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Arterial Stiffness and Vascular Aging

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Differences in Segmental β Response between Elastic and Muscular Arteries: A Comparison between Young and Adults

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Keywords
Cardio-ankle vascular index · Segmental β · Arterial stiffness · Aging · Vascular aging

Abstract
Introduction: The cardio-ankle vascular index (CAVI) is a noninvasive indicator used to assess arterial stiffness and predict atherosclerotic cardiovascular disease (ASCVD). CAVI represents a scale-converted form of the stiffness parameter β. Both CAVI and β reflect overall arterial stiffness from the heart to the ankle. However, there are distinct mechanistic pathways underlying the heterogeneous progression of ASCVD across the arterial tree (e.g., elastic and muscular arteries). Thus, the present study aimed to (1) examine differences in segmental β between elastic and muscular arteries at rest; (2) compare these differences between young and older adults at rest; and (3) further compare them with the segmental β responses observed after exercise. ***Methods:*** Eighty-three healthy individuals aged 18–52 years were recruited and divided into two groups: the young group (18–23 years, $n = 57$) and the adult group (31–52 years, $n = 26$). Cuffs were applied to both upper arms, the left thigh, and the right ankle. Segmental β was measured at rest as well as immediately after exercise using the Master's two-step exercise test. ***Results:*** At rest, muscular arterial stiffness (thigh-ankle β [taβ]) was 4.7 times higher in the young group and 2.8 times higher in the adult group, compared to that of the elastic arteries (heart-thigh β [htβ]). htβ and heart-ankle β (haβ) were higher in the adult group than in the young group ($p < 0.05$), whereas taβ was lower in the adult group ($p < 0.05$). After exercise, taβ, htβ, and haβ decreased in both groups. In the young group, exercise-induced β reduction was greatest in taβ, compared with htβ and haβ. This reduction was significantly greater in the young group than in the adult group (e.g., reduction in taβ was 4.9 times greater in the young group). ***Conclusion:*** This study demonstrated distinct segmental β values between elastic and muscular arteries, suggesting that the inherent stiffness of the arterial beds should ideally be assessed separately.

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Introduction

The cardio-ankle vascular index (CAVI) is a noninvasive and convenient method for assessing arterial stiffness [1, 2] and is a predictor of atherosclerotic cardiovascular disease (ASCVD) [3–6]. CAVI = a {(2 ρ / [systolic-diastolic BP]) × ln (systolic BP / diastolic BP) PWV^2} + b. BP is blood pressure, PWV is pulse wave velocity from the origin of the aorta to the tibial artery at the ankle through the femoral artery, ρ is blood density, and a and b are constants in order to adjust the values of CAVI to those of Hasegawa's PWV. CAVI employs the following equation derived from the β theory of stiffness parameters applying the Bramwell-Hill equation. β = (2 ρ / [systolic-diastolic BP]) × ln (systolic BP / diastolic BP) PWV^2. Takahashi et al. [2] reported that even when excluding the constants from the CAVI formula, β remains a useful indicator of arterial stiffness in both epidemiological and clinical research. Therefore, we used the CAVI, PWV, and β in the present study.

CAVI and β integrate the arterial stiffness across the arterial tree, from the heart to the ankle. However, within the arterial tree, the structure, stiffness, and composition of elastic and muscular arteries differ [7, 8]. Recent studies have reported that there are differential histological, pathological, and mechanistic pathways underlying the heterogeneous progression of ASCVD across the arterial tree [9]. The aorta and carotid arteries are elastic arteries with high concentrations of elastic fibers in the tunica media, allowing them to expand during systole and contract during diastole. In contrast, the brachial, coronary, radial, and femoral arteries are medium-sized vessels containing more connective tissue and fewer elastic fibers than the aorta and common carotid artery [9, 10]. Elastic and muscular arteries differ in structure, function, and mechanical properties and may also exhibit distinct patterns of adaptation to aging and exercise. Yamamoto et al. [11] reported that nitroglycerine administration reduced CAVI, the β theory-applied index of the aorta (htβ), and the femoral and tibial arteries (taβ), with varying rates in each index. We previously reported, using rabbit experiments, that segmental β of elastic and muscular arteries differed in response to BP changes due to several drugs or acute hypovolemia [12–15]. Evaluating the stiffness of different parts of the arterial tree separately allows for a deeper understanding of the morphological, mechanical, structural, and physiological differences between human elastic and muscular arteries. Furthermore, this aids in constructing a framework for growth and remodeling that explains vascular ageing [7, 16–18]. Thus, in the present study, we compared segmental β of elastic and muscular arteries at rest between two different age-groups and further compared these values with exercise-induced segmental β.

