European Review for Medical and Pharmacological Sciences 2016; 20: 912-918

Early and late aortic propagation velocity values in STEMI patients after successful primary PCI and their relationship with neutrophil to lymphocyte ratio

M. YAMAN[1], U. ARSLAN[1], O. BETON[2], H.E. PAMUKCU[2], O. DOGDU[3]

[1]Cardiology Clinic, Samsun Training and Research Hospital, Samsun, Turkey
[2]Cardiology Clinic, Department of Cardiology, Diskapi Training and Research Hospital, Ankara, Turkey
[3]Department of Cardiology, Faculty of Medicine, Firat University, Elazig, Turkey

Abstract. – OBJECTIVE: Atherosclerosis leads to increased arterial resistance through thickening and stiffening of the arterial wall, a phenomenon largely known as arterial stiffness. M-mode propagation velocity of the descending thoracic aorta, named aortic velocity propagation (AVP) is a novel method for the measurement of the aortic stiffness. We aimed to investigate the difference between early and late values of AVP after successful primary percutaneous coronary intervention (PCI) in ST-elevation myocardial infarction (STEMI) patients.

PATIENTS AND METHODS: A total of 103 (70 male, 67.9%) consecutive patients without a previous history of coronary artery disease, who presented with STEMI without hemodynamic compromise and underwent successful primary PCI were enrolled. Transthoracic echocardiography was performed in all patients after primary PCI at 12-24 hour in Intensive Care Unit (early measurements) and three months after the discharge during follow-up (late measurements). Doppler echocardiography, 2D and aortic M-mode propagation velocity measurements were recorded. Haematological and serum biochemical parameters of the study group were recorded.

RESULTS: There were no statistically significant differences in 2D echocardiography measurements between early and late evaluations. AVP values increased during 3 months follow-up in all patients. Mean AVP values were 33.7± 11.6 cm/sn and 44.4±10.5 cm/sn at early and late measurements, respectively (p<0.001). There were significant correlations between differences of AVP and neutrophil-lymphocyte ratio between early and late measurements.

CONCLUSIONS: We demonstrated for the first time that AVP values could improve after successful treatment in STEMI patients. The increment in AVP values was closely correlated with a decrement in neutrophil lymphocyte ratio. It can be postulated that AVP has strong correlations with the inflammatory markers.

Key Words:
Aortic propagation velocity, STEMI, Primary PCI, Inflammation.

Introduction

Ischemic heart disease is the major cause of mortality worldwide. Major clinical presentations of ischemic heart disease include stable angina pectoris, acute coronary syndromes, chronic ischemic cardiomyopathy, congestive heart failure, and sudden cardiac arrest. ST-elevation myocardial infarction (STEMI) is a clinical syndrome described by characteristic symptoms of myocardial ischemia in association with persistent electrocardiographic ST elevation and subsequent release of biomarkers of myocardial necrosis[1]. The characteristic initiating event of acute coronary syndrome is the coronary plaque rupture or fissure[2].

Atherosclerosis is a multifactorial and chronic disease, which also displays heterogeneity. Initiating event of the atherosclerosis is endothelial dysfunction[3]. Progression of atherosclerosis causes stiffening of the arterial wall and decrease in aortic distensibility and aortic strain. Therefore, atherosclerosis causes aortic stiffness. Higher aortic stiffness is associated with an increased risk for the first cardiovascular event[4]. To evaluate aortic stiffness, various parameters including aortic strain, aortic distensibility, augmentation index and pulse wave velocity were used in the previous studies[5]. Gunes et al[6] highlighted the importance of aortic propagation velocity and its usefulness for the detection of aortic stiffness, as well as prediction of coronary artery diseases (CAD). Sen et al[7] reported that there was a sig-

Corresponding Author: Mehmet Yaman, MD; e-mail: dr.yaman@windowslive.com

nificant relationship between aortic propagation velocity, aortic strain, and aortic distensibility. Aortic velocity propagation (AVP) was found to be useful in improving the diagnostic accuracy of exercise electrocardiography[8]. Gunes et al[9] reported that hypertensive patients had decreased AVP and flow-mediated dilatation (FMD) values, and increased carotid intima media thickness (CIMT), and AVP were directly correlated with FMD. They showed the decrement in AVP and Ankle-Brachial Index values, and their direct correlation one another in patients with isolated hypertension. All of the previous studies on AVP were performed in patients with stable CAD or patients without overt CAD. To the best of our knowledge, AVP has never been investigated in patients with acute coronary syndromes and also it is not known whether AVP values can change after treatment.

