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Age-Specific Determinants of Brachial-Ankle Pulse Wave Velocity among Male Japanese Workers

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Prevention of cardiovascular disease (CVD) is a public health challenge. Arterial stiffness is an index that indicates the risk of developing CVD. The lifestyle habits of working generations vary greatly with age; however, no study has examined the age-specific determinants of brachial-ankle pulse wave velocity (baPWV), an index of arterial stiffness. In this cross-sectional study, we aimed to identify the age-specific determinants of baPWV. From 2014 to 2017 fiscal years, health measurements were conducted at seven companies. Overall, 1,403 men, aged between 25 and 64 years, were categorized according to age. Their lifestyle habits, body composition, and hemodynamics were recorded. Multiple regression analyses using the stepwise method revealed that higher baPWV was associated with increasing age. baPWV was also increased with increasing systolic and diastolic blood pressure and heart rate across all age groups. The increased baPWV was significantly associated with the presence of metabolic syndrome component factors in the age group of 45-54 years, high smoking index in the age groups of 25-44 years and 55-64 years, low body mass index in the 55-64 age group, and low skeletal muscle index in the 35-54 age group. Total physical activity was inversely associated with baPWV in the two age groups of 45-54 and 55-64 years. In conclusion, hemodynamics significantly affected baPWV across all ages, while smoking index, total physical activity, body mass index, and skeletal muscle index affected baPWV depending on the age group. Thus, age-related strategies should be established for alleviating baPWV increase.

Keywords: age group; arterial stiffness; skeletal muscle index; smoking index; workers
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Introduction

Cardiovascular disease (CVD) is one of the leading causes of morbidity and mortality worldwide (GBD 2013 Mortality and Causes of Death Collaborators 2015; World Health Organization 2017), thus, its prevention is an urgent public health challenge. Arterial stiffness is an index that indicates the risk of developing CVD risk and the mechanical stiffness of the arterial wall (Safar et al. 2003; O'Rourke and Hashimoto 2007). Brachial-ankle pulse wave velocity (baPWV) is one way to evaluate arterial stiffness (Yamashina et al. 2002). The baPWV is obtained by measuring the time required for the pulse wave to propagate a certain distance in the blood vessel. The stiffer the arterial wall, the higher the velocity. The baPWV has been shown to be one of the predictors of CVD including coronary artery disease (Yamashina et al. 2003a; Imanishi et al. 2004; Vlachopoulos et al. 2012).

The increase in the baPWV is greatly affected by aging and an increase in blood pressure (Tomiyama et al. 2003). In addition, the presence of the risk of metabolic syndrome (MetS), such as diabetes and dyslipidemia, has also been reported as a factor that influences baPWV (Harada and Takeda 2004). As in these previous studies, examining the determinants that influence baPWV is important for the prevention of CVD. In particular, it has been shown that the risk of developing CVD among workers in Japan is on the rise due to the westernization of the living environment and the harsh working environment associated with the current socio-economic situation (Kitamura et al. 2010). However,

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the lifestyle habits of working generations vary greatly with age (Statistics Bureau, Ministry of Internal Affairs and Communications 2012). Furthermore, previous studies have not examined whether body composition, hemodynamics, and lifestyle habits influence the value of baPWV according to age. Therefore, it is unclear whether the same strategy to prevent an increase in baPWV can be applied to different age groups.

Herein, we conducted a cross-sectional study using body composition, hemodynamics, and lifestyle habits to identify the age-specific determinants that increase baPWV. This study aimed to establish a strategy to prevent the development of CVD in male workers.

