.00	1.00
	Intermediate	361	5	0.43 (0.15–1.32)	0.45 (0.15–1.36)
	High	304	15	1.88 (0.79–4.43)	1.98 (0.83–4.71)
Women:	Low	281	4	1.00	1.00
	Intermediate	314	2	0.47 (0.09–2.59)	0.39 (0.09–2.23)
	High	112	3	1.99 (0.44–8.97)	2.25 (0.48–10.41)
Job control:					
All:	High	1060	27	1.00	1.00
	Moderately low	405	8	0.96 (0.43–2.12)	1.04 (0.47–2.32)
	Low	150	3	1.06 (0.31–3.56)	1.12 (0.33–3.79)
Men:	High	674	24	1.00	1.00
	Moderately low	193	5	0.77 (0.29–2.03)	0.85 (0.32–2.26)
	Low	41	0	4.96E–06 (0.00– .)	4.26E–06 (0.00– .)
Women:	High	386	3	1.00	1.00
	Moderately low	212	3	2.13 (0.42–10.80)	2.25 (0.44–11.48)
	Low	109	3	3.61 (0.73–17.91)	4.42 (0.83–23.45)

^aIncident cases of CVE; ^bAge- and sex-adjusted RR for all participants and age-adjusted for men or women; ^cAdjusted for age, sex (if for all participants), mean SBP, BMI, total cholesterol, HDL-cholesterol, proteinuria, family history of stroke, left ventricular hypertrophy, ischemic ST-T change, atrial fibrillation and current smoking; 95% CI are shown in parentheses.

Table 4. Relative risks (RR) of cardiovascular events (CVE) according to job demands and job control dichotomized for classification of the job strain quadrant

Group		No.	Cases ^a	RR ^b	Multivariate RR ^c
Job demands:	All	Low ^d	1199	20	1.00
		High	416	18	2.74 (1.42–5.27)
	Men	Low	604	14	1.00
		High	304	15	2.77 (1.32–5.86)
	Women	Low	595	6	1.00
		High	112	3	2.74 (0.68–10.99)
Job control:	All	High ^e	1060	27	1.00
		Low	555	11	0.98 (0.48–2.00)
	Men	High	674	24	1.00
		Low	234	5	0.62 (0.24–1.63)
	Women	High	386	3	1.00
		Low	321	6	2.70 (0.66–10.94)

^{a, b, c}See footnote to Table 3; ^dLow job demand is defined as a score in the lower third or middle third, and high is defined in the upper third of the job demands scores; ^eHigh job control is classified as “high” response, and low is classified as “low” or “moderately low” response; 95% CI are shown in parentheses.

Table 5. Distribution of work-related factors and risk factors of cardiovascular disease according to job strain categories by sex, in the treated hypertensive workers aged 40–65 yr follow-up study, 1994–2000, Japan

Characteristic	Men					Women				
	Low strain	Passive	Active	High strain		Low strain	Passive	Active	High strain	
No.	148	456	218	86		266	329	57	55	
(% of No.)	(16)	(50)	(24)	(10)		(38)	(47)	(8)	(8)	
Mean age (p^a value)	54.5	54.7	52.2	52.0	(0.000)	53.1	54.8	53.7	53.6	(0.005)
($\pm$ SD)	(6.1)	(6.7)	(6.4)	(6.2)		(5.9)	(6.1)	(5.8)	(5.6)	
	%	%	%	%	p^b value	%	%	%	%	p^b value
Work status: Part-time employee	10	5	0	2	0.001	55	37	11	49	0.001
Full-time employee	77	63	61	78		32	27	59	34	
Self-employed	10	30	38	18		5	19	21	8	
Others	3	2	1	2		8	18	9	9	
Type of work: Hard physical work	28	20	21	28	0.001	17	11	20	39	0.704
Mild physical work	49	45	24	27		59	59	22	43	
Clerical or intellectual work	23	35	55	46		24	30	57	19	
Midnight work (≥ 4 times per month)	12	10	10	16	0.506	4	7	16	4	0.089
Long working hours (≥ 10 hours)	26	28	49	42	0.000	6	14	26	11	0.003
Alcohol intake (≥ 2 goc per day)	35	29	32	28	0.490	2	3	4	4	0.475
Current smoker	35	43	41	40	0.540	10	8	16	11	0.604
High SBP (≥ 140 mmHg)	65	63	67	56	0.525	62	63	63	67	0.511
Electrocardiograph findings ^d	44	35	53	54	0.042	32	35	35	44	0.405
Hypercholesterolemia	18	20	26	30	0.013	32	35	30	26	0.523
Obesity	29	38	48	29	0.164	41	49	25	34	0.263

^a p value by assessed one-way analysis of variance; ^b p value by assessed Pearson's chi-square test among distribution of categories;

^c1 go is equivalent to ethanol 29 ml; ^dEither left ventricular hypertrophy, ischemic ST-T changes, or atrial fibrillation.

multivariate RR=3.00, 95% CI: 0.72–12.46).

