Original Article

Association of Age with Carotid Intima-Media Thickness, Arterial Stiffness, and Brachial Artery Systolic Time Intervals in Thai People Undergoing a Routine Annual Physical Exam

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Background: Carotid intima-media thickness (CIMT), arterial stiffness measured by cardio-ankle vascular index (CAVI), and right brachial artery augmentation index (R-AI) have not been clearly correlated with age because of the presence of other cardiovascular risk factors. The association between age and brachial artery systolic time intervals (STIs) is not known.

Objective: To evaluate associations of CAVI, R-AI, right brachial artery STIs, and CIMT with age.

Materials and Methods: The present study was a cross-sectional, observational study. Thai people at least 18 years of age presented for an annual physical exam were enrolled. Medical histories were collected, physical examination performed, and CAVI, R-AI, right brachial artery STIs, and CIMT were assessed in all participants for statistical analyses.

Results: CAVI, R-AI, and CIMT demonstrated moderate, positive correlations with age, and their pattern of relationship were linear (p-value for F test <0.001). Right brachial artery STIs were weakly correlated with age. In multivariate analysis, age was an independent risk factor for arterial stiffness and CIMT (p<0.001).

Conclusion: Age is an independent factor for arterial stiffness, CAVI, R-AI, and CIMT, and these measurements represent aging of the arteries from the neck to the ankles.

Keywords: Age factor, Cardio-ankle vascular index (CAVI), Right brachial artery augmentation index (R-AI), Carotid intima-media thickness (CIMT), Right brachial artery systolic time intervals

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Because of longer life expectancy and better healthcare systems, preparing for the transition to an aging society is a global trend. According to the Department of Economic and Social Affairs of the United Nations, there were over 962 million people older than 60 years of age in 2017, with this number expected to more than double to around 2.1 billion people by 2030[1].

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According to the World Health Organization report in May 2017, cardiovascular disease remains the leading cause of death worldwide, and 85% of cardiovascular disease-related mortality is caused by heart attack and stroke[2]. The 2018 update on heart disease and stroke statistics by the American Heart Association showed that cardiovascular disease-related mortality increases with age and that the most common cause is coronary heart disease[3].

Arterial stiffness and carotid intima-media thickness (CIMT) have been linked to cardiovascular disease and mortality. Currently, arterial stiffness can be measured using three concepts: pulse wave velocity, augmentation index (AI), and distensibility. Each has advantages and disadvantages, which have

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been reviewed previously[4-6]. Cardio-ankle vascular index (CAVI) is a method to assess arterial stiffness that combines the principle of pulse wave velocity and stiffness parameter-β, a distensibility index[6]. Increased CAVI is associated with coronary artery disease, cardiovascular events, and mortality[7,8]. AI is an index of arterial stiffness that is calculated from the ratio between augmented pressure and pulse pressure[5]. Increased AI indicates greater arterial stiffness and is associated with impaired systolic and diastolic function[9]. CIMT is an early marker of atherosclerosis. Clinical studies have shown an association between increased CIMT and stroke and coronary heart disease events[10,11].

Systolic time intervals (STIs), which represent the timing of left ventricular contraction, consist of a pre-ejection period (PEP) and ejection time (ET). The PEP represents the time from the beginning of ventricular depolarization (the Q wave on an electrocardiogram [ECG]) to the beginning of left ventricular ejection. The ET represents the duration of the left ventricular ejection fraction. The PEP/ET ratio, or Weissler's index, is an indicator of left ventricular contraction. Longer PEP, shorter ET, and higher PEP/ET ratios are associated with poor left ventricular ejection fraction[12]. Su et al reported that brachial artery-derived STIs correlated well with cardiac STIs[13].

Arterial stiffness and CIMT increase with age[11,14]. Clinical research shows that arterial stiffness is also associated with cardiovascular risk factors[15-18]. Recently, Lind et al found that the level of cardiovascular risk factors is positively correlated with increasing age[19]. This leads to the important question of whether the association of arterial stiffness and CIMT with age is true or whether it is caused by the effect of other risk factors. The association between age and STIs is not known. The investigators conducted the present study to verify the true association among CAVI, CIMT, and right brachial artery augmentation index (R-AI), and to identify correlations with right brachial STIs.

