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Field Report

Low job control is associated with higher diastolic blood pressure in men with mildly elevated blood pressure: the Rosai Karoshi study

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Abstract: Job strain is a risk factor for hypertension, but it is not fully understood if components of job strain, or job demand or job control *per se* could be related to blood pressure (BP), and if so, whether the relationship differs between normotension and mildly elevated BP. We examined resting BP, and job stress components in 113 Japanese male hospital clerks (38.1 ± 4.4 yr). Subjects were classified into normotensive (NT) (<130/85 mmHg, n=83) and mildly elevated BP (ME) (≥130/85 mmHg) groups. Diastolic BP (DBP) showed a significant interaction between group and job control level (p=0.013). Subjects with low job control demonstrated higher DBP than those with high job control (89.1 ± 2.1 vs. 82.3 ± 2.3 mmHg, p=0.042) in ME group even after adjustments for covariates while DBP did not differ between low and high job control subjects in NT group. Systolic BP (SBP) did not differ between high and low job control subjects in both groups. Neither SBP nor DBP differed between high and low demand groups in either group. Among job strain components, job control may be independently related to BP in Japanese male workers with mildly elevated BP.

Key words: Job control, Job strain, Blood pressure, Men, Hypertension

Introduction

Work stress has been reported to increase the risk of coronary heart disease[1)] and stroke[2)]. In Japan, cardiovascular and cerebrovascular diseases resulting from overwork are known as *Karoshi*. In 2002, the Japanese government launched a comprehensive program to prevent *Karoshi*[3)]. However, the number of individuals suffering from related vascular diseases remains high, and this remains a major social problem in Japan[4)]. More than 95% of *Karoshi* cases occur in men[5)], and hypertension is the most common underlying disease. Thus, hypertensive men who do not receive adequate treatment seem to be at high risk for *Karoshi*.

Work stress is closely related to blood pressure (BP), as demonstrated using ambulatory BP monitoring to show that BP is higher at work sites[6, 7)], clinic[8)], home, and sleep[9)] in individuals reporting high job strain (combination of high job demand and low job control[10)]). In studies conducted in Western societies, some reports have shown that low job control, but not high job strain, is positively associated with high BP or hypertension risk in male workers[11, 12)], suggesting that the component of job strain *per se*, has a pathogenic effect on BP regulation.

In Japan, several cross-sectional studies have shown that high job strain, as opposed to middle or low strain is associated with increased BP or greater risk of hyperten-

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sion in male workers[13, 14]. It remains unclear if components of job strain could be independently related to BP in Japanese workers. Moreover, the influence of work stress on BP could differ between normotension and hypertension, as the BP response to stress is known to increase with increases in BP levels[15, 16].

The Job Content Questionnaire (JCQ)[17] is a commonly used measure to assess job strain and its components. In this study, we used an original questionnaire developed by the Ministry of Health, Labour and Welfare in Japan[18], which is now recommended for routine use among overworked employees in the workplace (Appendix 1). In this questionnaire, job demand is assessed by 7 items and job control is assessed by 3 items examining decision authority. On the other hand, job demand is assessed by 5 items and job control is assessed by the combination of 3 items for decision authority and 6 items for skill utilization in JCQ. There were 3 reversed scores in job demand and 2 reversed scores (one for decision authority and one for skill utilization) in job control of JCQ, while no reversed score was included in our original questionnaire. Moreover, there is a subtle difference in nuance between the sentences asking the same items. Therefore the two questionnaires are different both qualitatively and quantitatively. By means of this new questionnaire, we examined if the components of job strain are related to BP, and if so, whether the relationship differs between normotensive individuals and those with mild BP elevation.

Methods

Subjects

This multi-center study, named the Rosai Karoshi Study, examined the temporal relationship between work stress and cardiovascular risk among Japanese male workers. Nine Rosai hospitals (located in Iwamizawa, Sendai, Kamisu, Tokyo, Kawasaki, Nagoya, Sakai, Amagasaki, and Kure cities) agreed to participate in this study. Figure 1 shows the flow of the study subjects. Of 404 all hospital clerks, female workers were first excluded. Then, we excluded part time employees and manager class to minimize the influence of occupational class. Moreover, we focused on men aged from 30 to 49, who had got used to overall works in the hospital such as general affairs, account affairs, medical affairs, and manage planning affairs. Ultimately, 115 men were eligible for the study and the 114 agreed to participate in the study. This study was approved by the ethics committee of Japan Labour, Health and Welfare Organization. All subjects gave written informed consent.

