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Original Article

Differences in determinants affecting longitudinal change of brachial-ankle pulse wave velocity due to differences in baseline among Japanese male workers

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Abstract. [Purpose] No study has examined whether the determinants of longitudinal changes in brachial-ankle pulse wave velocity differ depending on the baseline brachial-ankle pulse wave velocity values. Therefore, this study aimed to extract these determinants in high- and low-value groups based on the FY2014 brachial-ankle pulse wave velocity values. [Participants and Methods] Participants were 97 male workers who underwent continuous health assessments from FY2014 to four years later. Their demographic, lifestyle, body-composition, and hemodynamic data were recorded. First-year data were subtracted from data obtained four years later for each continuous variable item, and the difference divided by the number of years was considered as the annual change. Based on the first-year median brachial-ankle pulse wave velocity, participants were classified into high- and low-brachial-ankle pulse wave velocity groups, i.e., high- and low-value groups, respectively. Multiple regression analysis was performed with the annual change in brachial-ankle pulse wave velocity serving as the dependent variable for both groups. [Results] In comparison with the values obtained in the first year, brachial-ankle pulse wave velocity obtained four years later increased significantly in the low-value group and tended to increase in the high-value group. Increased visceral fat area in the high-value group and increased diastolic blood pressure and heart rate in the low-value group were associated with worsening brachial-ankle pulse wave velocity. [Conclusion] The determinants of longitudinal changes in the brachial-ankle pulse wave velocity differed depending on the baseline brachial-ankle pulse wave velocity values.

Key words: Arterial stiffness, Longitudinal change, Male workers

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INTRODUCTION

Arterial stiffness represents the mechanical hardening of the arterial wall[1, 2)] and is one of the important indicators of the risk of cardiovascular disease (CVD). Brachial-ankle pulse wave velocity (baPWV) is a means to evaluate arterial stiffness[3)], obtained by measuring the time in which the pulse wave propagates a certain distance of the blood vessel. The baPWV has been proved to become faster as the arterial wall is stiffer and can be one of the predictors of CVD[4–7)]. Aging and increased

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blood pressure have significant effects on baPWV[8, 9]. In addition, it has been reported that exacerbation of baPWV greatly affects the presence of metabolic syndrome (MetS) risk such as impaired glucose tolerance and dyslipidemia[10, 11]. Examining the determinants affecting the value of baPWV will be an important issue for the prevention of the onset of CVD in the future. However, there are few reports examining the factors that influence the longitudinal change of baPWV[10, 12–14]. In particular, those with high and low baPWV baselines are considered to have different determinants of longitudinal changes in baPWV. However, none have been investigated, and further accumulation of strategies to suppress the deterioration of baPWV is required.

Therefore, the purpose of this study was to extract the determinants of changes in baPWV across four years from FY2014 to FY2018. Based on the FY2014 baPWV values, participants were divided into a high and a low value groups, and a longitudinal study was conducted considering lifestyle, body composition, and hemodynamics.

PARTICIPANTS AND METHODS

The Kyushu Rosai Hospital Research Center for the Promotion of Health and Employment Support conducted health assessments from FY2014 (first year) to FY2018 (four years later) at seven companies in the suburbs of Kitakyushu, Japan. In order to evaluate the health of workers, these health assessments measure body composition and hemodynamics and recorded the lifestyle of members at each company using measuring devices. In addition to explaining the results post assessment, guidance to improve their lifestyle was provided. This study was carried out with the provision of data processed by completely anonymizing the assessment data from the Kyushu Rosai Hospital Research Center for the Promotion of Health and Employment Support. The participants included 107 male workers who underwent health assessments consecutively from first year to four years later. Of these, a total of 97 (average age 47.2 ± 10.6 years) participants were included in the analysis, excluding 10 participants who did not complete the self-administered questionnaires (Fig. 1). Participants' occupations, based on the International Standard Classification of Occupations (major groups)[15], were as follows: managers (n=27); professionals, technicians, and associate professionals (n=48); clerical support workers (n=11); service and sales workers (n=5); craft and related trade workers (n=3); plant and machine operators/assemblers (n=1); and others (n=2). This study was approved by the Ethics Committee of the Kyushu Nutrition Welfare University, Higashi Chikushi Junior College (approval no. 1807).

