Relationship between Overtime Work Hours and Cardio-ankle Vascular Index (CAVI): A Cross-sectional Study in Japan

Koichi HATA1, Toru NAKAGAWA2, Masayuki HASEGAWA1, Hiroko KITAMURA1, Takeshi HAYASHI2 and Akira OGAMI1

1Department of Work Systems and Health, Institute of Industrial Ecological Science, University of Occupational and Environmental Health, Japan and 2Hitachi Health Care Center, Hitachi Ltd., Japan

Abstract: Relationship between Overtime Work Hours and Cardio-ankle Vascular Index (CAVI): A Cross-sectional Study in Japan: Koichi Hata, et al. Department of Work Systems and Health, Institute of Industrial Ecological Science, University of Occupational and Environmental Health, Japan—Objectives: The purpose of this research was to evaluate the relationship between overtime work hours and CAVI, a new index of arterial stiffness. Methods: We measured CAVI of Japanese workers (3,862 men) aged 26 to 59 years. Simultaneously, we obtained information on their monthly overtime work hours for the past few months using a self-administered questionnaire, with responses divided into five groups: <45, ≥45 and <60, ≥60 and <80, ≥80 and <100 and ≥100 hours/month. We calculated the odds ratios of CAVI≥9.0 for each group of overtime work hours. Results: In the full sample, there was no significant association between the average CAVI and overtime work hours. Taking <45 overtime hours/month as the reference category, the odds ratios of CAVI≥9.0 were as follows: OR=1.11, 95% CI=0.73–1.69 (≥45 and <60 hours/month); OR=0.92, 95% CI=0.48–1.76 (≥60 and <80 hours/month); OR=1.50, 95% CI=0.50–4.49 (≥80 and <100 hours/month); and OR=2.65, 95% CI=0.82–8.54 (≥100 hours/month). However, for workers in their 50 s, the odds ratio of CAVI≥9.0 was significantly higher among subjects with ≥100 hours/month than among those with <45 hours/month (OR=4.26, 95% CI=1.2–15.1) Conclusions: The present study suggests that CAVI is more likely to be 9.0 or higher in workers in their 50 s when they work ≥100 hours of overtime per month. (J Occup Health 2014; 56: 271–278)

Key words: Arterial stiffness, Atherosclerosis, Cardio-ankle vascular index, Overtime work

Excessive overtime work is observed all over the world and has been a serious social problem in East Asia, including Japan, for quite some time. An excessive workload due to long working hours would likely elevate the risk of hypertension, mental disorders, decreased cognitive function, cerebro-cardiovascular diseases, sleep disorders and injury1−8). In the 1970 s, deaths caused by cerebro-cardiovascular diseases due to overtime work in Japan were specifically reported as Karoshi (death from overwork), attracting a great deal of attention at the time9). Currently in Japan, it is suggested that an excess workload (mainly due to long working hours) can cause accelerated progression of arteriosclerosis beyond its natural course and lead to work-related cerebro-cardiovascular diseases. For this reason, the government has encouraged companies to implement shorter working hours and to have occupational physicians or other health-care service providers routinely interview workers with long working hours.

Various indexes for arteriosclerosis have been developed, including intima-media thickness (IMT), vascular endothelial function and angiography. Among the various methods, the brachial-ankle pulse wave velocity (baPWV) is frequently used to measure early arterial stiffness in healthy people because of its non-invasiveness and convenience. However, baPWV is highly dependent on blood pressure, and its values vary greatly depending on blood pressure at the time of measurement, making it sometimes difficult to evaluate arterial stiffness with baPWV10, 11). A new arterial stiffness measurement, the cardio-ankle vascular index (CAVI), was recently developed to compensate for the blood pressure dependence of baPWV. CAVI is an index reflecting the stiffness of the aorta, femoral artery and tibial artery and is calcu-
lated based on carotid echography. It is thought that CAVI becomes higher with the progression of arteriosclerosis. CAVI is characterized by relatively lower blood pressure dependence and a decreased influence of blood pressure on the obtained measurement value\(^{12}\). Some studies have reported that CAVI has a high correlation with baPWV and IMT, is better than baPWV as an index of arterial stiffness and shows an association with anatomical aspects of coronary arteriosclerosis\(^{11,13−15}\). Like baPWV, CAVI is a noninvasive and convenient measurement, and it is likely easy to use at medical checkups for healthy people. In the present study, we examined the association between overtime work hours and CAVI to determine whether CAVI could be used for early detection of arteriosclerosis, a condition premorbid to the onset of work-related cardiovascular diseases.

