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A new echocardiographic parameter of aortic stiffness and atherosclerosis in patients with coronary artery disease: Aortic propagation velocity

Taner Sen (MD)[a,*], Omac Tufekcioglu (MD)[b], Mustafa Ozdemir (MD)[c], Abdullah Tuncez (MD)[d], Belma Uygur (MD)[e], Zehra Golbasi (MD)[b], Halil Kisacik (MD)[b]

[a] Dumplupinar University Kütahya Evliya Celebi Education and Research Hospital, Cardiology, Turkey
[b] Turkiye Yuksek Ihtisas Education and Research Hospital, Cardiology, Turkey
[c] Kocaeli Derince Education and Research Hospital, Radiology, Turkey
[d] Konya Numune Hospital, Cardiology, Turkey
[e] Karaman State Hospital, Cardiology, Turkey

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ABSTRACT

Background: In this study, a novel echocardiographic parameter in the evaluation of the presence of coronary artery disease (CAD) and aortic stiffness, aortic propagation velocity, was measured and compared with other conventional aortic stiffness parameters such as aortic strain and aortic distensibility. Also, the relation between aortic propagation velocity and carotid intima media thickness was evaluated.
Method and results: A total of 51 patients with CAD and 42 patients with normal coronary arteries as a non-CAD group were included in the study. Aortic propagation velocity was significantly lower in the CAD group ($p < 0.001$). A statistically significant relation was detected between aortic propagation velocity and the maximum, mean, and overall carotid intima media thickness values for right and left carotid arteries ($p < 0.001$). There was a statistically significant relation between aortic propagation velocity, aortic strain, and aortic distensibility ($r = 0.556$, $p < 0.001$ and $r = 0.483$, $p < 0.001$ respectively).
Conclusion: Aortic propagation velocity is a novel and simple echocardiographic parameter of aortic stiffness which is feasible for non invasive cardiovascular risk stratification and selection of high risk individuals for CAD.

Introduction

Atherosclerosis is a chronic and multifactorial disease that affects whole arterial system [1]. Therefore, atherosclerotic changes in any part of the arteries give a clue about the atherosclerotic involvement of the arterial system. As the extension and severity of coronary artery disease (CAD) increase, the distensibility and strain of the aorta decrease. Parameters such as aortic strain (AS), aortic distensibility (AD), pulse pressure, augmentation index pulse wave propagation velocity in the detection of aortic stiffness were used in previous studies and a relationship with CAD was detected [2–6]. Yıldız et al. showed a relation between the presence and severity of CAD and AS [7]. Gunes et al. described the aortic propagation velocity and used it for the determination of aortic stiffness [8]. Recently, Gunes et al. showed that color M-mode-derived propagation velocity of the descending thoracic aorta (aortic propagation velocity-APV) was associated with coronary and carotid atherosclerosis and brachial endothelial function.

In this study, a novel echocardiographic parameter in the evaluation of the presence of CAD and aortic stiffness, aortic propagation velocity (APV), was measured and compared with other conventional aortic stiffness parameters such as AS and AD. Also, carotid intima media thickness (CIMT) which is an indicator of atherosclerosis was measured and the relation between APV and CIMT was evaluated. We also tried to investigate the power of APV to estimate the severity and the extent of CAD.

Patients and methods

The characteristics of the study

A total of 104 consecutive patients who had undergone coronary angiography between October 2010 and December 2010 were selected prospectively and randomized into a CAD group and a non-CAD group. Six patients did not want to join the study. Five patients were excluded from the study due to suboptimal suprasternal images. The study population was composed of 51 patients (25 male, 26 female) who had more than 50% stenosis in at least

* Corresponding author at: Dumlupinar Kutahya Evliya Celebi Education and Research Hospital, Cardiology, 43100, Turkey. Tel.: +905327064056; fax: +90 274 231 66 73.
E-mail address: medicineman_tr@hotmail.com (T. Sen).

