Original Article

Relation of the aortic stiffness with the GRACE risk score in patients with the non ST-segment elevation myocardial infarction

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Abstract: Background: Current guidelines recommend clinical risk scoring systems for the patients diagnosed and determined treatment strategy with in Non-ST-elevation elevation myocardial infarction (NSTEMI). Previous studies demonstrated association between aortic elasticity properties, stiffness and severity CAD. However, the associations between Aortic stiffness, elasticity properties and clinical risk scores have not been investigated. In the present study we have evaluated the relation between the Global Registry of Acute Coronary Events (GRACE) risk score and aortic stiffness in patients with NSTEMI. Method: We prospectively analyzed 87 consecutive patients with NSTEMI. Aortic elastic parameter and stiffness parameter were calculated from the echocardiographically derived thoracic aortic diameters (mm/m²), and the measurement of pulse pressure obtained by cuff sphygmomanometry. We have categorized the patients in to two groups as low ((n = 45) (GRACE risk score ≤ 140)) and high ((n = 42) (GRACE risk score > 140)) risk group according to GRACE risk score and compare the both groups. Results: Table 1 shows baseline characteristics of patients. Our study showed that Aortic strain was significantly low (3.5 ± 1.4, 7.9 ± 2.3 respectively, p < 0.001) and aortic stiffness index was significantly high (3.9 ± 0.38; 3 ± 0.35, respectively, p < 0.001) in the high risk group values compared to those with low risk group. The aortic stiffness index was the only independent predictor of GRACE risk score (OR: 119.390; 95% CI: 2.925-4872.8; p = 0.011) in multivariate analysis. Conclusion: We found a significant correlation between aortic stiffness, impaired elasticity and GRACE risk score. Aortic stiffness index was the only independent variable of the high GRACE risk score. The inclusion of aortic stiffness into the GRACE risk score could allow improved risk classification of patients with ACS at admission and this may be important in the diagnosis, follow up and treatment of the patients.

Keywords: Aortic stiffness, aortic elasticity, GRACE risk score, non ST-segment elevation myocardial infarction

Introduction

Acute coronary syndrome is correlated with high morbidity and mortality rates [1]. Guidelines recommend clinical risk score calculations for the planning of treatment [2, 3]. Aortic stiffness is related to mechanical aortic wall tension and elasticity [4]. Increased arterial stiffness by impairing especially large arterial dilatation capacity, decreases cardiac performance and adversely affects organ perfusion [5]. Increased pulse pressure due to large arterial stiffness also affects the coronary outcomes by increasing systolic blood pressure and after load [6]. Aortic stiffness can be evaluated by simple and noninvasive methods. Aortic strain is one of the aortic elasticity indexes. Aortic stiffness index represents aortic stiffness [7, 8]. In order to determine the treatment and follow up strategies of the patients with acute coronary syndromes, clinical risk scoring systems were generated according to the results of comprehensive clinical studies [9]. Global Registry of Acute Coronary Events (GRACE) risk score is one of the most important scoring system and it is found to be related to prognosis [9].

GRACE risk score includes laboratory parameters such as ECG changes, increase in cardiac markers and creatine value in addition to clinical characteristics of the patients such as age,
heart rate, systolic blood pressure, and degree of heart failure [9]. Echocardiography is used in all of the fields of cardiology; however there is no echocardiography parameter in these clinical scoring systems. Previous studies have demonstrated the relation between arterial stiffness and stroke [10], heart failure [11] and coronary artery disease [12]. Relation between the presence and the extent of coronary artery disease and aortic elastic properties were investigated in previous studies [12, 13]. However there is no study in the literature searching the relation between the aortic elastic parameters and stiffness measured by echocardiography parameters and clinical risk scores in acute coronary syndromes.

In the present study we have evaluated the relation between the GRACE risk score and Aortic stiffness measured by echocardiography in patients who were admitted to our hospital with the diagnosis of non ST elevation myocardial infarction (NSTEMI).

Materials and methods

Study population

Study population consisted of 107 patients who were referred to Ondokuz Mayis University emergency department with chest pain and had the diagnosis of non ST elevation acute coronary syndrome (NSTEMI) according to the results clinical, electrocardiographic and laboratory evaluation and admitted to coronary care unit between March 2012 and December 2012. Among 107 patients, 7 had no atherosclerosis on coronary angiography, 6 declined to have coronary angiography and 7 had poor quality of echocardiography images and subsequently excluded from study. Echocardiographic examinations were performed and parameters were recorded at the time of the diagnosis of acute coronary syndrome and after the recovery of acute ischemia, ECG and clinical complaints.