Participants and Methods

Participant recruitment

From 2014 fiscal year to 2017 fiscal year, the Kyushu Rosai Hospital research center for the promotion of health and employment support conducted health measurements at seven companies in Fukuoka Prefecture, Japan. The subjects included 1,659 male workers. In order to ensure an optimal health status of the workers, this health check measures the body composition, hemodynamics, and hearing lifestyle habits of the workers at each company. In addition to explaining the implications behind the measurements, individual guidance is provided to improve lifestyle habits. The present study was conducted in response to the provision of data obtained by completely anonymizing the health measurements provided. The data from the first year were used for those who had been receiving health measurements for multiple years since 2014 fiscal year. Of these 1,659 participants, a total of 1,403 (mean age 46.4 ± 10.6 years) were included in the analysis after excluding the 166 participants who submitted incomplete responses to the self-administered questionnaires and 90 participants under 25 years or over 65 years of age (Fig. 1). The participants' occupations (classified according to the major groups of the International Standard Classification of Occupations (International Labour Office 2012)) were classified as follows: managers (n = 468); professionals, technicians, and associate professionals (n = 503); clerical support workers (n = 249); services and sales workers (n = 68); skilled agricultural, forestry, and fishery workers (n = 1); craft and related trade workers (n = 21); plant and machine operators, and assemblers (n = 4); elementary occupations (n = 18); and others (n = 71).

This study was conducted with approval from the Ethics Committee of the Kyushu Nutrition Welfare University, Higashi Chikushi Junior College (approval no. 1807).

Participants' demographic information

Self-administered questionnaires were used to determine the participants' age, sex, height, disease under treatment, smoking status, drinking habits, and physical activity. The prevalence of MetS component factors (hypertension, dyslipidemia, diabetes, and obesity) was also determined based on the data obtained for disease under treatment. Those who had either one or more of the following: hypertension, dyslipidemia, diabetes, and obesity, were considered to have the factors constituting MetS. Smoking status was classified into "no smoking experience," "smoking experience (smoking cessation experience)," and "smoking experience (no smoking cessation experience)". For smokers, the smoking index was calculated by multiplying the average amount of cigarettes smoked per day by the number of years of smoking cigarettes. Drinking habits were estimated as the total amount of alcohol consumed in a week (g/week), calculated from the results of the type of alcohol and its frequency of consumption. Physical activity

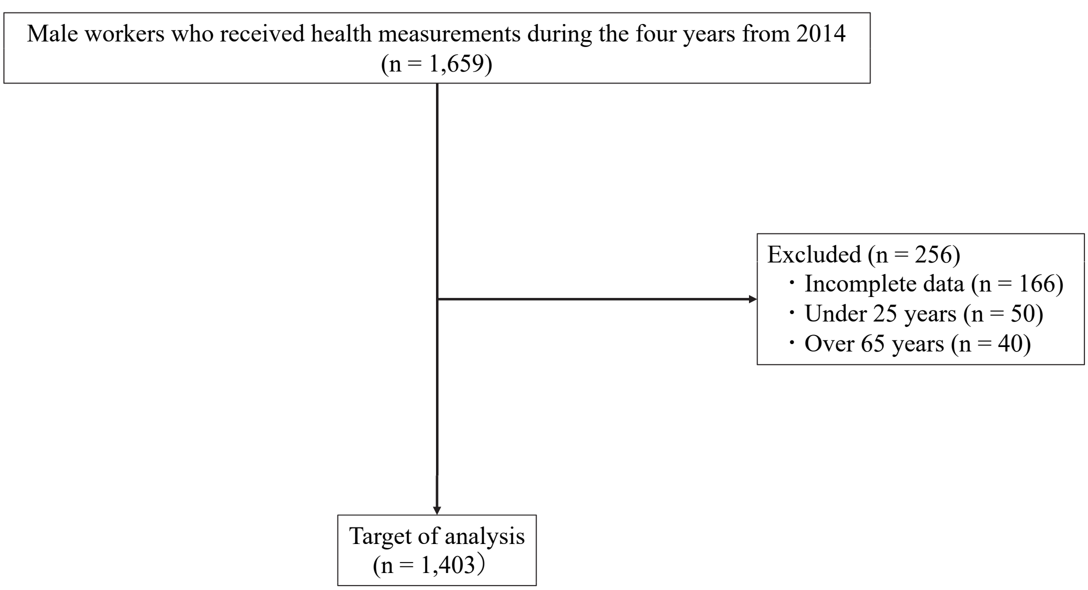

Fig. 1. Flow chart of participants for the study.