The purpose of this study is to investigate the difference between early and late values of AVP after successful primary percutaneous coronary intervention (PCI) in STEMI patients.

Patients and Methods

Characteristics of Patients

A total of 103 patients (70 men, 67.9%) who presented with STEMI and undergone successful primary PCI were enrolled prospectively in this study. All patients had no prior history of heart disease. Exclusion criteria were moderate or severe valvular stenosis or regurgitation, cardiomyopathy, atrial fibrillation/flutter, ventricular arrhythmias, congenital heart diseases, aortic aneurysms, presence of >50% stenosis in coronary arteries unrelated to the infarct, unsuccessful primary PCI, presence of critical stenosis at Left Main Coronary Artery, right ventricular Myocardial Infarction (MI) at admission, and pulmonary edema/shock at admission and during Intensive Care Unit. The study conformed to the standards set by the Declaration of Helsinki, and ethical approval was obtained from Medical Ethical Committee of Fırat University (Reference No: 02/12/2014-20-14). A written informed consent was obtained from each participant.

Coronary Angiography and Primary PCI

Selective coronary angiography was performed and patients who had a total thrombotic occlusion in one coronary artery were enrolled in the study. None of the participants had more than 50% stenosis in their coronary arteries other than culprit vessel. A successful primary percutaneous intervention was performed in all patients. None of the patient's received thrombolytic therapy before primary PCI. Tirofiban infusion (IV) was initiated in catheterization laboratory after passage of Percutaneous Transluminal Coronary Angioplasty guidewire distal to the culprit lesion and was continued for 18-24 hours.

Transthoracic Echocardiography

The transthoracic echocardiography (TTE) examination was performed 12-24 hours after primary PCI in Coronary Care Unit. Second TTE examination was performed three months later. The transthoracic echocardiographic examination was performed at rest in the left lateral decubitus position, using an echocardiographic device (Vivid 7, General Electric, Milwaukee, WI, USA) with a 2.5-3.5 MHz transducer, by a single experienced operator who was blinded to the clinical data. Echocardiographic examinations were performed in accordance with recommendations and standards of current guidelines[10]. Ejection fraction, left ventricular and left atrial diameters were measured. The pulsed Doppler sampling volume was placed between the tips of the mitral valve leaflets. Early diastolic flow (E), atrial contraction (A), E/A ratio, and deceleration time (DT), isovolumetric relaxation time (IVRT) were measured. Mitral annulus velocity was recorded by tissue Doppler imaging, mitral lateral and medial annulus motions were analyzed from apical views. E', A', and S' values were measured.

AVP is a marker of arterial stiffness[6]. It reflects the elastic characteristics of the vessel wall. From a suprasternal window at a supine position, the descending aorta was viewed, and color M-mode Doppler recordings were obtained with the cursor located at the center of the lumen and parallel to the direction of main flow in descending aorta. Color Doppler Nyquist limit is adapted to 30-50 cm/s and M-mode with recorder sweep rate was set to 200 mm/s, an M-mode spatiotemporal velocity map was viewed[6]. During the TTE examination, patient's systolic and diastolic blood pressures, as well as heart rate values were measured.

Statistical Analysis

Data were demonstrated as mean ±SD for normally distributed continuous variables, median (minimum-maximum) for skew-distributed con-

Table I. The clinical and demographic characteristics of patients (n= 103).

Age (years)	56.8±9.8
Men	70 (67.9%)
Body mass index (kg/m2), mean±SD	28.2±4.2
Hypertension	51 (49.5%)
Diabetes mellitus	25 (24.3%)
Current smokers	57 (55.3%)
Hyperlipidemia	25 (24.3%)
Medications at discharge	
Beta blockers	94 (91.3%)
Calcium channel blockers	6 (5.8%)
ACE inhibitör/ARB	103 (100%)
Statins	89 (86.4%)
Acetylsalicylic acid	103 (100 %)
Clopidogrel	103 (100 %)
Oral antidiabetics	15 (14.6%)
Insulin	18 (17.5%)
Spironolactone	6 (5.9%)
Diuretics	5 (4.9%)
MI location	
Non-anterior MI	81 (78.6%)
Anterior MI	22 (21.4%)
Culprit artery	
RCA	42 (40.8%)
CX	39 (37.9%)
LAD	22 (21.4%)

p: Level of significance (<0.05).

tinuous variables, and frequencies for categorical variables. Means of normally distributed continuous variables were compared by ANOVA. Skew-distributed continuous variables were compared by Mann-Whitney U test. Fischer's exact and Pearson's chi-square tests were used to compare categorical variables. Pearson r correlation was used to measure the degree of relationship between the two variables. For all statistics, a two-sided *p*-value <0.05 was considered to be statistically significant.