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one coronary artery in the CAD group and 42 patients (18 male, 24 female) who had normal coronary arteries or less than 50% coronary artery stenosis in the non-CAD group. All participants were informed about the study and their consents were obtained.

Exclusion criteria

- Moderate or severe valvular stenosis or regurgitation.
- Cardiomyopathy.
- Atrial fibrillation, atrial flutter, and other tachy–brady arrhythmias.
- Electrocardiographic bundle branch block.
- Early phase of acute myocardial infarction (within 6 weeks).
- Any congenital heart disease.
- Symptomatic heart failure.
- Systemic diseases affecting the aorta (Marfan, Ehler–Dahnlos).
- Aortic aneurysms (ascending or arcus aorta >44 mm).
- Inadequate echocardiographic image quality.
- Refusal of coronary angiography.
- Refusal of participation to the study.

Coronary angiography

Coronary angiography was performed with Toshiba Infinix CSI (Toshiba, Tokyo, Japan) and Siemens Axiom-Artis (Siemens, Munich, Germany) angiography devices. More than 50% lesions in left main coronary artery, left anterior descending artery, circumflex artery, and right coronary artery were evaluated as significant and the number of affected coronary arteries was determined. The severity of CAD was calculated by Gensini risk score [9].

Transthoracic echocardiographic examination

All patients underwent transthoracic echocardiographic examination by vivid 7 Dimension (General Electric, Fairfield, CT, USA) echocardiography device with a 2.5–3.5 MHz transducer. All echocardiographic examinations were performed by the same operator who was blinded to the groups of patients. Ejection fraction, left ventricular end-systolic, and end-diastolic diameters were noted. The systolic and diastolic diameters of the ascending aorta were measured with M mode echocardiography 3 cm above the aortic valve. The aortic systolic diameter was measured when the aortic valve was fully open whereas the diastolic diameter was measured according to peak of the QRS tracings. Five consecutive measurements were made and their average was calculated (Fig. 1). After routine echocardiographic examination, color M-mode Doppler recordings were obtained with the cursor parallel to the main flow of direction in the descending aorta from the suprasternal window. The Nyquist limit was adapted to 30–50 cm/s. A flame shaped M-mode spatio-temporal velocity map was displaced by switching to M-mode with the recorder sweep rate of 200 mm/s. Then, aliasing velocity was adjusted to get clear delineation of the velocity slope. The aortic propagation velocity was calculated by the division of the distance by time of the propagation slope just by tracing the velocity slope. The mean of at least three consecutive measurements was recorded as the APV value (Fig. 2a and b). AS and AD were calculated from the echocardiographically derived aortic diameters and the clinical blood pressure. Aortic pulse pressure was calculated by subtracting diastolic aortic pressure from systolic aortic pressure. AS and AD were used as aortic elasticity parameters. The formulas used to calculate the above mentioned parameters were as follows [10].

$$\mathrm{AS}\,(\%) = \frac{(\text{aortic systolic diameter} - \text{diastolic diameter}) \times 100}{\text{diastolic diameter}}$$

$$\mathrm{AD}\,(\mathrm{cm}^2/\mathrm{dyn}) = \frac{2 \times \mathrm{AS}}{\text{systolic pressure} - \text{diastolic pressure}}$$

Carotid intima media thickness measurement

The left and right common carotid arteries were examined by the same sonographer who was blinded to the clinical data of the patients with a Vivid Logiq 7 (GE) device with a 7.5 MHz linear array transducer. Patients were examined in the supine position, with the head turned 45° from the side being scanned. For the common carotid artery measurement, 10 mm of the common carotid artery segment after the bulbus was determined. On a longitudinal, two-dimensional ultrasound image of the carotid artery, the anterior (near) and posterior (far) walls of the carotid artery are displayed as two bright white lines separated by a hypoechogenic space. The distance between the leading edge of the first bright line of the far wall and the leading edge of the second bright line indicates the intima–media thickness (Fig. 3). CIMT measurements were made