was evaluated using the Japanese edition of the short version of the International Physical Activity Questionnaire, and its reliability and validity have been confirmed in previous studies (Murase et al. 2002; Craig et al. 2003). The average daily physical activity was calculated using the weekly physical activity duration and intensity (low, moderate, or vigorous) as shown by Murase et al. (2002). Daily physical activity according to intensity and total physical activity (kcal/day) was calculated using energy/ml of oxygen intake (= 0.005 kcal) and one metabolic equivalent unit (= 3.5 ml/kg/min).

Body composition

Body weight, body mass index, body fat percent, and muscle mass of the limbs were measured using a body-composition analyzer (InBody 720, InBody Co., Ltd., Seoul, Korea), which performed a bioelectric impedance analysis. The skeletal muscle index was calculated by dividing the muscle mass of the limbs by the square of height. This measurement was performed in a standing position for about 90 seconds.

A visceral fat measuring device (HDS-2000 DUALSCAN, Fukuda Corin Co., Ltd., Tokyo, Japan) was used to measure visceral fat area. This device measures visceral fat area by measuring the cross-sectional area, the lean body area, and subcutaneous fat area of the abdomen by the dual impedance method. The results of this measurement method are highly correlated with the results of visceral fat area obtained by X-ray computed tomography (Fukui et al. 2012). The measurement was performed in the supine position.

Hemodynamics

Systolic blood pressure, diastolic blood pressure, heart rate, and baPWV, which is an index of arterial stiffness—were measured using a blood pressure pulse wave tester (BP-203RPEIII, Fukuda Colin Co., Ltd., Tokyo, Japan). For this measurement, a manchette for blood pressure measurement was wrapped around the extremities in the supine position. Then, electrocardiogram clips were attached to both wrist joints, and a heart sound microphone was attached near the left margin of the 4th intercostal sternum. The measurement was performed after confirming the stability of the electrocardiogram signal. Systolic blood pressure and diastolic blood pressure adopted the measurement value of the upper right arm, and baPWV adopted the measurement value of the upper right and lower right limbs.

Statistical analysis

Participants were classified into the following age groups: 25-34 years, 35-44 years, 45-54 years, and 55-64 years (Health Bureau, Ministry of Health, Labour and Welfare 2002). Differences in baPWV according to age were examined using the Kruskal-Wallis test and Bonferroni correction. The age-specific determinants that increased baPWV were extracted by performing a multiple regression analysis using the stepwise method with baPWV as the dependent variable and age and height as the adjustment variables. 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 26.0 (IBM Co., Armonk, NY, USA). Two-tailed p values less than 0.05 were considered as statistically significant.

Results

The values obtained through the analysis process detailed in the previous section are described below as means ± standard deviations and categorical data are expressed as frequencies and percentage.

Table 1 shows the basic information of the study participants and the results of lifestyle, body composition, and hemodynamics analysis. This study included a total of 1,403 participants: 217 participants aged 25-34 years, 359 participants aged 35-44 years, 457 participants aged 45-54 years, and 370 participants aged 55-64 years. The proportion of participants with the MetS component factors increased with age, especially from the ages of 45-54 years. The proportion of non-smokers was decreased with age.

The differences in baPWV according to age are shown in Table 2. There was a significant difference in baPWV between each age group. The baPWV was significantly low among the participants aged 25-34 years, while the baPWV showed an increasing value in the order of 35-44 years, 45-54 years, and 55-64 years.

