Arterial Compliance and Carotid Artery Changes in Multiple Sclerosis

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Abstract: Limited studies show abnormal arterial compliance in multiple sclerosis (MS). We investigated possible carotid artery changes and arterial stiffness in MS patients. This study included 33 patients with clinically definite MS and 22 healthy control subjects. Expanded disability status scale (EDSS), Pulse wave velocity (PWV), Ankle brachial index (ABI), and carotid intima media thickness (CIMT) were measured in all participants. Brachial ankle PWV was significantly higher in MS patients compared to the healthy controls (P=0.014). There was no statistically significant difference between patients and control subjects as regards brachial femoral PWV, CIMT or ABI (P>0.05). Brachial femoral pulse wave velocity was significantly higher in the secondary progressive compared to the relapsing remitting MS patients (P=0.033). CIMT was significantly higher in the secondary progressive compared to the relapsing remitting MS patients (P=0.022). There were no statistically significant correlations between brachial ankle PWV, brachial femoral PWV or CIMT and EDSS scores in MS patients (P>0.05).Arterial wall changes may exist in MS patients. Its' value as potential biomarker for disease pathology or future atherosclerosis in MS patients remains questionable.

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1. Introduction

Carotid artery intima-media thickness (CIMT) and arterial stiffness are markers of structural and functional vessel wall properties(1). Arterial stiffness further describes the reduced ability of an artery to expand and recoil in response to pressure changes (2). It, collectively, describes indices like distensibility, compliance, and tensile elasticity of the arterial vascular system (3). Arterial stiffness can be detected before the appearance of clinically apparent vascular disease and is considered a powerful predictor of future cerebrovascular and cardiovascular events (4).

Increased CIMT and reduced arterial compliance have been previously reported in patients with autoimmune inflammatory disorders (5, 6). Few studies (7, 8) demonstrate significant differences in arterial compliance indices between multiple sclerosis (MS) patients, and healthy individuals. None, to our best knowledge investigated CIMT in MS patients.

The aim of this study is to investigate possible carotid artery changes and arterial compliance in MS patients.

2. Material and Methods

2.1. Study population:

This study included 33 clinically definite MS patients attending the MS Outpatient Clinic, MS research unit, Kasr Al-Ainy hospitals, Cairo University, Egypt; and 22 healthy control subjects; during the period from June 2012 to March 2013.

The age of patients ranged from 23 to 35 years with a mean of 29.48±3.35 years and the age of control subjects ranged from 25 to 35 years with a mean of 29.5±2.91 years (P>0.05).

The patients group included 18 female (54.55%) with an age range of 24 to 35 years and a mean of 29.67±3.18 years; and 15 male (45.45%) patients with an age range of 23 to 34 years with a mean of 29.27±3.63 years with no statistically significant difference (P>0.05).

MS patients were subdivided into 18 relapsing remitting MS (RRMS) (54.55%) with an age range of 23 to 34 years with a mean of 29.67±3.53 years; and 15 secondary progressive MS (SPMS) patients (45.45%) with an age range of 24 to 35 years with a mean of 29.27±3.22 years with no statistically significant age difference (P>0.05).

Patients were excluded if they have hypertension, diabetes mellitus, hyperlipidemia, ischemic cardiac disease or were smokers.

This study was approved by Cairo University research committee. All participants signed an informed consent.

2.2. Methods:

1. Expanded disability status scale (EDSS): The Kurtzke Expanded Disability Status Scale (9) was used for measurement of disability in MS patients.

2. Brain Magnetic resonance imaging (MRI): Contrast enhanced MRI of the brain and cervical spine was performed to all MS patients using a Phillips Intera© 1.5T scanner.

3. Pulse wave velocity measurement (PWV): Brachial/Ankle and Brachial/femoral PWVs were measured using Vasogurad apparatus (Nicolet Vasoguard, model p84, VIASYS Healthcare, USA). PWV was calculated as: Distance between 2 arterial recording sites / transit time (10).

4. Segmental arterial pressure measurement and ankle brachial index (ABI) calculation: Segmental blood pressure was measured by photoplethysmography method, using the Vasoguard machine (Nicolet Vasoguard, model p84, VIASYS Healthcare, USA).