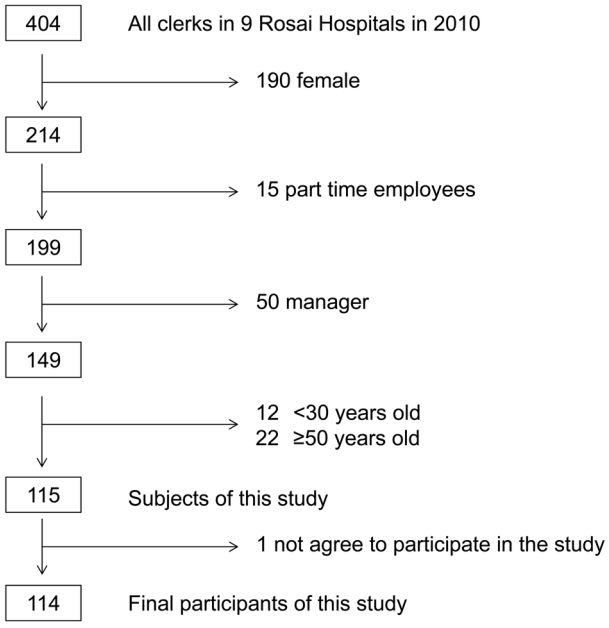

Fig. 1. Flow of the participants selection.

Protocol

Basic questionnaire

All subjects were asked to fill out a basic questionnaire regarding their family medical history, present illnesses, alcohol intake, smoking, and dietary and exercise habits. Daily alcohol intake was semiquantified as units of Japanese sake (one unit of Japanese sake contains 21.6 ml of ethanol), and the average daily alcohol intake (g) was calculated. Heavy drinkers were defined as those who ingested more than 12.6 ml of ethanol daily. Individuals were considered to exercise regularly if they participated in ≥30 min of moderate-intensity exercise at least twice per week, according to the Japanese Exercise Guideline 2006[19]. Subjects with currently treated hypertension (n=6), diabetes (n=1), dyslipidemia (n=1), and hypertension with diabetes (n=1) were included, as their conditions were well-controlled. They were requested not to change their medications throughout the study.

Assessment of work stress

In 2005, a revised Industrial Safety and Health Law legislated that employees who had worked overtime exceeding a certain limit of hours and reported fatigue must be interviewed by a healthcare physician[20]. Before the interview, work stresses such as job demand, job control, and work site social support are examined with an original

questionnaire developed by the Ministry of Health, Labour and Welfare[18]. Questions for job demand, job control, and work site social support consisted of seven, three, and six items, respectively. In this study, we used the data on job demand and job control (Appendix 1). All questions were coded on a 4-point scale (4=agree, 3=almost agree, 2=somewhat disagree, 1=disagree), with scores ranging from 7 to 28 for job demand (higher score means higher stress) and 3 to 12 for job control (lower score means higher stress). Thus the combination of high job demand scores and low job control scores indicates job strain condition. Cronbach's alpha coefficients for the scales in this study were 0.80 and 0.85, respectively. Pearson's correlation coefficients between job demand and control was −0.271 (p=0.004). Monthly overtime hours were calculated by examining pay slips. Overtime hours were defined as having worked overtime in three consecutive months between June and August.

Blood pressure measurements

After obtaining anthropometric measurements, systolic and diastolic BP (SBP and DBP), pulse pressure, heart rate (HR), and brachial-ankle pulse wave velocity (baPWV), a measure of systemic arterial stiffness, were measured by trained clinical laboratory technicians. Measurements were taken after at least 10 min of supine rest, using the AT-form PWV/ABI (Colin, Komaki, Japan). Details of this apparatus and its use have been described elsewhere[21, 22]. BP data consisted of mean values of 10-s readings. In this study, right brachial BP and right baPWV were used as representative values because the values obtained were similar for both the right and left sides in this sample. No subjects demonstrated an ankle-brachial index ≤0.9.