**Subjects and Methods**

**Subjects**

The subjects were 3,862 male workers aged 26 to 59 years. They worked in an engineering and electronics factory or for affiliated companies. In these companies, there were few female workers, and there were even fewer female workers who worked overtime. For this reason, we focused only on men in this study. The workers included in the study included 1,129 design workers, 448 inspection workers, 941 manufacturing workers, 167 research and development workers, 237 engineering workers, 475 administrative workers, and 465 workers of other types. The subjects enrolled voluntarily in the study, and their CAVIs were measured from April 2010 until March 2011 at annual medical checkups prescribed by the Industrial Safety and Health Law of Japan. When CAVI was measured, the ankle-brachial index (ABI) was simultaneously measured to examine the possibility of any peripheral vascular disorder. Subjects who met the following criteria were excluded because of the possibility of imprecise CAVI measurement: subjects who (1) were measured after a meal, (2) had abnormal electrocardiogram such as arrhythmia, (3) received unilateral measurement of CAVI, (4) had a history of abdominal or thoracic surgery, (5) had an ABI of less than 0.9 or (6) were receiving dialysis\(^{12}\). There were 4 subjects for which CAVI had been measured after a meal, 3 subjects with abnormal electrocardiograms, 3 subjects with ABIs of less than 0.9, 2 subjects with a history of abdominal or thoracic surgery, 5 subjects who had received unilateral measurements and 1 subject who was receiving dialysis. The final sample for this study included 3,844 male workers. Informed consent was obtained from the eligible subjects for use of their data for academic purposes. This study was approved by the Ethics Committee of the University of Occupational and Environmental Health, Japan.

**CAVI measurement**

CAVI was measured by a skilled technician using a VaSera VS-1000 (Fukuda Denshi, Tokyo, Japan). The subjects lay on their back with their head on a median line. Cuffs were wound bilaterally around the upper arms and the ankles. Electrocardiogram electrodes were placed on both wrists. A microphone was placed on the sternum to monitor the heartbeat. After these preparations, CAVI was measured during bed rest. It was calculated by using the following formula:

\[
\text{CAVI} = 2\rho \times \ln(\frac{P_s}{P_d}) \times \frac{\text{PWV}^2}{\Delta P},
\]

where \(\rho\) is the blood density, \(P_s\) is the systolic pressure, \(P_d\) is the diastolic pressure, \(\text{PWV}\) is the measured pulse wave velocity from the aortic valve to the ankle, and \(\Delta P\) is the difference between the systolic pressure and diastolic pressure.

The CAVI measurement process followed a previously reported procedure\(^{12}\). The measurements and calculations were automatically performed by the VaSera VS-1000 after setting them up. The present study used the average of the bilateral CAVI. Based on the results of a previous study, in which a half of the subjects with CAVI \(\geq 9.0\) showed coronary arteriosclerosis, we used CAVI=9.0 as the cutoff value for high arterial stiffness\(^{13}\).

**Laboratory data (blood test)**

In Japan, several examinations are required at periodical health checkups, based on the Industrial Safety and Health Law. The following results obtained from the periodical health checkups of individual subjects were used for the present study: glycated hemoglobin (HbA1c), blood glucose, total cholesterol, LDL-cholesterol (LDL-C), HDL-cholesterol (HDL-C) and triglycerides. These data were measured by Lavolute 7 and LABOSPECT 800 (Hitachi High-Technologies Corporation, Tokyo, Japan). Fasting blood samples were taken.