Materials and Methods

Study design and population

Five hundred and eleven Thai subjects, at least 18 years of age, who required an annual physical exam were enrolled between April and November 2018. The protocol was a cross-sectional, observational study and was approved by the Ethical Committee of Mae Fah Luang University on March 2, 2018 (EC number 019/2561).

Data collection

All study participants enrolled voluntarily and signed informed consent forms. Their age ranged from 18 to 80 years of age (mean ± standard deviation: 37.53±10.53 years). Medical and smoking histories were collected by interview. A positive smoking history included current and past smoking. Medication usage for hypertension, diabetes mellitus, dyslipidemia, or cardiovascular disease were noted. Arterial blood pressures, weight (kg), height (m), body mass index (kg/m²), waist circumference (inch), CAVI, and CIMT (mm) were measured. Blood samples were collected to assess complete blood count, fasting plasma glucose, and lipid profiles, including total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides. Waist circumference was measured in inches, and values >36 inches in men or >32 inches in women were considered excess waist circumferences[7]. Known cases of cardiovascular disease were defined as individuals who were undergoing treatment for heart disease or vascular disease. Hypertension was defined as a blood pressure of at least 140/90 mmHg at the time of the enrollment or current use of antihypertensive medication. Diabetes mellitus was defined as fasting blood sugar of >126 mg/dL, random blood sugar >200 mg/dL at the time of enrollment, known case of diabetes mellitus, or current use of a hypoglycemic agent. Dyslipidemia was defined as any or a combination of the following: known hyperlipidemia, current use of a lipid-lowering agent, serum total cholesterol >200 mg/dL, HDL cholesterol <40 mg/dL, LDL cholesterol >130 mg/dL, or triglyceride >150 mg/dL.

Cardio-ankle vascular index measurement and its by-products

CAVI was measured by the vascular screening system VaSera (model VS-1500; Fukuda Co., Ltd., Tokyo, Japan). During the examination, the subject was lying supine quietly. Four blood pressure cuffs were applied to both arms and both ankles for blood pressure examination. Limb-lead ECG electrodes were applied to obtain an ECG signal. The heart sound monitor was placed at the sternal border in the second intercostal space. The heart sound monitor could be located on the left or right side of the sternal border depending on the quality of signal received. After registering the subject's information (identification number, name, sex, age, height, and body weight), the CAVI examination began. The process included three blood pressure measurements; the machine automatically analyzed the arterial waveforms and time intervals. CAVI was calculated using the equation CAVI = 2(blood density)/(Ps−Pd)×[ln(Ps/Pd)]×PWV^2, where Ps and Pd represent the brachial systolic and diastolic pressures, respectively; ln Ps/Pd represents the natural logarithm of the ratio Ps/Pd; and PWV is the pulse wave velocity, which is derived from the ratio of vascular length from the heart to ankle divided by the time for blood to travel from the heart to the ankle. Right CAVI represents the measurement from the heart to right ankle, whereas left CAVI represents the same measurement on the left side. The details of CAVI measurement are as reported in the VaSera operation manual[20]. The CAVI data were transferred to the computer using the VaSera R data management program for later review. Ankle brachial index (ABI), brachial artery AI, and brachial artery STIs were obtained automatically during the CAVI examination. Brachial artery STIs comprise PEP and ET, and the PEP/ET ratio was calculated. Right ABI was calculated as the ratio of right ankle systolic pressure to brachial pressure, and left ABI was calculated as left ankle pressure over brachial pressure. Only the R-AI was available in the VaSera R data management program. The R-AI represents the hardness of the artery and was calculated from the equation visualized in Figure 1. PEP and ET, which represent the systolic time period of the left ventricle, were obtained from analysis of right brachial artery waveform, heart sounds, and ECG, as shown in Figure 2.

