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Arterial Stiffness and Its Correlation with the Extent of Coronary Artery Disease

Hoorak Poorzand[1], Ali Eshraghi[2*], Maliheh Layeghian[3], Mohammad Ramezani[4], Negar Morovatdar[5]

[1] *Echocardiologist, Atherosclerosis Prevention Research Center, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran*
[2] *Cardiologist, Atherosclerosis Prevention research Center, Mashhad University of Medical Sciences, Mashhad, Iran*
[3] *Cardiologist, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran*
[4] *Medical Student, Student Research Committee, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran*
[5] *Community Medicine Specialists, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran*

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ABSTRACT

Introduction: Coronary artery disease secondary to atherosclerosis is the most common cause of mortality. Coronary angiography is the most precise method for determining the extent of disease in the coronary vascular bed. Arterial stiffness has been proposed as a marker of atherosclerosis in some studies. One of the noninvasive methods for the determination of arterial stiffness is Doppler echocardiography. In this study, we aimed to find the correlation between arterial stiffness as measured by echocardiography and the extent of coronary artery disease as evaluated through angiography.

Material and Methods: Aortic pulse wave velocity (APWV) was measured by using the Doppler method in 70 patients, who were candidates for coronary angiography. The extent of coronary artery disease was determined quantitatively in terms of Friesinger index and semi-quantitatively as the number of vessels with stenosis of over 50%. Then, the correlation between arterial stiffness and these factors was evaluated.

Results: The mean APWV was 9.1±5 m/s. There was a direct relationship between APWV and Friesinger index, which was not statistically significant (P=0.67). The mean APWV for patients with one-vessel disease was 4.4±1.8 m/s, while it was 9.9±3.6 m/s in patients with two-vessel disease and 7.9±4 m/s in those with three-vessel disease, which did not show any statistically significant difference.

Conclusion: Doppler echocardiography to measure APWV was not considered as a promising tool to predict the extent of coronary artery disease.

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Introduction

Coronary artery disease (CAD)is the leading cause of death in the world (1) and intensive medical therapy considerably reduces the likelihood of recurrent major cardiovascular events and the related mortality(2, 3). Several invasive and noninvasive methods have been proposed to detect the presence of CAD(4) and much effort has been made to find optimal modalities with shorter diagnostic lag and lower cost, especially in the emergency situations (5,

**Corresponding author:* Ali Eshraghi, Atherosclerosis Prevention research Center, Mashhad University of Medical Sciences, Mashhad, Iran. Tel: +985138012739; Email: eshraghia@mums.ac.ir

6). Limited epidemiological studies have focused on arterial stiffness, which may represent a predictor of cardiovascular (CV) risk (7-10). Arterial stiffness can be assessed noninvasively by the measurement of pulse wave velocity (PWV), a simple and reproducible method. The elastic properties of the aorta and central arteries are important determinants of cardiovascular coupling, and the PWV measured along the aortic or aortoiliac pathway is the most clinically relevant one (11). A longitudinal study by Blacher et al. (12) demonstrated an independent relationship between arterial stiffness and all-cause and cardiovascular mortality in patients with end-stage renal disease (13). Another study indicated a relationship between arterial rigidity and the extent of coronary involvement in patients with myocardial infarction (MI), in which arterial stiffness was measured exclusively by methods other than Doppler modality (14). Transthoracic Echocardiography as a non-invasive and widely available tool, have promising role in diagnosis of cardiovascular diseases. APWV, derived by Doppler echocardiography, has been introduced as a reliable method, with a close correlation with invasive assessment (15). In another study on heart failure patients, it was found to have prognostic importance (16). In terms of CAD diagnosis or extent, the predictive value of aortic stiffness measured by Doppler echocardiography has not been established. This study was aimed at investigating the relationship between vascular stiffness and the extent of coronary heart disease. In this study, PWV of the aorta artery (APWV) was measured by Doppler echocardiography, and the extent of coronary disease was determined directly via angiography.

Materials and Methods

Participants

This cross-sectional study was conducted in the Cardiology Department of Imam Reza Hospital, Mashhad, Iran. With respect to α=0.05, β= 0.2 and moderate effect size as 0.7 by G.Power 3.1.9.9, sample size was calculated as 70 patients. We included 70 consecutive, unselected patients admitted for coronary angiography to be evaluated for coronary artery disease (CAD) from 2014 to 2015. Transthoracic echocardiography (TTE) was performed in all the patients. The exclusion criteria were history of any aortic surgeries, lack of sinus rhythm, significant aortic valve disease, and lack of accurate measurement of pulse wave velocity (PWV) due to improper acoustic windows. All the patients were studied while taking their medications regularly.

