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Original Article

Vascular age based on coronary calcium burden and carotid intima media thickness (a comparative study)

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Abstract: Background: Considering the importance of vascular age in the risk assessment of cardiovascular events and the presence of different methods for its estimation, this study aims to evaluate and compare vascular age according to coronary artery calcium scoring (CACS) and carotid ultrasonography. Methods: This study was conducted in Isfahan on patients who underwent CACS and carotid intima-media thickness (CIMT) assessments within 30 days. In patients who were candidates for CACS, calcium score was measured, then they were invited for carotid ultrasonography, and CIMT was measured. Vascular age was estimated based on these methods using available formulas. Results: In this study, 115 patients were enrolled. (Male 52.2%, female 47.8%). The mean chronological age was 59.08 ± 14.90 years old. The mean calcium score (CS) of patients was 48.23 ± 63.34. Mean CIMT was 0.73 ± 0.15 mm. The mean vascular age derived by CS and CIMT was 58.64 ± 12.63 and 53.99 ± 17.53 years, respectively. The vascular age obtained by CS was directly related to vascular age based on CIMT (P-value < 0.05). Conclusion: Calcium score is as helpful as CIMT for vascular age estimation.

Keywords: Vascular age, calcium score, carotid

Introduction

Cardiovascular disease is the leading cause of death worldwide. Coronary artery disease (CAD) accounts for half of all such deaths [1, 2]. At least 25% of patients experiencing nonfatal acute myocardial infarction or sudden cardiac death had no previous symptoms [3]. Identifying asymptomatic individuals at greater risk of experiencing future cardiovascular events is fundamental for the implementation of preventive strategies [4]. The determination of coronary artery calcification by computed tomography helps estimate total coronary atherosclerotic load and the risk of cardiovascular events [5]. In recent years, the development of methods for direct visualization of subclinical atherosclerosis has shown promise, by detecting early asymptomatic disease [6]. Two of the most promising techniques for the determination of subclinical atherosclerosis include computed tomography coronary calcium scoring [7] and B-mode ultrasonography assessment of carotid intima-media thickness (CIMT) [8]. Both of these techniques have demonstrated an increased sensitivity for detecting CAD risk versus traditional risk factor analyses [9].

Coronary artery calcium scoring (CACS) plays a relevant role in stratifying cardiovascular risk. Several studies have shown that the calcium score (CS) is significantly associated with the occurrence of major cardiovascular events (all-cause mortality, cardiac mortality, and nonfatal myocardial infarction) in the medium and long-term follow-up [10, 11]. In addition, it provides additional prognostic information on other cardiovascular risk markers [12].

Autopsy studies have shown that extracranial carotid atherosclerotic changes are correlated with coronary atherosclerosis. Studies support an association between cerebral ischemia and CAD [13]. It is known that hypertensive patients have increased intima-media thickness (IMT) values and also that hypertension is a risk factor for both coronary and carotid artery diseases [14]. While CIMT or CS assessment improves our ability to detect early disease, an

unresolved issue in atherosclerosis imaging is how to integrate the findings of these imaging studies into a patient's overall risk profile. A novel approach that has recently been proposed is CIMT or CS to define a patient's vascular age [15]. By redefining a person's age according to the results of CIMT or CS and using this vascular age to calculate the Framingham risk score (FRS) [16], one may be able to define better the likelihood of CAD developing beyond traditional risk factors. Individuals easily understand vascular age, so it would be better to find their CVD risk [1]. While CIMT and CS have been utilized to develop a vascular age, few data are available comparing these two modalities [17]. The goal of the present study was to compare the results of vascular age assessment in individual patients using both CS and CIMT.

Methods and material

Study design

This study was conducted in AL-Zahra hospital, Isfahan, Iran, from April 2020 to April 2021. A total of 115 patients underwent CACS and CIMT assessments within 30 days. According to the cardiologist's impression, a number of patients who have been referred for coronary computed angiography (CTA) and CACS entered the study. The Ethics Committee approved this study at Isfahan University of Medical Sciences (Ethics code: IR.MUI.MED.REC.1400.044). Consent was obtained from all patients. Patients were recruited from those referred for CTA. They did not have a history of cardiac interventions like coronary artery bypass graft surgery (CABG), percutaneous coronary intervention (PCI), or carotid interventions. Patients were excluded if we did not have needed data.

