[Original]

Cohabiting with Smokers Is an Independent Factor for Worsening Arterial Stiffness Even in Smoking Workers

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Abstract: Preventing cardiovascular disease (CVD) is an urgent public health challenge. Although brachial-ankle pulse wave velocity (baPWV) can indicate the risk of arterial stiffness and CVD, findings regarding whether baPWV is associated with smoking are inconsistent. This study considered the influence of smoking on arteriosclerosis, specifically focusing on secondhand smoke (SHS), and aimed to construct a strategy for preventing the worsening of arteriosclerosis. We recruited 295 male employees from five companies who had smoking habits such as being smokers, living with smokers, and exposure to SHS outside the home. We measured body composition and hemodynamics, including blood pressure and baPWV, and found that baPWV had significant positive correlations with age, smoking index, alcohol consumption, body-fat percentage, blood pressure, and heart rate, and significant negative correlations with height, fat-free mass, and lower-limb muscle mass. Moreover, baPWV showed a significant adverse effect on participants who had metabolic syndrome (MetS) risk factors such as hypertension, dyslipidemia, and diabetes. Multiple regression analysis showed that baPWV had significant positive relationships with age, height, MetS risk factors, cohabitation with smokers, blood pressure, and heart rate, and a significant negative relationship with lower-limb muscle mass. The same results were obtained when adjusting for current smoking status, smoking index, cohabitation with smokers at birth, and frequency of exposure to SHS outside the home. Exposure to tobacco smoke due to cohabitation with smokers increased baPWV regardless of the person's smoking habits. Thus, to prevent an increase in baPWV in housemates and smokers, it is necessary for smokers to quit smoking.

Keywords: arterial stiffness, smoking, tobacco smoke, workers.

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Introduction

Cardiovascular disease (CVD) is one of the primary causes of global morbidity and mortality [1-3], and prevention of CVD is an urgent public-health issue worldwide, including in Japan. Arterial stiffness, which is a mechanical hardening of arterial walls, is an indicator of CVD risk [4, 5]. One of the means for assessing arterial stiffness is the brachial-ankle pulse wave velocity (baPWV) test, which involves simply attaching blood-pressure cuffs to the four extremities [6]. One can determine baPWV by measuring the length of time it takes for pulse waves to propagate across blood vessels; a previous meta-analysis of 12 cohort studies reported that the stiffer the walls of arteries, the faster the wave velocity [7-9]. Thus, baP-WV can be used to predict CVD, including coronary artery disease.

Aging and high blood pressure can greatly worsen baPWV [10], and the presence of metabolic syndrome (MetS) related risks such as impaired glucose tolerance and dyslipidemia have also been reported to influence baPWV [11]. Meanwhile, among lifestyle habits, smoking is a major risk factor of cardiovascular events [12]. There have been several reports on the relationship between cigarette smoking and baPWV [10, 13, 14]; however, the findings have been inconsistent. A possible reason for this inconsistency is that, although there are health-related disadvantages for both mainstream smoking, which concerns smokers exhaling tobacco smoke, and passive smoking, which is the basis for secondhand smoke (SHS), prior studies have not considered the effects of SHS. SHS is considered to represent exposure both outside the home and in the home and workplace [15, 16], and examination of the influence of exposure to smoke in these environments is required.

Considering this, the purpose of this study was to examine the effects of smoking habits, including exposure to SHS situations, on arterial stiffness in workers who had not developed arteriosclerosis, as well as to construct a strategy for preventing future worsening of arteriosclerosis.