Biochemical measurements

Subjects visited each center after fasting overnight and laid in a supine position in a quiet room. Room temperature was held constant at 27°C. An indwelling catheter was inserted into the antecubital vein. After 30 min of rest, blood samples were obtained with minimal venous occlusion. Samples were immediately put on ice and centrifuged at 3,000 g for 5 min at 4°C. After separation, plasma was stored at −80°C until assayed. Standard assays were used to measure fasting glucose, hemoglobin A1c, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, creatinine, and uric acid levels. Plasma renin activity and aldosterone concentrations were measured using commercially available radioimmunoassay kits (TFB, Tokyo, Japan). Plasma adrenaline and noradrenaline concentrations were measured by high-performance liquid chromatography (TOSOH, Tokyo, Japan). Plasma adrenocorticotropic hormone levels were measured using an electro-chemiluminescence immunoassay kit (Roche Diagnostics, Tokyo, Japan), and plasma cortisol levels were measured using a radioimmunoassay kit (Beckman Coulter, Tokyo, Japan). Estimated glomerular filtration rate (eGFR) was calculated using the formula for men provided by the Japanese Society of Nephrology: eGFR (ml/min/1.73 m^2) = 194 × creatinine$^{-1.094}$ × age$^{-0.287}$.

To minimize seasonal influence on BP and biochemical parameters, the study was performed at the end of August and beginning of September 2010.

Statistical analysis

One subject was excluded from the analysis due to missing data, leaving 113 subjects. They were classified as mildly elevated BP (ME; SBP ≥130 mmHg or DBP ≥85 mmHg) and normotensive (NT; SBP <130 mmHg and DBP <85 mmHg) group. No subjects had SBP or DBP ≥160 mmHg or ≥100 mmHg, respectively. Each group was dichotomized by the median value of work stress scores, which was 19 for job demand and 9 for job control. Job strain was calculated using the median split of job demand and job control as the cutoff. Individuals who had job demand scores ≥19 and job control scores <9 were classified as the high job strain group and the remaining subjects were classified as the non-job strain group. Skewed data were logarithmically transformed.

Group comparisons were made using Student's t-test or the χ^2 test. Relationship between blood pressure and stress was analyzed by two-way analysis of variance (ANOVA) with work stress level (low vs. high) and group factors (NT vs. ME). Analysis of covariance (ANCOVA) was used to evaluate the effect of stress level independent of traditional risk factors such as age, body mass index (BMI), and HR. JMP (version 9.0.2 for Windows; SAS Institute, Cary, NC, USA) was used for statistical analysis. Statistical significance was defined as p<0.05.

Results

Table 1 shows the clinical characteristics of the NT and ME groups. BMI, baPWV, and HR were higher in the ME group than in the NT group, although age did not differ between groups. There were no significant differences in lifestyle characteristics, family history of hypertension, and frequency of receiving antihypertensive, antidiabetic, and antidyslipidemic medications between groups. Neither

Table 1. Clinical characteristics of the NT and ME groups

	NT (n=83)	ME (n=30)	*p*
Age (yr)	37.7 ± 4.2	39.2 ± 4.7	0.101
BMI (kg/m^2)	23.3 ± 2.8	25.4 ± 4.3	0.003
SBP (mmHg)	116.1 ± 6.9	138.6 ± 9.2	<0.001
DBP (mmHg)	69.1 ± 6.5	85.9 ± 9.8	<0.001
PP (mmHg)	46.9 ± 5.6	52.7 ± 7.3	<0.001
HR (bpm)	65.1 ± 9.0	72.5 ± 10.5	<0.001
BaPWV (cm/s)	1,231.8 ± 112.3	1,392.2 ± 163.0	<0.001
Current smoker (%)	25.3	23.3	0.830
Heavy drinker (%)	17.1	23.3	0.585
Regular exercise habits (%)	23.1	22.2	1.000
Family history of hypertension (%)	36.6	34.5	1.000
Hypertension (%)	3.6	10.0	0.190
Diabetes (%)	1.2	3.0	0.462
Dyslipidemia (%)	1.2	0.0	1.000
High job strain (%)	31.3	20.0	0.344
Job demand score	17.9 ± 3.7	18.3 ± 4.0	0.623
Job control score	7.8 ± 2.2	7.9 ± 2.2	0.792

NT: normotensive; ME: mildly elevated blood pressure; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; PP: pulse pressure; HR: heart rate; baPWV: brachial-ankle pulse wave velocity. Values are means ± SD.

work stress scores nor frequency of high job strain differed between groups.