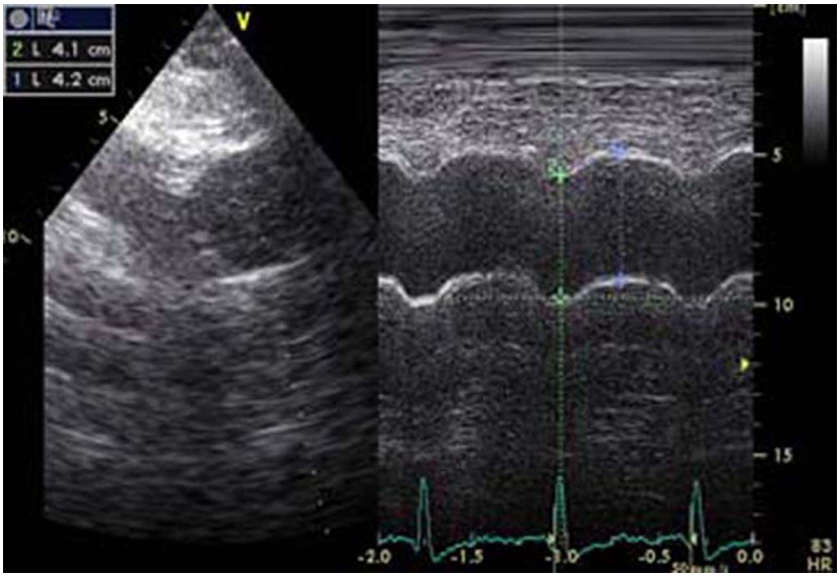

Fig. 1. Measurement of systolic and diastolic diameters of the ascending aorta with transthoracic M-mode echocardiography.

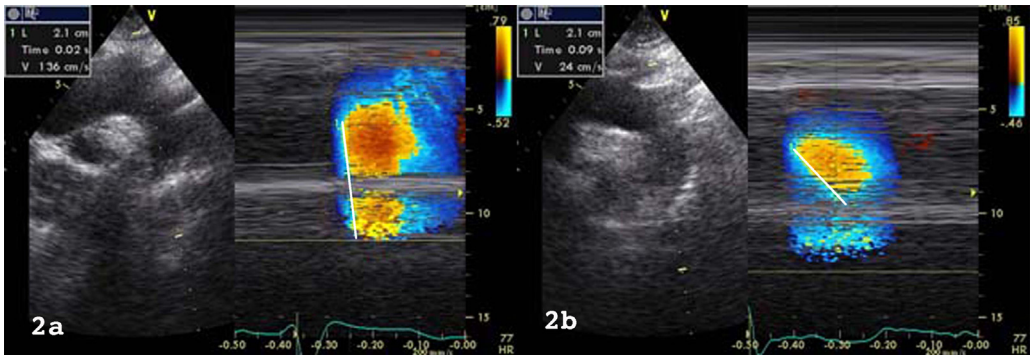

Fig. 2. (a) Aortic propagation velocity in a patient who has normal coronary arteries and (b) aortic propagation velocity in a patient with coronary artery disease.

from four different points apart 1 cm distance from each other and their mean value was calculated. The mean and maximum CIMT values for both the right and left carotid arteries and the overall maximum and mean values were determined.

Statistical analysis

All data were evaluated by the SPSS (Statistical Package for Social Sciences for Windows, version 15.0, Chicago, IL, USA). Parametric data were expressed as mean ± standard deviation and qualitative data as numbers and percentages. Differences between groups were assessed by the Student's *t*-test for normally distributed quantitative variables. Pearson test was used for correlation analysis of parametric data whereas Spearman correlation analysis was used to assess the correlations between nonparametric data. One-way ANOVA test was used for the comparison of the quantitative data between the groups. Parametric and nonparametric distribution of the variables was assessed by Kolmogorov Smirnov test. The results were considered statistically significant at the level of $p < 0.05$. Multivariate regression analysis was used to analyze the value of different baseline characteristics, stiffness parameters, and APV as independent predictors of CAD. The diagnostic ability of APV to detect significant CAD was evaluated with receiver operating characteristic (ROC) curves.