Design

Clinical and demographic information such as age, gender, and coronary risk factors were gathered in all patients. Systolic and diastolic blood pressure and pulse pressure were controlled at three times and under equal standard conditions. Using Phillips IE33 scanner (Phillips Ultrasound, Bottell, WA, USA) and X5S matrix probe, TTE echocardiography was performed to measure aortic pulse wave velocity (APWV). The following method was used to measure APWV: flow measurement was performed at two levels of the aortic arch and abdominal aorta. To measure flow at the level of the aortic arch, we placed the transducer in suprasternal notch and sample volume distal to the origin of the left subclavian artery. The distance between the transducer and the sample volume was measured by the echo 2D (D1). The R wave of the QRS complex, which was simultaneously recorded by the electrocardiography (ECG), was considered as a time reference. The time interval between the peak of the wave R in the electrocardiogram and the start of the aortic fluctuations in the Doppler was measured (T1). Flow in the abdominal aorta was assessed in subcostal window and the distance between suprasternal notch and the probe location on the abdominal skin surface measured (D2). The time interval between the peak of the R wave in ECG and the beginning of the aortic flow in Doppler signal was measured (T2; Figure 1). Finally, pulse wave velocity in the aorta was calculated as follows:

$$PWV = (D2 - D1) / (T2 - T1)$$

The patients then underwent coronary angiography. All angiographic images were assessed by an expert cardiologist. Obstructive CAD was defined as narrowing of more than 50% of the lumen diameter. In addition to this semi-quantitative method, coronary artery involvement in each case was calculated using a conventional numerical index (Friesinger index) with values ranging from 0 to 15. Each major coronary artery, received a number between 0 and 5,as the following:

Score 0: No stenosis along the vessel;

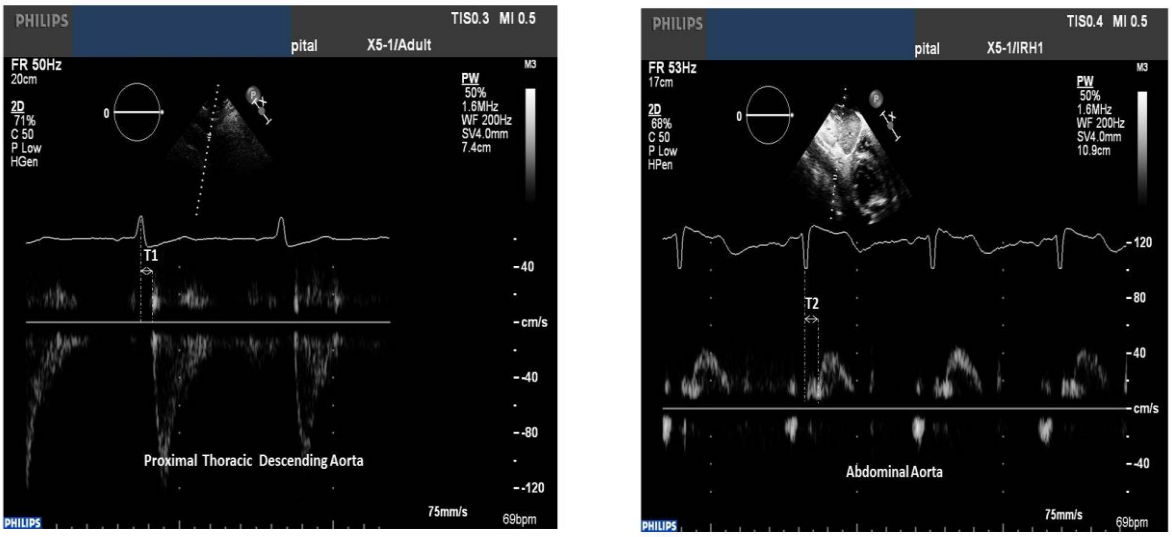
Score 1: Stenosis less than 30% of the lumen diameter;

Score 2: Localized stenosis between 30-70%;

Score 3: Multiple, tubular, or diffuse stenosis between 30-70%;

Score 4: Stenosis between 70-100%, provided that the vessel is not cut from the proximal part;

Score 5: The main vessel was cut from its proximal part.