DBP showed a significant interaction between job control level and groups [F (1, 109)=6.3, p=0.013] (Fig. 2a). DBP was significantly higher in subjects with low job control than in those with high job control in ME group even after adjustments for age, BMI and HR (89.1 ± 2.1 vs. 82.3 ± 2.3 mmHg, p=0.042) while it did not differ between low and high job control groups in NT group (69.7 ± 0.9 vs. 68.3 ± 1.0 mmHg, p=0.287). In SBP, there was no significant interaction between job control level and groups [F (1, 109)=2.0, p=0.156] (Fig. 2b). SBP were similar between subjects with low and high job control in both NT (116.7 ± 1.0 vs. 115.0 ± 1.1 mmHg, p=0.225) and ME (141.0 ± 2.1 vs. 135.9 ± 2.3 mmHg, p=0.114) groups. The interaction between job demand level and groups was not observed for both DBP and SBP [F (1, 109)=3.7, p=0.057) and F (1, 109)=3.2, p=0.078] (Fig. 2c and 2d). Both SBP and DBP did not differ between high and low job demand either in NT (116.2 ± 1.1 vs. 115.7 ± 1.0 mmHg, p=0.748 and 68.1 ± 1.0 vs. 69.8 ± 0.9 mmHg, p=0.219) or ME (140.9 ± 2.6 vs. 137.1 ± 2.1 mmHg, p=0.270 and 87.9 ± 2.7 vs. 84.6 ± 2.2 mmHg, p=0.360) groups.

When treated hypertensive subjects were excluded, an interaction between group and job control in DBP was attenuated [F (1, 102)=3.2, p=0.078] but DBP was still higher in low job control than in the high job control condition in ME group (87.9 ± 8.6 vs. 81.1 ± 7.7 mmHg, p=0.042).

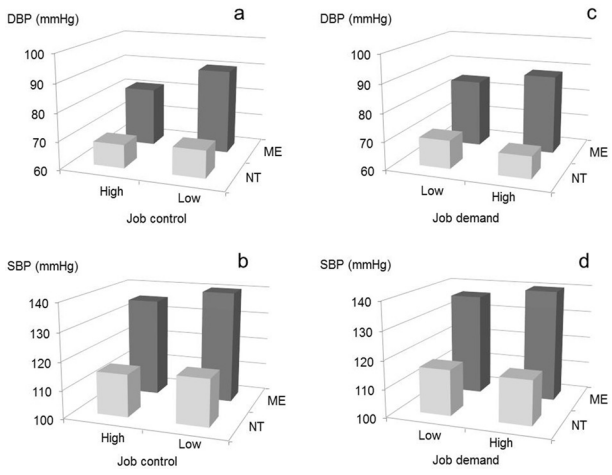

Fig. 2. Relationship between stress level and systolic and diastolic blood pressure (SBP and DBP, respectively) according to blood pressure category.

NT: normotensive group; ME: mildly elevated blood pressure group. There was a significant interaction between job control level (low vs. high) and group (NT vs. ME) in DBP, but not in SBP. There was no interaction between job demand and group either in SBP or DBP.

Table 2 compares the clinical data between high and

Table 2. Comparison of clinical data between high and low job control subjects among ME group