Results

One hundred and three consecutive patients were enrolled in this study. The mean age of study subjects was 56.8±9.8 years (range 34-76 years). Mean "angina to primary PCI" time was 170.4±118.2 minutes. Table I shows the basal characteristics of the patients at admission and Table II shows some characteristics both at admission and 3-month follow-up. There was a significant difference between first and second total cholesterol and LDL cholesterol levels. Fasting glucose and creatinine levels were not significantly different between two measurements.

There were no differences between the echocardiographic measurements in terms of LV and LA dimensions and aortic diameters (Table III). Left ventricular ejection fraction increased significantly at 3 months. There were no significant differences in Doppler echocardiography measurements, except for IVRT. Second IVRT values were significantly lower than the first values (103.7 ms *vs*. 95.7 ms, respectively $p<0.001$). Vital signs (blood pressure, and heart rate) of patients during echocardiographic assessment were not different between two measurements.

Mean AVP value was 33.7±11.6 (cm/s) at admission and 44.4±10.5 (cm/s) at 3-month follow-up, respectively ($p<0.001$) (Figure 1). Initial mean neutrophil lymphocyte ratio (NLR) was 6.2±5.0 and it was 2.8±1.2 at 3 months follow-up ($p<0.001$). A significant correlation was found between mean AVP values and NLRs both at admission (r= -0.61, $p<0.01$) and at 3rd month follow-up (r= -0.59, $p<0.01$).

Discussion

Endothelial dysfunction is considered to be the first stage in the development of atherosclerosis[11]. Progression of atherosclerosis increases the thick-

Table II. Laboratory measurements at 12-24th hours and at 3rd month.

	12-24th hour values	3rd month values	*p*-value
Fasting glucose (mg/dl)	105.3±27.7	106.4±27.7	0.139
Creatinine (mg/dl)	1.04±0.47	1.02±0.43	0.537
Hemoglobin (g/dl)	13.4±1.4	13.3±1.3	0.282
Total cholesterol (mg/dl)	200.1±33.7	167.0±26.2	0.001
LDL cholesterol (mg/dl)	112.9±28.8	96.4±24.7	0.001
Neutrophil lymphocyte ratio	6.2±5.0	2.8±1.2	<0.001

Table III. Echocardiographic measurements in 12-24th hour and 3rd month.

	12-24th hour values	3rd month values	*p*-value
2D echocardiography			
Aort (cm)	2.63±0.29	2.60±0.28	0.224
Left atrium (cm)	3.77±0.51	3.75±0.49	0.589
LAV (ml)	29.10±13.0	27.28±10.74	0.066
LVEDD (cm)	4.96±0.55	4.98±0.55	0.652
LVESD (cm)	3.16±0.70	3.14±0.69	0.682
LVEDV (mL)	91.23±30.40	95.63±39.15	0.132
LVESV (mL)	39.27±23.47	39.38±23.33	0.951
IVSd (cm)	1.09±0.17	1,11±0.38	0.609
PWd (cm)	1.06±0.14	1.05±0.12	0.193
EF (%)	48.4±12.8	50.9±11.1	0.021
Doppler echocardiography			
AVP (cm/sn)	33.7±11.6	44.4±10.5	<0,001
PASP (mmHg)	26.2± 3.3	25.9±2.7	0.253
E (cm/sn)	61.6±15.8	64.8±17.3	0.028
A (cm/sn)	70.9±16.1	71.0±15.4	0.946
E/A	91.2±33.7	96.3±35.7	0.120
EDT (ms)	288.0±47.4	276.2±32.5	0.015
IVRT (ms)	103.7±18.8	95.7±12.1	<0,001
LA lateral Sm velocity (cm/s)	8.9±2.7	8.7±2.8	0.622
LA lateral Em velocity (cm/s)	8.8±2.9	9.7±2.8	0.001
LA lateral Am velocity (cm/s)	11.4±3.3	10.9±3.1	0.146
LA medial Sm velocity (cm/s)	7.6±2.6	7.1±2.0	0.026
LA medial Em velocity (cm/s)	7.2±2.6	7.6±2.4	0.136
LA medial Am velocity (cm/s)	8.9±2.4	8.7±2.1	0.358
RA lateral Sm velocity (cm/s)	13.6±4.3	12.3±3.7	0.001
RA lateral Em velocity (cm/s)	9.7±3.3	9.6±3.0	0.645
RA lateral Am velocity (cm/s)	14.8±4.0	13.7±4.3	0.022
Vitals			
SBP (mmHg)*	128.6±13.9	127.1±14.6	0.139
DBP (mmHg)*	78.7±11.6	80.3±7.9	0.112
HR (bpm)*	72.5±6.9	71.4±4.9	0.127

