The Relation of Aortic Root 2D Speckle Strain to Aortic Stiffness as Predictors of Atherosclerosis in Vascular Beds

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The Relation of Aortic Root Two-dimensional Speckle Strain to Aortic Stiffness as Predictors of Atherosclerosis in Vascular Beds

Ahmed Magdy Ahmed Abd-Elgawada, Ali Mohammed Alamin, Ahmed Abdelraouf Mahdy, Mohammed Hamza Hamed

Abstract

Background: Two-dimensional speckle tracking (2D-ST) echocardiography is a promising new technique for imaging.

Aim: To evaluate feasibility of real-time 2D-ST echocardiography of the aortic root in relation to aortic stiffness for the early prediction of atherosclerosis in vascular beds.

Patients and methods: This cross-section study was carried out on 50 patients complaining of chest pain. All patients were subjected to blood pressure and aortic stiffness index measurement, invasive coronary angiography, resting transthoracic echocardiography, aortic speckle tracking echocardiography, carotid intima-media thickness (IMT), and ankle-brachial index (ABI). Patients were subdivided into two groups: atherosclerotic group included 32 patients who had lesions in one or more vascular bed and nonatherosclerotic group included 18 patients who had no affected vascular beds.

Results: Aortic distensibility and circumferential ascending aortic strain had a significant negative relationship with Gensini score ($r = -0.717$, $P < 0.001$, and $r = -0.789$, $P < 0.001$, respectively) and IMT ($r = -0.645$, $P < 0.001$, and $r = -0.788$, $P < 0.001$, respectively) and had a significant positive relationship with lowest ABI ($r = 0.610$, $P < 0.001$, and $r = 0.701$, $P < 0.001$, respectively). ABI was significantly lower in cases with LM lesions compared with those with no LM affection ($P < 0.001$). IMT was insignificantly different between patients with LM lesions compared with those with no LM affection.

Conclusions: Circumferential ascending aortic strain evaluated by 2D-ST echocardiography at rest predicted presence of significant coronary artery disease and recognized affection of different vascular beds.

Keywords: Aortic root, Aortic stiffness, Atherosclerosis, Two-dimensional speckle strain

1. Introduction

Arterial stiffening is an early manifestation of detrimental functional and structural vascular wall alterations. Atherosclerosis and degenerative arterial bed alterations (i.e. atherosclerosis) tend to coexist, leading to diffuse, progressive, and age-relevant deterioration in different vascular beds.

Increased aortic stiffness elevates the risk for cardiovascular diseases (CVD) and predicts cardiovascular mortality and morbidity, leading to more use of arterial stiffness assessment clinically. However, reproducibility and validity of the conventional techniques utilized for arterial stiffness evaluation locally, such as distensibility, stiffness index, and elastic modulus, are limited as they depend on blood pressure (BP) of the patient.

Two-dimensional speckle strain (2D-ST) echocardiography recognizes particular echogenic markers (i.e. speckles) in gray-scale images and tracks them in each beat. The outcome permits independent
calculations of deformation and motion variables, such as displacement, velocity, strain (e), and strain rate.3

The ankle-brachial index (ABI) acts as a measure of systemic atherosclerosis and thus is linked to atherosclerotic risk factors and prevalent CVD in other vascular beds.4

This trial aimed to evaluate the feasibility of real-time 2D-ST echocardiography of the aortic root in relation to aortic stiffness for the early prediction of atherosclerosis in vascular beds.

2. Patients and methods

This cross-section trial was carried out on 50 patients between the age of 18 and 65 years, who complained of chest pain and were subjected to coronary angiography and excluded evidence of structural heart disease.

The trial was conducted after approval from Ethics Committee. Moreover, informed written consent was obtained from the patients included.

Exclusion criteria were impaired left ventricular (LV) systolic function (EF < 50%), significant valvular heart diseases (more than mild valvular lesions), myocardial and pericardial diseases, congenital heart diseases, LV hypertrophy in which LV mass was less than 115 g/m² in men and less than 95 g/m² in women, chronic or inflammatory diseases and any form of malignancies, aortic aneurysms, systematic illnesses affecting the aorta such as Takayasu’s arteritis and Marfan’s syndrome, significant arrhythmias, and intraventricular conduction disturbances.

The study cases were divided into two groups: atherosclerotic group included 32 patients who had a lesion in one or more vascular beds, and nonatherosclerotic group included 18 patients who had no affected vascular beds.

