The effects of significant coronary stenosis and percutaneous coronary intervention on aortic stiffness

Ciddi koroner darlığın ve perkütan koroner girişimin aort sertliğine etkileri

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ABSTRACT

Objectives: Although aortic stiffness (AS) is a strong predictor of cardiovascular events, its value is unknown in patients who have coronary stenosis and undergo percutaneous coronary intervention (PCI). Our hypothesis was that AS might provide additional information about coronary hemodynamic status. In this context, we investigated the effects of coronary stenosis and PCI on AS.

Study design: The study included 107 patients undergoing coronary angiography. The patients were divided into three groups based on the angiographic results: 39 patients with significant lesions (≥50%) formed the 'critical group' and 38 patients with nonsignificant lesions (<50%) formed the 'noncritical group'. The control group (30 patients) had normal angiograms. Aortic stiffness was determined using the carotid-femoral aortic pulse wave velocity (PWV) method. All patients in the critical group underwent successful PCI and repeat PWV measurements.

Results: All baseline characteristics were similar in the three groups except for the mean PWV, which was significantly higher (9.4±2.2 m/sec) in the critical group compared to the control group (5.7±1.1 m/sec) and the noncritical group (5.8±1.1 m/sec) (p<0.0001). The latter two groups had similar PWV values (p=0.6). After PCI, the mean PWV decreased significantly by 24.4% to 7.1±2.0 m/sec (p=0.002); however, it was still significantly higher than that of the control group (p<0.0001). In correlation analysis, PWV showed significant correlations with age (r=0.412, p=0.01), systolic blood pressure (r=0.342, p<0.01), and hemoglobin (r=-0.370, p=0.02). Multiple logistic regression analysis showed that PWV was a predictor for significant stenosis [Exp(B) 3.960, 95% CI 2.014-7.786].

Conclusion: Our findings suggest that significant coronary stenosis is associated with significantly increased AS and successful PCI improves AS to some extent.

ÖZET

Amaç: Aort sertliği (AS) kardiyovasküler olayların güçlü bir öngördürücüsü olmasına karşın, ciddi koroner lezyonu olan ve perkütan koroner girişim (PKG) yapılan hastalarda AS'nin değeri bilinmemektedir. Aort sertliğinin koroner hemodinamik durum hakkında ek bilgiler verebileceğini düşünerek, çalışmamızda koroner darlığın ve PKG'nin AS üzerindeki etkisini araştırdık.

Çalışma planı: Çalışmaya koroner anjiyografi yapılan 107 hasta alındı. Anjiyografi sonuçlarına göre hastalar üç gruba ayrıldı. Anjiyografide bir koroner arterde %50'den fazla darlığı olan 39 hasta kritik grubu oluştururken, %50'den az darlığı olan 38 hasta kritik olmayan gruba ve koroner arterleri normal bulunan 30 hasta kontrol grubuna alındı. Aort sertliği, karotis-femoral aortik nabız dalga hızı (NDH) yöntemi kullanılarak ölçüldü. Kritik gruptaki tüm hastalara başarılı PKG yapıldı ve sonrasında NDH ölçümü tekrarlandı.

Bulgular: Üç grubun tüm başlangıç özellikleri NDH hariç benzerdi. Aortik NDH kontrol grubu (5.7±1.1 m/sn) ile kritik darlık olmayan grupta (5.8±1.1 m/sn) farklılık göstermezken (p=0.6), kritik darlık grubunda diğer iki gruba göre anlamlı derecede yüksekti (p<0.0001). Başarılı PKG'den sonra, ortalama NDH %24.4 oranında anlamlı düşüşle 7.1±2.0 m/sn bulundu (p=0.002); ancak, bu değer de kontrol grubundan anlamlı derecede yüksekti (p<0.0001). Korelasyon analizinde NDH yaş (r=0.412, p=0.01), sistolik kan basıncı (r=0.342, p<0.01) ve hemoglobin (r=-0.370, p=0.02) ile anlamlı ilişki gösterdi. Çoklu lojistik regresyon analizinde, NDH'nin anlamlı darlık için bağımsız bir öngördürücü olduğu görüldü [Exp(B) 3.960, %95 güven aralığı 2.014-7.786).

Sonuç: Bulgularımız koroner arterlerde ciddi darlık bulunmasının anlamlı derecede yüksek AS ile ilişkili olduğunu, başarılı PKG'nin de AS'yi bir dereceye kadar düzelttiğini göstermektedir.

