Original Article

The Relationship between the Prevalence and Complexity of Coronary Artery Disease and Aortic Stiffness in Myocardial Infarction Patients without ST-Segment Elevation

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Abstract

Background: The relationship between elastic properties of the aorta and presence of coronary artery disease (CAD) has been investigated in previous studies. However, the relationship of aortic stiffness (AS) with extent and complexity of CAD in patients with non-ST-segment elevation myocardial infarction (NSTMI) have not been evaluated in previous studies. **Aims and Objectives:** The aim of this study is to determine the relationship of AS with extent and complexity of CAD in patients with NSTMI. **Materials and Methods:** Study population includes 400 patients (265 men, 135 women, mean age 61,8 ± 10.4 years) who had coronary angiography (CAG) in our clinic between February 2013 and October 2013 with the diagnosis of NSTMI. Patients were divided into two groups according to the median SYNTAX score as SYNTAX score < 16,5 SYNTAXlow group; and SYNTAX score ≥ 16,5 SYNTAX high group. AS parameters containing pulse wave velocity (PWV) and augmentation index (AIx) were calculated using applanation tonometry. **Results:** PWV and AIx parameters were found to be significantly higher ($P < 0.001$ for each) in SYNTAX high group compared to SYNTAX low group. Also age, the frequency of HT (hypertension), HPL (hyperlipidemia) and DM (diabetes mellitus) were significantly higher ($P < 0.05$ for all) in SYNTAX high group. HT (β = 0.083, $P = 0.048$), DM (β = 0.160, $P < 0.001$), PWV (β = 0.520, $P < 0.001$), and AIx (β = 0.230, $P < 0.001$) were found to be independently associated with SYNTAX score in multivariate regression analysis. On the other hand, age (β = 0.255, $P < 0.001$), HT (β = 0.212, $P < 0.001$), NT-proBNP (β = 0.086, $P = 0.012$) and SYNTAX score (β = 0.494, $P < 0.001$) were independently associated with PWV in multivariate regression analysis. **Conclusion:** SYNTAX score was found to be independently associated with increased AS in NSTMI patients. Increased AS may be thought as a predictor of extent and complexity of CAD.

Keywords: AIx, aortic stiffness, coronary, NSTMI, PWV, SYNTAX

Introduction

Coronary artery disease (CAD) is one of the most important causes of morbidity and mortality worldwide. Scoring systems such as Gensini score, Negri score, and SYNTAX (Synergy between PCI and TAXUS™ and Cardiac Surgery) score can be used for determining the prevalence and severity of CAD. SYNTAX score is a quantitative score used to predict the prognosis of CAD, as well as the prevalence and severity of CAD.[1,2]

On the other hand, studies have shown that impaired elastic parameters of the aorta can predict the presence of CAD.[3-10] Aortic stiffness (AS), defined as the deterioration of the viscoelastic structure of the vessel wall, is the result of structural and hemodynamic changes of the cellular

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Received: 12-09-2019 **Revised:** 08-11-2019 **Accepted:** 20-11-2019
Published Online: 13-02-2020

Access this article online

Quick Response Code:

Website: http://www.ijcva.com

DOI: 10.4103/IJCA.IJCA_46_19

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How to cite this article: Arafat Y, Kucukosmanoglu M, Mustafa G. The relationship between the prevalence and complexity of coronary artery disease and aortic stiffness in myocardial infarction patients without ST-segment elevation. Int J Cardiovasc Acad 2020;6:16-21.

and structural elements that make up the vessels. The risk factors for AS are smoking, hyperlipidemia (HPL), diabetes mellitus (DM), hypertension (HT), and advanced age, and the risk factors for AS are the same as the CAD risk factors.[11] Pulse wave velocity (PWV) and augmentation index (AIx) are simple and accepted noninvasive methods used to determine AS.[12-15]

In the studies, the relationship between AS parameters obtained with echocardiography and applanation tonometer and the prevalence and severity of CAD was evaluated and limited information was obtained.[6,16-23] The aim of this study is to investigate the relationship between the prevalence and complexity of CAD and PWV and AIx, which are used as AS parameters in patients with acute myocardial infarction (non-ST-segment elevation myocardial infarction [NSTEMI]) without ST-segment elevation.

