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ORIGINAL ARTICLE

Evaluation of carotid-femoral pulse wave velocity, aortic stiffness index, and aortic distensibility in patients with fibromyalgia

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Abstract

Objective The aim of this study was to compare the carotid-femoral pulse wave velocity (CFPWV), aortic stiffness index (ASI), and aortic distensibility values of fibromyalgia patients with those of healthy subjects.

Methods This study was conducted as a case-control study between September 2017 and March 2018. Echocardiographic evaluations were administered by the same cardiologist. ASI, aortic distensibility, CFPWV, and other echocardiographic parameters of fibromyalgia patients and healthy subjects were compared. In addition, all patients were assessed using the Fibromyalgia Impact Questionnaire (FIQ), number of tender points, and Visual Analogue Scale (VAS) pain score.

Results The fibromyalgia group consisted of 67 female patients with a mean age of 48.54 ± 3.1 years (range, 42–55 years) and the control group consisted of 50 healthy subjects with a mean age of 49.76 ± 3.1 years (range, 42–55 years). No significant difference was observed between the groups in respect of age and body mass index ($p > 0.05$). CFPWV and ASI values were significantly higher in the fibromyalgia group than in the control group. Aortic distensibility values were significantly lower in the fibromyalgia group compared to the control group ($p < 0.05$ for all). There was a very strong, positive correlation between the CFPWV values and number of tender points ($r = 0.936$, $p < 0.001$), VAS ($r = 0.927$, $p < 0.001$), FIQ ($r = 0.941$, $p < 0.001$), and ASI ($r = 0.957$, $p < 0.001$).

Conclusion CFPWV and aortic stiffness seem to be increased and aortic distensibility seems to be decreased in patients with fibromyalgia. Alleviating pain and improving the disease severity may be helpful in preventing cardiovascular risk factors in patients with fibromyalgia.

Keywords Aortic stiffness · Coronary heart disease · Fibromyalgia · Pulse wave velocity

Introduction

Fibromyalgia is a rheumatic disorder characterized by widespread musculoskeletal pain with stiffness and localized tenderness accompanied by fatigue, sleep, or cognitive symptoms [1]. It has been well established that fibromyalgia is associated with cardiovascular disorders [2–4]. Fibromyalgia syndrome (FMS) has been previously found to be associated with increased carotid intima media thickness, coronary heart disease, and circadian blood pressure variability [2]. An increase in arterial stiffness, one of the significant markers of vascular aging, is a prognostic determinant of cardiovascular mortality [3, 4], but there have been few studies of arterial stiffness in fibromyalgia patients [5–7]. Brachial-ankle pulse wave velocity (BAPWV) has been studied in fibromyalgia, thereby highlighting endothelial dysfunction as a determinant of arterial stiffness [5]. Carotid-femoral pulse wave velocity (CFPWV) is the gold standard method for the determination of arterial stiffness and has a high predictive value for undesirable cardiovascular events [8]. However, to the best of our knowledge, there has been only one study evaluating CFPWV in fibromyalgia [6]. Therefore, the aim of this study was to compare CFPWV, aortic stiffness index (ASI) of fibromyalgia patients with those of healthy subjects.

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Materials and methods

Study design and participants

This case-control study was conducted between September 2017 and March 2018. The Fibromyalgia group consisted of patients aged 35–55 years who presented at the Physical Medicine and Rehabilitation Clinic and were diagnosed with fibromyalgia according to the American College of Rheumatology 1990 Criteria for the Classification of Fibromyalgia [9]. The control group was formed of subjects admitted to the cardiology clinic with non-specific symptoms with no cardiovascular or other systemic diseases. Patients with any history of coronary heart disease, hypertension, diabetes mellitus, chronic inflammatory disease, or endocrine disorders were excluded. Patients who had received any previous treatment for fibromyalgia were also excluded.