Table 3 shows the results of the multiple regression analysis using the stepwise method for each age group with baPWV as the dependent variable. In Table 3, only items that were significantly related to baPWV are listed. Systolic blood pressure, diastolic blood pressure, and heart rate showed a significant relationship with baPWV across all age groups and higher values for each variable correlated with higher baPWV. Furthermore, baPWV was increased as the smoking index increased among the participants aged 25-34 years ($p = 0.015$) and 35-44 years ($p = 0.009$), and baPWV was increased as the skeletal muscle index decreased among the participants aged 35-44 years ($p < 0.001$). We observed that baPWV was increased significantly in the participants aged 45-54 years ($p = 0.002$) with the MetS component factors and that baPWV was increased with higher total physical activity ($p = 0.021$). The baPWV appeared to increase as the smoking index increased among the participants aged 55-64 years ($p = 0.017$), but baPWV was increased as total physical activity ($p = 0.034$) and body mass index ($p < 0.001$) decreased. The multiple regression models were significant for all conditions (adjusted R-squared value were 0.413, 0.487, 0.481, and 0.545 in the age groups of 25-34 years, 35-44

Table 1. Demographics, lifestyle, body composition, and hemodynamics of the participants.

Variables	All participants (n = 1,403)			
	25-34 (n = 217)	35-44 (n = 359)	45-54 (n = 457)	55-64 (n = 370)
Participant's demographics				
Age (years)	28.8 ± 2.9	40.1 ± 2.8	49.4 ± 3.0	59.1 ± 2.8
Height (cm)	171.2 ± 5.6	172.0 ± 5.3	171.5 ± 5.8	168.8 ± 5.7
MetS component factor, n (%)	7 (3.2)	25 (7.0)	100 (21.9)	135 (36.5)
Lifestyle				
Smoking status				
Having no smoking experience, n (%)	130 (59.9)	170 (47.4)	168 (36.8)	112 (30.3)
Having smoking experience (having smoking cessation experience), n (%)	58 (26.7)	114 (31.8)	182 (39.8)	199 (53.8)
Having smoking experience (having no smoking cessation experience), n (%)	29 (13.4)	75 (20.9)	107 (23.4)	59 (15.9)
Smoking index	40.8 ± 64.7	163.7 ± 208.2	279.6 ± 285.2	392.2 ± 392.0
Alcohol consumption (g/week)	117.3 ± 550.8	159.9 ± 499.0	237.4 ± 743.3	235.8 ± 441.0
Total physical activity (kcal/day)	157.3 ± 224.7	152.1 ± 277.1	172.2 ± 300.2	176.5 ± 178.7
Low physical activity (kcal/day)	50.6 ± 75.7	61.5 ± 104.7	73.5 ± 102.8	98.0 ± 117.1
Moderate physical activity (kcal/day)	40.4 ± 83.1	38.3 ± 91.9	37.6 ± 122.4	38.1 ± 73.3
Vigorous physical activity (kcal/day)	66.4 ± 147.2	52.3 ± 145.5	61.1 ± 204.5	40.4 ± 104.7
Body Composition				
Weight (kg)	69.6 ± 12.6	73.3 ± 11.8	72.4 ± 10.3	68.4 ± 9.5
Body mass index (kg/m^2)	23.7 ± 4.1	24.8 ± 3.7	24.6 ± 3.1	24.0 ± 2.9
Body fat percentage (%)	21.5 ± 7.1	23.5 ± 6.8	23.5 ± 6.0	23.1 ± 6.0
Skeletal muscle index	7.9 ± 0.7	8.1 ± 0.7	8.1 ± 0.6	7.9 ± 0.6
Visceral fat area (cm^2)	63.8 ± 33.0	79.6 ± 36.9	84.0 ± 35.0	82.6 ± 34.1
Hemodynamics				
Systolic blood pressure (mmHg)	124.5 ± 11.4	130.2 ± 14.2	133.8 ± 15.4	136.3 ± 17.2
Diastolic blood pressure (mmHg)	72.1 ± 8.2	78.8 ± 10.4	83.3 ± 11.4	84.0 ± 11.2
Heart rate (beat/min)	67.7 ± 11.4	71.5 ± 11.8	70.7 ± 12.3	69.9 ± 11.4

The values were described as mean ± standard deviation. Categorical data were expressed as a frequency and percentage.
MetS, metabolic syndrome; baPWV, brachial-ankle pulse wave velocity.