All cases underwent detailed history, physical examination with special interest in cardiovascular risk factors (hypertension diagnosed and/or treated with medications, history of smoking, diet and/or exercise, dyslipidemia, diabetes mellitus, previous diagnosis of ischemic heart disease, family history of atherosclerotic coronary artery disease (CAD), and obesity, and standard 12-leads ECG.

BP and aortic stiffness index measurement: office BP was measured using a manual sphygmomanometer cuff at the left brachial artery with the patient in supine position. The aortic stiffness was assessed using aortic distensibility (D), which is calculated as D = 2(As-Ad)/[Ad (Ps-Pd)],7 where Ps = systolic BP, Pd = diastolic BP, and As = aortic systolic diameter, and Ad = aortic diastolic diameter.6

Invasive coronary angiography: left and right catheters were introduced through the sheath in right femoral artery via femoral or radial approach. A highly qualified operator analyzed the angiograms visually. The extension of coronary atherosclerosis was calculated using the Gensini score. Gensini score was determined by providing each coronary stenosis with a severity score: 32 points for complete obstruction, 16 points for 91–99% narrowing, eight points for 76–90% narrowing, four points for 51–75% narrowing, two points for 26–50% narrowing, and one point for less than or equal to 25% narrowing.

Resting transthoracic echocardiography is a widely used noninvasive imaging technique that aids in diagnosing multiple cardiovascular conditions and providing quantitative and qualitative information on pathophysiology and outcome. Transthoracic echocardiography was used to detect wall motion abnormalities and assess LV systolic function. All measures were carried out in accordance with the current American Society of Echocardiography recommendations (2015).7 Standard echocardiographic measurements were obtained including diameters of aortic root, left atrial diameter, left ventricular end-systolic diameter, left ventricular end-diastolic diameter, interventricular septum thickness, left ventricular posterior wall thickness, and left ventricular ejection fraction. Cardiac valves were assessed by a comprehensive Doppler study to exclude significant valvular heart diseases.

2.1. Aortic speckle tracking echocardiography

Circumferential strain of aortic root: strain of the aortic root was performed at the precise sample volume site for M-mode cut during measurements of aortic diameters. 2D echocardiography was performed from the left parasternal short-axis view at 2–3 cm above the level of aortic valve; a circular plane of the root of the aorta was obtained. At end expiratory apnea, 2D image acquisition was done. Ascending aortic strain was evaluated with the use of 2D-ST echocardiography. For accurate detection of rapid movement of the root of aorta, a very high-frame-rate image of ascending aorta was acquired. A circle was manually drawn onward the internal surface of aorta, and then another circle is spontaneously generated by the machine on the external surface of aortic wall. The width of area of interest was manually modified to the thinnest permitted thickness by the software due to the aortic wall low thickness. The software is programmed to divide the best fit aortic wall image into six equal color-coded
segments (green, yellow, blue, light blue, purple, and red). Variable color quantification curves were used to represent the strain of each aortic wall segment. Circumferential strain peaks values were detected in each segment, which usually were recognized just above the aortic valve closure. A circumferential ascending aortic strain (CAAS) was expressed as the mean of peak CAAS of the six segments. A corrected CAAS is measured by dividing the overall CAAS/pulse pressure. The optimal cutoff value for global CAAS is 0.149%/mmHg with a specificity of 73% and a sensitivity of 76%. Global CAAS was calculated and used to compare the values between patient with significant and nonsignificant atherosclerosis in vascular beds.

Carotid ultrasonographic examination: carotid artery measurements were done by a qualified operator blinded to clinical data as part of routine examinations. The carotid arteries were examined as far as could be made visible for plaques to detect atherosclerotic alterations. Intima-media thickness (IMT) of the carotid wall was evaluated as the length between the medial-adventitial and inner–intimal interfaces, and triplicate values were averaged and abnormal IMT is defined as a value greater than 0.7 mm².

The measurement of the ABI at rest was calculated for each leg by dividing the ankle systolic BP by the brachial pressure. ABI below 0.90 is considered as a marker for peripheral artery disease (PAD) diagnosis.

### 2.2. Statistical analysis

SPSS v26 was used for the statistical analysis (IBM Inc., Chicago, Illinois, USA). The unpaired Student’s t test was used to compare the two groups’ means and SDs for quantitative variables. The χ² test or Fisher’s exact test was used for statistical analysis of qualitative variables provided as frequencies and percentages. Analyses such as the receiver operating characteristic curve and the Pearson correlation were also conducted. When the P value was less than 0.05 using two-tailed testing, it was determined to be statistically significant.