CACS

We prepared a multi-slice CT scan for each patient. The patient was placed in the supine position, and a CT scan with a multi-slice device was performed. A Gated non-contrast examination was performed using a 128-slice GE Light Speed VCT Scanner (General Electric Medical Systems, Milwaukee, WI). Images were obtained at 2.5 mm and reconstructed at 2.5 mm. A coronary calcium score was obtained from scan data using a GE Advantage Windows 4.2 post-processing workstation.

Finally, the radiologist evaluated the obtained images using the desired software. Individual coronary artery calcium score was determined based on imaging findings obtained from personal CT scan using the Agatston method [18]. Smart score software was used to assess calcium scores. Also, in CT angiographic images, the severity of coronary artery stenosis was determined and scored [19]. The patient's vascular age was determined using a commonly available online MESA-based Tool [18]. Finally, data related to each patient were recorded in the patient profile.

CIMT

The thickness of the carotid intima at the site of the carotid bulb was measured, and the average size of both sides was calculated. CIMT data were obtained using standard ultrasound equipment with a 12-MHz linear array vascular ultrasound probe (Phillips Imaging Systems, Bothell, WA). Then, based on the thickness of the carotid intima and the study of Adolphe and colleagues, the vascular age of individuals was determined [20]. Finally, data related to each patient were recorded in the patient-specific profile. To establish CIMT-determined vascular age, we used each gender- and ethnic-training subset to regress the average measurement of CIMT for each individual on their chronologic age. Because there is some CIMT at birth that is greater than zero, and we had a minimum of 0.3 mm in study participants under the age of 20 years, we set a value of 0.2 mm at age zero years (at birth). The resulting gender- and ethnic-specific regression equations are as follows [21]: Males, Asian: Vascular Age CIMT-determined = 81.91321 × CIMT - 16.38264; Females, Asian: Vascular Age CIMT-determined = 121.51915 × CIMT - 24.30383.

Statistical analysis

Correlations between vascular age based on CS (VA-CS) and vascular age based on CIMT (VA-CIMT) were performed using Pearson correlation. Direct comparisons were performed using a Student t-test (for data with normal distribution) and repeated measures analysis of variance, Pearson correlation coefficient, and linear regression analysis. For all statistical analyses, a *p*-value of 0.05 was considered statistically significant. Statistical analyses were performed using SPSS version 24.

Table 1. Age, CS and CIMT description

		Mean (± SD)
CS		48.23 ± 68.346
CIMT (mm)		0.7339 ± 0.15716
Age	VA-CS	58.64 ± 12.631
	VA-CIMT	53.99 ± 17.533
	Chronologic	59.08 ± 14.904

Result

Study population

In this study, 115 patients were evaluated. Of these, 60 (52.2%) were male, 55 (47.8%) were female, and the mean chronological age was 59.08 ± 14.904 years old. The study showed that CS and CIMT age was lower than chronological age. CS and CIMT are shown in **Table 1**.

CS and CIMT correlation

We used Pearson correlation to examine the correlation between the two quantitative variables. When Pearson correlation is positive, the two variables are directly related. If the Pearson-correlation number is above 0.7, it indicates a strong relationship between the two variables. This study showed that the Pearson correlation between CS and CIMT was 0.904, a strong and direct relation. (*P*-value < 0.00). Details as shown in **Table 2**.

Chronological age, VA-CS and VA-CIMT

The number of people by age is shown in **Figure 1**, and the graphs of chronological age, VA-CS, and VA-CIMT are shown comparatively. As shown, age by CS and CIMT are strongly related to each other's and their distribution diagram is similar, which confirms in **Table 2**.