Participants' age, gender, height, diseases under treatment, smoking and drinking habits, and physical activity were recorded using a self-administered questionnaire, and the data from the first year and four years later were used. The presence or absence of MetS risk factors (hypertension, dyslipidemia, diabetes, and obesity) was also considered as diseases under treatment. If one or more of these conditions was present, MetS risk factors were considered to be present. Participants' smoking habits were classified into "having no smoking experience", "having smoking experience (smoking cessation experience)", and "having smoking experience (no smoking cessation experience)" according to the presence or absence of smoking/smoking cessation. For those who had smoking experience, the smoking index was calculated by multiplying the average number of cigarettes smoked per day by the number of years of smoking. Drinking habits were estimated as the total amount of pure alcohol consumed in a week (g/week) based on the results of the type and frequency of alcohol. Physical activity was evaluated using the Japanese edition of the short version of the International Physical Activity Questionnaire, whose reliability and validity have been confirmed in previous studies[16, 17]. Total physical activity per week (kcal/kg/week) was calculated based on the physical activity duration and intensity (classified as low, moderate, or vigorous)[17], the amount of energy per 1 mL of oxygen uptake (=0.005 kcal), and one metabolic equivalent (=3.5 mL/kg/min).

Body weight, body mass index, body fat percentage, and fat-free mass were measured with participants in a standing position for about 90 seconds using a body composition analyzer (InBody 720, InBody Japan Co., Ltd., Tokyo, Japan). This device measures body composition through a bioelectric impedance analysis. The measurement data of the first year and

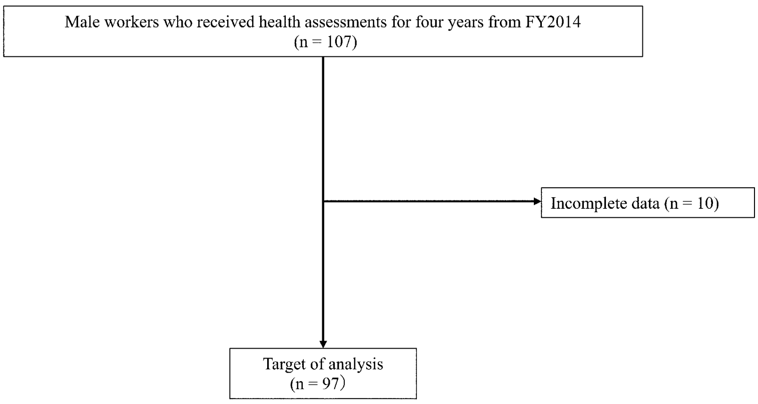

Fig. 1. Flow chart of study participants.

data from four years later were used. In addition, visceral fat area was measured using a visceral fat analyzer (HDS-2000 DUALSCAN, Fukuda Corin Co., Ltd., Tokyo, Japan). This device uses the dual impedance method to measure the visceral fat area in the supine position based on the two-step measurement of the cross-sectional area of the abdomen and of the fat-free area as well as the subcutaneous fat area measurement. This measurement result shows a very significant correlation with the visceral fat area by X-ray computed tomography[18]. The measurement data of the first year and four years later were used.

A non-invasive vascular screening device (BP-203RPEIII, Fukuda Colin Co., Ltd., Tokyo, Japan) was used to measure systolic blood pressure, diastolic blood pressure, heart rate, and baPWV, and the measurement data of the first year and four years later were used. The measurement was performed in the supine position and pneumatic cuffs were attached to the limbs of the participants, electrodes of the electrocardiograph were attached to both wrist joints, and a heart sound sensor was placed on the left edge of the 4th intercostal sternum. The measurement began after confirming the stability of the electrocardiogram. In this study, the systolic and diastolic blood pressure measured on the upper right arm and the value of the baPWV on the right side was used[9].