### 3. Results

Patients’ demographics and ECHO findings in both studied groups are shown in **Table 1**.

Aortic distensibility, CAAS, and corrected CAAS were significantly lower in atherosclerotic group compared with nonatherosclerotic group (P < 0.001). IMT, number of patients with PAD, and number of patients with Gensini score (>50) had considerably increased in the atherosclerotic group compared with the nonatherosclerotic group (P ≤ 0.001). Atherosclerotic group had significantly more affected vessels, more LM affections, and more severe lesions compared with nonatherosclerotic group (P < 0.001, P = 0.040). Carotid stenosis was insignificantly different between nonatherosclerotic group and atherosclerotic group. ABI was significantly lower (with mild or moderate PAD) in

Table 1. History, risk factor, blood pressure, and echo findings in atherosclerotic and nonatherosclerotic groups.

<table>
<thead>
<tr>
<th></th>
<th>Nonatherosclerotic (N = 18)</th>
<th>Atherosclerotic (N = 32)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>52.4 ± 9.68</td>
<td>58.2 ± 8.52</td>
<td>0.034*</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>10 (55.56)</td>
<td>23 (71.88)</td>
<td>0.391</td>
</tr>
<tr>
<td>Female</td>
<td>8 (44.44)</td>
<td>9 (28.13)</td>
<td></td>
</tr>
<tr>
<td>DM</td>
<td>1 (5.56)</td>
<td>11 (34.38)</td>
<td>0.036*</td>
</tr>
<tr>
<td>HTN</td>
<td>4 (22.22)</td>
<td>25 (78.13)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoker</td>
<td>3 (16.67)</td>
<td>22 (68.75)</td>
<td>0.001*</td>
</tr>
<tr>
<td>Nonsmoker</td>
<td>15 (83.33)</td>
<td>10 (31.25)</td>
<td></td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>3 (16.67)</td>
<td>13 (40.63)</td>
<td>0.117</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>117 ± 29.12</td>
<td>138.8 ± 11.29</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>79.6 ± 21.12</td>
<td>93.1 ± 8.96</td>
<td>0.003*</td>
</tr>
<tr>
<td>LVEDD (mm)</td>
<td>5 ± 0.52</td>
<td>4.9 ± 0.55</td>
<td>0.538</td>
</tr>
<tr>
<td>LVESD (mm)</td>
<td>3.5 ± 0.37</td>
<td>3.5 ± 0.44</td>
<td>0.915</td>
</tr>
<tr>
<td>EF (%)</td>
<td>57.5 ± 5.62</td>
<td>54.7 ± 6.91</td>
<td>0.147</td>
</tr>
<tr>
<td>LAD (mm)</td>
<td>3.4 ± 0.31</td>
<td>3.4 ± 0.32</td>
<td>0.659</td>
</tr>
<tr>
<td>ASD (mm)</td>
<td>3.1 ± 0.4</td>
<td>3.2 ± 0.46</td>
<td>0.759</td>
</tr>
<tr>
<td>ADD (mm)</td>
<td>2.8 ± 0.38</td>
<td>3 ± 0.44</td>
<td>0.067</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD and frequency (%).

ASD, atrial septal defect; DM, diabetes mellitus; EF, ejection fraction; HTN, hypertension; LAD, left anterior descending artery; LVEDD, left ventricular end diastolic diameter; LVESD, left ventricular end systolic diameter.

*Significant as P value less than or equal to 0.05.
patients with LM lesions compared to those with no LM affection ($P < 0.001$). IMT was insignificantly different between patients with LM lesions compared with those with no LM affection. Carotid stenosis has statically increased in patients with LM lesions compared with those with no LM affection ($P < 0.001$) (Table 2).

Table 3 shows the number of beds affected among atherosclerotic patients. Aortic distensibility and CAAS had a significant negative relationship with Gensini score ($r = -0.717$, $P < 0.001$, and $r = -0.789$, $P < 0.001$, respectively) and IMT ($r = -0.645$, $P < 0.001$, and $r = -0.788$, $P < 0.001$, respectively) and had a significant positive relationship with lowest ABI ($r = 0.610$, $P < 0.001$, and $r = 0.701$, $P < 0.001$, respectively). Gensini score had a significant positive relationship with IMT ($r = 0.739$, $P < 0.001$) and had a significant negative relationship with lowest ABI ($r = -0.755$, $P < 0.001$) (Table 4).