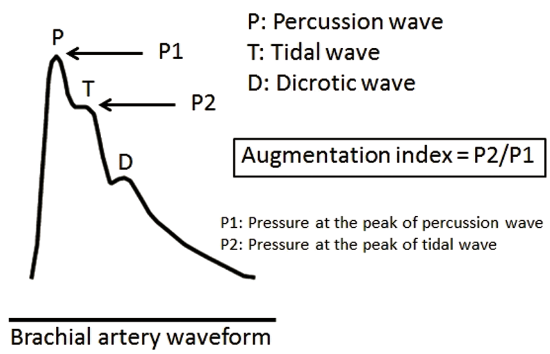

Figure 1. Calculation of right brachial artery augmentation index (R-AI) by VaSera vascular screening system, modified from the VaSera operation manual[20].

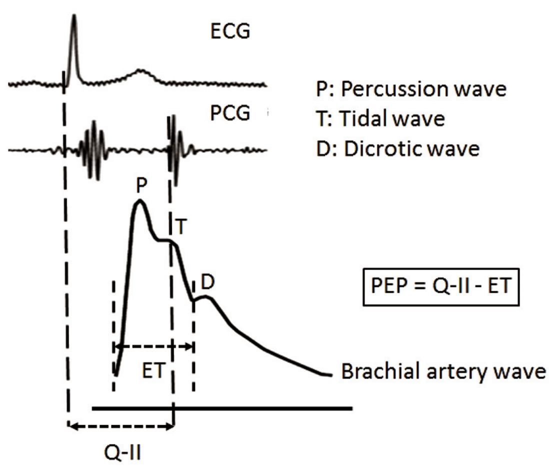

Figure 2. Evaluation of pre-ejection period (PEP) and ejection time (ET) by VaSera vascular screening system, modified from the VaSera operation manual[20]. PCG means phonocardiogram which is recorded by heart sound monitor.

Carotid intima-media thickness

Measurements of CIMT were obtained by using a vascular ultrasound machine (model Vivid-I, GE Company, Boston, MA, USA). A 10-MHz linear-array transducer was applied on the front of the neck to capture an image of the common carotid artery. After drawing a box over the far wall of the arterial region of measurement, the machine automatically calculated the average thickness, points of maximal and minimal thickness, and standard deviation of the measured data. The CIMT was measured on the distal part of the common carotid artery close to the bifurcation on both sides of the neck. The common carotid artery on both the right and left sides of the neck was measured.

Statistical analysis

Descriptive data, including clinical demographics, were presented as number and percentage of study population, and the measured parameters CAVI, R-AI, PEP, ET, PEP/ET, and CIMT were presented as mean and standard deviation. For continuous data, a test for normality was performed by using the Shapiro-Wilk test. The Pearson correlation coefficient was used to determine the strength of association of age (years) with arterial stiffness, brachial artery STIs, and CIMT. A linear regression model was performed to determine a linear relationship between age and the measured parameters. A p-value for F test less than 0.05 was accepted as statistically significant in the fitting of the linear equation model. Intercept (β_0) and slope (β_1) values in the linear equation were reported. Associations of risk factors, including sex, smoking status, presence of cardiovascular disease, hypertension, diabetes, dyslipidemia, and excess waist circumference, with the measured cardiovascular parameters were tested in univariate analysis by independent Student's t-test. Significant factors with p-value less than 0.05 in the univariate analysis were included in the multivariate analysis by using a multiple linear regression model to determine significant, independent variable factors and cardiovascular parameters. The SPSS statistical software (version 19.0; SPSS/IBM Corp., Armonk, NY, USA) was used to analyze all data. GraphPad Software Prism (version 8.0, GraphPad Inc., San Diego, CA, USA) was used to create the figures.

Table 1. Clinical characteristics of study population (n=511)

Variables	Frequencies n (%)
Sex	
Male	196 (38.4)
Female	315 (61.6)
Smoking status	
Current or past smoking	60 (11.7)
Never smoking	451 (88.3)
Known cardiovascular disease	5 (1.0)
Known renal impairment	3 (0.6)
Hypertension	140 (27.4)
Known diabetes mellitus	41 (8.1)
Known dyslipidemia	240 (47.1)
Medication use	89 (17.4)
Excess waist circumference	195 (38.6)
Body mass index	
Greater than 25 kg/m^2	172 (33.7)
Greater than 30 kg/m^2	46 (9.0)

Results

Clinical characteristics of the study population were presented in Table 1. Most study participants were female (61.6%), nonsmokers (88.3%), with no underlying history of cardiovascular disease (99.0%). Known cases of hypertension (27.4%), diabetes mellitus (8.1%), dyslipidemia (47.1%), excess waist circumference (38.6%), and high body mass index (>25 kg/m^2; 33.7%) were relatively common.

