

Decreased arterial compliance assessed by aortic pulse wave velocity is an important parameter for monitoring of blood pressure in patients with chronic inflammatory diseases

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Aim. Patients with chronic inflammatory diseases (CID), such as rheumatoid arthritis (RA) and familial Mediterranean fever (FMF) are more likely to have higher risk of cardiac events. Pulse wave velocity (PWV) can be used to measure the aortic distensibility and it is known as inversely related to the arterial compliance. Increased aortic stiffness which is assessed by PWV, is seem to be associated with arterial blood pressure. In this study, we investigated the arterial compliance by PWV in patients with CID including RA and FMF.

Material and methods. We studied 25 patients with RA, 33 patients with FMF and 31 healthy subjects without a history of any cardiovascular risk factors such as hypertension, diabetes mellitus, hyperlipidaemia (89 subjects in total). We measured the arterial compliance by automatic carotid-femoral (aortic) PWV using Complior Colson (France) device. $PWV (m/s) = distance (m)/transit time(s)$.

Results. It is seen that, patients with CID have higher carotid-femoral (aortic) PWV ($8,76 \pm 2,09$ vs $8,07 \pm 0,94$ m/s) compared to control groups ($p=0,03$). There were significant correlations between PWV and age, body-mass index, systolic blood pressure, diastolic blood pressure and mean blood pressure. ($p<0,001$, $r=0,65$; $p<0,001$, $r=0,36$; $p<0,001$, $r=0,42$; $p<0,001$, $r=0,46$; $p<0,001$, $r=0,48$, respectively).

Conclusion. Arterial compliance, which is assessed by carotid-femoral (aortic) PWV, is decreased in patients with CID such as RA and FMF when it is compared to healthy control group.

Keywords: arterial elasticity, pulse wave velocity, chronic inflammatory disease.

Relationships and Activities: none.

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Chronic immune and inflammatory diseases can present many complex problems for the cardiology, cardiothoracic surgery and anesthesiology practice. Rheumatoid arthritis (RA) and familial Mediterranean fever (FMF) are related with increased risk of cardiac events [1]. Endothelial dysfunction, which is also an early stage of atherosclerotic process, is associated with chronic inflammation [2]. When the arterial wall is damaged due to atherosclerosis, arterial stiffness increases, on the other hand arterial elasticity and compliance decreases [3]. Pulse wave velocity (PWV), inversely correlated with arterial distensibility and relative arterial compliance, is a noninvasive technique that helps to measure and understand such effects on the arterial system [3, 4]. Animal and preoperative studies suggested that PWV as arterial blood pressure changes with different hemodynamic conditions [5]. Increases in arterial blood pressure, heart rate, and systemic vascular resistance were associated with higher values for PWV in cardiothoracic surgical patients [6]. In this study, we investigated the arterial compliance by using PWV, especially in patients with chronic inflammatory diseases (CID), such as RA and FMF.

Material and methods

This cross-sectional study has a total number of 89 subjects including RA (25) who are diagnosed according to 2010 ACR/EULAR Classification Criteria for RA [7] and FMF (33) according to the Simplified FMF diagnosis criteria [8] and healthy subjects (31). All of the patients were inactive during the investigation. We excluded patients with history of previous myocardial infarction, peripheral arterial disease, carotid artery disease, congestive heart failure, renal failure (creatinine of plasma $>1,8$ mg/dl), arterial hypertension, insulin dependent diabetes mellitus, non-insulin dependent diabetes mellitus, hyperlipidemia, valvular heart disease, atrial fibrillation, anemia (hematocrit $<35\%$), obesity (body-mass index (BMI) >35 kg/m² and waist-hip ratio ≥ 1). Patients in this study were not treated with beta-blockers, calcium channel blockers, statins, hormone replacement therapy, diuretics, and angiotensin converting enzyme inhibitors, angiotensin receptor blockers and nitrates. The study was carried out in accordance with the standards of good clinical Practice (Good Clinical Practice) and the principles of the Helsinki Declaration. The study Protocol was approved by the Ethical committees of all participating clinical centers. Prior to being included in the study, written informed consent was obtained from all participants.