CAAS can significantly predict CAD [area under the curve (AUC) = 0.856, $P < 0.001$] at cutoff less than or equal to 0.05.
Table 4. Correlation of aortic distensibility and circumferential ascending aortic strain with intima-media thickness, Gensini score and ankle-brachial index, correlation of Gensini score with intima-media thickness and ankle-brachial index.

<table>
<thead>
<tr>
<th></th>
<th>Aortic distensibility</th>
<th>CAAS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td>P</td>
</tr>
<tr>
<td>IMT</td>
<td>−0.645</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>Gensini score</td>
<td>−0.717</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>Lowest ABI</td>
<td>0.610</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>Gensini score</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>r</td>
<td>P</td>
</tr>
<tr>
<td>IMT</td>
<td>0.739</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>Lowest ABI</td>
<td>−0.755</td>
<td>&lt;0.01*</td>
</tr>
</tbody>
</table>

ABI, ankle brachial index; CAAS, Circumferential Ascending aortic strain; IMT, intima-media thickness.

*Significant as P value less than 0.05.

than or equal to 6.6 with 79.95% sensitivity, 84.62% specificity, 88.2% positive predictive value (PPV), and 73.3% negative predictive value (NPV). Corrected CAAS can significantly predict CAD (AUC = 0.877, P < 0.001) at cutoff less than or equal to 0.16 with 89.47% sensitivity, 76.92% specificity, 85% PPV, and 83.3% NPV. Aortic distensibility can significantly predict CAD (AUC = 0.883, P < 0.001) at cut off less than or equal to 2.3 with 89.47% sensitivity, 76.92% specificity, 85% PPV, and 83.3% NPV. CAAS can significantly predict carotid artery disease (AUC = 0.844, P < 0.001) at cutoff less than or equal to 4.5 with 75% sensitivity, 82.14% specificity, 37.5% PPV, and 95.8% NPV. Corrected CAAS can significantly predict carotid artery disease (AUC = 0.875, P < 0.001) at cutoff less than or equal to 0.12 with 100% sensitivity, 71.43% specificity, 27.3% PPV, and 95.2% NPV. Aortic distensibility was an insignificant predictor of carotid artery disease. CAAS can significantly predict PAD (AUC = 0.831, P < 0.001) at cutoff less than or equal to 6 with 64% sensitivity, 100% specificity, 100% PPV, and 43.7% NPV. Corrected CAAS can significantly predict PAD (AUC = 0.751, P = 0.013) at cutoff less than or equal to 0.12 with 48% sensitivity, 100% specificity, 100% PPV, and 35% NPV. Aortic distensibility can significantly predict PAD (AUC = 0.837, P < 0.001) at cutoff less than or equal to 2.3 with 76% sensitivity, 85.71% specificity, 95% PPV, and 50% NPV.

By comparing between CAAS, corrected CAAS, and aortic distensibility as predictors at the same time, there was no significant variation between them in early prediction of CAD and carotid artery disease and PAD (Fig. 1).

Case 1. A 53-year-old male patient, hypertensive smoker, presented to our hospital with ACS (NON-STE-ACS). Laboratory investigation showed normal complete blood count and renal profile with elevated low-density lipoprotein level. Resting 12-lead ECG showed ST segment depression in inferior leads. Echocardiographic assessment showed normal LV dimensions and preserved systolic function (left ventricular ejection fraction = 50%) and normal aortic and left atrial diameters. Aortic distensibility was $1.3 \times 10^{-3}$ mmHg, whereas CAAS was 3.2%. Invasive CA revealed multivessel affection with distal LM lesion and Gensini score was 151. Carotid IMT was 1.4 mm, and there was 20% carotid stenosis. The lowest ABI was 0.7 (Fig. 2).

Case 2. A 53-year-old female patient, hypertensive not diabetic, presented to our hospital for elective coronary angiography. Laboratory investigation showed normal complete blood count, lipid profile, and renal function. Resting 12-lead ECG showed normal sinus rhythm. Echocardiographic assessment showed normal conventional transthoracic echocardiographic assessment with normal LV function and dimensions and normal aortic root and left atrial diameters. Aortic distensibility was $6 \times 10^{-3}$ mmHg, whereas CAAS was 15.6%. Invasive CA revealed normal coronaries and Gensini score was 0. Carotid IMT was 0.3 mm, and there was no carotid stenosis. The lowest ABI was 0.92 (Fig. 3).