Participants and Methods

Participant recruitment

To perform this study, an analysis on smoking habits including the SHS situation of male employees from five companies in Fukuoka Prefecture, Japan, was conducted over the course of two years, beginning in the 2016 fiscal year. Measurements were performed for those who wanted to participate in them during the standard health assessments that are conducted by the Kyushu Rosai Hospital research center for the promotion of health and employment support. The five companies were medium- to large-scale workplaces with good occupational health management. Of the 324 individuals who were approached for this study, 320 provided written consent, after being informed of the purpose of the study and being assured that their data would remain anonymous. Of these, a total of 295 healthy male workers were included in the analysis; seven participants with CVD (either past or present) and two with cerebrovascular disease (either past or present), which are arterial diseases, as well as three with cancer (either past or present), were excluded, along with 13 participants who submitted incomplete responses to the self-administered questionnaire that was used to gather background information. With regard to participants' occupations (classified according to the major groups of the International Standard Classification of Occupations [17]), the study comprised the following: managers (n = 95); professionals, technicians, and associate professionals (n = 155); clerical support workers (n = 31); services and sales workers (n = 8); craft and related trades workers (n = 2); and others (n = 4).

This study was conducted with approval from the Ethics Committee of the Kyushu Nutrition Welfare University, Higashi Chikushi Junior College (approval no. 1903).

Participants' demographic information

Self-administered questionnaires were used to determine the participants' age and height, and if they were currently receiving treatment for any disease. The prevalence of MetS risk factors (hypertension, dyslipidemia, diabetes, and obesity) was also determined through this "disease under treatment" item.

Participants' smoking situations and environments

The participants' exposure to smoking, including SHS, was determined through analysis of their smoking status, history of cohabitation with smokers (from birth to the present time), and frequency of exposure to SHS outside the home. For smoking status, participants were classified as "never-smokers," "ex-smokers," or "current smokers" [18]. The smoking index of ex-smokers and current smokers was calculated by multiplying the number of years they had been smoking by the average number of cigarettes smoked/day. As in a previous study [19], current smokers were classified as heavy smokers if they smoked more than 20 cigarettes/day. Regarding living with smokers, in order to improve the reliability of the responses, we asked not only whether respondents lived/live with smokers, but also who it was and when they lived together. To determine the frequency of exposure to SHS outside the home, participants were asked "Do you go to places where cigarettes are smoked?" If the participant replied "yes", the follow-up questions asked were "How frequently do you go to smoky places?" and "What kinds of places are they (e.g., pachinko parlors (a Japanese upright pinball game), restaurants, and pubs)?" [16] (Figure 1).

Lifestyle habits other than smoking

Aside from smoking, drinking and physical activity (PA) were also examined as other lifestyle habits that can impact health. PA was evaluated using the Japanese edition of the short version of the International physical activity questionnaire (IPAQ), for which the reliability and validity have been confirmed in previous studies [20, 21]. PA in kilocalories (kcals) was determined using the PA-intensity calculation developed by Murase *et al* [21]. The daily average PA was estimated using the weekly PA duration and intensity (low, moderate, or vigorous), which was determined using the IPAQ. Total PA (kcal/day) was calculated using energy/ml of oxygen intake (= 0.005 kcal) and the one metabolic equivalent unit (= 3.5 ml/kg/min).

Body composition

Body weight, body mass index, body fat percent, muscle mass of limbs and trunk, and fat-free mass were measured using a body-composition analyzer (InBody

- Q1. Have you ever had any respiratory illness?
- 1. No
- 2. Yes

If yes, please specify which: Bronchial asthma, Chronic obstructive pulmonary disease, Allergic rhinitis, Hay fever, Others