Results

Six patients did not want to join the study. Five patients were excluded from the study due to suboptimal suprasternal images.

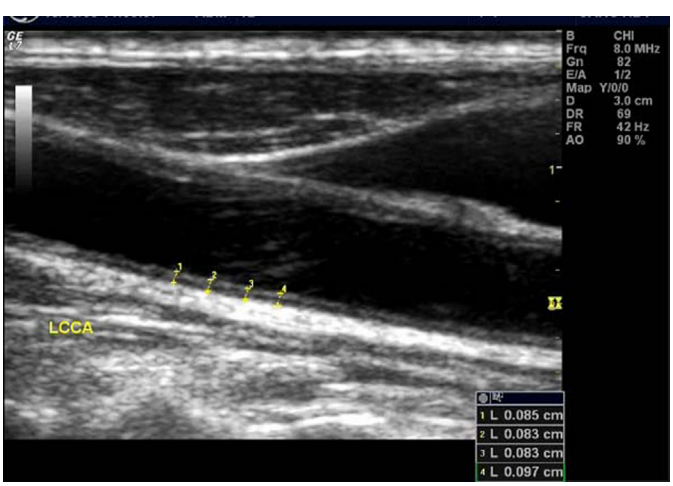

Fig. 3. Measurement of carotid artery intima media thickness of left common carotid artery. LCCA; left common carotid artery.

As a result, 51 patients in the CAD group (54.8%) and 42 patients (45%) in the non-CAD group were included. The CAD group was composed of 25 male and 26 female patients. Mean age of the CAD group was 55.2 ± 8.9 (range 35–75) years. The non-CAD group was composed of 18 male and 24 patients and their mean age was 52.3 ± 9.0 (range 33–72) years. The demographic and clinical characteristics of the groups were similar except for hyperlipidemia, waist circumference, and ejection fraction (Table 1).

Aortic systolic and diastolic diameters, systolic and diastolic blood pressure, and pulse pressure were not statistically different between the groups. Mean ascending aorta systolic diameter was 3.40 ± 0.39 cm in the CAD group and 3.39 ± 0.37 cm in the non-CAD group and mean ascending aorta diastolic diameter was 3.17 ± 0.42 cm in the CAD group and 3.03 ± 0.41 cm in the non-CAD group. AS and AD were significantly different between the groups ($p < 0.001$). APV was significantly lower in the CAD group than the non-CAD group ($p < 0.001$). APV was 39.2 ± 13.9 cm/s (range

Table 1
The clinical and demographic characteristics of the CAD and non-CAD groups.

	CAD group	Non-CAD group	*p*-Value
Age (year)	55.2 ± 8.9	52.3 ± 9.0	0.13
Male	25 (%49)	26(%51)	0.55
Female	18 (%42.9)	24(%57.1)	
Body mass index (kg/m^2)	29.5 ± 4.5	29.8 ± 5.4	0.79
Waist circumference (cm)	97.4 ± 12	91.3 ± 11.2	0.017
Hypertension (%)	66.7	59.5	0.47
Diabetes mellitus (%)	25.5	19	0.46
Hyperlipidemia (%)	76.5	40.5	0.001
Smoking (%)	25.5	23.8	0.85
Family history (%)	35.3	26.8	0.38
Total cholesterol (mg/dl)	191.4 ± 46.2	197.3 ± 40	0.52
LDL (mg/dl)	115.6 ± 36	120.5 ± 37.1	0.52
HDL (mg/dl)	41.8 ± 12.6	45.5 ± 11.4	0.15
Triglyceride (mg/dl)	173.5 ± 89.7	147.1 ± 61.9	0.11
Ejection fraction (%)	59.0 ± 6.9	62.3 ± 5.6	0.02

LDL, low-density lipoprotein; HDL, high-density lipoprotein; CAD, coronary artery disease; statistical significance $p < 0.05$.