The distribution of work-related factors and risk factors for cardiovascular disease according to job strain categories by sex is shown in Table 5. Sixteen percent of men were in low strain jobs, 50% in passive jobs, 24% in active jobs, and 10% in high strain jobs. The distribution in women was similar to that in men, i.e. 38%, 47%, 8% and 8%, respectively.

In both sexes, those in passive strain jobs were the oldest, and those in high strain jobs were the youngest in job strain groups. Men with high strain jobs were more likely to report being a full-time employee, and men with active jobs were more likely to report being self-employed. Men with both high strain and active jobs were more likely to report long working hours. Women with active jobs were more likely to report long working hours. The percentages of electrocardiogram findings and hypercholesterolemia among men were higher in both the high strain and active job groups than in other groups. Distributions of other factors in job strain groups in men or women were not significantly different.

Table 6 shows the relative risks of CVE according to

job strain categories by sex. Compared with the low strain job group, those with active jobs had a significant RR of CVE of 2.94 (95% CI: 1.36–6.38), and a significant multivariate RR of CVE of 2.89 (95% CI: 1.33–6.28). Those with high strain jobs also had higher RR of CVE of 2.44 (95% CI: 0.87–6.85), and a multivariate RR of CVE of 2.45 (95% CI: 0.87–6.93). For men, the risks of active jobs were significantly high at 2.75 (95% CI: 1.22–6.21) and 2.94 (95% CI: 1.29–6.73), respectively. For women, the risks of high strain jobs were significantly high (RR=6.66, 95% CI: 0.93–47.70 and multivariate RR=9.05, 95% CI: 1.17–69.86).

The risks of passive and active jobs in women were also higher, although these were not significant.

Using these data, the attributable fraction of high job demands for CVE was 54% in men, and 62% in women. The population attributable fraction of high job demands for CVE was 28% in men, and 20% in women.

Discussion

In this prospective study we found no significant association between long working hours and incidence

Table 6. Relative risks (RR) of cardiovascular events (CVE) according to job strain categories by sex, in the treated hypertensive workers aged 40–65 yr follow-up study, 1994–2000, Japan

Job strain categories		No.	Cases ^a	RR ^b	Multivariate RR ^c
All:	Low strain	414	6	1.00	1.00
	Passive	785	14	1.06 (0.40–2.78)	1.16 (0.44–3.08)
	Active	275	13	2.94 (1.36–6.38)	2.89 (1.33–6.28)
	High strain	141	5	2.44 (0.87–6.85)	2.45 (0.87–6.93)
Men:	Low strain	148	2	1.00	1.00
	Passive	456	12	0.54 (0.12–2.41)	0.61 (0.14–2.73)
	Active	218	12	2.75 (1.22–6.21)	2.94 (1.29–6.73)
	High strain	86	3	1.75 (0.49–6.29)	1.86 (0.51–6.75)
Women:	Low strain	266	4	1.00	1.00
	Passive	329	2	2.84 (0.51–15.72)	3.15 (0.55–18.05)
	Active	57	1	3.16 (0.28–35.02)	3.97 (0.34–46.88)
	High strain	55	2	6.66 (0.93–47.70)	9.05 (1.17–69.86)

^aIncident cases of CVE; ^bAge- and sex-adjusted RR for all participants and age-adjusted for men or women;

^cAdjusted for age, sex (if for all participants), mean SBP, BMI, total cholesterol, HDL-cholesterol, proteinuria, family history of stroke, left ventricular hypertrophy, ischemic ST-T change, atrial fibrillation and current smoking; 95% CI are shown in parentheses.

of CVE. On the other hand, job strain categories were significantly associated with an increased risk of CVE in treated hypertensive Japanese workers.

Although our previous study⁴⁾ showed that working more than 11 h a day increased risk of CVE (RR=2.7; 95% CI: 1.1–6.2) in treated hypertensive males in their fifth decade in the 1980s, neither working more than 10 h nor working more than 11 h (data not shown) were risks for CVE among men in the present study. The first reason may be the large change in the work environment after the collapse of the bubble economy in Japan. Japanese workers' annual working hours dropped dramatically from 2,100 h in the 1980s to 1,900 h after 1994. There was a large number of bankruptcies and increased unemployment. Reflecting the recession, workers suffered from both days with no work to do and days with urgent work due to short deadlines. One may conjecture that in such a work environment job stress can no longer be assessed by working hours only.

A second reason may be that risk was calculated without correction for work content. Recently, contradictory results have appeared in the relationship between long working hours and blood pressure in Japan. Hayashi *et al.* showed that among male white collar workers 24-h average blood pressure of a group working overtime was higher than that of a control group in a study in which the scores of subjective fatigue symptoms were higher in the overtime group than in the controls¹⁰⁾. Conversely, Nakanishi *et al.* showed that long working hours are negatively associated with the risk for hypertension in a prospective study of Japanese male

white collar workers in a major company¹¹⁾, in which professionals such as architects or research workers worked more overtime than clerks, and subjective symptoms such as headache, loss of appetite and general fatigue did not differ significantly among the groups.

These conflicting results in our two studies and in the two studies mentioned above suggest that further research is needed to investigate the association between long working hours and incidence of CVE with special attention being paid to differences in work environment and work content.