Transthoracic echocardiography was performed within 24 hours and coronary angiography was performed within 3-1.5 days. Evaluation of clinical risk in patients with NSTEMI was done according to GRACE risk score.

Exclusion criteria were severe ventricular arrhythmia, myocarditis, pericarditis, pulmonary emboli, severe heart failure or cardiogenic shock, presence of prosthetic valve, acute or chronic renal failure, musculoskeletal disease, presence of malignity, previous history of PCI or CABS, patients under regular medical treatment, severe hypertension, apparent DM, severe aortic valve disease, and dilatation of ascendant aorta. In addition patients who had cardioversion or exposed to trauma and patients who were followed medically and not undergone coronary angiography were also excluded from study.

Diagnosis of acute NSTE-ACS

NSTE-ACS was considered as presence of T-wave inversion or ST-segment depression and/or positive Troponin I in the absence of electrocardiographic (ECG) ST elevation in patients presenting with angina or equivalent [2].

Calculation of GRACE risk score

The main principle of the GRACE risk score has been described elsewhere [14]. The variables required for calculation of the score include age, heart rate, systolic blood pressure, baseline creatine level, history of congestive heart failure, in hospital percutaneous coronary intervention, history of MI, ST segment depression on admission electrocardiography (ECG) and elevated cardiac enzyme or marker levels. This study, we used single serum levels in this study, we used single serum levels of cTnI 0.1 ng/ml as the elevated cardiac marker. ST-segment depression was defined as decreased ST segment: 0.5 mV below the isoelectric line in any ECG lead. As is known patients who had GRACE risk score 140 over have bad clinical progression and poor prognosis that is why early invasive treatment strategies are recommended for these patients. For this reason we have categorized the patients in two groups as low (n = 45) (GRACE risk score ≤ 140)) and high (n = 42) (GRACE risk score > 140) risk group according to GRACE risk score and compare the both groups.

Measurements of aortic elasticity and stiffness parameters

In the present study, we used echocardiographically derived method for the evaluation of aortic elastic properties and stiffness. This meth-
Table 1. The demographic, laboratory characteristics, aortic strain and aortic stiffness index values of patients

<table>
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<tr>
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<th>Low risk group</th>
<th>High risk group</th>
<th>p</th>
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<tbody>
<tr>
<td></td>
<td>(n = 45)</td>
<td>(n = 42)</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>57.0 ± 6.2</td>
<td>60.0 ± 5.8</td>
<td>0.012</td>
</tr>
<tr>
<td>Gender M (%)</td>
<td>36 (80%)</td>
<td>28 (66.7%)</td>
<td>0.159</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>18 (40%)</td>
<td>25 (59.5%)</td>
<td>0.069</td>
</tr>
<tr>
<td>DM (%)</td>
<td>28 (84.4%)</td>
<td>30 (71.4%)</td>
<td>0.142</td>
</tr>
<tr>
<td>Smoking (%)</td>
<td>24 (53.3%)</td>
<td>12 (28.6%)</td>
<td>0.019</td>
</tr>
<tr>
<td>LDL cholesterol (mg/dL)</td>
<td>110.9 ± 41.9</td>
<td>114.5 ± 31.4</td>
<td>0.651</td>
</tr>
<tr>
<td>HDL cholesterol (mg/dL)</td>
<td>41.7 ± 10.4</td>
<td>39.1 ± 9.7</td>
<td>0.227</td>
</tr>
<tr>
<td>Total cholesterol (mg/dL)</td>
<td>180.9 ± 45.1</td>
<td>178.8 ± 41.8</td>
<td>0.819</td>
</tr>
<tr>
<td>Trygliceride (mg/dL)</td>
<td>146.1 ± 76.8</td>
<td>134 ± 59.3</td>
<td>0.436</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>124.6 ± 12.6</td>
<td>128.1 ± 15.4</td>
<td>0.256</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>78.4 ± 7.6</td>
<td>74.8 ± 7.6</td>
<td>0.031</td>
</tr>
<tr>
<td>Heart rate</td>
<td>73.4 ± 8.9</td>
<td>85.5 ± 11</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Creatine (mg/dL)</td>
<td>0.78 ± 0.22</td>
<td>0.94 ± 0.24</td>
<td>0.02</td>
</tr>
<tr>
<td>Trophonin I (ng/dL)</td>
<td>2.3 ± 7.6</td>
<td>10.1 ± 2.9</td>
<td>0.02</td>
</tr>
<tr>
<td>Aortic Strain (%)</td>
<td>7.9 ± 2.3</td>
<td>3.5 ± 1.4</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Aortic stiffness index</td>
<td>3.0 ± 0.35</td>
<td>3.9 ± 0.38</td>
<td>&lt; 0.001</td>
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</table>