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Aortic stiffness is associated with cardiovascular risk factors and atherosclerosis.[1-3] It has been shown that AS is a powerful predictor of future cardiovascular events and cardiovascular mortality.[4] Because of this strong relationship, the current guidelines suggest that AS be used in patients with hypertension as a tool for the assessment of subclinical target organ damage.[5] Moreover, current analyses support the measurement of AS in clinical practice for patients who have a high cardiovascular risk.[4]

The relationship between coronary circulation and AS has been investigated in several studies. In hypertensive patients, AS has a diagnostic value in the determination of impaired coronary microcirculation.[6] There is a significant correlation between the degree of coronary atherosclerosis and AS, as well.[7]

Despite the proven clinical significance of AS, the role of AS values in patients with coronary artery stenosis and undergoing percutaneous coronary intervention is not well known. Noninvasive prediction of coronary circulation is a crucial issue in the evaluation of patients with suspected coronary artery disease. Our hypothesis was that AS might provide additional information about coronary hemodynamic status. To test this hypothesis, we evaluated AS using pulse wave velocity in patients with coronary artery stenosis and undergoing PCI.

PATIENTS AND METHODS

Study population

A total of 107 patients undergoing coronary angiography were included in the study between November 2010 and January 2011. The patients were divided into three groups based on the results of coronary angiography. Thirty-nine patients 22 men, 17 women; mean age 64±10 years) who were found to have significant lesions (≥50%) in only one coronary artery formed the 'critical group'. The 'non-critical group' consisted of 38 patients (21 men, 17 women; mean age 62±9 years) who had a non-significant coronary lesion (1%-50%). The control group involved 30 matched patients (16 men, 14 women; mean age 62±10 years) who had normal coronary angiograms. All patients in the critical group underwent successful PCI.

Exclusion criteria were high blood pressure (≥140/90 mmHg), heart failure, diabetes mellitus, chronic kidney disease, any cardiac arrhythmia, current tobacco use, valvular heart disease, and body mass index greater than 30 kg/m^2. Subjects who were taking drugs that could potentially affect pulse wave reflection measurements (calcium channel blockers, alpha-blockers, and nitrates) were also excluded. All patients were informed about the study, and all gave written consent. The study was approved by the local ethics committee and was conducted in accordance with the Declaration of Helsinki.

Abbreviations:

AS	*Aortic stiffness*
CAD	*Coronary artery disease*
PCI	*Percutaneous coronary intervention*
PWV	*Pulse wave velocity*

Pulse wave velocity

Carotid-femoral aortic PWV is a simple, noninvasive, robust, and highly reproducible method for the determination AS.[8] All PWV measurements were performed in a quiet, temperature-controlled room, with subjects resting in the supine position. Systolic and diastolic blood pressures were measured twice using a semi-automated noninvasive oscillometric sphygmomanometer following a 10-min rest period. Pulse wave analysis was performed using the carotid and femoral arteries on a PWV machine (Micro Medical Pulse Trace, Rochester, UK) in accordance with the manufacturer's recommendations and PWV was calculated by measuring the time for the pulse wave to travel between the carotid and femoral arteries. All measurements were performed by the same operator blinded to patients' data in the following morning after coronary angiography and PCI procedures.

Pulse wave velocity was determined by means of a noninvasive analysis of the propagation time and distance of the pulse wave between the two acquisition points [PWV (m/sec) = Distance (meters) / Time (seconds)]. The transducers were positioned over the carotid and femoral arteries always on the right side of the body and the signals were sent to the Complior System (Colson, Les Lilas, France). Signal acquisition was performed by a skilled observer who was unaware of the patient's condition before and after exertion on a stationary bike, and 15 sequential pulse waves were preferentially recorded. The subject was sent to the evaluation bed for data acquisition as soon as the predicted heart rate was reached or observation of exercise-interruption criteria.