Echocardiographic evaluation

CFPWV evaluations were performed by a single cardiologist using a SphymoCor® system, (AtCor Medical, Sydney, Australia) and the echocardiographic evaluations were applied using a 3.5-MHz transducer (Vivid S5, GE Medical System). Following a routine conventional echocardiographic examination, each patient was positioned to be slightly recumbent on the left side and two-dimensional guided M-mode tracings were recorded from the ascending aorta. The measurements were taken at 3 cm above the aortic valve. Using a caliper, internal aortic diameters were measured as the distance between the trailing edge of the anterior aortic wall and the leading edge of the posterior aortic wall in systole and diastole. Aortic systole diameter (AoSD) was measured when the aortic valve was fully open, and aortic diastole diameter (AoDD) was measured at the peak of QRS complex on the electrocardiogram. The two diameter values were used to calculate the ASI:

$$\text{Arterial diameter change (mm)} = \text{SD}-\text{DD}$$

- Arterial strain = (SD-DD)/DD.

Then, aortic distensibility and CFPWV were calculated according to the following formulae [9–11]:

- ASI β = Ln (SBP/DBP)/strain (Ln: natural logarithm)
- Arterial distensibility = (2 × strain)/(SBP-DBP)

Pulse wave velocity was measured from the right carotid and right femoral arteries. These arterial pulse waves were digitized at 1200 Hz, and the pulse transit time between the carotid and femoral sites (ΔTcf) was also calculated based on phase velocity theory. The path length from the suprasternal notch to the femur (ΔDsf) was calculated as ΔDsf = 0.5643 −height (m) × 18.381. The path length from the suprasternal notch to the carotid site (ΔDsc) was calculated as ΔDsc = 0.2437−height (m) × 19.0. The CFPWV was calculated using the following formula that was used from the device: (ΔDsf-ΔDsc)/ΔTcf [11, 12].

Fibromyalgia impact questionnaire and visual analogue scale

The Fibromyalgia Impact Questionnaire (FIQ) is a measurement tool that was developed to evaluate the status, progress, and outcomes of fibromyalgia patients. The FIQ includes 10 items covering the areas of physical impairment, general well-being, work missed, work accomplished, pain, fatigue, rest, stiffness, anxiety, and depression. Each item is scored from a maximum of 10 points with higher scores indicating a greater effect of the syndrome on the patient [13]. Pain severity was assessed using the Visual Analogue Scale (VAS), where 0 = no pain and 10 = intolerable pain.

Statistical analysis

Data obtained in the study were analyzed using IBM SPSS version 20.0 software (IBM Corp., Armonk, NY, USA). Conformity of the data to normal distribution was checked using the Kolmogorov-Smirnov test and histograms. Descriptive statistics were stated as mean ± standard deviation. Between-group comparisons were made using the Mann-Whitney U test or Student's t test, according to the distribution. Correlation analyses were made using Pearson's Correlation test. A value of $p < 0.05$ was accepted as statistically significant.

Results

A total of 117 subjects were included in this study as the FMS group consisting of 67 female patients with a mean age of 48.54 ± 3.1 years (range, 42–55 years) and the control group of 50 healthy subjects with a mean age of 49.76 ± 3.1 years (range, 42–55 years). No significant difference was observed between the groups in respect of age and BMI ($p > 0.05$).

Comparisons of the echocardiographic measurements are shown in Table 1. CFPWV and aortic stiffness values were significantly higher in the FMS group than in the control group. Aortic distensibility values were significantly lower in the FMS group compared to the control group ($p < 0.05$ for all).

The correlation analyses of the FMS patients ($n = 67$) are shown in Table 2. A very strong, positive correlation was