Methods

Study Participants

This study was conducted at Fukushima Medical University School of Health Sciences. We recruited healthy individuals with no history of smoking, hypertension, diabetes mellitus, dyslipidemia, or ASCVD. Eighty-three healthy individuals (mean 25.7 ± 10.7 years; 35 males, 42.2%) were recruited. The participants were divided into two groups: older adolescents and young adults, with an age range of 15–24 years (young group; $n = 57$) and adults aged 25–59 years (adult group; $n = 26$) [19]. In this study, we (1) examined differences in segmental β between elastic and muscular arteries at rest; (2) compared these differences between the young and adult groups; and (3) further compared them with exercise-induced segmental β.

Evaluation of Arterial Stiffness (Segmental β)

Cuffs were applied to both upper arms, the left thigh, and the right ankle, and pulse waves were measured at each segment (Fig. 1a). The participant remained at rest for 10 min prior to measurement. Segmental β, PWV, and BP were measured using a CAVI device (VaSera VS-3000 TE; Fukuda Denshi Co., Ltd., Tokyo, Japan). BP at the left upper brachial artery was used for all arterial stiffness calculations [11]. The stiffness of the elastic artery (htβ), muscular artery (taβ), and overall arterial tree (haβ) was calculated from BP and PWV measurements between the heart and left thigh (htPWV; aortic origin to left femoral artery), left thigh and right ankle (taPWV; left femoral to right tibial artery), and heart and right ankle (haPWV; aortic origin to right tibial artery), respectively [1]. As it is difficult to measure ipsilateral haPWV and taPWV simultaneously here, we employed the right tibial artery instead of the left tibial artery for measurement. This is consistent with a method reported by Yamamoto et al. [11]. CAVI was calculated from haβ and coefficients a and b [2]. CAVI0 was calculated using a method developed by Spronck et al. [20].

Exercise Methods

The Master's two-step exercise test is a widely used exercise stress test due to its relatively simple technique and lack of requirement for specialized exercise

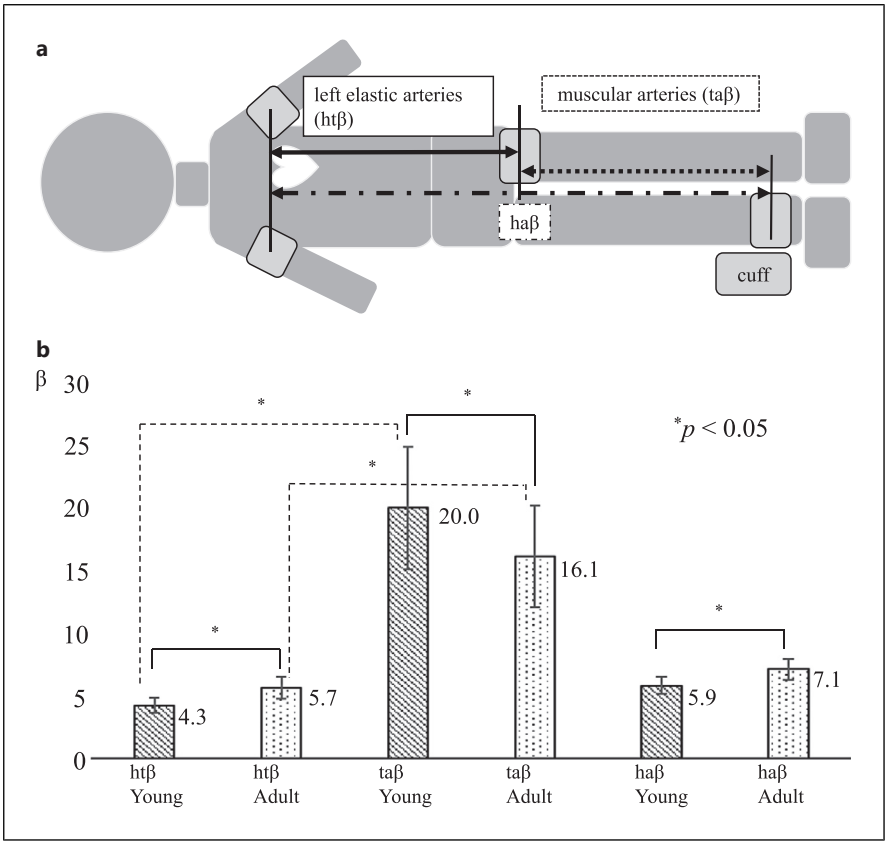

Fig. 1. a Measurement sites for haβ, htβ, and taβ. Segmental β response was measured using the vessels from the aortic origin to the left femoral artery (heart-thigh, htβ) as the elastic artery and from the left femoral artery to the right ankle (thigh-ankle, taβ) as the muscular artery haβ was measured using the vessels from the aortic origin to the ankle (heart-ankle). **b** Comparisons of haβ, htβ, and taβ between the young and adult groups at rest. Data are expressed as mean ± standard deviation. htβ and haβ were higher in the adult group than in the young group, whereas taβ was lower in the adult group.