Information on arterial stiffness, CIMT, and brachial artery STIs were summarized in Table 2. Mean values of CIMT and right and left CAVI increased with age. Mean values of R-AI also increased with age but less consistently than CAVI.

According to Table 3, CAVI, R-AI, and CIMT showed moderate, positive correlations with age. Pearson correlation coefficients between age and these parameters were 0.605, 0.555, 0.376, 0.531, and 0.620 for right CAVI, left CAVI, R-AI, right CIMT, and left CIMT, respectively. All of these correlations were fit with the linear model, with p-value for F test <0.001. The difference in the linear relationship between age and CAVI of men and women was shown in Figure 3. The mean value of CAVI was markedly greater in men than in women in all age intervals, p<0.001 for right and left CAVI.

The differences in CAVI, R-AI, and CIMT values for each cardiovascular risk factor were studied by univariable analysis. As shown in Table 4, CAVI scores were significantly higher in men and in participants with known cardiovascular disease,

Table 2. Cardiovascular parameters in different age intervals

	Mean (SD)	Min-Max	Age interval (years), Mean±SD							
			<20	20 to 29	30 to 39	40 to 49	50 to 9	60 to 69	70 to 79	>80
RCAVI	6.71 (1.25)	1.2 to 10.3	5.74±0.45	5.92±0.96	6.47±0.99	7.12±1.16	7.94±1.08	8.43±0.87	9.32±0.48	9.4
LCAVI	6.70 (1.19)	1.2 to 13.3	5.72±0.54	6.02±0.91	6.50±0.96	7.08±1.30	7.59±0.84	8.31±0.86	9.44±0.58	9.4
R-AI	0.97 (0.21)	0.6 to 2.1	0.75±0.16	0.87±0.14	0.95±0.16	1.02±0.22	1.13±0.31	1.06±0.17	1.06±0.20	1.2
PEP	87.63 (16.8)	8 to 150	77.6±22.7	84.9±17.8	87.5±17.4	87.8±14.7	91.6±15.4	97.9±15.5	90.0±6.8	86
ET	300.11 (21.2)	195 to 361	296.2±14.1	299.2±17.1	299.5±21.0	303.8±21.2	299.0±25.8	288.8±32.5	313.6±19.2	320
PEP/ET	0.30 (0.06)	0.03 to 0.79	0.26±0.08	0.29±0.06	0.30±0.06	0.30±0.07	0.31±0.06	0.35±0.08	0.29±0.04	0.27
RCIMTa	0.52 (0.11)	0.28 to 1.16	0.45±0.04	0.47±0.07	0.49±0.07	0.56±0.10	0.63±0.15	0.67±0.18	0.63±0.05	0.85
LCIMTa	0.54 (0.12)	0.35 to 1.12	0.44±0.03	0.48±0.07	0.51±0.08	0.59±0.10	0.69±0.14	0.73±0.20	0.75±0.15	0.98

SD=standard deviation; Min=minimal value; Max=maximal value; RCAVI=right cardiac ankle vascular index; LCAVI=left cardiac ankle vascular index; R-AI=right brachial artery augmentation index; PEP=pre-ejection period (millisecond); ET=ejection time (millisecond); PEP/ET=ratio PEP over ET; RCIMTa=average thickness of right common carotid artery on CIMT measurement; LCIMTa=average thickness of left common carotid artery on CIMT measurement; CIMT=carotid intimal media thickness

Table 3. Linear regression model between age (years) and the measured cardiovascular parameters

	r	p-value for F test	Intercept (β_0)	p-value of the β_0	Slope (β_1)	p-value of the β_1
RCAVI	0.605	<0.001	4.044	<0.001	0.071	<0.001
LCAVI	0.555	<0.001	4.360	<0.001	0.062	<0.001
R-AI	0.376	<0.001	0.689	<0.001	0.007	<0.001
RCIMTa	0.531	<0.001	0.310	<0.001	0.006	<0.001
LCIMTa	0.620	<0.001	0.278	<0.001	0.007	<0.001