A B

Figure 1. Pulsed Doppler signals, taken from proximal part of thoracic descending aorta (A) and abdominal aorta (B) to measure the time interval between R wave in electrocardiogram and the initiation of systolic signal

Ethics

The study design was approved by the review board/Ethics committee of the Research Council, Mashhad University of Medical Sciences. The study protocol was explained to all participants and an informed consent was obtained prior to study entrance. Before obtaining written informed consent, the purpose and procedures of the study were explained to all the participants.

Statistical analysis

Statistical analysis was performed using SPSS version 16 (SPSS Inc, Chicago, USA). Categorical and continuous data were presented using proportions and means and standard deviations respectively. The T test was used to compare descriptive variables for normally distributed variables and Mann-Whitney test for non-normally distributed variables. Comparison between categorical variables were made using Chi-square test or Fisher's exact test. Correlations were assessed by Spearman's rank correlation coefficient test. P-value less than 0.05 was considered statistically significant.

Results

The baseline clinical characteristics of our patients are summarized in Table 1. Most of the participants were male (n =37; 52.9%), with a mean age of 59.7±9.8 years. The mean systolic and diastolic blood pressure in the study population were respectively 127±20 mmHg and 79±9 mmHg. The minimum and maximum systolic blood pressure were 95 mmHg and 197 mmHg, respectively. Diastolic blood pressure in this study varied from 53 mmHg to 106 mmHg. The Fisher's test showed a significant difference between males and females in terms of diabetes (P<0.002; Table 1).

The mean APWV of the patients was 9.17±5.08 m/s, and its minimum and maximum values were 2 m/s and 27 m/s. Mann-Whitney test did not reflect any significant differences in the mean APWV values in relation to gender (p=0.5) and hypertension (p=0.9). No significant correlation was found between APWV and age (p=0.57). The mean Friesinger index was 6.8±4.1. There was a significant difference between the two groups of women and men in the Friesinger index (P=0.004).

Table 1. Baseline characteristics of the patients

Study Variables	Total (n=70)	Female (n=33)	Male (n=37)	P value
Age (year), mean±sd	59.7±9.8	60.18±9.14	59.27±10.45	0.7
Hypertension, n(%)	20 (28.6)	11 (33.3)	9 (24.3)	0.4
Systolic blood pressure (mmHg), mean±sd	127.4±20.1	129.9±20.4	125.1±19.8	0.2
Diastolic blood pressure (mmHg), mean±sd	78.9±9.2	79.6±10.2	78.2±8.3	0.5
Diabetes, n(%)	11 (15.7)	10 (30.3)	1 (2.7)	0.002
Coronary artery stenosis > 50% in one vessel ,n(%)	14 (20)	6 (18.2)	8 (21.6)	
Coronary artery stenosis > 50% in two vessels, n(%)	19 (27.1)	7 (21.2)	12 (32.4)	0.1
Coronary artery stenosis > 50% in three vessels, n(%)	17(24.3)	6 (18.2)	11 (29.7)	

Table 2. Mean APWV and Friesinger index of study patients

Population	Variables					
	Mean APWV			Friesinger index		
	APWV	TEST	P value	Friesinger index	TEST	P value
Male Female	8.5±4.2 9.8±5.8	Z=0.55	P=0.57	5.34±3 8.23±6	Z=-2.91	P=0.004
Diabetic Non-diabetic	7.6±6.2 9.4±4.8	Z=-1.97	P=0.048	7.33±7 6.74±2	Z=-0.42	P=0.67
Hypertensive Normotensive	9.1±5 9.1±4.9	Z=0.05	P=0.95	6.3±4 7.4±2	Z=-0.53	P=0.59