	High job control (n=14)	Low job control (n=16)	*p*
Age (yr)	37.9 ± 4.4	40.4 ± 4.8	0.147
BMI (kg/m^2)	25.5 ± 4.6	25.3 ± 4.2	0.886
PP (mmHg)	54.2 ± 8.5	51.3 ± 5.9	0.283
HR (bpm)	70.5 ± 9.4	74.3 ± 11.4	0.330
baPWV (cm/s)	1,339.9 ± 137.5	1,438.0 ± 173.6	0.101
LDL (mg/dl)	111.4 ± 38.0	106.6 ± 29.8	0.697
HDL (mg/dl)	48.1 ± 16.0	52.1 ± 10.0	0.414
FBS (mg/dl)	111.2 ± 25.6	101.3 ± 14.3	0.195
HbA1c (%)	5.5 ± 0.9	5.0 ± 0.4	0.065
Renin (ng/ml/h)	1.0 (0.3, 1.5)	1.0 (0.5, 1.6)	0.747
Aldosterone (pg/ml)	83.3 (57.4, 93.6)	57.7 (47.4, 101.4)	0.909
Cortisol (μg/dl)	14.6 ± 4.2	14.8 ± 5.4	0.387
ACTH (pg/ml)	23.4 ± 7.1	25.4 ± 11.6	0.560
Adrenaline (pg/ml)	39.4 (20.5, 51.8)	43.0 (28.0, 46.5)	0.645
Noradrenaline (pg/ml)	276.1 (164.0, 366.3)	245.0 (159.0, 279.8)	0.535
Creatinine (mg/dl)	0.78 ± 0.07	0.79 ± 0.08	0.708
Uric acid (mg/dl)	7.0 ± 1.5	6.6 ± 1.2	0.459
eGFR (ml/min/1.73 m^2)	91.0 ± 10.8	88.1 ± 11.2	0.487
Current smoker (%)	0.0	43.8	0.006
Heavy drinker (%)	14.3	31.3	0.399
Regular exercise habits (%)	23.1	21.4	1.000
Family history of hypertension (%)	28.6	40.0	0.700
Hypertension (%)	0.0	25.0	0.103
Diabetes (%)	7.1	0.0	0.467
Dyslipidemia (%)	0.0	0.0	–
Overtime (h)	113.6 ± 51.5	108.8 ± 63.5	0.822
Job demand score	18.2 ± 3.3	18.4 ± 4.6	0.882
Job control score	9.7 ± 1.1	6.4 ± 1.8	<0.001

ME: mildly elevated blood pressure; BMI: body mass index; PP: pulse pressure; HR: heart rate; baPWV: brachial-ankle pulse wave velocity; LDL: low-density lipoprotein cholesterol; HDL: high-density lipoprotein cholesterol; FBS: fasting blood sugar; HbA1c: hemoglobin A1c; eGFR: estimated glomerular filtration rate; ACTH: adrenocorticotropic hormone. Values are means ± SD or median (25th, 75th).

low job control subjects in the ME group. Current smokers were more prevalent in the low job control group than in the high job control group, while no other parameters differed between the two groups. DBP was still higher in the low job control group than in the high job control group even after adjustments for smoking status in addition to age, BMI and HR (80.4 ± 3.0 vs. 88.8 ± 2.1, p=0.030).

Both SBP and DBP showed significant interactions between job strain level and groups [F (1, 109)=10.4, p=0.002 and F (1, 109)=6.7, p=0.011]. In the ME group, high job strain group showed higher SBP than non-job strain group even after adjustments for age, BMI, and HR (147.1 ± 3.3 vs. 136.5 ± 1.6 mmHg, p=0.001). Although DBP was also higher in the high strain group, the effect did not reach a statistically significant level after adjustments for covariates (91.9 ± 3.8 vs. 84.5 ± 1.8 mmHg, p=0.100). Both SBP and DBP were similar between job strain and non-job strain groups in the NT group.

Discussion

This study examined the relationship between job strain components, or job demand and job control, and BP in Japanese male workers. We found a significant interaction between job control and groups suggesting that relationship between job control and BP differ between subjects

with normotension and those with mildly elevated BP. In subjects with mildly elevated BP, low job control was significantly associated with higher DBP, even after adjusting for age, BMI, HR, and smoking, while high job demand was not. Moreover, neither job control nor job demand was related to BP in normotensive subjects. These data suggest that low job control could increase BP in Japanese men with mild hypertension.

The mean DBP difference between high and low job control individuals in ME group was about 7 mmHg. An increase in DBP of 5 mmHg reportedly increases the mortality risks of coronary artery disease and stroke by about 28%[23] and 14.5%[24], respectively. The present results, therefore, suggest that low job control may increase the mortality risks of coronary artery disease and stroke by approximately 39.2% and 20.3%. EPOCH-JAPAN has reported that cardiovascular mortality risk continuously increases from optimal to high-normal BP category in middle-aged Japanese[25]. Thus, stress management may be an effective strategy for reducing cardiovascular disease risks in working men with mildly elevated BP.