**Body weight and height**

The body weight and height of each subject were obtained by an automatic measurement instrument (Tanita BF-220, Tokyo, Japan) with the subject wearing a very light hospital gown. Body mass index (BMI) was calculated by dividing the body weight (Kg) by the squared height (m). BMI was classified into the following categories based on the body mass standard provided by the WHO: underweight (BMI<18.5), normal weight (BMI=18.5 and <25), overweight, (BMI ≥25 and <30) and obese (BMI≥30).
Blood pressure

Blood pressure was measured by a skilled nurse while the subjects were in a seated position after they had rested sufficiently. Pulse was measured simultaneously. Blood pressure was remeasured in cases where the systolic pressure was ≥140 mmHg or the diastolic pressure was ≥90 mmHg. The ES-H55 Blood Pressure Monitor (Terumo, Tokyo, Japan) was used to measure blood pressure.

Questionnaire

A self-administered questionnaire was used to obtain information about the following lifestyle-related items: smoking habits (nonsmoker, ex-smoker, or smoker); clinical history of diabetes, hypertension or hyperlipidemia; average weekly alcohol consumption; routine exercise; and average daily sleeping hours. Average weekly alcohol consumption was measured in units of gou. A gou, a traditional Japanese unit of alcohol consumption, is equivalent to 23 g of ethanol. The subjects were asked to choose one of the following categories for daily sleeping hours: <5 hours, ≥5 and <6 hours, ≥6 and <7 hours and ≥7 hours. Information on the subjects’ working hours was also obtained from the self-administered questionnaires. The subjects were asked to choose between five categories for their average overtime work hours in the past 2 to 3 months: <45 hours/month (below 45 hours), ≥45 and <60 hours/month (45 to 60 hours), ≥60 and <80 hours/month (60 to 80 hours), ≥80 and <100 hours/month (80 to 100 hours), and ≥100 hours/month (100 hours or more).

Statistical analysis

CAVI was compared among the 5 overtime work hours groups based on their answers. Because CAVI is known to be age dependent, the results were simultaneously compared by age-adjusted analysis of covariance. The odds ratio for each overtime work hours group was calculated by logistic regression analysis predicting high arterial stiffness (CAVI≥9.0). The following covariates were used because of their influence on CAVI: smoking habits (smoker, ex-smoker or nonsmoker), hypertension, dyslipidemia, diabetes, WHO body mass standard (underweight, normal weight, overweight, or obese), age, average amount of weekly alcohol consumption and routine exercise.

Hypertension was defined as systolic pressure ≥140 mmHg, diastolic pressure ≥90 mmHg or receipt of medical treatment for hypertension. Diabetes was defined as HbA1c ≥6.5%, fasting blood glucose ≥126 mg/dl or receipt of medical treatment for diabetes. Dyslipidemia was defined as triglycerides ≥150 mg/dl, HDL-C ≤40 mg/dl or receipt of medical treatment for dyslipidemia.

We then divided the participants into three age groups: 30 s, 40 s, and 50 s. We calculated the odds ratio for each overtime work hours group. To determine the correlation with sleeping hours, a cross tabulation was constructed based on “the average overtime work hours in the past 2 to 3 months” and “the average daily sleeping hours”.

Results

Characteristics of the study population

The characteristics of the subjects are shown in Table 1. The answers to the questionnaires, which were obtained from all 3,844 subjects, revealed that there were 2,384 subjects with below 45 hours of overtime, 832 with 45 to 60 hours of overtime, 416 with 60 to 80 hours of overtime, 140 with 80 to 100 hours of overtime and 72 with 100 hours or more hours of overtime in the past 2 to 3 months. The average age for each group was as follows: 49.5 years for those with below 45 hours of overtime, 47.4 years for those with 45 to 60 hours of overtime, 46.5 years for those with 60 to 80 hours of overtime, 45.9 years for those with 80 to 100 hours of overtime, and 45.4 years for those with 100 hours or more of overtime. Those with below 45 hours of overtime were significantly older than the other groups. There were no significant differences in BMI, HDLC, triglycerides, LDLC, total cholesterol, systolic pressure, diastolic pressure, fasting blood glucose or HbA1c between the overtime work hours categories. The smoking rate was slightly higher among those with 100 hours or more of overtime (40.3%) than for the other groups, although this difference was not significant. There was also no significant difference in alcohol consumption between these groups.