equipment. A wooden step with a height of 9 inches per step was used for Master's two-step exercise test. The width of each step in its longest dimension was 24 inches. There are two steps, and the participants must continuously ascend and descend the steps at the specified pace for 3 min without stopping [21, 22]. The number of steps was determined according to each participant's age, sex, and body weight. In the present study, the Master's two-step exercise test using the double method (3 min) was adopted, and this exercise intensity corresponds to approximately six metabolic equivalents of task. Measurements of htβ, taβ, haβ, heart rate (HR), systolic BP, and diastolic BP were obtained at rest before exercise and immediately after exercise.

Statistical Analysis

Normality of the data was assessed using the Shapiro-Wilk test. Normally distributed data are expressed as mean ± standard deviation. Comparisons of parametric variables between groups were performed using independent *t* tests, while paired *t* tests were employed for comparisons within groups. Relationships between parametric variables (e.g., age, weight, HR, BP, β, PWV) were examined using Pearson's correlation coefficients. To determine associations between arterial stiffness parameters and confounding variables, simple regression analysis and multiple regression analysis were performed. A p value of < 0.05 was considered statistically significant in all analyses. All analyses were conducted using IBM SPSS Statistics version 26 (IBM, Armonk, NY, USA).

Results

Comparisons of htβ, taβ, and haβ at rest between the young (18–23 years, $n = 57$) and adult (31–52 years, $n = 26$) groups are presented in Figure 1b. The stiffness of muscular arteries (taβ) was 4.7 times higher than that of elastic arteries (htβ) in the young group and 2.8 times higher in the adult group. htβ and haβ were higher in the adult group than in the young group ($p < 0.05$), whereas taβ was lower in the adult group ($p < 0.05$). Simple correlations are presented in Table 1. A strong correlation was observed between haβ and both CAVI and CAVI0 ($R = 0.996$, $p < 0.01$; $R = 0.934$, $p < 0.01$). CAVI0

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Table 1. Simple correlation analysis

	Age, years	Height, cm	Weight, kg	BMI, kg/m^2	HR, bpm	SBP, mm Hg	DBP, mm Hg	htPWV, cm/s	htβ	taPWV, cm/s	taβ	haPWV, cm/s	haβ	CAVI	CAVI0
Age, years	–	0.325*	0.503*	0.426*	0.142	0.349*	0.414*	0.693*	0.684*	−0.202	−0.332*	0.670*	0.637*	0.639*	0.581*
Height, cm	–	–	0.675*	0.196	0.008	0.348*	0.185	0.365*	0.321*	−0.134	−0.231**	0.342*	0.270**	0.291*	0.327*
Weight, kg	–	–	–	0.853*	0.239**	0.520*	0.323*	0.480*	0.382*	−0.204	−0.366*	0.371*	0.194	0.209	0.225**
BMI, kg/m^2	–	–	–	–	0.310*	0.440*	0.284*	0.364*	0.264**	−0.183	−0.326*	0.232**	0.048	0.052	0.053
HR, bpm	–	–	–	–	–	0.313*	0.409*	0.124	−0.038	0.098	−0.042	0.106	−0.121	−0.127	−0.244**
SBP, mm Hg	–	–	–	–	–	–	0.734*	0.587*	0.288*	0.048	−0.323*	0.596*	0.190	0.190	0.158
DBP, mm Hg	–	–	–	–	–	–	–	0.730*	0.469*	0.051	−0.310*	0.742*	0.382*	0.384*	0.120
htPWV, cm/s	–	–	–	–	–	–	–	–	0.933*	−0.177	−0.434*	0.937*	0.805*	0.804*	0.674*
htβ	–	–	–	–	–	–	–	–	–	−0.253**	−0.387*	0.845*	0.884*	0.879*	0.796*
taPWV, cm/s	–	–	–	–	–	–	–	–	–	–	0.916*	0.060	0.047	0.045	0.036
taβ	–	–	–	–	–	–	–	–	–	–	–	−0.220**	−0.070	−0.073	−0.024
haPWV, cm/s	–	–	–	–	–	–	–	–	–	–	–	–	0.882*	0.880*	0.754*
haβ	–	–	–	–	–	–	–	–	–	–	–	–	–	0.996*	0.934*
CAVI	–	–	–	–	–	–	–	–	–	–	–	–	–	–	0.930*
CAVI0	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–

BMI, body mass index; HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; htPWV, heart-thigh pulse-wave velocity; htβ, heart-thigh β; taPWV, thigh-ankle pulse-wave velocity; taβ, thigh-ankle β; haPWV, heart-ankle pulse-wave velocity; haβ, heart-ankle β; CAVI, cardio-ankle vascular index. *p < 0.01. **p < 0.05.