Job strain categories, the other category of work-related stress, were investigated with a simple method devised with reference to Karasek's model, and both active jobs and high strain jobs were found to be significant risk factors for CVE.

That is, high job demands was a significant risk factor for CVE in all participants, and increased the risk of CVE in both sexes. On the other hand, low job control did not increase the risk. We found that low control has a different effect on CVE between the sexes. That is, low control in women tended to increase the risk, but low control in men tended to decrease the risk. As a result, low control in all participants did not increase the risk.

In four strain categories, active jobs were significant risk factors for CVE in all participants (both RR and multivariate RR were significant). High strain in all participants, which did not have significant discriminatory power, also increased the risk of CVE. In women high strain was a significant risk factor for CVE. These data are totally in agreement with Karasek's job strain model.

Our results are similar to those from a few other prospective investigations that have looked at the relationship between Karasek's model and cardiovascular disease.

In a prospective cohort study (Whitehall II study), job strain, high job demands and, to some extent, low decision latitude were shown to be associated with an increased risk of coronary heart disease among British civil servants¹²⁾. In that study, an active job was not associated with risk of coronary heart disease.

In a 25-yr follow-up study of 812 office workers in Finland, employees with a high job strain had a 2.2-fold cardiovascular mortality risk compared with their colleagues with low job strain¹³⁾. In that study, high demands were not associated with risk of cardiovascular mortality, although low control and high strain increased the risk. Data on active jobs was not shown. Thus, the evidence in these studies for an association between job strain categories and cardiovascular disease was not totally consistent.

In our study, active jobs, as well as high strain, were risks for CVE. The active jobs group in both men and women had the highest proportions of people with long working hours in job strain groups. An additional effect of long working hours on the risk from active jobs may be considered.

In Japan, Iso *et al.* showed prospectively that perceived mental stress was associated with increased mortality from stroke for women and with coronary heart disease for men and women, although a relation between job stress and mortality was not shown¹⁴⁾.

Previous studies produced different results on the relation between job strain and CVE incidence in women, and some reports have shown no relation between job strain and incidence of CVE in women¹⁵⁾. One of the reasons for the null findings in women may be, as the authors said¹⁵⁾, that the study had insufficient variability across categories of job conditions for a single occupation (registered nurses), unlike our study population that included various occupations.

In our study, high job strain in women was a significant risk factor for CVE. Compared with men, the proportion with low job control was 1.8 times higher in women, and the RR was also higher than in men. These findings suggest the features of working women in Japan. Since the working rate for women is rising in Japan, further research will be needed to examine the relation between job strain and the incidence of CVE in women.

The results for attributable fraction of high job demands (i.e. active jobs and high strain jobs) for CVE showed that in the high job demands group, 54% of events in men and 62% of events in women were excessive as a result of high job demands. The results for the population attributable fraction of high job demands for CVE showed that, in workers treated for hypertension overall, 28% of

events in men and 20% of events in women were excessive because of high job demands. The large distribution indicates that a highly demanding job is a serious risk for hypertension.

Our cohort was not general workers but treated hypertensives. Stress is clearly related to hypertension, and there is considerable evidence that job stress is related to the onset of hypertension and cardiovascular impairments¹⁶⁻¹⁸⁾. To our knowledge, no prospective study has examined the association between job strain and incidence of CVE in treated hypertensive workers.

From our data one may conjecture that job strain exacerbates hypertension in treated hypertensives, and causes damage to the cardiovascular system. Since hypertensives are also a high risk group in which CVEs tend to occur, job strain is likely to be a stronger risk for CVE than in normotensive persons.

This study has several limitations. First, the cohort was small with a small number of CVEs. The number of women in particular was small. The variability in such a small group may be one reason significant differences were not seen in some points.

Second, at the end of the follow-up period in 2000 the follow-up rate was 75%, which was insufficient. Cases of CVE may therefore have gone undetected, possibly leading to a bias that could have altered the results. The main reasons participants could not be followed were 1) the person in charge left his or her position and participants could not be followed, 2) participants moved to different areas, and 3) participants had an accident and were hospitalized in a different hospital. Reasons 1) and 2) are not likely to have affected the conclusions. Reason 3) may have decreased the number of recognized cases and diluted our results, but would not have been large enough to have changed our conclusions. Furthermore, there were no significant differences in the follow-up period of the long working hours group and all others (5.61 ± 1.54 yr versus 5.66 ± 1.50 yr), or in the job strain groups. In both the analyzed database group and excluded cases that were not followed at all, the proportions of those with long working hours and of those with job demands were also similar: 390/1,615 (24%) versus 11/44 (25%) and 416/1,615 (26%) versus 14/44 (32%), respectively. These data showed the practice of follow-up influenced the results only a little.

Third, job stress was assessed with a simple method. Job strain in this study was assessed using a simple 3-question self-reported questionnaire. Low job control was defined by only one question. The questionnaire was prepared with reference to Karasek's model, but differed from the standard questionnaire in that model. Even though the questionnaire was simple the results were in agreement with Karasek's model.

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