RCAVI=right cardiac ankle vascular index; LCAVI=left cardiac ankle vascular index; R-AI=right brachial artery augmentation index; RCIMTa=average thickness of right common carotid artery on CIMT measurement; LCIMTa=average thickness of left common carotid artery on CIMT measurement; CIMT=carotid intimal media thickness; r=Pearson's correlation coefficient

The p-values in this table which are lesser than 0.05 represented the fitting model in linear relationship between age and the measured parameters and also accepting intercept (β_0) and slope (β_1) values in the linear equation

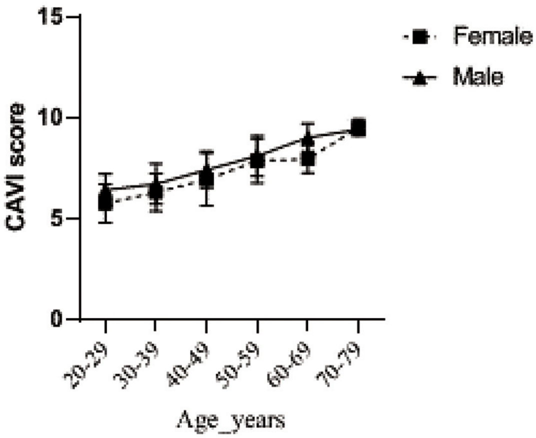

Figure 3. The mean and standard deviation of cardio-ankle vascular index (CAVI) score according to age group and sex.

hypertension, diabetes, or dyslipidemia. Current or past smoking was not a significant factor for CAVI in this study. The R-AI value was significantly higher in participants with excess waist circumference, known cardiovascular disease, or hypertension. The clinical factors sex, smoking status, diabetes mellitus, and dyslipidemia were not significant for R-AI score. The mean CIMT value was higher in men and in participants with excess waist circumference, hypertension, diabetes mellitus, dyslipidemia, or the presence of cardiovascular disease. However, the associations of sex with left CIMT and dyslipidemia with right CIMT did not reach statistical significance. Smoking status was not associated with CIMT.

The factor variables including age (years) and significant factors in univariable analysis were selected for multivariate analysis. In the final analysis, age was only an independent factor for CAVI, R-AI, and CIMT values. These findings confirmed that CAVI, R-AI, and CIMT were truly associated with age (Table 5). Male sex was associated only with CAVI, not with R-AI or CIMT. Excess waist circumference and hypertension were correlated with CIMT but not with CAVI or R-AI. Known case of diabetes was associated only with left CIMT. The presence of cardiovascular disease was associated with right CAVI, R-AI, and CIMT but not with left CAVI.

Discussion

According to the results of the present study, CAVI, R-AI, and CIMT were truly associated with age and were moderately correlated; whereas PEP, ET, and PEP/ET ratio were poorly correlated. The relationship between CAVI, R-AI, CIMT, and age was linear. Some conventional cardiovascular risk factors, including male sex, hypertension, excess waist circumference, and the presence of diabetes were also associated with these parameters.

The linear relationship between age and CAVI was found previously in a large Japanese population reported by Namekata et al[14]. Although a large number of cardiovascular disease risk factors were observed, the CAVI scores of the Thai participants in the current study were lower than the mean CAVI scores of the cardiovascular risk-free group in the Japanese population for each age interval. This difference might be explained by ethnicity, as different ethnicities have their own CAVI patterns. This idea is supported by the study of Wohlfahrt et al[21], in which a quadratic relationship was observed between CAVI and age in a Caucasian population in Brno, Czech Republic. A linear relationship was found only in the group with optimal blood pressure[21].