Statistical analysis

Data were processed using the SPSS 15.0 statistical software. Continuous variables were given as mean±SD and categorical variables as percentages. Comparisons between the groups were carried out using the independent-samples t-test. Correlation analy-

Table 1. Baseline characteristics of the study groups

	Critical stenosis (n=39) (Mean±SD)	Noncritical stenosis (n=38) (Mean±SD)	Control group (n=30) (Mean±SD)	*p*
Age (years)	64±10	62±9	62±10	0.872
Body mass index (kg/m^2)	25±8	24±6	24±6	0.642
Blood urea nitrogen (mg/dl)	23±9	22±8	21±7	0.468
Creatinine (mg/dl)	1.1±0.3	1.1±0.4	1.0±0.3	0.699
Total cholesterol (mg/dl)	202±51	200±48	198±46	0.744
HDL cholesterol (mg/dl)	38±5	38±6	37±6	0.278
LDL cholesterol (mg/dl)	139±43	139±41	137±34	0.686
Triglyceride (mg/dl)	106±71	108±73	102±69	0.472
Hemoglobin (mg/dl)	12.7±1.5	13.1±1.8	12.9±1.6	0.732
White blood count (x10^9/μl)	10.1±3.8	9.6±2.9	9.9±3.3	0.464
Platelet (x10^3/μl)	296±112	287±101	292±98	0.950
Systolic blood pressure (mmHg)	116±19	119±21	117±16	0.429
Diastolic blood pressure (mmHg)	77±11	79±13	78±12	0.564
Pulse (beats/min)	68±6	69±6	72±6	0.320

sis was performed using the Pearson's correlation coefficient. Multiple logistic regression analysis was used to evaluate the predictive role of PWV for significant coronary stenosis, which also included age, body mass index, and cholesterol level as variables. A *p* value of less than 0.05 was considered to be significant.

RESULTS

Baseline characteristics of the study groups are shown in Table 1. The three groups were similar with respect to age, body mass index, systolic and diastolic blood pressures, and heart rate. The mean PWV was 5.7±1.1 m/sec in the control group and 5.8±1.1 m/sec in patients in the noncritical group (p=0.6). The mean PWV was 9.4±2.2 m/sec in the critical group and was significantly higher compared to both the control and noncritical groups (p<0.0001, Fig. 1).

Following successful PCI in the critical group, the mean PWV decreased significantly by 24.4% to 7.1±2.0 m/sec (p=0.002). However, the postprocedural PWV values were still significantly higher than those in the control group (Fig. 1).

Based on the site of critical lesions, significant decreases were seen in PWV values following PCI for lesions in the left anterior descending coronary artery (from 9.5±2.2 to 7.1±2.1 m/sec, p<0.001) and in the right coronary artery/circumflex artery (from 8.9±2.2 to 7.1±1.8 m/sec, p=0.001). On the other hand, both preprocedural and postprocedural PWV values were similar in lesions in the left anterior descending coronary artery and the right coronary artery/circumflex artery.

In correlation analysis, PWV showed significant correlations with age (r=0.412, p=0.01), systolic blood pressure (r=0.342, p<0.01), and hemoglobin (r=-0.370, p=0.02). However, cholesterol levels, left ventricular ejection fraction, creatinine, and diastolic blood pressure showed no correlation with PWV.

In multiple logistic regression analysis, PWV was a predictor for significant stenosis [Exp (B) 3.960, 95% confidence interval 2.014-7.786].

DISCUSSION

The prognostic role of AS measurement in cardiovascular disease was demonstrated in previous studies.[4,9-11] These data suggest that AS is a simple, useful and noninvasive technique in the evaluation of cardiovascular disease. In this study, we investigated the relation between CAD and AS. Our study demonstrated that aortic PWV was significantly related with the degree of CAD severity, suggesting that AS might be a helpful clinical tool in the evaluation of patients with significant coronary artery lesions.

Several studies investigated the relationship between AS and coronary circulation.[7,12] It has been