LDL, Low-density lipoprotein; HDL, High-density lipoprotein; DBP, Diastolic blood pressure; SBP, Sistolic blood pressure.

We have used the aortic strain as aortic elasticity parameter. Impaired aortic elasticity properties are association with aortic stiffness [15, 16].

These parameters give information on structure of aorta [17]. Abnormality in these parameters means structural alteration of arterial wall [17]. Elastic properties of aorta are useful not only in representing basic mechanical behavior of the arterial system but also in predicting outcome [17].

Statistical analyses

All continuous variables were given as mean ± standard deviation. Normal distribution was assessed by Kolmogorov–Smirnov test. Then, student t-test and Mann Whitney U-test were used when appropriate. Categorical variables were analyzed by Chi-square test and Fischer-exact test. Multivariable logistic regression analysis was used to assess the relationship between increased GRACE score and other variables. A p value < 0.05 was considered statistically significant. SPSS 15.0 statistical program (SPSS Inc, Chicago, IL USA) was used to statistical analysis.

Results

The study population consisted of 87 patients with NSTEMI. There were 64 (74%) men and 23 (26%) women in the study population. Mean age of patients was 58.4±4. In all, 58 (66.6%) patients were diabetic, 43 (49%) patients were hypertensive and 36 (41.3%) patients were smokers. According to the GRACE risk score, 42 (48.2%) patients were in the high risk score group and 45 (51.8%) patients were in the low risk score group. The demographic, laboratory characteristics, the aortic elasticity properties and aortic stiffness of patients in GRACE risk score groups are presented in Table 1. High risk group was older (60.0 ± 5.8, 57.0 ± 6.2, respectively, p = 0.012) heart rate (85.5 ± 11, 73.4 ± 8.9, respectively, p < 0.001) creatine (0.94 ± 0.24, 0.78 ± 0.22, respectively, p = 0.02), and trophonin I (ng/dl) (10.1 ± 2.92, 3.0

Aortic stiffness and GRACE risk score
Aortic stiffness and GRACE risk score

Results of our study have demonstrated that there is a significant relation between the aortic stiffness and clinical risk score in patients with NSTEMI and we have also demonstrated that aortic stiffness index is the independent determinant of high GRACE risk score. Previous studies have revealed that there is a relation between aortic stiffness and extend and the severity of coronary artery disease and also the cardiovascular events [4, 12, 18]. There are several studies that have demonstrated the increased cardiovascular morbidity and mortality with the increased in arterial stiffness [19, 20]. Willum-Hansen et al. have investigated the arterial stiffness in general population and put forth the relation between the aortic stiffness and cardiovascular events and mortality [21]. Study of Akinori et al. has demonstrated that there is a marked increase in CAVI (cardio-ankle vascular index) in patients with acute coronary syndrome [22]. However there is no study evaluating the relation between the Grace risk score which is used in the routine clinical practice for the diagnosis and treatment of the patients with acute coronary syndrome and aortic elasticity parameters (aortic strain) and aortic stiffness index which can easily be measured with echocardiographic examination. GRACE scoring system is an important scoring system which is composed of specific parameters and advised by the current guidelines for the diagnosis and the determination of treatment strategies in patients with acute coronary syndrome [2]. Among the GRACE risk scoring parameters, there is no echocardiographic parameter. Previous studies have demonstrated the relation between GRACE risk score and cardiovascular events and prognosis in patients with ACS.

Figure 1. Aortic stiffness index in the study groups.