Overtime work hours and CAVI

Figure 1 indicates the average CAVI for each overtime work hours group: 7.62 ± 0.82 for those with below 45 hours of overtime, 7.50 ± 0.80 for those with 45 to 60 hours of overtime, 7.44 ± 0.75 for those with 60 to 80 hours of overtime, 7.41 ± 0.80 for those with 60 to 80 hours of overtime, and 7.36 ± 0.86 for those with 100 hours or more of overtime. The average CAVI was significantly higher for those with below 45 hours of overtime than for those with 45 to 60 hours of overtime, 60 to 80 hours of overtime, and 80 to 100 hours of overtime. However, there was no significant difference between those with below 45 hours and those with 100 hours or more of overtime. The age-adjusted CAVI of each overtime work-hours group was as follows: 7.56 ± 0.82 for those with below 45 hours of overtime, 7.56 ± 0.80 for those with
45 to 60 hours of overtime, 7.56 ± 0.75 for those with 60 to 80 hours of overtime, 7.57 ± 0.80 for those with 80 to 100 hours of overtime and 7.55 ± 0.86 for those with 100 hours or more of overtime. There was no significant difference among the groups, but the difference between groups was reduced compared with the pre-adjustment calculations (Fig. 2).

Overtime work hours and CAVI≥9.0
The odds ratio of CAVI≥9.0 (vs. CAVI<9) was predicted using logistic regression analysis (Table 2). With the subjects having below 45 hours of overtime used as the reference category, the odds ratios of CAVI≥9.0 were as follows: 1.11 (95%CI 0.73–1.69) for 45 to 60 hours of overtime, 0.92 (0.48–1.76) for 60 to 80 hours of overtime, 1.50 (0.50–4.49) for 60 to 80 hours of overtime and 2.65 (0.82–8.54) for 100 hours or more of overtime. None of these effects were significant. Significant differences were found in the age, overweight, obesity, diabetes, ex-smoker, smoker and pulse rates. When the model was estimated separately for the three age groups, the overtime work hours categories had no significant effect on CAVI≥9.0.
on having a CAVI≥9 for workers in their 30 s or 40 s. However, when the same analysis was performed with only workers in their 50 s, using the group with below 45 hours of overtime as the reference category, the odds ratio of CAVI≥9.0 was 4.26 (1.2−15.1) for those having 100 hours or more of overtime (Table 3).

Sleeping hours, overtime work hours and CAVI

Table 4 shows a summary of the associations between sleeping hours and overtime work hours. In the group with below 45 hours of overtime, 4.9% answered that their sleeping hours were <5 hours, whereas in the group with 100 hours or more of overtime, 37.5% answered that their sleeping hours were <5 hours. When overtime work hours were higher, sleeping hours were lower. Logistic regression analysis predicting CAVI≥9 with sleeping hours included in the model instead of the overtime work hours revealed no significant effect of the sleeping hours groups, but the odds ratios had a tendency to be larger for the groups with fewer sleeping hours (Data not shown).

Table 2. Odds ratios of the subjects with CAVI≥9.0 (for all subjects)

<table>
<thead>
<tr>
<th>Overtime work hours/month</th>
<th>Odds ratio</th>
<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Below 45 hours</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>45 to 60 hours</td>
<td>1.11</td>
<td>0.73−1.69</td>
</tr>
<tr>
<td>60 to 80 hours</td>
<td>0.92</td>
<td>0.48−1.76</td>
</tr>
<tr>
<td>80 to 100 hours</td>
<td>1.50</td>
<td>0.50−4.49</td>
</tr>
<tr>
<td>100 hours or more</td>
<td>2.65</td>
<td>0.82−8.54</td>
</tr>
<tr>
<td>Routine exercise</td>
<td>1.04</td>
<td>0.75−1.44</td>
</tr>
<tr>
<td>Age (actual number)*</td>
<td>1.26</td>
<td>1.21−1.31</td>
</tr>
</tbody>
</table>