(*) At the time of echocardiographic measurement. A: peak mitral valve flow velocity during atrial contraction, Am: tissue Doppler late diastolic wave, AVP: aortic flow propagation velocity, DBP: diastolic blood pressure, E: peak mitral valve flow velocity during the early rapid filling phase, Em: tissue Doppler early diastolic wave, EDT: deceleration time of early phase of mitral valve flow, EF: ejection fraction, HR: heart rate, IVDd: interventricular septum diameter, IVRT. isovolumetric relaxation time, LAV: left atrial volume, LVEDD: left ventricular end diastolic diameter, LVEDV: left ventricle end diastolic volume, LVESD: left ventricular end systolic diameter, LVESV: left ventricle end systolic volume, PASP: pulmonary artery systolic pressure, PWd: posterior wall diameter, SBP: systolic blood pressure, Sm: tissue Doppler systolic wave.

ness of tunica media[12]. As the aorta gets stiffer and thicker; aortic distensibility decreases. As the arteries get thicker, arterial resistance increases. In recent years, several methods for the assessment of arterial stiffness have been described, including the home arterial stiffness index, the ambulatory arterial stiffness index, the central and peripheral augmentation index, and the pulse wave velocity. Overall, carotid-femoral pulse wave velocity measurement is considered to be the gold standard technique for this approach[13]. Previous studies[14,15] have shown that aortic stiffness was assosiated with CAD. Aortic stiffness is predictive of all-cause and cardiovascular mortalities, coronary events, and fatal strokes in patients with uncomplicated essential hypertension[16-18], type 2 diabetes[19], end-stage renal disease[20,21], and elderly population[22].

AVP is a novel echocardiographic parameter in the assessment of aortic stiffness. Gunes et al[6] described AVP and used it for the evaluation of aortic stiffness. The color M-mode propagation velocity of the descending aorta was significantly lower in patient with CAD and they stated that AVP predicted coronary atherosclerosis more powerfully than other methods of ultrasonographic aortic stiffness measurements. They further proposed to use this method in patient selec-

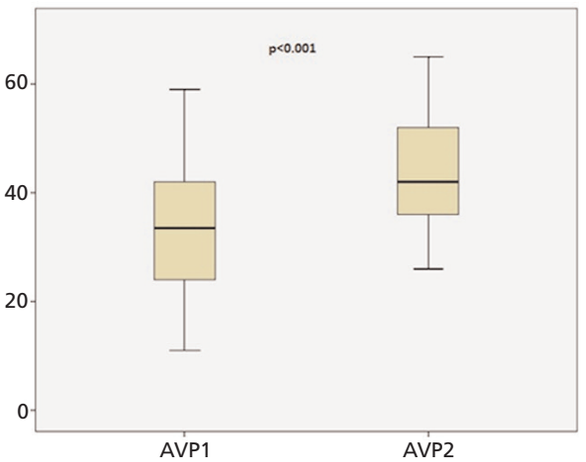

Figure 1. Initial and 3-month follow-up measurements of aortic velocity propagation (AVP).

tion for primary prevention of atherosclerosis. AVP was also useful to improve the diagnostic accuracy of exercise electrocardiography test[8]. Guntekin et al[23] found significant associations between AVP and CIMT and FMD in patients without significant coronary atherosclerosis or subclinical atherosclerosis. They found a significant association between AVP and FMD in patients with slow coronary flow without significant coronary atherosclerotic involvement. Therefore, they suggested AVP as an indicator of endothelial dysfunction[24]. Sen et al[7] showed that AVP was feasible for cardiovascular risk stratification and selection of high-risk individuals with CAD. In their study, AVP values were significantly lower in the CAD group when compared with the non-CAD group. However, CAD group did not include acute MI patients.