Table 1 Demographic and echocardiographic data of the groups

Variables	Fibromyalgia group ($N = 67$)	Control group ($N = 50$)	P value
Age (years)	48.54 ± 3.178	49.76 ± 3.178	0.055
Body mass index (kg/m^2)	23.01 ± 1.2	23.12 ± 1.1	0.233
Smoking, n (%)			
- Yes	11 (16,4)	9 (18,0)	0,153
- No	56 (83.6)	41 (82)	
Systolic blood pressure (mmHg)	125.16 ± 7.995	123.00 ± 8.767	0.167
Diastolic blood pressure (mmHg)	76.48 ± 6.9	73.18 ± 9.0	0.060
Mean arterial pressure (mmHg)	92.79 ± 7.07	89.78 ± 8.3	0.058
Heart rate (bpm)	74.50 ± 6.6	73.62 ± 8.3	0.536
CFPWV (m/s)	7.24 ± 1.0	6.19 ± 0.3	< 0.001
Ejection fraction (%)	62.53 ± 2.5	62.80 ± 2.5	0.577
Mitral valve early diastolic velocity	81.64 ± 10.6	86.20 ± 8.4	0.014
Mitral valve late diastolic velocity	65.07 ± 5.4	69.20 ± 6.8	0.001
Left ventricle deceleration time	65.07 ± 5.4	69.20 ± 6.8	0.385
Isovolumic relaxation time	179.85 ± 15.37	182.00 ± 9.4	0.280
Systolic myocardial velocity	10.59 ± 0.6	11.28 ± 0.7	< 0.001
Annular early diastolic velocity	11.79 ± 0.7	11.42 ± 0.9	0.023
Annular late diastolic velocity	10.07 ± 0.6	10.52 ± 0.6	< 0.001
Systolic aortic diameter (mm)	30.01 ± 2.6	30.48 ± 2.8	0.363
Diastolic aortic diameter (mm)	28.20 ± 3.0	28.28 ± 2.9	0.900
Aortic stiffness	5.64 ± 1.1	4.03 ± 0.3	< 0.001
Aortic distensibility	3.85 ± 0.49	4.18 ± 0.3	< 0.001
Aortic wall systolic velocity	11.49 ± 0.5	11.78 ± 0.6	0.014
Aortic wall late diastolic velocity	9.55 ± 0.7	10.48 ± 0.7	< 0.001
Aortic wall late diastolic velocity	10.86 ± 0.7	10.38 ± 0.5	< 0.001

CFPWV carotid-femoral pulse wave velocity

determined between the CFPWV values and the number of tender points ($r = 0.936$, $p < 0.001$), VAS ($r = 0.927$, $p < 0.001$), FIQ ($r = 0.941$, $p < 0.001$), and aortic stiffness ($r = 0.957$, $p < 0.001$). A very strong, negative correlation was determined between the aortic distensibility values and the number of tender points ($r = -0.816$, $p < 0.001$), VAS ($r = -0.881$, $p < 0.001$), FIQ ($r = -0.876$, $p < 0.001$), CFPWV ($r = -0.876$, $p < 0.001$), and aortic stiffness ($r = -0.888$, $p < 0.001$).

Discussion

The aim of this study was to compare the CFPWV, ASI, and aortic distensibility values of fibromyalgia patients with those of healthy subjects. There were three main outcomes of the study. CFPWV and aortic stiffness values were significantly higher in the fibromyalgia group. Second, aortic distensibility values were significantly lower in the fibromyalgia group, and third, CFPWV, aortic stiffness, and aortic distensibility were significantly correlated with the severity of fibromyalgia.

The mechanism of cardiovascular events in fibromyalgia is not clearly understood, although (inappropriate) sympathetic discharges, autonomic nervous system changes, reduced heart rate variability, neurohumeral activation, and pro-inflammatory cytokines have been proposed as possible mechanisms [2, 7, 14]. Arterial stiffness is one of the earliest actions of structural and functional changes within the arterial wall. Increased aortic stiffness may contribute to atherosclerotic progression and endothelial dysfunction [15, 16]. In this context, pulse wave velocity is the gold standard measurement of AS and is an independent predictor of mortality and stroke in the general population and in various chronic diseases [14, 15].