In a meta-analysis of a US database of 12,555 men, lower job control was associated with significantly higher SBP, while job demand was not related to SBP[26]. Cesana *et al.*[27] demonstrated in men of the combined population of WHO-MONICA and PAMELA studies that, in the tertiles of job control dimension, SBP but not DBP progressively increased from high to low groups in both normotensive and hypertensive populations, although job demand was not related to either measure of BP. It has been reported that ambulatory mean SBP and DBP were 3.3 mmHg and 2.9 mmHg higher in low job control than in high job control group[11]. Thus, some cross-sectional studies conducted in Western countries also suggest that job control is related more to BP than job demand.

There are, however, some differences between those reports and ours. First, SBP was not related to the job control dimension in our study. This discrepancy may be explained by the difference in age. The mean age of our subjects with mildly elevated BP was 37.7, which is younger than previous reports. Thus, DBP may be more sensitive to work stress than SBP.

Second, significant relationship between job control and BP was not observed in the normotensive group in our results. The sample size of our NT group was 83, considerably smaller than that used in previous reports, reducing statistical power. Previous reports demonstrated that ambulatory BP is raised at work, but not at the clinic, in normotensive individuals who report high job strain[6]. In this study, BP was measured at resting supine condition. In other words, we cannot exclude the possibility that BP is raised at work even in normotensive subjects who reported low job control. To clarify this issue, a study using ambulatory BP monitoring is required.

In our study, none of the parameters of pituitary-adrenal, sympatho-adrenal, and renin-angiotensin-aldosterone systems differed between high and low job control individuals in the ME group although the two groups showed significant difference in DBP. Our data differ from the previous reports showing that higher work stress condition is associated with increased urinary norepinephrine[28] or higher salivary cortisol concentration[29] compared with low work stress condition. The small number of subjects might fail to detect the statistical difference but alternative explanation is an involvement of unkown mechanisms in BP evlavation in low job control condition. Further study is required to clarify the mechanisms and this should be a future issue.

High job strain ME subjects demonstrated higher SBP than did the remaining ME subjects after adjusting for age, BMI, and HR. BP did not differ between normotensive subjects with high job strain and the remaining normotensive individuals. Again, our data do not preclude the possibility that BP at work is raised in normotensive individuals with high job strain, as has been suggested by previous reports[6].

It has been shown that the influence of work stress on BP differs considerably across occupational classes, and is opposite between low and high occupational classes[30]. To minimize the influence of occupational class, we studied non-managerial male clerks with similar degree of work experience. In other words, we could exclude the possibility that socioeconomic status affected the results.

There were several limitations to this study. First, this study included 83 NT subjects and 30 ME subjects, and thus the ME group was considerably smaller. Nonetheless, a significant relationship between job control and BP was observed in ME group, supporting the positive results of this study. Second, we used resting supine BP, which would not reflect worksite BP. To further confirm our results, we need a study using ambulatory BP monitoring. Third, all subjects were non-managerial hospital clerks. Hence, it is unclear if the present results could apply to different classes of occupation. Fourth, this study was cross-sectional. To clarify whether low job control increases the risk of incident hypertension, a long-term follow-up study is required.

In conclusion, low job control was associated with

elevated DBP among mildly hypertensive Japanese men. Hypertension has been suggested to be an important risk factor for work-related cardiovascular events (i.e., *Karoshi*). To further clarify the pathogenic role of low job control in Japanese workers, a study focusing specifically on BP at work is required.

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Appendix 1. Questionnaire for overworked workers

Degree of job demand

1) I must do much amount of work
2) I can't finish my work within a given time
3) I must work very hard
4) My work needs considerable degree of concentration
5) I am engaged in a difficult task needed for high level of knowledge and skill
6) I must always consider my work while on duty
7) My work needs much amount of physical effort

Degree of job control

1) I can do my work with my own pace
2) I can decide order as well as way of work by myself
3) I can put my opinion on work plan