In our study, we demonstrated for the first time that AVP values could improve after successful treatment in STEMI patients. Initial AVP values were found to be low in the first 12-24 hours of MI. The degree of inflammation is very high in the early hours of myocardial infarction, with a state of hypercoagulability, and tendency to vasoconstriction and thrombus formation[25]. Histological analysis of autopsy specimens taken from patients who died of acute coronary syndromes has shown that unstable or ruptured atherosclerotic plaques are characterized by the presence of foam cells, macrophages, lymphocytes, and mast cells[26].

Elevations in inflammatory markers and changes in leukocyte subset distributions were reported in patients with CAD[27-29]. Recent trials have demonstrated the role of neutrophils in all stages of atherosclerosis and plaque destabilization leading to acute coronary syndromes[30]. Neutrophil counts and NLR are promising markers for the presence and severity of CAD[31-33]. Neutrophil/lymphocyte ratios are predictors of mortality and cardiovascular events in high-risk patient groups[34].

There is also evidence coming from ischaemic heart disease models that functional endothelial abnormalities may occur as a result of neutrophil interaction with the endothelium of coronary arteries[35]. In our study population, the first mean NLR was 6.2±5.0; and the second was 2.75±1.2 (p<0.001). This significant reduction might be due to the regression of inflammation process. Acute inflammation triggered in acute MI causes an increase in neutrophil counts. Increased neutrophil counts may also accelerate endothelial abnormalities in acute phases of MI. In our study population, initial AVP values were low. That low values might be due to an activated acute inflammation, an increased neutrophil values and endothelial dysfunction, as well as an increased arterial resistance. The increased arterial resistance acts to decrease the flow propagation speed within the arterial lumen[7]. The decrease in vasoconstriction and inflammation may lead to normalization of the flow in the aortic lumen and also the regression of the severity of endothelial dysfunction may be the reason of elevation in AVP values.

In our study, first mean AVP value of STEMI patients was 33.7±11.6 (cm/s). The mean second AVP value at third month was 44.4±10.5 (cm/s) (p<0.001). The significant correlations between AVP and NLR both at admission and 3-month follow-up in the setting of STEMI made us think that AVP is an important echocardiographic marker for the presence of inflammation rather than the left ventricular functions. AVP may be a novel marker as a negative acute phase reactant in patients with acute myocardial infarction.

The limited suprasternal images of some patients may be a handicap to the measurement of AVP. Reproducibility of the acquisition of the images and AVP were also limitations. On the other hand, other modalities like FMD as indicative of endothelial dysfunction could have been applied to our patients and the association between AVP and FMD could have been analyzed in our patients. Moreover, the number of our study population is limited. We did not include patients with unsuccessful PCI for comparison of AVP values.

Conclusions

We demonstrated for the first time that AVP values could improve after successful treatment in STEMI patients. Increments in AVP values were closely correlated with decrements in NLR. AVP values may be useful in monitoring MI patients in terms of determining the inflammatory status during follow-up.

Conflict of Interest

The Authors declare that they have no conflict of interests.