Table 2. Changes in parameters at rest and after exercise

	At rest	Immediately after exercise	*p* value
Systolic blood pressure, mm Hg	120.3±11.7	136.4±13.6	<0.001
Diastolic blood pressure, mm Hg	73.2±8.7	79.8±8.8	<0.001
Mean blood pressure, mm Hg	88.9±9.0	98.7±9.9	<0.001
Heart rate, bpm	65.3±9.2	76.4±14.2	<0.001
htPWV, cm/s	526.7±67.5	530.7±76.8	0.387
htβ	4.7±0.9	4.3±1.0	<0.001
taPWV, cm/s	1044.4±129.5	986.3±142.6	0.001
taβ	18.8±5.0	15.0±4.5	<0.001
haPWV, cm/s	608.6±61.6	605.8±77.8	0.544
haβ	6.3±0.9	5.6±1.2	<0.001
CAVI	6.0±0.8	5.5±1.0	<0.001
CAVI0	8.4±1.1	7.6±1.5	<0.001

htPWV, heart-thigh pulse-wave velocity; htβ, heart-thigh β; taPWV, thigh-ankle pulse-wave velocity; taβ, thigh-ankle β; haPWV, heart-ankle pulse-wave velocity; haβ, heart-ankle β; CAVI, cardio-ankle vascular index.

showed no correlation with either systolic BP or diastolic BP. htβ was positively correlated with age, height, weight, body mass index (BMI), systolic BP, diastolic BP, htPWV, haPWV, haβ, CAVI, and CAVI0 and negatively correlated with taPWV and taβ. In contrast, taβ was negatively correlated with age, height, weight, BMI, systolic BP, diastolic BP, htPWV, htβ, and haPWV and was positively correlated with taPWV.

We have performed univariable and multivariable regression analyses regarding stiffness parameters at rest (htPWV, htβ, taPWV, taβ, haPWV, haβ, CAVI, and CAVI0) and possible confounding variables (age, height, weight, heart rate, mean BP), as shown in online supplementary Table 1 (for all online suppl. material, see https://doi.org/10.1159/000551759). Since there was multicollinearity in BMI with height and weight, and mean BP with systolic and diastolic BP, we adopted height, weight, and mean BP as confounding variables. In the multiple regression analysis, only variables ($p < 0.10$) in the univariable regression analyses were employed. In the multiple regression analysis, almost all arterial stiffness parameters, except for taPWV and taβ, were independently associated with age (online suppl. Table 1).

Changes in systolic BP, diastolic BP, mean BP, HR, and arterial stiffness parameters at rest and immediately after the Master's two-step exercise test are presented in Table 2. Systolic BP, diastolic BP, mean BP, and HR increased, while htβ, taPWV, taβ, haβ, CAVI, and CAVI0 decreased after exercise.

Figure 2 shows comparisons of %changes in exercise-induced segmental β between the young and adult groups. After exercise, htβ, taβ, and haβ decreased in both groups. In the young group, exercise-induced β reduction was greater in taβ compared with htβ and haβ. Compared with the adult group, the young group showed significantly greater exercise-induced β reductions (e.g., 4.9 times in taβ).

As with the resting state, regression analysis was performed for exercise-induced changes in arterial stiffness parameters. In multiple regression analysis, taβ, taPWV, and CAVI0 were independently associated with age (online suppl. Table 2).