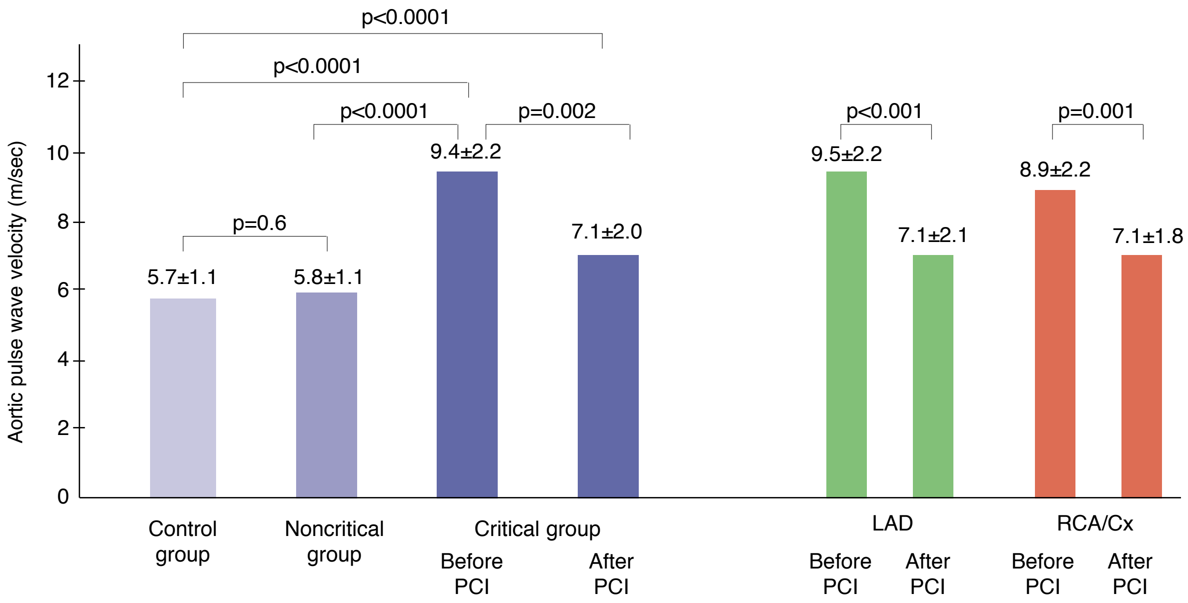

Figure 1. Baseline PWV values of the study groups and of those of the related arteries treated with PCI for critical stenotic lesions, with comparisons between pre- and postprocedural values. PWV: Pulse wave velocity; PCI: Percutaneous coronary intervention; LAD: Left anterior descending artery; RCA: Right coronary artery; Cx: Circumflex artery.

shown that AS results in changes in coronary perfusion.[13] Kingwell et al.[14] found AS to be a predictor of myocardial ischemic threshold in patients with CAD. Fukuda et al.[7] showed that PWV increased and was significantly correlated with the number of diseased vessels. Similarly, we found significantly higher PWV values in patients with critical coronary lesions compared to those without critical lesions and controls.

Noninvasive evaluation is an important clinical issue for patients with suspected CAD. Despite the presence of various diagnostic tools, diagnosis of significant CAD may be a difficult clinical challenge. Compared to healthy subjects, we found that patients with significant coronary lesions had significantly higher PWV values (9.4±2.2 *vs*. 5.7±1.1 m/sec). However, patients with normal coronary vessels and noncritical stenosis had similar PWV values. These findings suggest that PWV may be a noninvasive indicator of significant coronary stenosis. However, as the underlying mechanism is not clear, further studies are needed to explain this mechanism.

Consistent with previous studies, our results show that PWV may be a useful diagnostic tool in identifying severe CAD. However, aortic PWV may be influenced by many confounding factors, including age, mean arterial pressure, and sex.[15] We observed that PWV values significantly decreased after PCI in patients with significant stenosis. However, the exact mechanism for the decrease in AS after PCI is uncertain. Successful PCI have been associated with hemodynamic and biochemical effects in the early term, especially improvements in left ventricular function and neurohumoral activation.[16-18] Significant correlations have been found between AS and parameters of left ventricular diastolic and systolic functions.[16,19] These changes after PCI may be responsible for PWV changes in the early term. Further studies are needed to clarify improvements in AS following PCI.

It is known that AS is influenced by certain drugs such as nitrates, angiotensin-converting-enzyme inhibitors, angiotensin II receptor antagonists, calcium channel blockers, and alpha-blockers.[20] However, beta-blockers alone have little or no effect on PWV or wave reflections, but they enhance the augmentation index by reducing the heart rate.[21] In our study, we excluded patients who were taking nitrates and calcium channel blockers to minimize the effects of medications on our results. The use of angiotensin-converting-enzyme inhibitors and beta-blockers was similar in the critical and noncritical groups.

The main limitation of our study is its small sample size. On the other hand, neuromediators such as nitric oxide and brain natriuretic peptide may be responsible for acute changes in PWV after PCI procedures, but we did not measure these potential mediators.

In conclusion, patients with significant stenotic lesions in the coronary arteries have high AS values. Determination of AS by the PWV method is simple and noninvasive. It may prove useful in showing significant coronary stenotic lesions.

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Key words: Angioplasty, balloon, coronary; blood flow velocity; coronary angiography; coronary stenosis; elasticity; vascular resistance.

Anahtar sözcükler: Anjiyoplasti, balon, koroner; kan akım hızı; koroner anjiyografi; koroner darlık; elastisite; vasküler direnç.