Based on the median baPWV (1,306.0 cm/sec) in the first year, the participants were classified into two groups, a high baPWV group (n=48) and a low baPWV group (n=49). The median baPWV is lower than the cut-off value (1,400 cm/sec), which is reported to increase the risk of arteriosclerosis and CVD[6]. However, the value was close to the measured baPWV value (1,358.5 ± 17.4 cm/sec) of the group with a low-risk of arteriosclerosis (the group with a low cumulative number of risk factors such as hypertension, impaired glucose tolerance, hypercholesterolemia, hypertriglyceridemia, and obesity) shown in a previous study[19]. The first-year data was subtracted from the data four years later for each of the continuous variable items of participant information, body composition, and hemodynamics. The annual change was calculated by dividing the data by the number of years. Each item in the first year between the two high and low baPWV groups was compared using the two-sample t-test, the Mann-Whitney U test, or the χ^2 test. Multiple logistic regression analysis was performed to compare the data four years later with the first-year data for each item of lifestyle, body composition, and hemodynamics, and the odds ratios (OR) and 95% confidence interval (95% CI) were calculated. The relationship between the annual change of baPWV and the first-year data and the annual change of each item was examined using Pearson's correlation coefficient or Spearman's rank correlation coefficient in both the high and low baPWV groups. Based on the results of this univariate analysis, the item for which $p<0.1$ in either the high or low baPWV group was set as the independent variable. A multiple regression analysis was performed by the stepwise method with the annual change of baPWV as the dependent variable, and the determinants of the annual change of baPWV were extracted for each of the high and low baPWV groups. The first-year age, height, MetS risk factors, systolic blood pressure, and diastolic blood pressure were used as adjusting variables. The MetS risk factors were considered to be dummy variables with reference to those that did not exist in the first year and four years later. To avoid potential issues of multicollinearity, we confirmed that the variance inflation factor of the independent variables was less than 10 [9]. 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 are described below as means ± standard deviations or medians (inter-quartile range 25–75%). Categorical data are expressed as frequencies and percentages.

Table 1 shows the information, lifestyle, body composition, and hemodynamic results of the first-year study participants. Compared with the low baPWV group, the proportion of those in the high baPWV group who were older and had MetS risk factors was higher. In addition, the smoking index, obesity-related items such as body fat percentage and visceral fat area, and hemodynamics were high in the high baPWV group.

Table 2 shows the annual changes of each item and the results of multiple logistic regression analysis with the first year as the baseline. Compared with the first year, the baPWV four years later increased significantly in the low baPWV group ($p<0.01$), and tended to increase in the high baPWV group ($p=0.084$). No significant change was observed in other items.

Table 3 shows the results of the correlation analysis of the relationship between the annual change in baPWV and each item in each of the high and low baPWV groups. In the high baPWV group, a significant positive relationship was found with the first-year age, systolic blood pressure, and diastolic blood pressure, as well as with the annual changes in body fat percentage and visceral fat area. Meanwhile, a significant positive relationship was found with the annual changes in systolic blood pressure, diastolic blood pressure, and heart rate in the low baPWV group. There was no significant association between lifestyle and baPWV in either group.

Table 4 shows the results of multiple regression analysis by the stepwise method with the annual change of baPWV as the dependent variable. This model was adjusted for first-year age, first-year height, MetS risk factors, first-year systolic blood pressure, and first-year diastolic blood pressure. As a result, in the high baPWV group, a significant relationship was found between the annual change in visceral fat area and the annual change in baPWV, with the baPWV increasing as visceral fat area increased (adjusted R-square=0.236). In the meanwhile, in the low baPWV group, the annual changes in diastolic blood pressure and heart rate were found to be significantly related to the annual changes in baPWV, with baPWV increasing as diastolic blood pressure or heart rate increased (adjusted R-square=0.441). The multiple regression models were significant for all conditions.