Discussion

To the best of our knowledge, the present study is the first to present differences in segmental β responses in elastic and muscular arteries at rest and those induced by exercise between young and adult groups. The segmental β response of muscular arteries (taβ) at rest was three to five times higher than that of elastic arteries (htβ), which is consistent with the results of a previous report [23]. Elastic arteries are composed of abundant elastic fibers and possess a large vessel diameter, whereas muscular

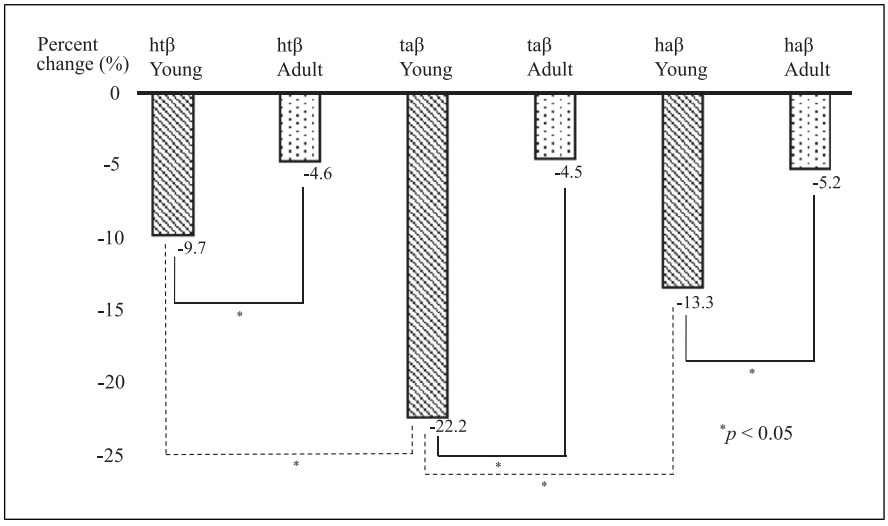

Fig. 2. Comparisons of %changes in exercise-induced segmental β (immediately after exercise-at rest) between the young and adult groups. Date are expressed as mean values. After exercise, taβ, htβ, and haβ decreased in both groups. In the young group, the exercise-induced β response reduction was greatest in taβ compared with htβ and haβ.

arteries are primarily composed of smooth muscle fibers, possess a smaller vessel diameter, and exhibit higher impedance than elastic arteries [24]. htβ and haβ were higher in the adult group than in the young group, and taβ was conversely lower in the adult group. Additionally, htβ was positively correlated with age, weight, BMI, and BP, all of which are well-known risk factors for arteriosclerosis. In particular, htβ, an indicator of elastic arteries, showed a strong correlation with age. Moreover, it was found that htPWV, htβ, haPWV, haβ, CAVI, and CAVI0 – which include elastic arteries – remained strongly associated with age even after adjusting for height, weight, and BP. On the other hand, taβ was negatively correlated with age, height, weight, BMI, and BP. After adjusting for height, weight, and BP, no association with age was observed for taPWV and taβ, which are indicators of muscular arteries.

Elastic arterial stiffness increases with age due to spatial disorganization and fragmentation of elastin, as well as accumulation and cross-linking of collagen [25, 26]. Regarding muscular arteries, Davy et al. [27] reported that limb vasoconstrictor responsiveness to sympathetic nervous activation may be attenuated with age [28, 29].

After the Master's two-step exercise test, htβ, taβ, and haβ decreased. In the young group, the decrease in taβ was greater than that in htβ or haβ. Moreover, the decrease in taβ in the young group was greater than that in the adult group. With respect to decreases in htβ, taβ, and haβ, the increases in HR, stroke volume, and cardiac output induced by exercise are thought to cause vasodilation, particularly via shear stress on the muscular vessels of the lower limb; therefore, this is inferred to have led to a reduction in arterial stiffness. Concordant with the present study, Saz-Lara et al. [30] reported in a meta-analysis that a decrease in PWV was observed at both central and peripheral levels in the first hour after exercise [31]. On the contrary, Pewowaruk et al. [32] reported nitroglycerin-induced vasodilation was found to both increase and decrease arterial stiffness depending on the ratio of passive-to-active stiffness along the continuum of young-to-old, healthy-to-diseased, and elastic-to-muscular arteries studied. However, since we did not evaluate arterial diameter, the relationship between reduced vascular stiffness and vasodilation could not be clearly established in this study.

In the young group, the exercise-induced β response of muscular arteries (%taβ) appeared larger and more labile than that of elastic arteries (%htβ). Ashor et al. [33] reported that the magnitude of the effect of aerobic exercise training on PWV was greater in peripheral (ba-PWV) rather than in central (cf-PWV) indices of arterial stiffness. This difference might be explained by the apparently greater shear stress-enhanced release of nitric oxide (NO) in the peripheral exercising limbs and the NO-producing small conduit arteries [33]. In the regression analysis of arterial stiffness parameters following exercise loading, it was found that only taPWV and taβ – indicators of muscular arteries – were affected by age, even after adjusting for height, weight, and BP. This suggests that the response of muscular artery stiffness to exercise loading can be affected by aging. Trinity et al. [34] stated that in young healthy men, passive leg movement elicits a robust NO-dependent increase in leg blood flow and that these responses diminish with advancing age. Hearon et al. [29] reported that with advancing age, the normal regulation of blood