4. Discussion

Increased aortic stiffness elevates the risk for CVD and predicts cardiovascular morbidity and mortality. 10 2D strain echocardiography enables a fast, precise, angle-independent determination of regional myocardial deformities. 11 Aortic elasticity can be linked to CAD degree. 12 Hence, it would be appealing if the evaluation of ascending aortic strain by 2D-ST echocardiography could enhance coronary artery stenosis diagnosis. 13, 14

The current work showed that CAAS and corrected CAAS were significantly lower in atherosclerotic group compared with nonatherosclerotic group (P < 0.001).

Consistently, Hamdy Abd El-Aziz et al. 15 reported that CAAS was significantly lower in atherosclerotic group compared with nonatherosclerotic group (P < 0.001).

Regarding the IMT and carotid stenosis in the current study, our results agree with those documented by Kim et al. 16 who showed that IMT was significantly higher in CAD group compared with...
non-CAD group (0.72 ± 0.17 mm in the non-CAD group and 0.82 ± 0.16 mm in the CAD group; \( P = 0.009 \)). Moreover, carotid stenosis was insignificantly different between both studied groups.

Our results revealed that atherosclerotic group had significantly higher number of cases with PAD in compared with nonatherosclerotic group (\( P < 0.001 \) and \( P = 0.040 \)) and a significantly higher number of cases with Gensini score (>50) compared with nonatherosclerotic group (\( P = 0.001 \)).

In agreement with our trial, Trihan et al.\(^{17}\) found that the patient group had significantly more number of patients with PAD (mild and moderate) compared with controls (\( P < 0.05 \)). Patients had significantly more affected vessels, more LM affections, and more severe lesions compared with nonatherosclerotic group (\( P < 0.001 \) and \( P = 0.040 \)).
Fig. 2. (a) 2D transthoracic Echo, long axis view, MM at level of aortic root and LA, (b) 2D transthoracic echo, long axis view, MM at the tip of mitral valve leaflets, (c) circumferential ascending aortic root strain, (d) coronary angiography, (e) carotid IMT of the case. 2D, two dimensional.
affections, and more severe lesions compared with controls.

In agreement with our trial, Korkmaz et al. demonstrated that PAD prevalence is quite high even if cases do not show any symptoms linked to PAD. Moreover, these cases showed more complex coronary lesions and there was a strong relationship between the coronary lesion complexity and ABI. Kim et al. found that CAD group had significantly lower carotid strain and strain rate and there was variation between CAD group graded according to vessel number with more than moderate stenosis. CAAS was negatively correlated with carotid IMT. CAD group had significantly higher carotid IMT and significantly lower strain and strain rate. They also found a significant positive relationship between Gensini score and IMT ($r = 0.639$, $P < 0.05$).

In consistent with our results, Hamdy Abd El-Aziz et al. reported that CAAS can significantly predict ischemic heart disease at cutoff less than or equal to 9.1 with 96.7% sensitivity, 92% specificity, 95.1%
PPV, and 79.3% NPV, with an accuracy of 98.8%. Aortic distensibility can significantly predict ischemic heart disease at cutoff less than or equal to 3.03 with 73.3% sensitivity, 64% specificity, 78.6% PPV, and 57.1% NPV, with an accuracy of 77.5%. By comparing between CAAS and aortic distensibility as predictors at the same time, CAAS has more sensitivity, accuracy than aortic distensibility in predicting ischemic heart disease.

Limitations: this is a single-center trial with relatively smaller sample size. Reproducibility and validity of the study techniques are limited due to their dependence on the BP of the patient and now can be replaced by new strain methods. 2D-ST echocardiography is a semiautomated technology that requires examiners to draw a line along the aortic wall inner side manually. Thus, this technique depends on the examiner limiting its wide use clinically, 2D-ST echocardiography software is available for LV not for aorta, so it was unfortunately used for aortic strain measurement.

4.1. Conclusions

CAAS evaluated by 2D-ST echocardiography at rest predicted significant CAD presence and recognized multi-vessel illness. Aortic stiffness index and distensibility are old methods used for evaluation of arterial stiffness locally. Therefore, the CAAS may be useful to aid in clinical judgment, although exclusive use of this tool requires further research studies.

Conflict of interest

Authors declare that there is no conflict of interest, no financial issues to be declared.

References