- Q2. Do you currently smoke cigarettes?
- 1. Yes, I currently smoke.
 - Q1-1. How many cigarettes do you smoke a day?
 - Q1-2. For how many years have you been smoking?
 - Q1-3. How old were you when you first smoked a cigarette?
 - Q1-4. How old were you when you started smoking habitually?
- 2. I smoke sometimes, but not every day.
 - Q2-1. How many cigarettes do you smoke at a time?
- Q2-2. How many times do you smoke in a month?
- Q2-3. How old were you when you first smoked a cigarette?
- Q2-4. How old were you when you started smoking habitually?
- 3. I have smoked in the past.
 - Q3-1. When did you stop smoking?
 - Q3-2. How many cigarettes did you smoke a day at that time?
- Q3-3. For how many years did you smoke cigarettes?
- Q3-3. How old were you when you first smoked a cigarette?
- Q3-4. How old were you when you started smoking habitually?
- 4. I have never habitually smoked.
- Q3. Do your cohabitants currently smoke regularly?
- 1. No
- 2. Yes
 - Q2-1. Please specify: Spouse / Father / Mother / Child / Others
 - Q2-2. How long have you been living with smokers?
- Q4. Did your cohabitants smoke habitually until you were 18 years of age?
- 1. No
- 2. Yes
 - Q2-1. Please specify: Father / Mother / Grandfather / Grandmother / Others
 - Q2-2. How long have you lived with smokers?
- Q5. Do you go to places where cigarettes are smoked?
- 1. No
- 2. Yes
 - Q2-1. How frequently do you go to smoky places?
 - Q2-2. What kinds of places are they (e.g., pachinko parlors, restaurants, and pubs)?

Figure 1. Questions about participants' smoking situations and environments.

720, InBody Co., Ltd., Seoul, Korea) that performed bioelectric impedance analysis. These measurements were conducted while participants were in a standing position.

Hemodynamics

Systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), and baPWV, as indices of arterial stiffness, were measured using a blood-pressure pulse wave examination device (BP-203RPE III, Fukuda Colin Co., Ltd., Tokyo, Japan). Cuffs for blood-pressure measurement were wound around the limbs while the participant was in a supine position; then, electrocardiogram clips were attached to both hand joints, and a heart-sound microphone was attached near the sternum at the left border of the fourth intercostal space. The stability of the electrocardiogram signal was confirmed before measurement was performed. SBP and DBP were determined through the values measured from the right brachium, while baPWV was determined through the values measured on the two right-sided limbs.

Statistical analysis

For statistical analysis, the relationships between participants' information, lifestyle, body composition, and baPWV were analyzed, with Spearman's rank correlation coefficient used for continuous variables and the Mann-Whitney U test used for categorical variables. Based on these results, a multiple stepwise linear regression analysis was performed, with baPWV set as the dependent variable; this served to investigate the factors that influence baPWV. Meanwhile, variables related to smoking habits and SHS and factors for which the univariate analysis returned P-values of less than 0.1 were set as independent variables. Through this multiple regression analysis, factors related to smoking habits and SHS that were excluded as independent variables were reanalyzed as adjustment variables. In order to avoid potential issues of multicollinearity, we confirmed that the variance inflation factor of the independent variables was less than 10. All analyses were performed using SPSS Statistics 25.0 (IBM Co., Armonk, NY, USA). Two-tailed Pvalues less than 0.05 were considered to indicate statistical significance. The values obtained through the

analysis process detailed in the previous section are described below as means \pm standard deviations and as median values (interquartile range 25–75%) for normally and not normally distributed data, respectively. Meanwhile, categorical data are expressed as frequencies and percentages.

Results

Participants' characteristics

Table 1 presents the characteristics of the 295 male participants in terms of demographics, smoking habits, lifestyle, body composition, and hemodynamics. The smoking rate was 22.7% for both light and heavy smokers. At the age of 0, about half of all the participants had lived with smokers, but only about 5% of all participants lived with smokers at present.

Analysis of the correlation between baPWV and other factors

Table 2 shows the correlation between baPWV and the participants' demographics, lifestyles, body compositions, and hemodynamics. We found significant positive correlations between baPWV and age (P<0.01), smoking index (P<0.01), alcohol consumption (P<0.01), body fat percentage (P<0.01), SBP (P<0.01), DBP (P<0.01), and heart rate (P<0.01), whereas height (P<0.05), fat-free mass (P<0.01), and lower-limb muscle mass (P<0.01) correlated negatively with baPWV.