References

1) O'Gara PT, Kushner FG, O'Gara PT, Kushner FG, Ascheim DD, Casey DE Jr, Chung MK, de Lemos JA, Ettinger SM, Fang JC, Fesmire FM, Franklin BA, Granger CB, Krumholz HM, Linderbaum JA, Morrow DA, Newby LK, Ornato JP, Ou N, Radford MJ, Tamis-Holland JE, Tommaso CL, Tracy CM, Woo YJ, Zhao DX, Anderson JL, Jacobs AK, Halperin JL, Albert NM, Brindis RG, Creager MA, DeMets D, Guyton RA, Hochman JS, Kovacs RJ, Kushner FG, Ohman EM, Stevenson WG, Yancy CW; American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation 2013; 127: e362-425.
2) Santos-Gallego CG, Picatoste B, Badimón JJ. Pathophysiology of acute coronary syndrome. Curr Atheroscler Rep 2014; 16: 401.
3) Juonala M, Viikari JS, Laitinen T, Marniemi J, Helenius H, Rönnemaa T, Raitakari OT. Interrelations between brachial endothelial function and carotid intima-media thickness in young adults: the cardiovascular risk in young Finns study. Circulation 2004; 110: 2918-2923.
4) Mitchell GF, Hwang SJ, Vasan RS, Larson MG, Pencina MJ, Hamburg NM, Vita JA, Levy D, Benjamin EJ. Arterial stiffness and cardiovascular events; the Framingham Heart Study. Circulation 2010; 121: 505-511.
5) Cohn JN, Finkelstein S, McVeigh H. Non-invasive pulse wave analysis for the early detection of vascular disease. Hypertension 1995; 26: 503-518.
6) Güne Y, Tuncer M, Yildirim M, Güntekin U, Gümrükçüo lu HA, Sahin M. A novel echocardiographic method for the prediction of coronary artery disease. Med Sci Monit 2008; 14: MT42-46.
7) Sen T, Tufekcioglu O, Ozdemir M, Tuncez A, Uygur B, Golbasi Z, Kisacik H. A new echocardiographic parameter of aortic stiffness and atherosclerosis in patients with coronary artery disease: aortic propagation velocity. J Cardiol 2013; 62: 236-240.
8) Güne Y, Gümrükçüo lu HA, Kaya Y, Tuncer M. Incremental diagnostic value of color M-mode propagation velocity of the descending thoracic aorta to exercise electrocardiography. Turk Kardiyol Dern Ars 2010; 38: 551-557.
9) Güneş A, Güntekin Ü, Yıldız S, Kaya BC, Deveci E, Kaya Z, Sezen Y, Yeşilay AB, Demirbağ R. Association of aortic flow propagation velocity with ankle-brachial blood pressure index in patients with hypertension an observational study. Anadolu Kardiyoloji Dergisi 2012; 12: 568-573.
10) Douglas PS, DeCara JM, Devereux RB, Duckworth S, Gardin JM, Jaber WA, Morehead AJ, Oh JK, Picard MH, Solomon SD, Wei K, Weissman NJ; American Society of Echocardiography Standards; American College of Cardiology Foundation. Echocardiographic imaging in clinical trials: American Society of Echocardiography Standards for echocardiography core laboratories: endorsed by the American College of Cardiology Foundation. J Am Soc Echocardiogr 2009; 22: 755-765.
11) Adams MR, Celermajer DS. Detection of presymptomatic atherosclerosis: a current per-spective. Clin Sci 1999; 97: 615-624.
12) Park SM, Seo HS, Lim HE, Shin SH, Park CG, Oh DJ, Ro YM. Assessment os aterial stiffness index as a clinical parameter for atherosclerotic coronary artery disease. Clinical J 2005; 69: 1218-1222.
13) Laurent S, Cockcroft J, Van Bortel L, Boutouyrie P, Giannattasio C, Hayoz D, Pannier B, Vlachopoulos C, Wilkinson I, Struijker-Boudier H. European Network for Non-invasive Investigation of Large Arteries: Expert consensus document on arterial stiffness: methodological issues and clinical applications. Eur Heart J 2006; 27: 2588-2605.
14) Simon AC, Levenson J, Bouthier J, Safar ME, Avolio AP. Evidence of early degenerative changes in large arteries in human essential hypertension. Hypertension 1985; 7: 675-680.
15) Eren M, Gorgulu S, Uslu N, Celik S, Dagdeviren B, Tezel T. Relation between aortic stiffness and left ventricular diastolic function in patients with hypertension, diabetes, or both. Heart 2004; 90: 37-43.
16) Boutouyrie P, Tropeano AI, Asmar R, Gautier I, Benetos A, Lacolley P, Laurent S. Aortic stiffness is an independent predictor of primary coronary events in hypertensive patients: a longitudinal study. Hypertension 2002; 39: 10-15.
17) Laurent S, Boutouyrie P, Asmar R, Gautier I, Laloux B, Guize L, Ducimetiere P, Benetos A. Aortic stiffness is an independent predictor of all-cause and cardiovascular mortality in hypertensive patients. Hypertension 2001; 37: 1236-1241.
18) Laurent S, Katsahian S, Fassot C, Tropeano AI, Gautier I, Laloux B, Boutouyrie P. Aortic stiffness is an independent predictor of fatal stroke in essential hypertension. Stroke 2003; 34: 1203-1206.

19) Cruickshank K, Riste L, Anderson SG, Wright JS, Dunn G, Gosling RG. Aortic pulse-wave velocity and its relationship to mortality in diabetes and glucose intolerance: an integrated index of vascular function? Circulation 2002; 106: 2085-2090.