CAVI is an indicator of arterial stiffness from the heart valve to the ankle. The higher the CAVI value,

Table 4. Univariate analysis between cardiovascular parameters (CAVI, R-AI, PEP, ET, PEP/ET, and CIMT) and their risk factors

Cardiovascular parameters/ risk factors	Sex, Mean (SD)		Smoking, Mean (SD)		Excess waist circumference, Mean (SD)		Hypertension, Mean (SD)		Diabetes mellitus, Mean (SD)		Dyslipidemia, Mean (SD)		Known CVD, Mean (SD)	
	Male (n=196)	Female (n=314)	Yes (n=60)	No (n=450)	Yes (n=195)	No (n=315)	Yes (n=140)	No (n=370)	Yes (n=41)	No (n=467)	Yes (n=41)	No (n=467)	Yes (n=5)	No (n=505)
RCAVI	7.03*	6.51*	6.83	6.70	6.82	6.64	7.30*	6.50*	7.30*	6.70*	6.90*	6.50*	8.90*	6.70*
	(1.15)	(1.27)	(1.09)	(1.27)	(1.46)	(1.08)	(1.40)	(1.10)	(1.60)	(1.20)	(1.20)	(1.20)	(1.20)	(1.20)
LCAVI	6.99*	6.52*	6.84	6.68	6.78	6.65	7.10*	6.50*	7.10*	6.65*	6.90*	6.50*	8.60*	6.70*
	(1.12)	(1.20)	(1.16)	(1.19)	(1.47)	(0.97)	(0.40)	(0.05)	(1.70)	(1.10)	(1.30)	(1.10)	(1.30)	(1.10)
R-AI	0.94	0.98	0.95	0.97	1.00*	0.94*	1.02*	0.94*	0.92	0.97	0.98	0.95	1.31*	0.96*
	(0.21)	(0.21)	(0.19)	(0.21)	(0.23)	(0.18)	(0.25)	(0.18)	(0.14)	(0.21)	(0.20)	(0.19)	(0.28)	(0.02)
PEP	88.85	86.87	85.59	87.90	87.60	87.60	89.40	86.90	85.30	87.80	88.70	86.60	99.00	87.50
	(14.77)	(18.01)	(18.42)	(16.64)	(16.40)	(17.20)	(16.40)	(16.90)	(18.10)	(16.80)	(16.90)	(16.70)	(18.90)	(16.80)
ET	294.02*	303.91*	296.51	300.58	293.30*	302.40*	290.30*	303.80*	290.00*	300.90*	297.90*	302.10*	294.80	300.20
	(19.89)	(21.18)	(24.11)	(20.81)	(23.90)	(19.10)	(23.40)	(19.10)	(23.10)	(20.80)	(22.70)	(19.70)	(24.10)	(21.20)
PEP/ET	0.31*	0.29*	0.29	0.30	0.30	0.29	0.31*	0.29*	0.29	0.29	0.30*	0.29*	0.33	0.29
	(0.07)	(0.06)	(0.07)	(0.06)	(0.07)	(0.06)	(0.06)	(0.06)	(0.07)	(0.06)	(0.07)	(0.06)	(0.07)	(0.06)
RCIMTa	0.54*	0.51*	0.52	0.52	0.56*	0.49*	0.58*	0.49*	0.58*	0.51*	0.52	0.51	0.69*	0.51*
	(0.11)	(0.11)	(0.11)	(0.11)	(0.12)	(0.09)	(0.13)	(0.08)	(0.13)	(0.10)	(0.12)	(0.09)	(0.10)	(0.11)
LCIMTa	0.56	0.54	0.52	0.55	0.59*	0.52*	0.62*	0.52*	0.65*	0.54*	0.56*	0.53*	0.74*	0.54*
	(0.12)	(0.12)	(0.10)	(0.12)	(0.13)	(0.10)	(0.14)	(0.01)	(0.19)	(0.11)	(0.13)	(0.11)	(0.19)	(0.12)

SD=standard deviation; RCAVI=right cardiac ankle vascular index; LCAVI=left cardiac ankle vascular index; R-AI=right brachial artery augmentation index; PEP=pre-ejection period; ET=ejection time; RCIMTa=average thickness of right common carotid artery on CIMT measurement; LCIMTa=average thickness of left common carotid artery on CIMT measurement; CIMT=carotid intimal media thickness; CVD=cardiovascular disease