Body mass classification

- Normal
- Underweight
- Overweight*
- Obese*
- Diabetes*

Smoking habits

- Nonsmoker
- Ex-smoker*
- Smoker*

Pulse rate (actual number)*

The odds ratios for each overtime work hours group were calculated by logistic regression analysis for subjects with CAVI≥9.0. The covariates were overtime work hours, routine exercise, age, body mass classification, diabetes, dyslipidemia, hypertension, smoking habits and pulse rate. CAVI=9.0 is cut-off value for arterial stiffness. *p<0.05.

Table 3. Odds ratios of the subjects with CAVI≥9.0 in their 50 s

<table>
<thead>
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<th>Overtime work hours/month</th>
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<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Below 45 hours</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>45 to 60 hours</td>
<td>1.13</td>
<td>0.72−1.76</td>
</tr>
<tr>
<td>60 to 80 hours</td>
<td>0.79</td>
<td>0.37−1.65</td>
</tr>
<tr>
<td>80 to 100 hours</td>
<td>1.33</td>
<td>0.37−4.73</td>
</tr>
<tr>
<td>100 hours or more*</td>
<td>4.26</td>
<td>1.20−15.08</td>
</tr>
<tr>
<td>Routine exercise</td>
<td>0.93</td>
<td>0.66−1.31</td>
</tr>
<tr>
<td>Age (actual number)*</td>
<td>1.29</td>
<td>1.21−1.38</td>
</tr>
</tbody>
</table>

Body mass classification

- Normal
- Underweight
- Overweight*
- Obese*
- Diabetes*

Smoking habits

- Nonsmoker
- Ex-smoker*
- Smoker*

Pulse rate (actual number)*

Odds ratios were calculated using logistic regression analysis predicting CAVI≥9.0. The covariates were overtime work hours, routine exercise, age, body mass classification, diabetes, dyslipidemia, hypertension, smoking habits and pulse rate. *p<0.05.

Discussion

The Japanese Ministry of Health, Labour and Welfare stated that 9.2% of the workers in Japan worked 60 or more hours per week in 2010\(^22\). The present study observed that 5.5% of workers had 80 or more hours of overtime monthly (Table 1), which likely corresponds to weekly working hours of 60 or more. This percentage is lower than that in the report by the Japanese Ministry of Health, Labour and Welfare. This difference is probably the result of the subjects in the present study being workers at relatively large companies. The average age was highest among those with below 45 hours of overtime and lowest among those with 100 hours or more of overtime. A similar tendency was found in the Ministry of Health, Labour and Welfare in Japan research, which pointed out that the number of overtime work hours was greatest among workers in their 30 s.

The present study compared CAVI between different categories of overtime work hours, and the results in Fig. 1 show that CAVI for those with less than 45 hours of overtime was significantly higher than for those in the other groups. However, the significant difference disappeared after adjusting for age. It
seems that CAVI for those with less than 45 hours of overtime was high because of their age.

In the logistic analysis, there were no significant differences in the full sample, although the odds ratios tended to be higher when overtime work hours were higher (Table 2). Some studies on the association between working hours and cerebro-cardiovascular disease have found a higher frequency of these diseases with an increase in working hours. Thus, arterial stiffness is likely to worsen prior to the development of cerebro-cardiovascular diseases caused by overwork.

Table 3 shows a significant effect of overtime work hours on CAVI ≥9.0 for subjects in their 50s; the odds of CAVI ≥9.0 were significantly higher for the group with >100 hours of overtime monthly, compared with the same odds for those with <45 hours of overtime monthly. The results of the present study are likely to be reasonable considering that the number of people diagnosed with work-related cerebro-cardiovascular diseases in Japan is larger for those in their 50s. Although it should be noted that CAVI depends on age, our results suggest that measurement of arterial stiffness in Japanese workers in their 50s would be useful in helping to determine the onset of cerebro-cardiovascular diseases induced by overtime work.