Discussion

The concept of using vascular age in place of chronologic age is based on the theory that the assessment of subclinical atherosclerosis by direct vascular imaging would be helpful in the early detection of at-risk individuals. In this regard, conversion of a patient's chronologic age to the "Vascular age" or an age at which the amount of that patient's subclinical atherosclerosis could be represented would lead to a more accurate assessment of a patient's actual cardiovascular risk-improving our success in decreasing unexpected cardiovascular events in the population. In other words, it could be a good indicator for screening and risk assessment.

In this study, the vascular age obtained with a CS score was directly and strongly related to the vascular age obtained by CIMT. We showed that the higher the CS, the higher the CIMT. It had been demonstrated that CS was more effective in predicting cardiovascular events in asymptomatic patients than CIMT. Still, the relationship between the two methods was not assessed in determining vascular age [22]. Two other studies have shown the superiority of CS over CIMT in predicting cardiovascular events [23, 24] but their relationship was not investigated in terms of vascular age. In 2010, in a study by Khalil and colleagues [16], the two methods were compared for the first time. In this study, 20 patients were evaluated with a mean age of 55.8 years. When CS was used to calculate a vascular age, a mean vascular age of 67 was obtained, or an average addition of 11.3 years to the mean chronological age of 55.7 (P = 0.011). When CIMT was used to calculate vascular age, mean vascular age of 68.5 was obtained, or an average addition of 12.8 years to the mean chronological age (P = 0.016).

Thus, both CS and CIMT yielded vascular ages that added significantly to the chronologic ages. It was reported that CS and CIMT provide similar information in the assessment of vascular age. In our study, hence vascular age based on CS and CIMT was well matched; the mean vascular age was less than chronological age, in contrast to the survey by Khalil. In other studies comparing vascular age and chronological age (Although none have surveyed the correlation of age derived by CIMT and CS), mean vascular age has shown more than chronological age [17, 25-28]. Our different results could be related to our patient selection bias. Most cases in our study were selected from patients with low calcium levels.

Our study was performed during the COVID-19 pandemic, and many patients refused to do sonography to measure CIMT. As we need their consent, we could not oblige them. Those patients with a better medical situation, who generally had fewer calcium scores, were more

Table 2. Corelation between vascular ages determined by CS and CIMT

		VA-CS	VA-CIMT	chronological age
VA-CS	Pearson Correlation	-	0.904	0.933
	P value		0.000	0.000
chronological age	Pearson Correlation	0.933	0.893	-
	P value	0.000	0.000	

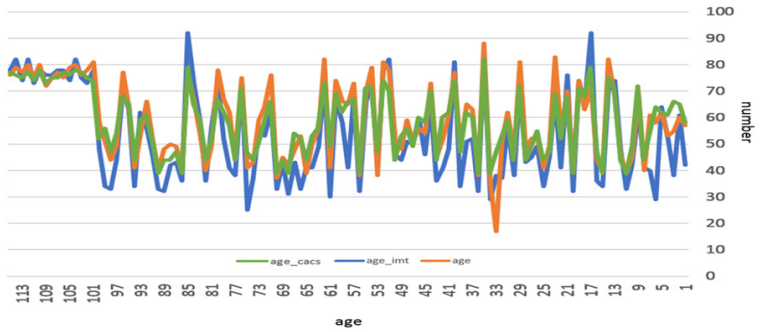

Figure 1. Relation between ages determined by CAC & CIMT and chronological age. (age_cacs is VA-CACS, age_imt is VA-CIMT and age means chronological age).

cooperative. As a result, the mean CS of our patient was 48.23, which probably doesn't correctly represent the average population. Selection biases were our main limitation, whereas having this limitation, CIMT & CS-derived age were correlative, which was a valuable finding. Finally, further studies with a larger population avoiding our limitations are recommended.

Conclusion

In the present study, it was shown that the vascular age derived by CS and CIMT are well correlated. Conversion of a patient's chronologic age to the "Vascular age" or an age at which the amount of that patient's subclinical atherosclerosis could be represented would lead to a more accurate assessment of a patient's actual cardiovascular risk.

Disclosure of conflict of interest

None.

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