* p-value of independent student-t test with lesser than 0.05 represented association between cardiovascular parameter and risk factor

Table 5. Multivariate analysis by multiple linear regression model between cardiovascular parameters and their risk factors

Variables	Intercept	Age	Sex	Smoking	Excess waist circumference	Hypertension	Diabetes mellitus	Dyslipidemia	Known CVD
RCAVI	3.988	0.068	0.382	NA	NA	NS	NS	NS	1.190
	(<0.001)	(<0.001)	(<0.001)						(0.007)
LCAVI	4.272	0.610	0.357	NA	NA	NS	NS	NS	NS
	(<0.001)	(<0.001)	(<0.001)						
R-AI	0.698	0.007	NA	NA	NS	NS	NA	NA	0.257
	(<0.001)	(<0.001)							(<0.001)
RCIMTa	0.330	0.004	NS	NA	0.019	0.055	NS	NS	0.116
	(<0.001)	(<0.001)			(0.027)	(<0.001)			(0.004)
LCIMTa	0.301	0.006	NA	NA	0.036	0.044	0.055	NS	0.114
	(<0.001)	(<0.001)			(<0.001)	(<0.001)	(<0.001)		(<0.001)

RCAVI=right cardiac ankle vascular index; LCAVI=left cardiac ankle vascular index; R-AI=right brachial artery augmentation index; RCIMTa=average thickness of right common carotid artery on CIMT measurement; LCIMTa=average thickness of left common carotid artery on CIMT measurement; CIMT=carotid intimal media thickness; CVD=cardiovascular disease; NA=non-available or no significant in univariate analysis; NS=non-significant in multivariate analysis

The data represents coefficient value and p-value of the beta coefficient which is in the bracket. The p-value that is lesser than 0.05 demonstrates significantly accepted intercept (β_0) and beta coefficient or slope (β_1) to fit linear regression equation model the greater the stiffness of the arteries. A CAVI value of 9.0 is commonly used as the cut-off for cardiovascular disease[6]. In Thai people, a CAVI value greater than 8.0 is associated with obstructive coronary artery disease[7]. The results of Yingchoncharoen et al[7] imply that arterial stiffness from heart to ankle increases with age and that people aged 60 years or greater with a CAVI value >8.0 are at risk for cardiovascular disease, especially coronary artery disease. In a large clinical study of Japanese people, CAVI scores in people with cardiovascular disease risks were higher than in those without risk factors[14]. The cardiovascular risk factors in the Japanese report included borderline hypertension, hypertension, dyslipidemia, impaired fasting glucose, diabetes mellitus, ischemic ECG findings, and arteriolar sclerotic change of the retina[14]. The CAVI values of participants in the current study showed similar trends, as shown in Table 4 and 5.

R-AI, which represents the stiffness of the local artery, was moderately correlated with age (r=0.3759) in the current study. This may imply that peripheral arterial stiffness (i.e., R-AI) changed in a similar manner to regional artery stiffness (i.e., CAVI) in the Thai participants of the present study. The R-AI values were higher in participants with excess waist circumference, hypertension, or known cardiovascular disease. The R-AI values were also higher in women than in men and in those with dyslipidemia than without, although differences of R-AI among different gender, presence of dyslipidemia and without dyslipidemia did not reach statistical significance. The study of Chung et al[22] found that peripheral and central augmentation indices were correlated with age: r=0.320 for peripheral and r=0.305 for central augmentation indices; peripheral augmentation indices were higher in women and in those with hyperlipidemia.

Brachial artery STIs, PEP, ET, and PEP/ET were not correlated with age. Increased PEP and PEP/ET ratio and decreased ET have been shown to be correlated with decreased left ventricular contraction[12]. The PEP/ET ratio or Weissler coefficient in the present study showed a trend toward increasing from the youngest age interval to 69 years, suggesting that left ventricular function may decrease in older people. However, the correlation coefficients of these parameters with age were low or very low.