5. Carotid artery intima media thickness measurement: B mode ultrasonographic images of both common carotid arteries were obtained by (AcusonAntras Siemens) with a 7.5 MHZ high frequency linear transducer. Distance between the echoes arising from the blood intima surface and the media adventitia interface was taken as the measurement of intima media thickness (11)

2.3. Statistical analysis

The data were analyzed using the statistical package IBM SPSS version 15 (SPSS Inc., Chicago, IL). Statistical differences between groups were tested using Chi Square test for qualitative variables and independent sample t-test for quantitative normally distributed variables while Nonparametric Mann Whitney U test was used for non-normally distributed variables.Correlations were done to test linear relationship between variables. A *P*-value of 0.05 or less was considered statistically significant.

3. Results

Brachial ankle pulse wave velocity (baPWV) was significantly higher in MS patients compared to the healthy controls (*P*=0.014). There were no statistically significant differences between MS patients and the control subjects as regards brachial femoral pulse wave velocity (bfPWV), ABI or CIMT (*P*>0.05) (Table 1).

baPWV was significantly higher in the MS male patients compared to females (*P*<0.001). bfPWV was significantly higher in the MS male patients compared to females (*P*=0.006). CIMT was significantly higher in the MS male patients compared to females (*P*=0.005) (Table 2). EDSS score of female MS patients ranged from 2.5 to 7.5 with mean of 5.47 ±1.41 and was significantly higher compared to the score of male MS patients which ranged from 2 to 7.5 with a mean of 4.07 ±1.76 (*P*=0.022).

CIMT was significantly higher in the SPMS compared to the RRMS patients (*P*=0.022). bfPWV was significantly higher in the SPMS compared to the RRMS patients (*P* =0.033) (Table 3). EDSS score of SPMS patients ranged from 5.5 to 7.5 with a mean of 6.37 ± 0.74 and was significantly higher compared to the RRMS patients which ranged from 2 to 5.5 with a mean of 3.56 ± 1.11 (*P*<0.001).

There were no statistically significant correlations between baPWV, bfPWV or CIMT and EDSS scores in all groups of MS patients (*P*>0.05).

Table 1. Comparison of ABI, baPWV, bfPWV and CIMT among MS patients to healthy control subjects

	MS patients (n=33)	Healthy controls (n=22)	*P*-value
ABI	1.08 ± 0.8	1.05±0.09	0.229
baPWV (m/s)	7.66 ± 1.95	6.72 ±0.78	0.014*
bfPWV (m/s)	9.12±1.67	8.49±1.54	0.162
CIMT (cm)	0.058±0.008	0.058±0.008	0.922

ABI (Ankle/Brachial Index), baPWV (brachial ankle pulse wave), bfPWV (brachial femoral pulse wave velocity)
*Significant

Table 2. Comparison of ABI, baPWV, bfPWV and CIMT among male and female MS patients

	Female MS patients n=18	Male MS patients n=15	*P*-value
ABI	1.07 ± 0.08	1.08±0.08	0.969
baPWV (m/s)	6.63± 1.13	8.89 ±2.04	<0.001*
bfPWV (m/s)	8.42±1.38	9.96 ±1.63	0.006*
CIMT (cm)	0.053±0.008	0.065±0.016	0.005*

ABI (Ankle/Brachial Index), baPWV (brachial ankle pulse wave), bfPWV (brachial femoral pulse wave velocity)
*Significant

Table 3. Comparison of ABI, baPWV, bfPWV and CIMT among relapsing remitting and secondary progressive subgroups of MS patients.

	RRMS patients n=18	SPMS patients n=15	*P*-value
ABI	1.085 ± 0.0719	1.068±0.088	0.561
baPWV (m/s)	7.64± 1.71	7.68 ±2.27	0.953
bfPWV (m/s)	8.47±1.15	9.66±1.86	0.033*
CIMT (cm)	0.053±0.007	0.063±0.015	0.022*

ABI (Ankle/Brachial Index), baPWV (brachial ankle pulse wave), bfPWV (brachial femoral pulse wave velocity)
*Significant

4. Discussion

Pulse wave velocity is considered a marker of arterial stiffness (12). In the present study brachial ankle pulse wave velocity was significantly higher in MS patients compared to the healthy controls indicating that multiple sclerosis patients have stiffer arteries.