Table 2. Difference in baPWV for each age group.

Variables	baPWV (cm/sec)	Contrasts
25-34 (n = 217)	1179.7 ± 122.5	b, c, d
35-44 (n = 359)	1283.3 ± 168.0	a, c, d
45-54 (n = 457)	1348.3 ± 197.4	a, b, d
55-64 (n = 370)	1494.9 ± 243.3	a, b, c

a: $p < 0.01$ vs. 25-34, b: $p < 0.01$ vs. 35-44, c: $p < 0.01$ vs. 45-54, d: $p < 0.01$ vs. 55-64 assessed by Kruskal-Wallis test and Bonferroni correction.
baPWV, brachial-ankle pulse wave velocity.

years, 45-54 years, and 55-64 years, respectively, with an analysis of variance $p < 0.001$ in all age groups).

Discussion

Although the factors affecting baPWV have already been examined in previous studies (Tomiyama et al. 2003; Harada and Takeda 2004; Inomoto et al. 2014; Konishi et al. 2014), these factors have not been examined according to age. It was unclear whether the same strategy to prevent increase in baPWV should be applied to different age groups. However, the results of this study indicate that hemodynamics significantly affect baPWV in any age group, which may support the findings of previous studies on all age groups (Tomiyama et al. 2003, 2010; Inomoto et al. 2014; Konishi et al. 2014). Among the results, the association between diastolic blood pressure and baPWV was stronger than systolic blood pressure and baPWV in the younger generations (25-34 years and 35-44 years) compared with the 45-54 years and 55-64 years age groups. In general, baPWV is often associated with systolic blood pressure and is often poorly associated with diastolic blood pressure, resulting in interesting results (Tomiyama et al. 2003; Yamashina et al. 2003b; Hiroshige et al. 2012; Inomoto et al. 2014). Systolic blood pressure rises with age until old age, but diastolic blood pressure shows a transition from rising to declining after the fifth decade of life (Health Bureau, Ministry of Health, Labour and Welfare 2020). Therefore, it is presumed that systolic blood pressure has a large effect on the risk of coronary artery disease in young and middle-aged people, and diastolic blood pressure has a large effect in elderly people.

Table 3. Result of multiple regression analysis with baPWV as the dependent variable.

Variables	Unstandardized coefficients	Standardized coefficients	95% CIs	VIF
25-34 (n = 217)				
Smoking index	0.254	0.134*	0.05 - 0.46	1.11
Systolic blood pressure	2.375	0.221**	0.59 - 4.16	2.61
Diastolic blood pressure	5.263	0.351**	2.70 - 7.82	2.77
Heart rate	1.377	0.128*	0.20 - 2.56	1.14
35-44 (n = 359)				
Smoking index	0.082	0.101**	0.02 - 0.14	1.05
Skeletal muscle index	−39.384	−0.164**	−59.25 - −19.52	1.24
Systolic blood pressure	2.448	0.207**	0.69 - 4.20	3.98
Diastolic blood pressure	6.444	0.400**	3.99 - 8.89	4.17
Heart rate	3.247	0.229**	2.08 - 4.41	1.21
45-54 (n = 457)				
MetS component factor	52.323	0.110**	19.05 - 85.59	1.11
Total physical activity	0.053	0.080*	0.01 - 0.10	1.05
Skeletal muscle index	−44.099	−0.143**	−69.86 - −21.34	1.24
Systolic blood pressure	4.774	0.372**	3.03 - 6.52	4.20
Diastolic blood pressure	3.774	0.218**	1.40 - 6.15	4.30
Heart rate	3.405	0.212**	2.28 - 4.53	1.12
55-64 (n = 370)				
Smoking index	0.054	0.087*	0.01 - 0.10	1.08
Total physical activity	−0.104	−0.076*	−0.20 - −0.01	1.04
Body mass index	−17.241	−0.205**	−23.34 - −11.14	1.10
Systolic blood pressure	6.820	0.483**	4.75 - 8.89	4.50
Diastolic blood pressure	3.575	0.165*	0.36 - 6.79	4.64
Heart rate	5.509	0.257**	3.94 - 7.07	1.12

* $p < 0.05$
** $p < 0.01$
baPWV, brachial-ankle pulse wave velocity; MetS, metabolic syndrome; CIs, confidence intervals; VIF, variance inflation factor.