Relationship between baPWV and other factors

The relationship between baPWV and the presence of MetS risk factors and the lifestyle-related variables are shown in Table 3. Here, baPWV shows significantly higher values when MetS risk factors (hypertension, dyslipidemia, and diabetes) are present. Among the current smokers, heavy smokers showed higher baPWV than never-smokers. Living with smokers at present showed no significant difference, but baPWV did tend to increase (P=0.076). In addition, according to the result of the Shapiro–Wilk test, the baPWV of the 16 persons who lived together with smokers at present had a normal distribution, although they were few.

Table 1. Participants' information regarding demographics, smoking habits, lifestyle, body composition, and hemodynamics

Variables	Values								
Participants' demographic information	tion		varues						
Age (years)		0 (39.0-	57.0)					
Height (cm)	170.	`		37.0)					
MetS risk factors (n, %)	63	(
Hypertension (n, %)	37	(
Dyslipidemia (n, %)	25	`.	8.5)						
Diabetes (n, %)	16		5.4)						
Obesity (n, %)	3	(1.0)						
• , , ,									
Participants' smoking situations and smoking-related environments									
Smoking status			40.0						
Never-smokers (n, %)	144								
Ex-smokers (n, %)	84	(
Current light smokers (n, %)	28	(9.5)						
Current heavy smokers (n, %)	39	`	13.2)						
Smoking index (Ex- and current smokers only)	300.	0 (150.0-	620.0)					
Cohabitation with smokers at birth (n, %)	163	(55.3)						
Cohabitation with smokers at present (n, %)	16	(5.4)						
Frequency of exposure to SHS outside the home (times/month)	1.	0 (0.0-	6.0)					
Lifestyle habits other than smoking	<u>o</u>								
Alcohol consumption (g/week)		4 (0.0-	197.6)					
Total physical activity (kcal/day)		`		238.2)					
		,		<i>'</i>					
Body composition Weight (Irg)	69	2 (62.0-	75.2)					
Weight (kg) Rody mass index (kg/m²)			62.0 – 21.5 –						
Body mass index (kg/m²) Body fat percentage (%)		4 (18.7-						
Fat-free mass (kg)		1 (
	_	_ `							
Upper-limb muscle mass (kg)		`	5.1-	6.1)					
Lower-limb muscle mass (kg)			2.1	24.7)					
Trunk muscle mass (kg)	23.	2 (21.6-	24.7)					
Hemodynamics									
Systolic blood pressure (mmHg)									
Diastolic blood pressure (mmHg)	77.	1 (68.9-	86.7)					
Heart rate (beats/min)	68.	0 (61.0-	78.0)					
baPWV (cm/sec)	1288.	0 (1177.0-	1477.0)					

The values are described as means \pm standard deviation and median values (interquartile range 25–75%), for normally and not normally distributed data, respectively. Categorical data are expressed as frequencies and percentages. MetS: metabolic syndrome, SHS: secondhand smoke, baPWV: brachial-ankle pulse wave velocity

Table 2. Correlation analysis of baPWV and other factors

Variables C	orrelation coefficient
Age (years)	0.585**
Height (cm)	-0.146*
Smoking index	0.271**
Frequency of exposure to SHS outside (times/month)	the home 0.008
Alcohol consumption (g/week)	0.173**
Weight (kg)	-0.025
Body mass index (kg/m ²)	0.068
Body fat percentage (%)	0.162**
Fat-free mass (kg)	-0.164**
Upper-limb muscle mass (kg)	-0.077
Lower-limb muscle mass (kg)	-0.157**
Trunk muscle mass (kg)	-0.099
Total physical activity (kcal/day)	0.034
Systolic blood pressure (mmHg)	0.659**
Diastolic blood pressure (mmHg)	0.722**
Heart rate (beats/min)	0.367**

^{**} P<0.01 and *P<0.05, assessed using Spearman's rank correlation coefficient. baPWV: brachial-ankle pulse wave velocity, SHS: secondhand smoke