Methods

Four hundred consecutive patients who applied to the Cardiology Clinic of Adana City Training and Research Hospital, between February and October 2013, with the presenting complaint of typical chest pain, and received the diagnosis of NSTEMI were included in this study. The patients were included in the study after the approval of the local ethics committee. NSTEMI diagnosis, the presence of HT and DM, and low-density lipoprotein (LDL) elevation were established according to the recommendations of current guidelines in the literature.[24] Patients who were smoking, including those who had quit smoking in the last month, were named smokers. Patients with previously known CAD, severe valvular disease, chronic liver disease, chronic kidney disease, active malignancy, known hematological disease, presence of active infection, pregnancy, and/or suspected pregnancy were excluded from the study. In addition, patients who refused to participate in the study and did not give written consent were not included.

Coronary angiography (CAG) was performed with Siemens (Axiom Sensis XP, Berlin, German) and Toshiba (Infinix CSI, Tokyo, Japan) devices using standard techniques. CAG evaluation and SYNTAX scoring were performed by two experienced interventional cardiologists. Patients with 50% stenosis in the left main coronary artery and/or more than 70% stenosis in other coronary arteries were included in the study. SYNTAX score was calculated with a digital system.[25]

The patients were laid down on a hospital bed in a quiet room reserved for measurement, in the first 24 h after diagnostic angiography, at least 5 minutes after rest and without smoking or consuming caffeinated beverages in the last 30 minutes. AS parameters including PWV and AIx were measured using an applanation tonometer, a "MOBILE GRAPH New generation 24 h ABPM Classic" brand arteriography device. Height, weight, sex, and birth dates of the patients were entered in the relevant data places on the MOBILE GRAPH device. The cuff was inflated above the currently determined systolic pressure (at least 35 mmHg higher), after the pressure measurement was done by the device. This way, brachial artery occlusion was performed and blood flow was stopped as a procedure condition during the measurement period (only 8–20 s, average 8 s). The signals obtained through the tonometer were transferred to the computer through infrared, wireless network. AIx and PWV values and pressure waves were recorded together with the software developed for this purpose. In order to optimize the pressure recordings, records with operator index 90% and above were evaluated.

Statistical analysis

Kolmogorov–Smirnov test is used to determine whether the distribution of continuous variables was normal or not. Continuous variables in the group data are showed as mean standard deviation. Categorical variables are given as numbers and percentages. A comparison of continuous variables according to their distribution between groups was made by Student's *t*-test or Mann–Whitney U-test. Chi-square test and Fisher's exact test were used to compare categorical variables. Pearson correlation analysis was performed to investigate the relationship between SYNTAX score and NDH. Multivariate linear regression analysis was used to determine independent relationships between the parameters found significant in this study. $P < 0.05$ is considered statistically significant. Analyses were performed using SPSS 17.0 (Chicago, IL, USA) statistical software package.

Results

Totally 400 patients included to the study (mean age: 62.1 ± 10.3 years, 66.2%, $n = 265$ males). Patients were divided into two groups according to the median SYNTAX score. Patients with a SYNTAX score <16.5 were considered to be the low SYNTAX score group ($n = 200$), and patients with a SYNTAX score ≥16.5 were considered to be the high SYNTAX score group ($n = 200$). The demographic characteristics of the patients are shown in Table 1. There was no difference

Table 1: Comparison of baseline demographic characteristics of patients ($n=200$)