Measurements. Weight of the patients were measured in kilograms as being in light clothes and without shoes and measurements of their height

Table 1
Basic data and hemodynamic values
in control subjects and patients with CID

Parameters	CID	Healthy Group	p
Age (years)	34,5 \pm 14,5	37,3 \pm 10,8	0,31
BMI (kg/m ²)	24,57 \pm 3,99	25,65 \pm 3,39	0,18
Waist/Hip	0,83 \pm 0,73	0,86 \pm 0,08	0,07
SBP (mmHg)	110,26 \pm 15,6	115,00 \pm 13,10	0,13
DBP (mmHg)	71,38 \pm 10,67	72,10 \pm 7,61	0,71
MBP (mmHg)	84,34 \pm 11,58	86,19 \pm 8,07	0,38
Pulse Pressure (mmHg)	38,88 \pm 10,13	42,90 \pm 11,67	0,11
Heart Rate (beat/min)	78,93 \pm 10,30	76,32 \pm 9,08	0,22
PWV (m/s)	8,76 \pm 2,09	8,07 \pm 0,94	0,03

Abbreviations: BMI — body mass index, CID — chronic inflammatory diseases, DBP — diastolic blood pressure, MBP — mean blood pressure, PWV — pulse wave velocity, SBP — systolic blood pressure.

were taken. BMI (kg/m²) were calculated dividing body weight in kilograms by square of body height in meters. Waist circumference is measured between the last rib and *crista iliaca* on the midline while the patient was standing. Hip circumference is measured by using the line between right and left trochanter major of femur. The circumference of waist dividing them by circumference of hip, waist-hip ratios were calculated.

PWV and blood pressure measurements. Systolic (SBP), diastolic (DBP), mean blood pressure (MBP) and pulse pressures were measured in consonant with European Society of Cardiology (ESC) and the European Society of Hypertension (ESH) guidelines [9], using a mercury sphygmomanometer with appropriate cuff sizes, in patients who rest for 20 min (Korotkoff phase I for SBP and V for DBP).

Pulse pressure = SBP — DBP

MBP = [SBP + 2 X DBP] / 3

Arterial elasticity was measured by automatic carotid-femoral (aortic) PWV by using the Complior Colson (France) device; the technical characteristics of this device have been described [4]. PWV of the aorta can be measured by two ultrasounds or strain-gauge transducers (using a TY-306 Fukuda pressure sensitive transducer non-invasively — Fukuda, Tokyo, Japan) that fixed transcutaneously into arteries by a known distance: the right femoral and right common carotid arteries. We repeated the measurements over ten different cardiac cycles, and used the mean value for the final analysis. PWV is calculated with pulse transit time and the distance (between femoral and right common carotid artery

which was measured from the body surface) traveled by the pulse between two recording sites, according to the following formula:

$PWV (m/s) = \text{distance (m)} / \text{transit time (ms)}$.

Statistical analysis. Statistics were obtained using the ready-to-use program of SPSS version 8.0. All the values were expressed as mean \pm standard deviation. The obtained results were assessed by Mann-Whitney U test. Correlations were calculated with the Spearman test. $P < 0,05$ was accepted as statistically significant.

Results

It is seen that, patients with CID have higher carotid-femoral (aortic) PWV ($8,76 \pm 2,09$ vs $8,07 \pm 0,94$ m/s) compared to control groups ($p = 0,03$) (Table 1). There were significant correlations between PWV and age, BMI, SBP, DBP and MBP ($p < 0,001$, $r = 0,65$; $p < 0,001$, $r = 0,36$; $p < 0,001$, $r = 0,42$; $p < 0,001$, $r = 0,46$; $p < 0,001$, $r = 0,48$, respectively).