flow to exercising muscles is impaired, which may lead to metabolic dysregulation and exercise intolerance. The age-associated impairments in vascular conductance are thought to result from (1) altered bioavailability of endothelium-derived substances (e.g., endothelial NO synthase) and (2) the impaired ability to blunt sympathetic vasoconstriction within active tissues (e.g., adenosine triphosphate). Changes in skeletal muscle feed arteries in the regulation of blood flow during exercise may explain the attenuated perfusion of skeletal muscle with advancing age and could lead to exercise intolerance in the elderly [35]. By evaluating segment β of elastic and muscular arteries separately in this manner, and by applying exercise stress, this approach may yield a more clinically meaningful assessment.

Future Prospects

Evaluating segmental β of elastic and muscular arteries separately may enable a more detailed assessment of arterial stiffness and vascular aging. htβ, which primarily reflects the aorta and other elastic arteries, may serve as a stable marker of vascular dysfunction or arterial stiffness, as well as a specific marker of arteriosclerosis. On the other hand, taβ at rest and exercise-induced segmental taβ response are thought to reflect an age-related reduction in responsiveness to endothelium-derived substances or sympathetic nervous activation. To evaluate the prognostic significance of segmental β of elastic and muscular arteries for future risk of ASCVD, further cross-sectional and longitudinal studies are needed.

Study Limitations

First, this study is a cross-sectional study including only healthy subjects and did not include patients with ASCVD, hypertension, diabetes, dyslipidemia, or a history of smoking. Thus, we could not analyze the impacts of such disease on segmental β. In addition, we did not evaluate the prognostic significance of segmental β for future occurrence of ASCVD in the study. Second, relevant biochemical data, such as lipid profiles and blood glucose levels, were not obtained. Third, BP for the calculation of CAVI, htβ, and taβ should ideally be measured in each arterial segment, but this was not possible in this clinical study. We used BP measured at the upper brachial artery.

Conclusion

This study demonstrated that segmental β differed between elastic arteries and muscular arteries. Elastic arteries showed a strong association with age at rest. The exercise-induced β response of muscular arteries was particularly labile, and this instability was greater in the young group. These findings suggest that the intrinsic stiffness of different arterial beds should ideally be assessed separately.

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Statement of Ethics

The studies involving humans were approved by the Research Ethics Committee of Fukushima Medical University (No. 2021-186). Written informed consent for participation in this study was provided. Written informed consent was obtained from the individual for the publication of any potentially identifiable images or data included in this article.

Conflict of Interest Statement

The authors declare there is no conflict of interest in this study.

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Author Contributions

Yuko Horikoshi and Akiomi Yoshihisa designed this study, conducted the experiment, analyzed the data, and drafted the manuscript. Toa Kotani and Takumu Watanabe conducted the experiment, analyzed the data, and discussed the results. Rie Sakuraba-Hirata, Shin-ichiro Katsuda, and Yasuchika Takeishi designed this study, discussed the results, and drafted the manuscript. All authors have read and agreed to submit the manuscript to Pulse.

Data Availability Statement

The data that support the findings of this study are not publicly available due to privacy reasons but are available from the corresponding author, data sharing committee, or other source upon request.

References

1 Shirai K, Utino J, Otsuka K, Takata M. A novel blood pressure-independent arterial wall stiffness parameter; cardio-ankle vascular index (CAVI). J Atheroscler Thromb. 2006;13(2):101–7. https://doi.org/10.5551/jat.13.101

2 Takahashi K, Yamamoto T, Tsuda S, Okabe F, Shimose T, Tsuji Y, et al. Coefficients in the CAVI equation and the comparison between CAVI with and without the coefficients using clinical data. J Atheroscler Thromb. 2019;26(5):465–75. https://doi.org/10.5551/jat.44834

3 Tavolinejad H, Erten O, Maynard H, Chirinos JA. Prognostic value of cardio-ankle vascular index for cardiovascular and kidney outcomes: systematic review and meta-analysis. JACC Adv. 2024;3(7):101019. https://doi.org/10.1016/j.jacadv.2024.101019

4 Sato Y, Yoshihisa A, Ichijo Y, Watanabe K, Hotsuki Y, Kimishima Y, et al. Cardio-ankle vascular index predicts post-discharge stroke in patients with heart failure. J Atheroscler Thromb. 2021;28(7):766–75. https://doi.org/10.5551/jat.58727