Table 1. Participants' information, lifestyle, body composition, and hemodynamics in the first-year (FY2014)

Variables	All (n=97)	High baPWV group (n=48)	Low baPWV group (n=49)	p-value
Participants' information				
Age (years)	48.0 (40.0–56.0)	53.0 (43.0–59.0)	44.0 (37.5–52.0)	0.002[b]
Height (cm)	169.9 ± 5.5	170.2 ± 5.6	169.6 ± 5.5	0.596[a]
MetS risk factors (n, %)	19 (19.6)	15 (31.3)	4 (8.2)	0.004[c]
Lifestyle				
Smoking habits				0.058[c]
Having no smoking experience (n, %)	46 (47.4)	17 (35.4)	29 (59.2)	
Having smoking experience (smoking cessation experience) (n, %)	39 (40.2)	23 (47.9)	16 (32.7)	
Having smoking experience (no smoking cessation experience) (n, %)	12 (12.4)	8 (16.7)	4 (8.2)	
Smoking index	20.0 (0.0–387.5)	125.0 (0.0–500.0)	0.0 (0.0–180.0)	0.012[b]
Drinking habits (g/week)	70.0 (0.0–184.0)	75.0 (0.0–210.0)	70.0 (0.0–164.0)	0.609[b]
Total physical activity (kcal/kg/week)	11.6 (3.8–25.2)	10.6 (2.2–22.8)	15.8 (5.4–28.9)	0.323[b]
Body Composition				
Weight (kg)	67.5 (61.4–73.8)	68.6 (63.0–74.2)	65.4 (61.1–73.3)	0.276[b]
Body mass index (kg/m^2)	23.1 (21.7–25.4)	23.4 (22.2–25.3)	22.3 (21.4–25.6)	0.192[b]
Body fat percentage (%)	21.9 ± 5.5	23.1 ± 5.3	20.9 ± 5.6	<0.050[a]
Fat-free mass (kg)	53.3 ± 5.3	53.1 ± 5.3	53.4 ± 5.4	0.810[a]
Visceral fat area (cm^2)	71.5 (47.1–93.4)	73.2 (57.5–96.5)	64.9 (42.8–81.2)	0.023[b]
Hemodynamics				
Systolic blood pressure (mmHg)	126.0 (118.0–137.0)	134.0 (120.3–143.8)	122.0 (115.0–129.0)	<0.001[b]
Diastolic blood pressure (mmHg)	78.5 (69.7–86.5)	83.6 (76.4–89.3)	73.0 (67.0–80.4)	<0.001[b]
Heart rate (beat/min)	66.6 ± 10.7	69.3 ± 10.5	63.9 ± 10.3	0.012[a]
baPWV (cm/sec)	1,306.0 (1,170.5–1,459.0)	1,459.0 (1,385.3–1,555.3)	1,172.0 (1,109.5–1,253.0)	<0.001[b]

The values were described as mean ± standard deviation or medians (interquartile range 25–75%). Categorical data were expressed as a frequency and percentage.
[a] two-sample t-test, [b] Mann-Whitney U test, [c] χ^2 test.
MetS: metabolic syndrome; baPWV: brachial-ankle pulse wave velocity.

Table 2. Annual change of each item and results of multiple logistic regression analysis with first-year baseline

Variables	First year	High baPWV group			Low baPWV group		
	Baseline	Annual change	OR	95% CIs	Annual change	OR	95% CIs
Lifestyle							
Smoking index	1.0	−41.94 ± 183.26	1.000	0.998–1.001	33.16 ± 90.92	1.001	0.999–1.002
Drinking habits (g/week)	1.0	−73.58 ± 447.99	1.000	0.998–1.001	−38.96 ± 729.01	1.000	1.000–1.000
Total physical activity (kcal/kg/week)	1.0	2.16 ± 19.45	1.005	0.986–1.025	6.47 ± 18.37	1.018	0.995–1.041
Body composition							
Weight (kg)	1.0	0.09 ± 3.44	1.001	0.956–1.048	0.40 ± 2.49	1.005	0.962–1.049
Body mass index (kg/m^2)	1.0	0.05 ± 1.17	1.007	0.865–1.172	0.12 ± 0.83	1.012	0.889–1.153
Body fat percentage (%)	1.0	0.53 ± 2.95	1.019	0.945–1.099	0.07 ± 2.36	1.003	0.932–1.079
Fat-free mass (kg)	1.0	−0.28 ± 1.81	0.990	0.917–1.069	0.29 ± 1.38	1.011	0.937–1.090
Visceral fat area (cm^2)	1.0	−1.40 ± 24.86	0.998	0.985–1.012	−1.86 ± 16.36	0.998	0.986–1.011
Hemodynamics							
Systolic blood pressure (mmHg)	1.0	0.40 ± 9.66	1.002	0.976–1.028	2.59 ± 9.86	1.024	0.985–1.063
Diastolic blood pressure (mmHg)	1.0	−1.69 ± 7.20	0.981	0.940–1.024	1.04 ± 8.18	1.011	0.970–1.054
Heart rate (beat/min)	1.0	0.90 ± 10.39	1.007	0.972–1.044	1.76 ± 13.28	1.013	0.978–1.050
baPWV (cm/sec)	1.0	62.90 ± 138.99	1.002	1.000–1.005	83.55 ± 128.06	1.006	1.002–1.010**