Associations between CIMT and age have also been studied in white, black, and Asian populations. The mean CIMT of white and black people aged between 45 and 64 years in the ARIC study[23] ranged from 0.5 to 1.0 mm, but the prevalence of cardiovascular disease and its risk factors were not reported. For Korean people in the ARIRANG study[24], the mean common CIMT in people without cardiovascular disease or risk factors ranged from 0.39 to 0.99 mm in participants from 40 to 70 years old. The range of CIMT in Thai people in the current study was greater, from 0.28 to 1.16 mm, than in the previous reports. The possible reasons for these differences are the wider range of ages, different ethnicities, differences in risk factors, and presence of cardiovascular disease. The effects of age and ethnicity are supported by the report from the Multi-Ethnic Study of Atherosclerosis (MESA)[11]. Combined hyperlipidemia and simple hypercholesterolemia were also associated with increased CIMT in the MESA study[17].

Because CAVI and R-AI are markers of arterial stiffness, whereas CIMT is a marker of early atherosclerosis, correlations between age and these parameters indicate that increased arterial stiffness, CAVI, R-AI, and CIMT scores are important cardiovascular changes associated with aging. Because healthy aging and wellbeing are common goals in the modern era, a better understanding of the science of aging is needed. Moreover, biomarkers of aging are needed to indicate at what stage a person is in his or her lifespan. Several features of a biomarker of aging were proposed by the American Federation for Aging Research[25], as follows: 1) it must predict the rate of aging; 2) it must monitor a basic process that underlies the aging process, not the effects of disease; 3) it must be able to be tested repeatedly without harming the person; and 4) it must be something that works in humans and in laboratory animals.

CAVI, R-AI, and CIMT may serve these purposes. These parameters, especially CAVI and CIMT, change with age, and several clinical studies have shown increased cardiovascular events, cardiovascular disease, and mortality in people with high values of CAVI and CIMT[8,11]. Cardiovascular events, cardiovascular disease, and mortality have long been known as manifestations of aging. Measuring CAVI, R-AI, and CIMT is easy and noninvasive. Thus, CAVI, R-AI, and CIMT are good biomarkers of cardiovascular aging. Furthermore, vascular age may be the preferred method to evaluate the risk of atherosclerotic cardiovascular disease instead of traditional cardiovascular risk assessment, and it may be an easier way for patients to understand their own risks[26]. However, the rate and magnitude of the changes in these parameters are not yet known.

Limitation

Because the present study was a cross-sectional study, the investigators could not assess the cause-effect relationship between age and these parameters. Blood samples such as fasting plasma glucose and lipid profiles could not be collected in some participants, which might affect the study results.

Conclusion

Age is an independent factor for arterial stiffness and CIMT, measurements that represent the aging character of the arteries from the neck to the ankles. Arterial stiffness and CIMT have been used as tools to evaluate cardiovascular risk but not to estimate the age of the cardiovascular system. Recently, the "vascular age" approach to cardiovascular risk estimation was introduced because it is an easier way for people to understand their own risks. To manage cardiovascular system aging, biomarkers of aging are required. Based on our results, CAVI, R-AI and CIMT are good biomarkers of cardiovascular aging.

What is already known on this topic?

Arterial stiffness and carotid intimal media thickness have been known for their relationship with age. In addition to age factor, other cardiovascular risk factors including; hypertension, smoking, excess waist circumference, diabetes mellitus and dyslipidemia, are relate to such measurements and the prevalence of these risk factors increase with age. Moreover, the information about these measurements in Thai people are still lacking.

What this study adds?

This study points out that chronologic age is an independent factor which associates with arterial stiffness measured by CAVI and CIMT. According to the recent criteria proposed by American Foundation of Aging Research, CAVI and CIMT are the excellent biomarker of cardiovascular aging over the region from neck to both ankles.

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Author's contributions

The first author, Jularattanaporn V, is a student in the Ph.D. program of the School of Anti-Aging and Regenerative Medicine, Mae Fah Luang University, and he designed the study topic, protocol, and data collection, and wrote this manuscript. Chalermchai T, the second adviser, analyzed the data and wrote the statistical analysis part of the study. Tongyoo S, co-adviser, and Nararatwanchai T, the first adviser, reviewed the final manuscript before submission.

Conflict of interest

The authors declare no conflicts of interest.

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