Letter to the Editors

Increased aortic stiffness in patients with fibromyalgia: results of a prospective study on carotid-femoral pulse wave velocity

Sirs,

Fibromyalgia (FM) affects about 0.5-5% of the population and is one of the most common reasons for referring a patient to a rheumatologist (1, 2). An important pathophysiological aspect of FM is an aberrant function of the sympathetic nervous system (3). Interestingly, sympathetic nerve hyperactivity has been reported to be associated with an increased risk of cardiovascular (CV) disease (4). CV risk in the general population can be assessed through carotid femoral pulse wave velocity (cfPWV), a marker of aortic stiffness (5). The aims of this study were therefore to test the hypothesis of increased cfPWV in a group of patients with FM and to examine its association with FM associated parameters and selected traditional CV risk factors.

Measurements of cfPWV in 99 FM patients and 102 controls were performed via a validated non-invasive oscillometric device (Vicorder®, SMT medical). cfPWV was measured as the velocity value calculated through the distance between the suprasternal notch and right femoral artery in meters divided by the time that one pulse wave needed to cover this distance in seconds ($\Delta s/\Delta t$) (m/s). The examination procedure was in accordance with the recommendations of the American Heart Association (6). Subsequently, measurements of systolic (SP) and diastolic pressure (DP) were performed over the brachial artery. Exclusion criteria were: malignancy, pregnancy, age<18 years, known CV disease, kidney failure, class II/III obesity [Body Mass Index (BMI)≥35 kg/m^2], diabetes mellitus and statin therapy. All included patients met the modified 2010 American Rheumatism Association (ACR) diagnostic criteria for FM (7). Patients gave their informed consent and the assessment was approved by the Local Standing Committee for Clinical Studies in adherence to the Declaration of Helsinki.

The descriptive characteristics of both groups are seen in Table I. cfPWV average was significantly higher in the patients group compared to the control group (p=0.004). The correlation remained significant even after adjusting for statistically identified confounding factors [age, mean arterial pressure (MAP) and BMI, p_{adj}=0.044]. cfPWV associated significantly with age in both the patients and the control group (Spearman's: *rho*=0.614, p<0.001 and *rho*=0.678, p<0.001 accordingly). In the control group, age adjusted multiple regression analysis showed significant correlations of cfPWV with SP, DP, MAP (p<0.001, p=0.013 and p<0.001 accordingly) and with BMI (p=0.003). In the patients group, the same age adjusted statistical model showed no significant correlations between cfPWV and FM related parameters [EuroQol-VAS (pain), tender points], laboratory markers (lipids, inflammation markers, rheumatoid factor, antinuclear antibodies) or CV risk factors (nicotine use, blood pressure, antihypertensive drugs, BMI≥30 kg/m^2) (all p_{adj}> 0.05).

To our knowledge, this is the largest study to examine the gold standard assessment method of aortic stiffness in FM patients and the first one to find increased cfPWV values in comparison to healthy subjects. One further analysis did not find higher cfPWV values in a small group of female FM patients in comparison to controls (8). Nevertheless, more recent reports show that FM could be associated with a higher CV disease risk profile (9). However, the main result of our exploration cannot be solely explained through the presence of traditional CV risk factors (exclusion criteria, statistical adjustments for confounding factors). Therefore, there could be an independent, probably FM associated parameter which lead to an increase of aortic stiffness such as sympathetic hyperactivity which has been found to correlate independently with cfPWV (10).

As a limitation, we did not account for medications such as pain killers and antidepressants or for the presence of thyroid autoantibodies.

In conclusion, we report for the first time that patients with FM have increased cfPWV in comparison to healthy controls and could therefore be under high CV risk.

Table I. Descriptive characteristics by group.

	Controls (n=102)	Patients (n=99)	Significance (p)
cfPWV (m/s)†	7.50 (6.78–8.40)	8.00 (7.20–9.30)	0.004*
Age (years)†	50 (38.25–56.25)	53 (46.00–59.00)	0.025*
Gender (female)	92 (90.2 %)	93 (93.9 %)	0.436
Nicotin (smokers)	21 (20.6 %)	28 (28.6 %)	0.250
Antihypertensive drugs	16 (15,2%)	35 (36,1%)	0.001*
BMI† (kg/m^2)	23.74 (21.08–27.05)	26.50 (23.80–30.81)	<0.001*
SP† (mmHg)	120 (110-136)	120 (110–130)	0.770
DP† (mmHg)	80 (70–85)	80 (70–80)	0.426
MAP† (mmHg)	92.33 (85–100)	93 (83.33–96.67)	0.586
Heart rate† (/min)	66.00 (59.00–73.0)	72.00 (66.00–90.0)	0.001*
Cholesterine§ (mg/dl)	-	222.8 ± 44,4	-
HDL† (mg/dl)	-	65 (54-77.5)	-
LDL† (mg/dl)	-	140 (108.50–173.50)	-
Triglycerides† (mg/dl)	-	105 (74.50–156.00)	-
Tender points (18/18 positive)	-	52 (52.5 %)	-
CRP† (mg/l)	-	1.67 (1.00–4.62)	-
ESR† (mm/h)		13.50 (8–18)	
RF (positive)	-	11 (11.1 %)	-
ANA (> 1:80)	-	5 (5.1%)	-
EQ-VAS† (%)	-	45 (35–60)	

†Data are presented as median (inter quartile range) as they are not normally distributed. §Data are presented as mean ± standard deviation as they are normally distributed. The rest of data are presented as absolute (n) and relative frequency (%). cfPWV: carotid femoral pulse wave velocity, BMI: body mass index, SP: systolic pressure, DP: diastolic pressure, MAP: mean arterial pressure, HDL: high density lipoprotein, LDL: low density lipoprotein, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, RF: rheumatoid factor, ANA: antinuclear antibodies.
*p<0.05.

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