Meanwhile, certain components of lifestyle and body composition suggested as the age-specific determinants that increase baPWV differ according to age. Thus, it is speculated that the strategies to prevent increases in baPWV should differ depending on age. It was specifically clarified that the baPWV of those who smoke cigarettes was affected by the smoking index among younger generations (25-34 years, 35-44 years), who have few smoking habits. Younger generations possess an arterial wall with a higher sensitivity to cigarette smoke and may be more susceptible to its effects, even if they do not have a significant smoking history (Mahmud and Feely 2003). The smoking index used in the present study did not contribute to an increase in baPWV in participants aged 45-54 years, but was shown to be associated with baPWV in the participants aged 55-64 years. Fukui et al. (2006) reported that long-term smoking may influence baPWV. It has also been reported that smoking cessation for one year improved baPWV (Takami and Saito 2011). Therefore, while the effects of smoking were not observed in the participants aged 45-54 years, early smoking cessation is necessary to prevent arterial stiffness and reduce long-term exposure to cigarette smoke.

Total physical activity was also shown to be related to baPWV. However, the relationship between total physical activity and baPWV was contradictory among participants aged 45-54 years and 55-64 years. Generally, it has been reported that as the amount of physical activity increases, the arterial stiffness decreases in middle-aged and elderly individuals (Tanaka et al. 2000; Gando et al. 2010). The reason for the contradiction in this study may be that the participants aged 45-54 years were anxious about theirhealth status (e.g., worsening baPWV) and therefore, they were more likely to have improved their health through regular exercise habits. However, this is only a speculation, and it is necessary to examine the behavioral habits and health perceptions of this age group.

Further, in terms of body composition, baPWV increased as the skeletal muscle index—one of the diagnostic criteria for sarcopenia—decreased among participants aged 35-44 and 45-54 years. Previous studies (Hiroshige et al. 2012; Yang et al. 2020) that examined a wide range of age groups also clarified the relationship between baPWV and skeletal muscle index; however, the results of this study suggest that the relationship between skeletal muscle index and baPWV differs depending on age. In addition, this study showed that baPWV increased as the body mass index decreased between the ages of 55 and 64 years, and previous studies (Zhang et al. 2019; Rong et al. 2020) reported that baPWV increased with sarcopenia, which was diagnosed by skeletal muscle index and muscle strength or physical function in the elderly over 65 years of age. It is necessary to improve muscle mass in the younger generation and to maintain and improve muscle mass and strength as well as to improve nutrition (Higuchi et al. 2013) in the middle-aged age groups.

Except for lifestyle and body composition, it was shown that MetS component factors were associated with an increase in baPWV between the ages of 45 and 54 years. Previous studies have also shown a relationship between baPWV and MetS components (Harada and Takeda 2004; Inomoto et al. 2014). Therefore, attention must be paid to prevent an increase in MetS component factors not only in this age group but also in the previous age groups.

The limitation of this study is that the presence of MetS component factors that influence baPWV (Harada and Takeda 2004) was only reported in the self-administered questionnaire. In this study, we were unable to obtain medical examination data from the target companies including in this study; therefore, the data were solely based on the self-administered questionnaire on whether each item of the MetS component factors was diagnosed or not. Therefore, the MetS component factors of this study were different from the selection criteria for periodic medical examinations (Ningen Dock) (Ministry of Health, Labour and Welfare 2020). Further, this study was a cross-sectional study. Considering the factors that have been shown to be related to baPWV in this study, it is necessary for future studies to longitudinally examine the factors that affect the temporal change in baPWV.

Conflict of Interest

The authors declare no conflict of interest.

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