Parameter	Low SYNTAX score group	High SYNTAX score group	*P*
Age (years)	59.5±11.3	64.1±9.6	<0.001
Sex (male), *n* (%)	132 (66.0)	133 (66.5)	0.500
BMI (kg/m^2)	28.7±4.9	28.1±4.6	0.226
HT (%), *n* (%)	72 (36.0)	134 (67.0)	<0.001
DM (%), *n* (%)	47 (23.5)	111 (55.5)	<0.001
Smoking, *n* (%)	80 (40.0)	81 (40.5)	0.500
HPL, *n* (%)	68 (34.0)	85 (42.5)	0.049
Family history, *n* (%)	17 (8.5)	10 (5.0)	0.116
SBP (mmHg)	121.4±23.5	122.2±20.3	0.733
DBP (mmHg)	75.8±12.8	76.9±13.2	0.421
PP (mmHg)	44.6±13.4	45.1±13.9	0.703
Pulse (beat/min)	84.5±15.4	87.0±15.7	0.266

BMI: Body mass index, HT: Hypertension, DM: Diabetes mellitus, HPL: Hyperlipidemia, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, PP: Pulse pressure

Table 2: Comparison of laboratory and echocardiographic findings of patients (n=200)

Parameter	Low SYNTAX score group	High SYNTAX score group	*P*
Glucose (mg/dl)	137.9±69.1	157.1±81.1	0.011
Total cholesterol (mg/dl)	192.5±46.4	183.8±41.0	0.046
Triglyceride (mg/dl)	165.9±104.2	162.5±94.0	0.732
LDL-C (mg/dl)	136.4±126.6	118.2±36.1	0.052
HDL-C (mg/dl)	40.8±10.9	40.0±10.9	0.497
Creatinine (mg/dl)	0.9±0.7	0.9±0.8	0.419
Uric acid (mg/dl)	5.5±1.6	5.5±1.5	0.816
Hs-CRP (mg/dl)	1.5±2.7	2.0±3.5	0.079
NT-proBNP (pg/ml)	781.8±2655.9	1500.1±3976.8	0.034
CKMB (ng/ml)	11.2±24.5	18.1±33.5	0.019
Troponin (pg/ml)	399.4±980.9	590.8±1040.9	0.059
Hemoglobin (mg/dl)	13.8±2.3	13.9±7.0	0.879
WBC (u/mL)	9.1±2.6	8.9±2.8	0.580
Left atrium diameter (cm)	3.7±0.4	3.8±0.4	0.508
Left ventricle diameter (cm)	4.6±0.4	4.7±0.4	0.435
Interventricular septum thickness (cm)	1.08±0.14	1.09±0.14	0.527
Left ventricle posterior wall thickness (cm)	1.05±0.14	1.06±0.17	0.956
EF (%)	55.6±7.9	54.8±9.7	0.331
PWV (m/s)	7.6±1.4	9.6±2.0	<0.001
AIx (%)	16.9±7.7	22.7±9.3	<0.001

LDL-C: Low-density lipoprotein-cholesterol, HDL-C: High-density lipoprotein-cholesterol, NT-proBNP: N-terminal pro-b-type natriuretic peptide, Hs-CRP: High-sensitivity C-reactive protein, WBC: White blood cell, PWV: Pulse wave velocity, AIx: Augmentation index, EF: Ejection fraction, CKMB: Creatinine kinase myocardial band

Table 3: Correlation of SYNTAX score and pulse wave velocity with demographic and laboratory parameters and multivariate logistic regression analysis

Parameters	*r*	*P*	β	*P*
SYNTAX score				
Age	0.315	<0.001	−0.032	0.419
HT	0.440	<0.001	0.083	0.048
DM	0.371	<0.001	0.160	<0.001
HPL	0.133	0.008	−0.014	0.719
Total cholesterol	−0.190	<0.001	−0.043	0.246
LDL-C	−0.154	0.002	−0.048	0.190
NT-proBNP	0.138	0.006	−0.053	0.142
PWV	0.670	<0.001	0.520	<0.001
AIx	0.453	<0.001	0.230	<0.001
PWV				
Age	0.488	<0.001	0.255	<0.001
DM	0.286	<0.001	−0.036	0.326
HT	0.519	<0.001	0.212	<0.001
NT-proBNP	0.168	0.001	0.086	0.012
SYNTAX score	0.670	<0.001	0.494	<0.001
SBP	0.186	<0.001	0.078	0.094
DBP	0.114	0.022	−0.002	0.966