5 Watanabe K, Yoshihisa A, Sato Y, Hotsuki Y, Anzai F, Ichijo Y, et al. Cardio-ankle vascular index reflects impaired exercise capacity and predicts adverse prognosis in patients with heart failure. Front Cardiovasc Med. 2021;8:631807. https://doi.org/10.3389/fcvm.2021.631807

6 Miyoshi T, Shirai K, Horinaka S, Higaki J, Yamamura S, Saiki A, et al. Association between cardio-ankle vascular index and heart failure outcomes: insights from a prospective multicenter cohort. JACC Adv. 2025;4(12 Pt 2):102187. https://doi.org/10.1016/j.jacadv.2025.102187

7 Jadidi M, Razian SA, Habibnezhad M, Anttila E, Kamenskiy A. Mechanical, structural, and physiologic differences in human elastic and muscular arteries of different ages: comparison of the descending thoracic aorta to the superficial femoral artery. Acta Biomater. 2021;119:268–83. https://doi.org/10.1016/j.actbio.2020.10.035

8 Leloup AJ, Van Hove CE, Heykers A, Schrijvers DM, De Meyer GR, Fransen P. Elastic and muscular arteries differ in structure, basal NO production and voltage-gated Ca(2+)-Channels. Front Physiol. 2015;6:375. https://doi.org/10.3389/fphys.2015.00375

9 Soehnlein O, Lutgens E, Doring Y. Distinct inflammatory pathways shape atherosclerosis in different vascular beds. Eur Heart J. 2025;46(33):3261–72. https://doi.org/10.1093/eurheartj/ehaf054

10 Betts Gordon. Anatomy and physiology 2e open stax; 2022.

11 Yamamoto T, Shimizu K, Takahashi M, Tatsuno I, Shirai K. The effect of nitroglycerin on arterial stiffness of the aorta and the femoral-tibial arteries. J Atheroscler Thromb. 2017;24(10):1048–57. https://doi.org/10.5551/jat.38646

12 Horikoshi Y, Katsuda SI, Fujikura Y, Hazama A, Shimura H, Shimizu T, et al. Opposing responses of the calcium channel blocker nicardipine to vascular stiffness in the elastic and muscular arteries in rabbits. J Atheroscler Thromb. 2021;28(12):1340–8. https://doi.org/10.5551/jat.60848

13 Katsuda SI, Fujikura Y, Horikoshi Y, Hazama A, Shimizu T, Shirai K. Different responses of arterial stiffness between the aorta and the iliofemoral artery during the administration of phentolamine and atenolol in rabbits. J Atheroscler Thromb. 2021;28(6):611–21. https://doi.org/10.5551/jat.57364

14 Katsuda SI, Horikoshi Y, Shiomi M, Kitajima S, Ito T, Hazama A, et al. Arterial stiffness of the aorta and iliofemoral artery and their responses to nitroglycerin administration in myocardial infarction-prone watanabe heritable hyperlipidemic rabbits. J Hypertens. 2024;42(3):441–9. https://doi.org/10.1097/HJH.0000000000003608

15 Ito T, Katsuda SI, Horikoshi Y, Funyu T, Hazama A, Tsuyoshi S, et al. The responses of arterial stiffness parameter beta-derived index of the aorta and Illiac-Femoral artery to acute hypovolemia in rabbits. Pulse. 2024;12(1):76–84. https://doi.org/10.1159/000539480

16 Bossuyt J, Engelen L, Ferreira I, Stehouwer CD, Boutouyrie P, Laurent S, et al. Reference values for local arterial stiffness. Part B: femoral artery. J Hypertens. 2015;33(10):1997–2009. https://doi.org/10.1097/HJH.0000000000000655

17 Basu P, Sen U, Tyagi N, Tyagi SC. Blood flow interplays with elastin: collagen and MMP: TIMP ratios to maintain healthy vascular structure and function. Vasc Health Risk Manag. 2010;6:215–28. https://doi.org/10.2147/vhrm.s9472

18 Horikoshi Y, Sakuraba-Hirata R, Suzuki N, Inomata Y, Oikawa M, Kotani T, et al. Associations between obesity and arterial stiffness assessed by cardio-ankle vascular index in healthy children and adolescents. Front Cardiovasc Med. 2025;12:1633849. https://doi.org/10.3389/fcvm.2025.1633849

19 Diaz T, Strong KL, Cao B, Guthold R, Moran AC, Moller AB, et al. A call for standardised age-disaggregated health data. Lancet Healthy Longev. 2021;2(7):e436–43. https://doi.org/10.1016/S2666-7568(21)00115-X