Table 4 shows a significant effect of overtime work hours on CAVI ≥9.0 for subjects in their 50s; the odds of CAVI ≥9.0 were higher for the group with >100 hours of overtime monthly, compared with the same odds for those with <45 hours of overtime monthly. The results of the present study are likely to be reasonable considering that the number of people diagnosed with work-related cerebro-cardiovascular diseases in Japan is larger for those in their 50s. Although it should be noted that CAVI depends on age, our results suggest that measurement of arterial stiffness in Japanese workers in their 50s would be useful in helping to determine the onset of cerebro-cardiovascular diseases induced by overtime work.

In this study, we used CAVI = 9.0 as the general cutoff value for arterial stiffness. Although the accepted cutoff value for CAVI is 9.0 at present, this might change in the future because of new findings. For this reason, we repeated our analysis using the cutoff value of CAVI = 8.0. The results of this analysis demonstrated that those with 100 hours or more of overtime had the highest odds of CAVI ≥8.0, but there was no significant difference between the overtime work hours groups (data not shown). CAVI might be high among workers with overtime work even if we use another cutoff value.

As shown in Table 2, CAVI was higher according to age, BMI, smoking habits, presence of diabetes, and pulse. These results are consistent with previous studies except for the finding concerning BMI. In the present study, BMI was negatively associated with CAVI ≥9.0. Specifically, the odds ratios of CAVI ≥9.0 for the overweight and obese groups were significantly lower than those for the normal weight group. The association between body weight and coronary artery diseases/arteriosclerosis is controversial. Some studies have reported that BMI is not associated with death from coronary artery disease; rather, being overweight lowers the rate of mortality due to coronary artery diseases. These studies have suggested the possibility that not obesity but rather an increase in body weight causes arteriosclerosis and that BMI cannot classify body fat percentage or lean body mass.

Because previous studies have reported that sleeping hours strongly affect the development of cerebro-cardiovascular diseases brought on by long working hours, the present study examined the association of sleeping hours with overtime work and high CAVI. As was found in previous studies, sleeping hours were shorter in the groups with overtime work. Although there was no significant difference, the odds ratio of CAVI ≥9.0 tended to be higher for the groups with fewer sleeping hours. A previous report showed that the incidence of coronary artery diseases in Japanese male workers is 3 times higher for those with less than 6 hours of sleep daily than for those with 7 to 7.9 hours of sleep daily. Another report has found that carotid-wall intima-media thickness was larger for those with <5 hours of sleep daily than for those with ≥7 hours of sleep daily, especially among older people. Thus, the effect of a decreased number of hours of sleep due to longer working hours on arterial stiffness may be stronger in older people.

There are some limitations to the present study. First, this was a cross-sectional study, so causal relationships could not be proven. Consequently, a long-term follow-up study is needed to determine whether overtime work causes an elevation in CAVI. Second,
the present study could not examine the psychological aspects of overtime work or occupational hazards. A previous work has reported that there is a clear association between the stress from work and coronary artery diseases\(^\text{30,31}\). However, cross-sectional studies in Japan using pulse wave measurement have not found any clear association between workplace stress and arterial stiffness\(^\text{30,31}\). Moreover, past studies have found a relationship between noise and cardiovascular disease. Further longitudinal studies that take psychological factors into account are needed to elucidate the association of workplace stress caused by long working hours with CAVI. Third, there was a problem with bias due to the healthy worker effect. In the present study, it is possible that the healthy workers could work longer hours than the unhealthy workers. Therefore, this study design probably underestimates the differences by working hours. Consequently, there might be a greater influence of overwork on CAVI.

Conclusions

We examined the association between overtime work hours and CAVI, a new arteriosclerosis index, in male Japanese workers and found no clear association in the full sample. However, among male workers in their 50s, CAVI was more likely to be 9.0 or higher in workers with ≥100 hours of overtime. CAVI can be useful for early detection of arteriosclerosis, especially in workers aged 50 or older who work overtime.

Acknowledgments: This work was supported by the Fukuda Foundation for Medical Technology.

References