**p<0.01 versus first-year, assessed using multiple logistic regression analysis to estimate odds ratios (OR) and 95% confidence intervals (CIs).
baPWV: brachial-ankle pulse wave velocity.

Table 3. Correlation coefficient with the annual change of baPWV

Variables		High baPWV group	Low baPWV group
Age (years)		0.415††	0.150
Height (cm)		−0.039	−0.036
Smoking index	First-year	0.066	0.036
	Annual change (/year)	−0.273	−0.094
Drinking habits	First-year (g/week)	0.069	−0.018
	Annual change (g/week/year)	−0.209	0.114
Total physical activity	First-year (kcal/kg/week)	0.081	0.239
	Annual change (kcal/kg/week/year)	−0.112	−0.203
Weight	First-year (kg)	0.162	−0.213
	Annual change (kg/year)	0.223	−0.007
Body mass index	First-year (kg/m^2)	0.192	−0.213
	Annual change (kg/m^2/year)	0.232	−0.020
Body fat percentage	First-year (%)	0.003	−0.148
	Annual change (%/year)	0.337*	0.010
Fat-free mass	First-year (kg)	0.177	−0.223
	Annual change (kg/year)	−0.054	0.011
Visceral fat area	First-year (cm^2)	0.088	−0.095
	Annual change (cm^2/year)	0.366*	0.015
Systolic blood pressure	First-year (mmHg)	0.315†	−0.275
	Annual change (mmHg/year)	−0.081	0.373††
Diastolic blood pressure	First-year (mmHg)	0.340*	−0.061
	Annual change (mmHg/year)	−0.123	0.418††
Heart rate	First-year (beat/min)	0.088	−0.161
	Annual change (beat/min/year)	0.248	0.542††

*p<0.05, assessed using Pearson's correlation coefficient, ††p<0.01, †p<0.05, assessed using Spearman's rank correlation coefficient.
baPWV: brachial-ankle pulse wave velocity.

Table 4. Results of multiple regression analysis with baPWV annual change as the dependent variable

Variables	Unstandardized coefficients	Standardized coefficients	95% CIs	VIF
High baPWV group				
Smoking index (/year)				1.32
Total physical activity (kcal/kg/week)		0.116		1.26
Body fat percentage (%/year)		0.146		1.67
Visceral fat area (cm^2/year)	2.226	0.398**	0.67–3.79	1.17
Systolic blood pressure (mmHg/year)		0.019		1.30
Diastolic blood pressure (mmHg/year)		0.074		1.72
Heart rate (beat/min/year)		0.115		1.27
Low baPWV group				
Smoking index (/year)		−0.149		1.31
Total physical activity (kcal/kg/week)		0.062		1.14
Body fat percentage (%/year)		−0.206		1.32
Visceral fat area (cm^2/year)		−0.129		1.29
Systolic blood pressure (mmHg/year)		−0.109		4.17
Diastolic blood pressure (mmHg/year)	4.507	0.288*	0.47–8.54	1.40
Heart rate (beat/min/year)	5.250	0.544**	2.90–7.60	1.24

**p<0.01, *p<0.05, first-year age, first-year height, MetS risk factors, first-year systolic blood pressure, and first-year diastolic blood pressure were adjusted.
baPWV: brachial-ankle pulse wave velocity; CIs: confidence intervals; VIF: variance inflation factor; MetS: metabolic syndrome.