Carotid artery compliance was previously shown to be significantly lower in MS patients compared to healthy subjects (8). Fjeldstad et al (7) compared arterial compliance in younger to older MS patients. Arterial compliance was significantly lower in the young group, compared to the healthy control group, whereas the older group showed no significant differences when compared to the healthy control group.

Increased arterial stiffness in patients with chronic inflammatory diseases may result either from endothelial dysfunction, which is considered an early step towards overt arterial stiffness (13-15), or from inflammation which may act as a contributing factor to vascular stiffening initiation and progression (8, 13). Several studies revealed that patients with multiple sclerosis have altered endothelial function (14, 16) as well as increased serum and CSF levels of inflammatory mediators (17, 18) which are believed to promote white cell infiltration into arteries, and cause changes in vascular smooth muscle phenotype. resulting in release of a number of matrix metalloproteinases (MMP), including MMP-9, which in turn degrade elastin, and therefore may result in stiffening of arteries (19). In addition, corticosteroids commonly used in MS relapse treatment, may improve arterial compliance as has been shown with other autoimmune disorders (20).

In the present study, there was no statistically significant difference as regards CIMT between the MS patients and the control groups. Similar results were shown by a previous study (8).

The presence of significantly higher brachial ankle pulse wave velocity with no significant difference regarding the intima media thickness in our patients compared to the healthy controls may be explained by the results of Aggoun et al (21) who reported that an early phase of alteration of the mechanical properties of the arterial wall with functional consequences,may precede the clinical and echographic appearance of atherosclerosis.

In the present study, brachial ankle, brachial femoral pulse wave velocity and CIMT were significantly higher in male compared to the female patients. Fjeldstad et al (7) found no statistical significant difference for arterial compliance between young male or female patients with multiple sclerosis. Yet, this may be contributed to wider age range of MS patients and different method of measurement of arterial stiffness as compared to the present study.

Interestingly, many studies revealed that male patients with MS have demonstrated testosterone levels significantly below the normal range (22, 23) which may correlate with arterial stiffness (24) but this was not examined in the present study.

In the present study, brachial femoral pulse wave velocity was significantly higher in patients with secondary progressive multiple sclerosis compared to patients with relapsing remitting multiple sclerosis but not when compared to healthy controls indicating that SPMS patients have relatively stiffer arteries compared to RRMS patients.

Fjeldstad et al (7) found no statistical significant differences regarding small or large arterial compliance in the relapsing remitting multiple sclerosis patients or in the secondary progressive multiple sclerosis patients when compared to the healthy controls.

Results of the present study may be attributed to reduced physical activity in the secondary progressive multiple sclerosis group as EDSS scores ranged from 5.5 to 7.5 indicating that the patients had either restricted ambulation or walked with assistance or were wheel chair bound, compared to the relapsing remitting multiple sclerosis group whom their EDSS ranged from 2 to 5.5 which indicated that the patients were either fully ambulant or had only restricted

ambulation. This hypothesis is supported by the results of Ranadive et al (8) who demonstrated that the physical activity of multiple sclerosis patients was significantly correlated with their central pulse wave velocity. In addition, daily ambulatory activity "particularly the cadence of at least 30 continuous minutes of ambulation" was shown to be predictive of favorable large arterial elasticity in young healthy individuals(25).

In the current study, intima media thickness was significantly higher in the secondary progressive multiple sclerosis patients. These results may be explained by the results of Pahkala et al (26) who reported that physical activity favorsa rather normal intima media thickness and endothelial function in young age, and that a physically active lifestyle in healthy young population is preventive against subclinical atherosclerosis. Same result would also explain higher CIMT in male MS patients in the present study as mean EDSS score was significantly higher and would imply less mobility.

The limitations of the current study were the narrow age range of MS patients included which was different from the population of similar studies and comparison was sometimes not conclusive, In addition, the study design did not allow us to confirm the cause/consequence relationship between arterial changes and MS. Another issue was the limited number publications covering this perspective, thus narrowing the scope of discussion and drawing conclusions.

In conclusion, Arterial stiffness may be found in MS patients, yet its relationship to MS type or degree of disability is not well established. CIMT may be higher in SPMS compared to RRMS patients but not when compared to healthy subjects. The clinical significance of these findings and the value of arterial compliance and CIMT changes as potential markers for MS disease pathology or predictors of higher risk of future atherosclerosis in MS, are yet to be confirmed.

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