Table 3. Relationship between baPWV and other factors

Variables	n	baPWV (cm/sec)
MetS risk factors		
Yes	67	1,452 (1,338-1,662) **
No	228	1,258 (1,161-1,428)
Hypertension		
Yes	37	1,491 (1,436-1,745) **
No	258	1,263 (1,164-1,430)
Dyslipidemia		
Yes	25	1,467 (1,349-1,655) **
No	270	1,271 (1,173-1,454)
Diabetes		
Yes	16	1,530 (1,329-1,920) **
No	279	1,280 (1,173-1,466)
Obesity		
Yes	3	1,318 (1,031-1,400)
No	292	1,288 (1,178-1,477)
Smoking status		
Never-smokers	144	1,261 (1,163-1,437)
Ex-smokers	84	1,317 (1,219-1,484)
Current light smokers	28	$1,265 (1,134-1,419)^{\dagger}$
Current heavy smokers	39	1,443 (1,222-1,662) §§
Cohabitation with smokers	at birth	
Yes	163	1,290 (1,215-1,491)
No	132	1,281 (1,153-1,463)
Cohabitation with smokers	at prese	ent
Yes	16	1,460 (1,203-1,803)
No	279	1,284 (1,175-1,467)

The values are described as median values (interquartile range 25–75%). **P<0.01 versus no, assessed using the Mann-Whitney U test. $^{\dagger}P$ <0.05 versus ex-smokers, assessed using the Kruskal-Wallis test and Bonferroni correction. §§P<0.01 versus non-smokers, assessed using the Kruskal-Wallis test and Bonferroni correction. baPWV: brachial-ankle pulse wave velocity, MetS: metabolic syndrome

Multiple regression analysis with baPWV set as the dependent variable

Table 4 shows the results of the multiple regression analysis that included baPWV as the dependent variable. While baPWV shows a significant positive relationship with age, height, MetS risk factors, cohabitation with smokers, SBP, DBP, and heart rate, it has a significantly negative relationship with lower-limb muscle mass. The same results were also obtained after adjusting for current smoking status (non-smoker, ex-smoker, light smoker, heavy smoker), smoking index, cohabitation with smokers at birth, and frequency of exposure to SHS outside the home. The multiple regression model created for both conditions was significant.

Discussion

Increased arterial stiffness is associated with a risk of developing CVD; therefore, to prevent CVD, it is important to identify the factors that cause an increase in arterial stiffness. The results of this study show that aging, blood pressure, heart rate, presence of MetS risk factors, and lower-limb muscle mass make significant contributions in this regard, which accords with the findings of several previous studies [10, 11, 22–24]. However, this study also presents a novel finding: co-

habitation with smokers at present is correlated with an adverse effect on baPWV regardless of smoking status.

Our examination showed that living with smokers is associated with baPWV. We also examined the effect of exposure to SHS through cohabitation with smokers at birth and the frequency of exposure to SHS outside the home, but did not find these to be significantly associated with baPWV. Thus, cohabitation with smokers at present is a greater risk for an increase in baPWV than occasional exposure to passive smoking outside the home. These results support the suggestion made in previous studies that spouse's smoking leads to an increased risk of coronary artery disease [25]. Although few previous studies have examined the relationship between SHS and baPWV, those studies have shown that SHS has an adverse effect on baPWV [14, 26]. However, this study's results indicate that cohabitation with smokers at present affects baPWV for smokers and never-smokers alike.

When a smoker lives with other smokers, the smoker might be more likely to smoke in the home without hesitation, especially in the living room and bedroom, which may increase the frequency of smoking and the number of cigarettes smoked. Smoking at home is a particular cause of exposure to high concentrations of tobacco smoke, especially in Japanese houses where

Table 4.	Multiple	regression	analysis	with ba	PWV	set as	the de	enendent	variable