20) Blacher J, Guerin AP, Pannier B, Blacher J, Marchais SJ, Darne B, Metivier F, Adda H, Safar ME. Impact of aortic stiffness on survival in end-stage renal disease. Circulation 1999; 99: 2434-2439.

21) Shoji T, Emoto M, Shinohara K, Kakiya R, Tsujimoto Y, Kishimoto H, Ishimura E, Tabata T, Nishizawa Y. Diabetes mellitus, aortic stiffness, and cardiovascular mortality in end-stage renal disease. J Am Soc Nephrol 2001; 12: 2117-2124.

22) Meaume S, Benetos A, Henry OF, Rudnichi A, Safar ME. Aortic pulse wave velocity predicts cardiovascular mortality in subjects 70 years of age: Arterioscler Thromb Vasc Biol 2001; 21: 2046-2050.

23) Guntekin U, Gunes Y, Gunes A, Ceylan Y, Gumrukcuoglu HA, Yucel Y, Simsek H, Tuncer M. Noninvasive assessment of atherosclerosis in patients with isolated hypertension. Echocardiography 2010; 27: 155-160.

24) Simsek H, Sahin M, Gunes Y, Akdag S, Akil MA, Akyol A, Gumrukcuoglu HA, Yaman M. A novel echocardiographic method as an indicator of endothelial dysfunction in patients with coronary slow flow. Eur Rev Med Pharmacol Sci 2013; 17: 689-693.

25) Demetz G, Ott I. The interface between inflammation and coagulation in cardiovascular disease. Int J Inflam 2012; 2012: 860301.

26) Kohchi K, Takebayashi S, Hiroki T, Nobuyoshi M. Significance of adventitial inflammation of the coronary artery in patients with unstable angina: results atautopsy. Circulation 1985; 71: 709-716.

27) Pai JK, Pischon T, Ma J, Manson JE, Hankinson SE, Joshipura K, Curhan GC, Rifai N, Cannuscio CC, Stampfer MJ, Rimm EB. Inflammatory markers and the risk of coronary heart disease in men and women. N Engl J Med 2004; 351: 2599-2610.

28) Nijm J, Wikby A, Tompa A, Olsson AG, Jonasson L. Circulating levels of proinflammatory cytokines and neutrophil-platelet aggregates in patients with coronary artery disease. Am J Cardiol 2005; 95: 452-456.

29) Turkmen S, Dogdu O, Tekin K, Kucukdurmaz Z, Cagliyan CE, Sarikaya S, Yucel H, Karapinar H, Ozkan B, Uysal OK, Basara A, Sancaktar E, Yilmaz A. The relationship between neutrophil/lymphocyte ratio and the TIMI flow grade in patients with STEMI undergoing primary PCI. Eur Rev Med Pharmacol Sci 2013; 17: 2185-2189.

30) Soehnlein O. Multiple roles for neutrophils in atherosclerosis. Circ Res 2012; 110: 875-888.

31) Kawaguchi H, Mori T, Kawano T, Kono S, Sasaki J, Arakawa K. Band neutrophil count and the presence and severity of coronary atherosclerosis. Am Heart J 1996; 132(1 Pt 1): 9-12.

32) Arbel Y, Finkelstein A, Halkin A, Birati EY, Revivo M, Zuzut M, Shevach A, Berliner S, Herz I, Keren G, Banai S. Neutrophil/lymphocyte ratio is related tothe severity of coronary artery disease and clinical outcome in patients undergoing angiography. Atherosclerosis 2012; 225: 456-460.

33) Kalay N, Dogdu O, Koc F, Yarlioglues M, Ardic I, Akpek M, Cicek D, Oguzhan A, Ergin A, Kaya MG. Hematologic parameters and angiographic progression of coronary atherosclerosis. Angiology 2012; 63: 213-217.

34) Duffy BK, Gurm HS, Rajagopal V, Gupta R, Ellis SG, Bhatt DL. Usefulness of anelevated neutrophil to lymphocyte ratio in predicting long-term mortality after percutaneous coronary intervention. Am J Cardiol 2006; 97: 993-996.

35) Kloner RA, Giacomelli F, Alker KJ, Hale SL, Matthews R, Bellows S. Influx ofneutrophils into the walls of large epicardial coronary arteries in response to ischemia/reperfusion. Circulation 1991; 84: 1758-1772.