HT: Hypertension, DM: Diabetes mellitus, HPL: Hyperlipidemia, LDL-C: Low-density lipoprotein-cholesterol, NT-proBNP: N-terminal pro b-type natriuretic peptide, PWV: Pulse wave velocity, Aix: Augmentation index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure

between the groups in terms of sex, smoking, and family history, but the mean age (59.5 ± 11.3 vs. 64.1 ± 9.6; P < 0.001), DM (23.5% vs. 55.5%; P < 0.001), HT (36.0% vs. 67.0%; P < 0.001), and dyslipidemia (34.0% vs. 42.5%; P = 0.049) was significantly higher in the high SYNTAX score group. The basal laboratory values and echocardiography parameters of the patients are shown in Table 2. The mean fasting blood glucose (137.9 ± 69.1 vs. 157.1 ± 81.1; P = 0.011), NT-proBNP (781.8 ± 2655.9 vs. 1500.1 ± 3 976.8; P = 0.034), and peak creatinine kinase myocardial band (CKMB) (11.2 ± 24.5 vs. 18.1 ± 33.5; P = 0.019) was significantly higher in the high SYNTAX score group. In addition, the AS parameters, i.e. NDH and AIx, were significantly higher in the high SYNTAX score group (7.6 ± 1.4 vs. 9.6 ± 2.0; P < 0.001 and 16.9 ± 7.7 vs. 22.7 ± 9.3; P < 0.001, respectively) [Table 2]. Table 3 summarizes the correlation between SYNTAX score and demographic and laboratory parameters. There was a significant and positive correlation between SYNTAX score and age, HT, DM, HPL, NT-proBNP, PWV, and AIx, whereas there was a significant negative correlation between total cholesterol and LDL-C [Table 3]. Multivariate logistic regression analysis showed that SYNTAX score was independently associated with HT (P = 0.048), DM (P < 0.001), PWV (P < 0.001), and AIx (P < 0.001) [Table 3]. Multivariate logistic regression analysis showed that PWV was independently associated with age (P < 0.001), HT (P < 0.001), NT-proBNP (P = 0.012), and SYNTAX score (P < 0.001) [Figure 1].

Discussion

Two important results were obtained in our study: (i) PWV and AIx were higher in the group with a high SYNTAX score and (ii) increased AS parameters independently predicted patients with a high SYNTAX score. These results suggest that

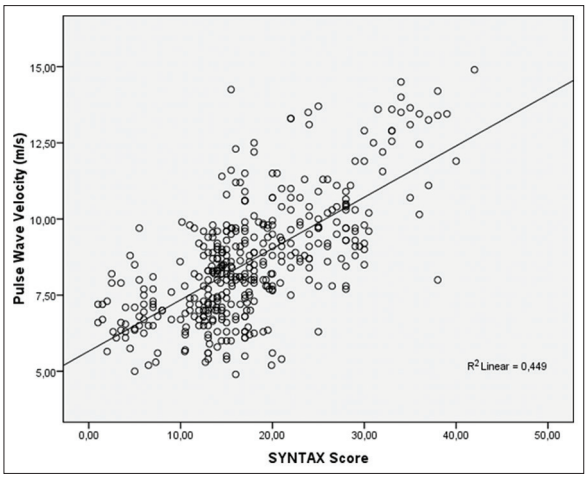

Figure 1: Relationship between pulse wave velocity and SYNTAX score (R^2 linear = 0.449)