Table 2
Aortic stiffness parameters in the CAD and non-CAD groups.

	CAD group	Non-CAD group	*p*-Value
Diastolic diameter (cm)	3.17 ± 0.42	3.03 ± 0.41	0.106
Systolic diameter (cm)	3.40 ± 0.39	3.39 ± 0.37	0.889
Systolic blood pressure (mmHg)	131.6 ± 17.0	129.1 ± 20.6	0.528
Diastolic blood pressure (mmHg)	79.8 ± 8.4	79.0 ± 12.2	0.730
Aortic strain (%)	7.4 ± 3.3	12.4 ± 5.4	<0.001
Aortic distensibility (cm^2 dyn^{-1} 10^{-3})	2.46 ± 1.63	4.17 ± 2.39	<0.001
APV	39.2 ± 13.9	81.4 ± 21.4	<0.001

APV, aortic propagation velocity; CAD, coronary artery disease; statistical significance $p < 0.05$

10–80 cm/s) in the CAD group whereas it was 81.4 ± 21.4 cm/s (range 30–133 cm/s) in the non-CAD group (Table 2).

The mean and maximum CIMT values for both right and left carotid arteries and the overall maximum and mean values were significantly higher in the CAD group (Table 3). APV was positively correlated with left, right, and overall CIMT ($p < 0.001$). APV was also significantly correlated with AD and AS ($r = 0.556$, $p < 0.001$ and $r = 0.483$, $p < 0.001$ respectively). As the CAD group was divided according to number of affected coronary arteries (one, two, and three vessels), there was no statistically significant correlation between APV and the number of affected coronary arteries ($p < 0.142$). APV was not significantly related with Gensini score in the CAD group ($p = 0.092$) (Table 4). Multivariate regression analysis including age, body mass index, systolic blood pressure, left ventricular ejection fraction, CIMT, LDL cholesterol, APV, AS, and AD revealed that only APV (beta = 0.743, $p < 0.001$) was a significant predictor of CAD (Table 5). An APV value of ≤60.5 cm/s, determined by ROC curve analysis, predicted CAD with 90.5% sensitivity and 92.2% specificity.

Table 3
Carotid intima media thickness in the CAD and non-CAD groups.

Carotid intima media thickness	CAD group	Non-CAD group	*p*-Value
Left			
Highest (mm)	0.741 ± 0.15	0.627 ± 0.15	0.001
Mean (mm)	0.672 ± 0.14	0.557 ± 0.14	<0.001
Right			
Highest (mm)	0.687 ± 0.18	0.599 ± 0.12	0.008
Mean (mm)	0.626 ± 0.17	0.532 ± 0.11	0.003
Overall			
Highest (mm)	0.757 ± 0.18	0.658 ± 0.14	0.006
Mean (mm)	0.658 ± 0.14	0.548 ± 0.12	<0.001

CAD, coronary artery disease; statistical significance $p < 0.05$.

Table 4
The relationship between aortic propagation velocity and carotid intima media thickness, aortic strain, aortic distensibility, number of affected vessels, and Gensini score.

	APV	
	r value	*p value*
Left common carotid intima media thickness		
Highest (mm)	−0.447	<0.001
Mean (mm)	−0.466	<0.001
Right common carotid intima media thickness		
Highest (mm)	−0.390	<0.001
Mean (mm)	−0.403	<0.001
Overall common carotid intima media thickness		
Highest (mm)	−0.392	<0.001
Mean (mm)	−0.490	<0.001
Aortic strain (%)	0.556	<0.001
Aortic distensibility ($cm^2\ dyn^{-1}\ 10^{-3}$)	0.483	<0.001
Number of affected vessels		0.142
Gensini score	−0.239	0.092

APV, aortic propagation velocity; statistical significance $p < 0.05$.