DISCUSSION

In this study, we investigated whether the determinants of the longitudinal change of baPWV differ depending on the difference in the baseline of baPWV in the first year (FY2014). Previous studies[13] on the relationship between baPWV and hemodynamics reported that longitudinal changes in blood pressure affect the development of baPWV, regardless of initial blood pressure. Another study[12] reported that a high heart rate at the beginning of the study and an increase in heart rate during the study period had a great effect on the age-related increase in baPWV. However, this study revealed that increased diastolic blood pressure and heart rate were associated with the development of baPWV only in the low baPWV group. In general, diastolic blood pressure undergoes a transition from rising to falling after the fifth decade of life[20]. In this study, the median age of the high baPWV group was 53.0 years, while that of the low baPWV group was 44.0 years. Therefore, we expected that the high baPWV group would be particularly unaffected because the increase in diastolic blood pressure was poor. In addition, the average age of the participants in the previous study[12], which revealed an increase in heart rate and progress in baPWV, was 40 ± 8 years, which was younger than that of the low baPWV group in this study. Therefore, this study indicates that the risk of developing cardiovascular disease among those in the relatively young age group of the early 40s, who show low baPWV, is greatly affected by the increase in diastolic blood pressure and heart rate.

In the meanwhile, the study did not show an association with systolic blood pressure in either the high or low baPWV group. In general, baPWV is often associated with systolic blood pressure[8, 13, 21]. The reason for this difference in results could be that we predicted that the high baPWV group would be affected by systolic blood pressure in the first year, so the effect of systolic blood pressure after that was small. Furthermore, we speculated that the low baPWV group would be more susceptible to diastolic blood pressure than systolic blood pressure. However, the fact that the adjusted R-square was particularly low in the high baPWV group and the number of participants was small may also affect this result. In the future, it will be necessary to increase the number of subjects and examine the effects of blood pressure in detail.

Regarding the relationship between baPWV and body composition, it was shown that an increase in visceral fat area affects the deterioration of baPWV in the high baPWV group. In contrast, no similar relationship was found in the low baPWV group, which was an interesting result. Previous studies[22, 23] suggest that adiponectin abnormalities due to visceral fat accumulation promote arteriosclerosis either directly or through the induction of insulin resistance and the development of metabolic syndrome. Several studies have also reported multiple positive correlations between baPWV and visceral fat area[18, 24] and a significant association between increased baPWV and visceral fat accumulation in patients with type 2 diabetes[25, 26]. The results of this study present a novel finding: Those with a high baPWV baseline are particularly affected by visceral fat accumulation. Thus, in order to suppress further increase in arterial stiffness in the future, those with high baPWV may need to pay particular attention to changes in visceral fat area.

In this study, the lifestyle items were not extracted as determinants of longitudinal changes in baPWV. In the past, we conducted a cross-sectional study to investigate the determinants of baPWV according to age group[9]. The study showed that smoking index and total physical activity were associated with baPWV. However, these two items were not associated with baPWV in all age groups, and the association differed depending on the age group. Participants in this study were divided into two groups according to their baPWV value (high baPWV group and low baPWV group) regardless of age, and as expected, this study did not show a relationship between lifestyle and baPWV. In the future, it will be necessary to further examine these two groups according to age.

One of the limitations of this study is that we were unable to obtain medical examination data from the target companies and the self-administered questionnaire was used to determine the presence or absence of MetS risk factors that affect baPWV[11]. Therefore, the presence or absence of diagnosis of MetS risk factors was derived from the participants' own self-report and may differ according to the selection criteria of periodic medical examinations (Ningen Dock)[27].

The determinants of longitudinal changes in baPWV differ depending on the baseline of baPWV. This study has revealed that an increase in visceral fat area in the high baPWV group and an increase in diastolic blood pressure and heart rate in the low baPWV group may affect the increase in baPWV. Individual guidance is required to suppress the deterioration of baPWV according to the baseline of baPWV. In the future, it will be necessary to increase the number of participants and accumulate more information.

Conflicts of interest

The authors declare that they have no conflict of interest.

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