As regards the evaluation of pulse wave velocity in fibromyalgia patients in the literature; increased aortic stiffness was shown in 99 fibromyalgia patients by Triantafyllias et al. [6]. BAPWV was evaluated in a prospective controlled trial comprising 108 female fibromyalgia patients and 76 healthy subjects. The patients with fibromyalgia showed significantly increased arterial stiffness. In addition, BAPWV showed a significant positive correlation with the severity of fibromyalgia [5]. In another study consisting of 27 postmenopausal women and 29 healthy controls, the three regional pulse wave

Table 2 Correlation analyses of the FMS patients ($N = 67$)

Variables		Number of tender points	VAS	FIQ	CFPWV	Aortic stiffness	Aortic distensibility
Number of tender points	Pearson correlation	1	.897**	.901**	.936**	.920**	− .816**
	Sig. (two-tailed)		.000	.000	.000	.000	.000
VAS	Pearson correlation	.897**	1	.921**	.924**	.927**	− .881**
	Sig. (two-tailed)	.000		.000	.000	.000	.000
FIQ	Pearson correlation	.901**	.921**	1	.950**	.941**	− .872**
	Sig. (two-tailed)	.000	.000		.000	.000	.000
CFPWV	Pearson correlation	.936**	.924**	.950**	1	.957**	− .876**
	Sig. (two-tailed)	.000	.000	.000		.000	.000
Aortic stiffness	Pearson correlation	.920**	.927**	.941**	.957**	1	− .888**
	Sig. (two-tailed)	.000	.000	.000	.000		.000
Aortic distensibility	Pearson correlation	− .816**	− .881**	− .872**	− .876**	− .888**	1
	Sig. (two-tailed)	.000	.000	.000	.000	.000	

**Correlation is significant at the 0.01 level (two-tailed)

velocities of the two groups at the aorta-femoral, femoral-dorsalis, and aorta-radialis arteries were similar [7].

Since arterial stiffness is primarily associated with aging and hypertension [14], patients with HT were excluded from this study, and the groups were age-matched. According to the results obtained in the study, the CFPWV and aortic stiffness values were significantly higher in the fibromyalgia patients, which was consistent with literature. However, the main strength of this study was that pulse wave velocity was evaluated from the carotid-femoral arteries rather than brachial-ankle, aorta-femoral or other arteries.

CFPWV depends on mean arterial pressure (and in some cases heart rate) at the time of CFPWV measurement. According to the recommendations for improving and standardizing vascular research on arterial stiffness of the American Heart Association, these two parameters should be always taken into account when performing CFPWV examinations, due to their possible confounding effect on the results [17]. In our study, no significant difference was observed between the groups in terms of systolic blood pressure, diastolic blood pressure, mean arterial pressure, or heart rate.

Distensibility refers to the ability of the artery to expand during systole, and it can be defined as the relative change in the cross-sectional area of the artery (strain) divided by the local pulse pressure. Therefore, increased aortic stiffness can be expected to be accompanied by decreased aortic distensibility. From this point of view, Özcan et al. [18] suggested that elastic properties of the aorta are impaired in patients with severely symptomatic fibromyalgia. Likewise, the aortic distensibility was decreased in the fibromyalgia patients in the current study and there was a strong negative correlation between aortic distensibility and the severity of fibromyalgia.

There are some important drawbacks to this study. First, there was no evaluation of pro-inflammatory cytokines. The cross-sectional design rather than a prospective cohort was another limitation. This study lacks using the new classification criteria for fibromyalgia patients [1]. The control group could be formed of healthy persons (in a strict manner) rather than subjects admitted to the cardiology clinic with non-specific symptoms with no cardiovascular or other systemic diseases. Finally, CFPWV was evaluated on the right side only, and the lack of left side evaluations can be considered a limitation.

In the light of the current study results, CFPWV and aortic stiffness seem to be increased and aortic distensibility seems to be decreased in patients with fibromyalgia. In addition, these parameters are significantly associated with the severity of the disease. Alleviating pain and lessening disease severity may be helpful in preventing cardiovascular risk factors in patients with fibromyalgia. In this context, we would like to highlight that patients with fibromyalgia, particularly the severe cases, can be examined regarding the cardiovascular risk factors. Besides, exercise and obesity, which have an impact on both fibromyalgia and cardiovascular diseases, should be focused on, and patients should be encouraged for weight loss and exercise.

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H.A.: study design, acquisition of data, writing and drafting the manuscript, and final approval

T.E.: study design, statistical analyses, writing and drafting the manuscript, and final approval

Compliance with ethical standards

Disclosures None.

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