20 Spronck B, Avolio AP, Tan I, Butlin M, Reesink KD, Delhaas T. Arterial stiffness index beta and cardio-ankle vascular index inherently depend on blood pressure but can be readily corrected. J Hypertens. 2017;35(1):98–104. https://doi.org/10.1097/HJH.0000000000001132

21 Master AM. The master two-step test. Am Heart J. 1968;75(6):809–37. https://doi.org/10.1016/0002-8703(68)90042-2

22 Kumar A, Hegde N, Kumaravel J, Mohindra R, Soni RK, Rathod R, et al. Comparison of master two-step exercise stress test versus six-min walk test in patients tested positive for SARS-CoV-2. J Fam Med Prim Care. 2022;11(11):7008–14. https://doi.org/10.4103/jfmpc.jfmpc_1111_22

23 Watahiki M, Horinaka S, Ishimitsu T, Toyoda S, Inoue T. Comparing the heart-thigh and thigh-ankle arteries with the heart-ankle arterial segment for arterial stiffness measurements. Vasc Health Risk Manag. 2020;16:561–70. https://doi.org/10.2147/VHRM.S284248

24 Lacolley P, Regnault V, Segers P, Laurent S. Vascular smooth muscle cells and arterial stiffening: relevance in development, aging, and disease. Physiol Rev. 2017;97(4):1555–617. https://doi.org/10.1152/physrev.00003.2017

25 Uejima T, Dunstan FD, Arbustini E, Loboz-Grudzien K, Hughes AD, Carerj S, et al. Age-specific reference values for carotid arterial stiffness estimated by ultrasonic wall tracking. J Hum Hypertens. 2020;34(3):214–22. https://doi.org/10.1038/s41371-019-0228-5

26 Reference Values for Arterial Stiffness' Collaboration. Determinants of pulse wave velocity in healthy people and in the presence of cardiovascular risk factors: "establishing normal and reference values". Eur Heart J. 2010;31(19):2338–50. https://doi.org/10.1093/eurheartj/ehq165

27 Davy KP, Seals DR, Tanaka H. Augmented cardiopulmonary and integrative sympathetic baroreflexes but attenuated peripheral vasoconstriction with age. Hypertension. 1998;32(2):298–304. https://doi.org/10.1161/01.hyp.32.2.298

28 Dinenno FA, Tanaka H, Stauffer BL, Seals DR. Reductions in basal limb blood flow and vascular conductance with human ageing: role for augmented alpha-adrenergic vasoconstriction. J Physiol. 2001;536(Pt 3):977–83. https://doi.org/10.1111/j.1469-7793.2001.00977.x

29 Hearon CM Jr, Dinenno FA. Regulation of skeletal muscle blood flow during exercise in ageing humans. J Physiol. 2016;594(8):2261–73. https://doi.org/10.1113/JP270593

30 Saz-Lara A, Cavero-Redondo I, Alvarez-Bueno C, Notario-Pacheco B, Ruiz-Grao MC, Martinez-Vizcaino V. The acute effect of exercise on arterial stiffness in healthy subjects: a meta-analysis. J Clin Med. 2021;10(2):291. https://doi.org/10.3390/jcm10020291

31 Maeda S, Tanabe T, Otsuki T, Sugawara J, Ajisaka R, Matsuda M. Acute exercise increases systemic arterial compliance after 6-month exercise training in older women. Hypertens Res. 2008;31(2):377–81. https://doi.org/10.1291/hypres.31.377

32 Pewowaruk RJ, Hein AJ, Carlsson CM, Korcarz CE, Gepner AD. Effects of nitroglycerin-induced vasodilation on elastic and muscular artery stiffness in older Veterans. Hypertens Res. 2022;45(12):1997–2007. https://doi.org/10.1038/s41440-022-00981-6
33 Ashor AW, Lara J, Siervo M, Celis-Morales C, Mathers JC. Effects of exercise modalities on arterial stiffness and wave reflection: a systematic review and meta-analysis of randomized controlled trials. PLoS One. 2014;9(10):e110034. https://doi.org/10.1371/journal.pone.0110034
34 Trinity JD, Groot HJ, Layec G, Rossman MJ, Ives SJ, Morgan DE, et al. Passive leg movement and nitric oxide-mediated vascular function: the impact of age. Am J Physiol Heart Circ Physiol. 2015;308(6):H672–9. https://doi.org/10.1152/ajpheart.00806.2014
35 Park SY, Ives SJ, Gifford JR, Andtbacka RH, Hyngstrom JR, Reese V, et al. Impact of age on the vasodilatory function of human skeletal muscle feed arteries. Am J Physiol Heart Circ Physiol. 2016;310(2):H217–25. https://doi.org/10.1152/ajpheart.00716.2015