Univariate and multivariate relationships of GRACE risk score

GRACE risk score was associated with age (OR: 1.1000, p = 0.016), smoking (OR: 0.350, p = 0.021), lower diastolic blood pressure (OR: 0.937, p = 0.036) higher aortic stiffness index (OR: 230.460, p < 0.001) and lower Aortic strain (OR: 0.493, p < 0.001) on Univariate logistic regression analysis (Table 2). Multivariate analysis was performed in order to evaluate the independent determinants of GRACE risk score (Table 2). The aortic stiffness index was the only independent predictor of GRACE risk score (OR: 119.390; 95% CI: 2.925-4872.8; p = 0.011) in multivariate analysis (Table 2).
Aortic stiffness and GRACE risk score

Table 2. Relationship between increased GRACE score and other variables

<table>
<thead>
<tr>
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<th>Univariate analysis</th>
<th>Multivariate analysis</th>
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<tbody>
<tr>
<td></td>
<td>OR</td>
<td>P</td>
</tr>
<tr>
<td>Age</td>
<td>1.100</td>
<td>0.016</td>
</tr>
<tr>
<td>DBP</td>
<td>0.937</td>
<td>0.036</td>
</tr>
<tr>
<td>HT</td>
<td>2.206</td>
<td>0.071</td>
</tr>
<tr>
<td>Smoking</td>
<td>0.350</td>
<td>0.021</td>
</tr>
<tr>
<td>Aortic Strain</td>
<td>0.493</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Aortic Stiffness index</td>
<td>230.460</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

DBP, Diastolic blood pressure; HT, Hypertension.

[23]. For this reason there may be a relation between the GRACE risk score and aortic stiffness.

Aortic stiffness has an adverse effect on arterial wall integrity, coronary perfusion and left ventricular function in patients with cardiovascular disease. Arterial stiffness is related to large arterial mechanical tension [4, 24]. As a result, increased arterial stiffness or decreased elasticity increase the left ventricular burden and myocardial oxygen demand and impair left ventricular function and coronary blood flow [22, 24, 25]. Besides, it was reported that, in patients with moderate coronary artery disease, large arterial stiffness is the major determinant of exercise myocardial ischemia [26]. Fukuda et al. have searched the relation between Ao-bracial PWV index which is related to aortic stiffness. FFR and found that coronary flow is decreased in patients with aortic stiffening [5]. Deterioration in aortic elasticity and stiffness parameters may increase the myocardial ischemia by decreasing coronary blood flow and increasing myocardial oxygen demand in addition to atherosclerotic lesions.

As a result, poor clinical condition results in high Grace score. In addition to this, previous studies have revealed the relation between the deterioration in aortic elasticity and stiffness parameters and complicated atherothrombotic lesion [27]. Selwaness et al have demonstrated the relation between arterial stiffness and carotid plaque hemorrhage and vulnerability [28]. There may be a correlation between vessels that have impaired elasticity, increased stiffness and unstable atherosclerotic plaques and extent of ischemia, high risk scores and bad prognosis. In our study, there was a strong correlation between aortic stiffness and clinical risk score. There was a significant correlation between the aortic strain and stiffness index and GRACE risk score at Univariate logistic regression analysis, however aortic stiffness was the only independent variable in multivariate analysis. We found a significant correlation between aortic elasticity and stiffness and GRACE risk score. Aortic stiffness index was the only independent variable of the high GRACE risk score. Based on our knowledge, this is the first study to correlate aortic stiffness with GRACE risk score.

Limitations of study

Major limitation of our study is the low number of the patients. Besides, aortic elasticity and stiffness calculations done with the echocardiography by measuring the diameter changes in ascendant aorta is not a gold standard [17]. However it gives information about local stiffness and can be done with echocardiography machine which can easily be reached even in intensive care units and it is practical and cheap. In addition we have planned our study to find a method which can be used in routine clinical practice. As is known that social security systems in many countries do not pay the price of the gold standard systems that measures the aortic stiffness, however echocardiography is practical and easily reachable.

In conclusion, the determination of aortic stiffness may be useful parameter for risk stratification of patients with NSTEMI during the hospitalization period. The inclusion of aortic stiffness parameters into the GRACE risk score could allow improved risk classification of patients with ACS at admission and this may be important in the diagnosis, follow up and treatment of the patients. Large, prospective, multicenter registries are necessary to confirm our results.

Disclosure of conflict of interest

None.
Aortic stiffness and GRACE risk score

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References


Van Sloten TT, Schram MT, van den Hurk K, Dekker JM, Nijpels G, Henry RM. Stehouwer
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