Variables		Unadjusted ar	nalysis	Adjusted analysis [#]				
	Unstandardized coefficients	Standardized coefficients	95% CIs	VIF	Unstandardized coefficients	Standardized coefficients	95% CIs	VIF
Age (years)	6.737	0.296**	4.84 - 8.63	1.45	6.518	0.286**	4.46 - 8.57	1.69
Height (cm)	8.659	0.195**	3.15 - 14.17	3.20	8.699	0.196**	3.12 - 14.28	3.25
MetS risk factors	63.135	0.100**	15.36 - 110.91	1.18	57.185	0.090*	8.27 - 106.10	1.23
Cohabitation with smokers at present	99.008	0.086*	18.14 - 179.88	1.04	86.247	0.075*	1.45 - 171.04	1.13
Lower-limb muscle mass (kg)	-46.029	-0.370**	-61.3230.74	3.16	-45.816	-0.368**	-61.3830.25	3.24
Systolic blood pressure (mmHg)	5.741	0.332**	3.23 - 8.25	4.40	5.521	0.320**	2.98 - 8.06	4.47
Diastolic blood pressure (mmHg)	4.137	0.193*	0.74 - 7.54	5.24	4.288	0.200*	0.85 - 7.73	5.31
Heart rate (beats/min)	3.772	0.179**	2.16 - 5.38	1.22	3.462	0.165**	1.79 - 5.13	1.30

^{**}P<0.01, *P<0.05. ** Smoking status, smoking index, cohabitation with smokers at birth, and frequency of exposure to SHS outside the home were adjusted. baPWV: brachial-ankle pulse wave velocity, MetS: metabolic syndrome, CIs: confidence intervals, VIF: variance inflation factor

room sizes are small and poorly ventilated [27]. Individuals can smoke in their homes for an unlimited time, which increases the risk of others' exposure to high concentrations of tobacco smoke over time.

In this study, 10 out of 16 participants (62.5%) who lived with smokers were current smokers themselves, and consumption of cigarettes was higher in smokers (n=10) who lived with other smokers, as compared to smokers who did not live with smokers (n=57) (P=0.053). It is not surprising that never-smokers are affected by tobacco smoke emitted by living together with smokers, but even among smokers, living with other smokers may have an adverse effect on baPWV due to the combined exposure to tobacco smoke generated by themselves and their cohabitants.

Meanwhile, even though heavy smokers were found to have higher baPWV values than never-smokers in this study, multiple regression analysis did not extract smoking status as a factor affecting baPWV. This result is similar to that of Jang et al [28], who suggested that smoking is not a factor related to increased baP-WV. However, Tomiyama et al [29] reported that continued smoking increases baPWV, and other researchers have reported that the acute effects of smoking can cause an increase in arterial stiffness [13]. The reason for the difference between these results and those of the present study may be that the effects of passive smoking were not considered in the other studies, and the age group was different. Future research should examine changes in baPWV among smokers by age group using a longitudinal design that has a wide range of age groups with a large sample size, which would allow for a detailed examination of the influence of smoking on baPWV.

Three limitations of this study are worth noting. First, only the presence of cohabitation with smokers at birth or at present could be analyzed; we were not able to investigate the extent of the cohabitant's smoking and the smoking locations, as would be required to estimate the amount and time of SHS exposure. Further, assessing cohabitation with smokers in the past may have been influenced by recall bias. Second, the presence or absence of MetS risk factors and their effect on baPWV [11] was only determined through the self-administered questionnaire. We did not obtain data from companies' health-examination records, so whether a participant

had been diagnosed with MetS risk factors was only determined through the participant's self-report. This means that our approach differed from the selection criteria of periodic medical checkups (Ningen Dock) [30]. Third, the number of target companies was small, at five. Since one of the five companies had a closed smoking room and the other four companies had open outdoor smoking areas, there are some differences in level of exposure to SHS during work hours. In addition, as the smoking rate of men in their 30s to 50s in Japan ranges from 33% to 40% [31], the smoking rate in the five companies was quite low at 23.7%. Since the subjects in this study volunteered to participate in the health measurement, it is expected that they had a high level of health consciousness. In the future, it will be necessary to examine the relationship between smoking and baPWV in workplaces that have similar measures against passive smoke, as well as to examine companies with a smoking rate similar to the average of similarly aged workers.

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Conflicts of Interest

The authors declare that they have no conflict of interest.

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J UOEH 42(3): 251 - 259(2020)