APWV: Aortic pulse wave velocity

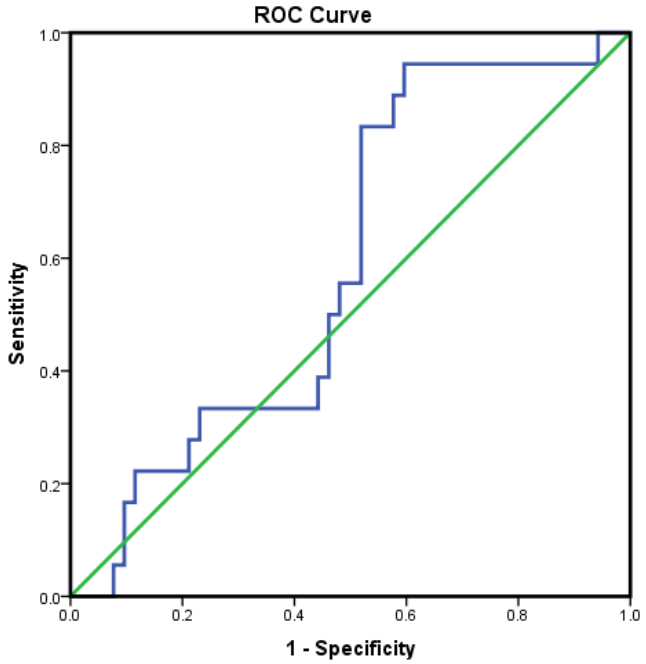


Figure 2. Different aortic pulse wave velocity values for predicting the disease with a sensitivity and specificity for each value

Mann-Whitney test did not show a significant difference in the Friesinger index between the two groups of diabetic and non-diabetic patients (P=0.67). No significant correlation was found between APWV and the Friesinger index (p= 0.67, r= 0.051). Overall, APWV could not define the severity of coronary artery involvement considering Friesinger index (Table 2). APWV was significantly reduced in diabetic patients versus non-diabetics (p=0.048).

In very low APWV values, the sensitivity of the test was high, but its specificity was low. In high APWV values, on the other hand, these values were controversial. APWV levels within the range of 6-9 m/s can be considered with a sensitivity and specificity of 73% and 52%, respectively (area under curve [AUC]=0.58, 95% CI= 0.45-0.72; p=0.2) for predicting coronary three-vessel disease, but it not reach to a significant level (Figure 2).

Discussion

The main result of this study was defining a direct relationship between APWV and Friesinger index, which was not statistically significant. Age, gender, or hypertensive state did not show any significant effect on APWV. APWV calculated in the diabetic group was lower than that in the non-diabetic group. The Freisinger index, which is a conventional numerical index of the extent of coronary artery diseases, was significantly different between the two genders.

Despite the fact that APWV was higher in the group of patients with two- and three-vessel diseases, there was a direct non-significant correlation between APWV and Freisinger index.

According to the Receiver Operating Characteristic (ROC) curve (Figure 2), APWV levels within the range of 6.9ms with a sensitivity and specificity of 73% and 52% respectively, can be considered for predicting the presence of three–vessel disease.

The increase in PWV may be associated with coronary events though multiple mechanisms.

Arterial stiffness can result in the return of reflected waves at end systole, increased central pulse pressure (PP) and work load on the ventricle, decreased ejection fraction, and elevated myocardial oxygen demand. Arterial

stiffness is associated with left ventricular hypertrophy, a risk factor for coronary events in both normotensive and hypertensive patients (17). Increased systolic blood pressure, which raises left ventricular afterload and myocardial work, and decreased diastolic one, by reducing coronary perfusion, result in sub-endocardial ischemia (18). Arterial stiffness is correlated with atherosclerosis, probably through the effects of cyclic stress on arterial wall thickening. Aortic stiffening accompanying age and CHD risk factors is caused by various changes, including fibrosis, breaks in elastin fibers, calcifications, and diffusion of macromolecules within the arterial wall (19). Thus, the measurement of aortic stiffness through integrating such changes may also reflect associated lesions in coronary vasculature. Increased PP, a manifestation of elevated arterial stiffness, and systolic blood pressure are known as independent risk factors for CHD (20).

Study Limitation:

Abdominal obesity could affect accurate Doppler measurement. Invasive assessment of aortic stiffness would provide more accurate data, but in this research, we tried to define the value of APWV taken by a simple non-invasive method and compare it with angiographic findings.

The presence of aortic artery or proximal iliac artery stenosis may lead to weakened or delayed pressure wave.

Conclusion

Measuring aortic stiffness by Doppler echocardiography did not identify the extent of coronary artery disease in diabetic or hypertensive patients. APWV was significantly reduced in diabetic cases, but more studies with follow up are needed to find its prognostic importance.

Authors' contribution

Hoorak Poorzand proposed the idea and supervised all the echocardiography procedures. Ali Eshraghi supervised all the angiographic procedures and their interpretations. Maliheh Layeghian performed all the echocardiographies and filled out data sheets. Mohammad Ramezani and Negar Morovatdar contributed to data analysis and writing the article draft. Finally, all the authors reviewed the article and approved its final corrections.

Acknowledgments

None.

Conflict of Interest

The authors declare no conflict of interest.

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