Table 5
Multivariate regression analysis.

Variables	*B*	STD	Beta	*T*	Sig *T*
Age (year)	−0.009	0.005	−.155	−1.726	0.089
BMI (kg/m^2)	−0.002	0.008	−0.020	−0.245	0.807
SBP (mmHg)	0.002	0.003	0.089	0.857	0.394
LVEF (%)	0.004	0.007	0.045	0.550	0.584
CIMT (mm)	−5.775	15.370	−0.173	−0.376	0.708
LDL (mg/dl)	−0.001	0.001	−0.097	−1.312	0.194
AS (%)	−0.032	0.019	−0.296	−1.651	0.103
AD ($cm^2\ dyn^{-1}\ 10^{-3}$)	0.030	0.052	0.122	0.583	0.562
AVP	−0.014	0.002	−0.743	−8.025	0.0001

BMI, body mass index; SBP, systolic blood pressure; LVEF, left ventricle ejection fraction; CIMT, carotid intima media thickness; LDL, low density lipoprotein; AS, aortic strain; AD, aortic distensibility; AVP, aortic propagation velocity. Statistical significance ($p < 0.05$).

Discussion

Aortic stiffness is associated with cardiovascular risk factors such as CAD, smoking, obesity, hypertension, glucose tolerance, diabetes, and older age [11–16]. As the extent and the severity of the atherosclerosis increase, AD and AS decrease. As atherosclerosis progresses, tunica media increases in thickness and tunica media gets stiffer [17,18]. Therefore, it is very valuable to detect atherosclerotic disease before clinical disease comes out via a noninvasive method. Endothelial dysfunction is the first stage of the atherosclerosis. Atherosclerosis increases arterial wall thickness and the stiffness of the aorta. The arterial resistance will increase as the arterial wall gets stiff and thick. Increase in arterial resistance decreases the flow APV. In our study, AS, AD, and APV were significantly lower in the CAD group compared to the non-CAD group. As a result of atherosclerotic process in patients with CAD, the aorta gets stiff, so the APV decreases. Furthermore, our study showed that APV was statistically correlated with the other conventional aortic stiffness parameters as AS and AD.

CIMT is significantly related with CAD. CIMT measurement with B-mode ultrasonography has been frequently used in the detection of atherosclerosis in many epidemiological studies. It is cheap and a noninvasive method [19–21]. According to the guideline of European Society of Cardiology, the level of CIMT > 0.9 mm was accepted as the target organ injury cut off point [22]. In our study, the mean and maximum CIMT values for both right and left carotid arteries and the overall maximum and mean values were significantly higher in the CAD group. APV was positively correlated with left, right, and overall CIMT. It is important that APV was significantly correlated with CIMT which is a valuable marker of atherosclerosis. In our study, we could not show that APV was correlated with the number of the affected coronary arteries and Gensini score. It is thought that the number of the patients in the CAD group was not large enough to reach statistical significance. Larger studies are required to show the correlation between Gensini score and APV.

APV is a simple and easy echocardiographic parameter which could be used in daily echocardiographic examination. The best clinical utilization of APV would be in noninvasive cardiovascular risk stratification and management of patients and for better selection of cardiovascular high-risk individuals. This method also might enable physicians to select patients for primary prevention of atherosclerosis and to identify patients who will benefit from further diagnostic tests for CAD.

Limitations

The suprasternal images of some of the patients were not suitable enough to get clear measurement of APV. Furthermore, the patient sample size may not be large enough to reach statistical significance to show the correlation between Gensini score and APV.

Conclusion

Our study showed that APV could be used as a new echocardiographic parameter in detection of aortic stiffness in patients with CAD. Furthermore, APV is significantly correlated with CIMT which is a well-known marker of atherosclerosis. As a conclusion, APV is a novel and simple echocardiographic parameter of aortic stiffness which is feasible for noninvasive cardiovascular risk stratification and selection of high-risk individuals for CAD.

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