AS increases as the prevalence and complexity of CAD increase in NSTEMI patients. In addition, another important finding in our study was that the arterial stiffness parameters, i.e. PWV, age, HT frequency, NT-proBNP, and SYNTAX scores, were closely related. Several scores have been used to determine the presence and severity of CAD, and recent guidelines emphasize the use of the SYNTAX score.[1,2,23,26,27] Previous studies have shown that DM and HT, which are among the traditional and modifiable risk factors of CAD, are directly proportional to the prevalence and severity of CAD.[28-30] Similarly, in our study, it was shown that the prevalence and complexity of CAD with the SYNTAX score were independently associated with the presence of DM and HT. AS risk factors are smoking, HPL, DM, HT, renal failure, high systolic blood pressure, serum uric acid level, and advanced age, and they are similar to CAD risk factors.[11] PWV measurement is the most simple, accepted, and most commonly used examination method in the evaluation of AS.[12-15] In addition to PWV detected by applanation tonometer, AIx detected by the same method, PWV detected by Doppler ultrasonography, and AS detected by echocardiography can also be used as AS parameters.[31] In our study, we used PWV and AIx as AS parameters. Distortion of the elastic parameters of the aorta predicts the presence of CAD, as it has been shown in previous studies.[3-7,10] In the Rotterdam study, 3000 elderly patients were included and it was shown that AS detected by PWV clearly predicted CAD and stroke development.[9] In other studies, contradictory relationships were found between the deterioration of AS parameters obtained by echocardiographic and applanation tonometry in stable CAD and the presence, prevalence, and severity of CAD.[6,16-23] In the majority of studies, the prevalence and severity of CAD were associated with AS.[16-21] However, in several studies, AS parameters were associated with the presence of CAD but not with the severity of CAD.[6,22,23] In our study, it was found that AS was independently associated with the prevalence and severity of CAD in accordance with previous studies. In the study of Alarhabi *et al*., PWV was found to be closely related to the severity of CAD, in addition to the presence of CAD.[4] However, in this study, the prevalence of CAD was determined according to the number of patient vessels, which is the simplest method. Similar findings were also found by Lim *et al*.[32] Although the findings of our study were similar to these two studies, there were significant differences. First of all, the severity of CAD was determined by the more acceptable and more current scoring method, SYNTAX score; second, an association with CAD severity in AIx other than PWV was established; and finally, patients with NSTEMI were also included in the study. A study similar to our study has recently been concluded. In this study conducted by Xiong *et al*., a positive and independent correlation was found between SYNTAX score and PWV in stable CAD patients.[21] In the literature, there are no other data showing the relationship between AS and the prevalence and severity of CAD in NSTEMI patients. In some studies, PWV, which is an AS parameter, was found to be associated with the presence of CAD but not with the prevalence and severity of CAD.[6,22,23] In these three studies,[6,22,23] it was thought that PWV was not associated with CAD severity due to some limitations. In a study by Gaszner *et al*., PWV was not associated with SYNTAX score, but the number of patients in this study was relatively small (125 people). Another study was conducted by Seo *et al*., and there was no relationship between AS and CAD severity.[23] The most important limitation of this study was the use of the Gensini score, which is of less importance in CAD severity. Gensini score is not a current scoring system and does not provide important information about CAD complexity. The study conducted by Chae *et al*. was retrospective, and its data were thought to be insufficient in clearly determining the severity of CAD.[6]

The relationship between severity of AS and CAD have been shown in the previous studies. However this relationship has not been demonstrated in patients with NSTEMI. Our study is the first study showing the relationship between AS and the prevalence and severity of CAD in NSTEMI patients.[16] Deterioration in both atherosclerosis and AS parameters is probably due to a general process involving all vessels. The risk factors for both conditions are similar, and these are common risk factors such as HT, DM, smoking, age, HPL, and sex.[33-44] Noninvasive AS parameters, which are evaluated in this field, seem to be an important parameter in predicting the presence and severity of CAD in the future.

Limitations

The most important limitation of our study is that it is a single centeer study and with a small sample size. Other important limitation is that our study did not provide prognostic information due to the lack of follow-up studies. A prognostic evaluation may be performed by studies with more patients in the future.

Conclusion

In NSTEMI patients, SYNTAX score was independently associated with increased AS. In this patient group, increased

AS may be a predictor of the prevalence and complexity of CAD.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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