Discussion

In this study, arterial compliance assessed by carotid-femoral (aortic) PWV, an indicator of arterial stiffness, is decreased in patients with CID such as RA and FMF, when we compared to the healthy group. Although, the underlying mechanisms of vascular pathologies in patients with CID are not well understood, predominant histopathologic reason is known as vascular inflammation, which is related with endothelial cell injuries [10]. Vascular fibrosis and smooth muscle cell proliferation forms the basis of vascular inflammation, which increases arterial stiffness and decreases arterial compliance. Increased arterial stiffness associated with increased carotid-femoral PWV or decreased arterial compliance may lead left ventricular afterload to increase or myocardial oxygen supply to decrease [10].

RA is an inflammatory and systemic immune disease, which may cause acceleration in atherosclerotic progress and an increase in cardiovascular morbidity and mortality [11]. The mortality of RA patients has remained high even if the standardized mortality ratio of the general population improvements has improved over the years and that might have been the of the most important discoveries over the past twenty years. This inflammation becomes an important factor of the initiation or the progression of atherosclerosis due to impairing endothelial function, arterial compliance and arterial elasticity [12]. Some studies have discovered that RA patients have their arterial elasticity reduced [12, 13].

FMF happens to be an autosomal recessive disorder that has its own ethnicity originating from the Middle East: Sephardic Jews, Armenians, Arabs,

Druze and Turks [14]. Recurrent episodes of arthritis, chest/stomach pain, and serosal inflammation mostly along with the fever are the main symptoms of FMF. On the other hand, the main issue with untreated patients is the development of amyloidosis. Inflammation with infiltration by neutrophils is seen in histopathologic examinations. It is shown that arterial elasticity and/or compliance is reduced in patients with FMF [2, 14].

Atherosclerotic cardiovascular disease can be characterized by thickening of the vessel wall. It is possible to come across with atherosclerosis in different stages by non-invasive techniques like carotid-femoral (aortic) PWV and that is important to clinically describe patients under high cardiovascular risks including hypertension, hyperlipidemia, and diabetes mellitus [2, 4]. PWV is inversely proportional to arterial elasticity and relative arterial compliance [4]. Some studies have searched the effects of the different factors on the PWV, such as age, sex, height, weight, inflammatory markers, heart rate and blood pressure [2, 6]. In our study, we observed that the most important factors contributing to increased aortic PWV is age and BMI, because of arterial compliance decreasing caused by decrease in elastin fiber, and increase in collagenous material. Normally, the total elastin and collagen protein levels should be almost the same in all aortic wall parts. Endothelial dysfunction and increased arterial medial calcification cause changes in the extracellular matrix by smooth muscle cell proliferation and increased synthesis of structural proteins including collagen, which are also some of the findings of advanced age [3]. Increased BMI, is traditional cardiovascular risk factors, could be a sign of inactivity and could be associated with inflammation and decreasing arterial distensibility, and/or compliance, as in our study [6]. PWV also depends on blood pressure levels including SBP, DBP and MBP, as in our study, and it decreases at low blood pressure, while increases at high blood pressure [3, 4]. Experimental and preoperative studies demonstrated that PWV as arterial blood pressure changes with different hemodynamic conditions [5, 6]. Increased arterial blood pressure have found with increased PWV in cardiothoracic surgical patients [4].

Study limitations. We took great care to exclude subjects with active RA, FMF and with a history of previous myocardial infarction, diabetes mellitus, hyperlipidemia, heart valve disease, aortic aneurysm, choric renal disease, peripheral arterial disease, cerebrovascular disease. In addition, we are aware that the study could be done with more cases. Therefore, the study will need confirmation in large sample size.

Conclusion

Increased aortic stiffness, measured by PWV while the preoperative anesthetic evaluation, is related with more pronounced hypotension during the induction [1, 15]. Structural changes like smooth muscle hypertrophy, changes of extracellular matrix and increased collagen levels of the vessel wall seems to be cause of reduced arterial elasticity in increased blood [3].

In conclusion, patients with RA, FMF have decreased arterial compliance assessed by carotid-femoral (aortic) PWV — an index of arterial stiffness and a marker of atherosclerosis — when we compared to healthy controls.

Relationships and Activities: none.

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