Vascular Dysfunction and Physical Activity in Multiple Sclerosis

SUSHANT M. RANADIVE, HUIMIN YAN, MADELINE WEIKERT, ABBI D. LANE, MELLISSA A. LINDEN, TRACY BAYNARD, ROBERT W. MOTL, and BO FERNHALL

Department of Kinesiology and Community Health, University of Illinois at Urbana-Champaign, Urbana, IL

ABSTRACT

RANADIVE, S. M., H. YAN, M. WEIKERT, A. D. LANE, M. A. LINDEN, T. BAYNARD, R. W. MOTL, and B. FERNHALL. Vascular Dysfunction and Physical Activity in Multiple Sclerosis. Med. Sci. Sports Exerc., Vol. 44, No. 2, pp. 238–243, 2012. Background: Multiple sclerosis (MS) is an inflammatory disorder of the brain and spinal cord. Disability status and progression are associated with reduced physical activity (PA) and cardiovascular function. Lack of adequate PA combined with inflammation may create high susceptibility to subclinical atherosclerosis and vascular dysfunction. Purpose: The purpose of this study was to compare subclinical atherosclerosis and arterial function between individuals with and without MS matched for age, sex, and body mass index. Methods: Thirty-three individuals diagnosed with MS and 33 controls underwent strain gauge plethysmography for resting forearm blood flow (FBF) and peak reactive hyperemia for the microvascular function. Intima–media thickness and arterial compliance (AC) were measured using carotid ultrasound for vascular function. C-reactive protein and PA (7-d accelerometer data) were also measured. Results: There was a significant difference ($P < 0.05$) in resting FBF, peak reactive hyperemia, central pulse wave velocity, and AC between the MS and control groups. PA was associated with peak FBF and central pulse wave velocity but not FBF and carotid AC. Individuals with MS exhibited reduced arterial function but similar intima-media thickness compared with controls. Persons with MS had significantly reduced PA levels compared with controls, and PA accounted for differences in arterial function between groups. Conclusions: These results indicate that subclinical markers of atherosclerosis are higher in individuals with MS, suggesting a higher risk of cardiovascular disease in this population. However, the higher levels of subclinical atherosclerosis were accounted for by the low PA in persons with MS, suggesting that increasing PA may reduce the increase in cardiovascular disease risk in patients with MS. Key Words: PULSE WAVE VELOCITY, REACTIVE HYPEREMIA, ARTERIAL COMPLIANCE, PHYSICAL ACTIVITY

Multiple sclerosis (MS) is a chronic inflammatory disease involving demyelination and transection of axons in the CNS (3). This disease process manifests in excessive fatigue, loss of limb function and sensation, impairment of balance and coordination, pain, and autonomic dysfunction (11). Over time, such consequences likely result in a cycle of increased disability and reduced physical activity (PA) (29).

The inflammatory nature of MS combined with physical inactivity might be associated with increased risks of morbidity. MS is associated with similar or increased risk of cardiovascular disease (CVD) compared with the general population (5), and this risk is exaggerated in the first year after diagnosis (7). Importantly, vascular comorbidities are associated with delays in diagnosing MS and increased disability at diagnosis (24) and result in more rapid progression of disability over time (25).

The observation of increased CVD risk in MS is not surprising because chronic inflammation is a predictor of CVD morbidity and mortality and is involved in atherosclerotic plaque formation (6,21). An indicator and a proinflammatory cytokine like C-reactive protein (CRP) have been shown to be significantly higher in patients with MS (44). Inflammation further decreases endothelial function and increases arterial stiffness (1,23), and arterial dysfunction is present long before measurable atherosclerotic lesions and CVD symptoms (2). These changes in arterial function coupled with greater intima-media thickness (IMT) provide evidence for early subclinical atherosclerosis and are prominent in other autoimmune diseases (20,45), but little information exists in persons with MS.

Conversely, PA (4,40) is a potent protective factor against the development of CVD in healthy adults perhaps through decreased systemic inflammation (12,18). This is based on the association between PA and arterial structure and function in the general population (7,10). Nevertheless, persons with MS typically engage in low levels of PA (27,35), and some researchers have linked this with increased risk for CVD in...
MS (10,29). We recently reported in a cross-sectional study that PA was inversely associated with self-reported cardiovascular comorbidities in persons with MS (28). To that end, persons with MS might have increased levels of subclinical atherosclerosis in the absence of overt CVD symptoms because of the rate of physical inactivity.

This study compared measures of subclinical atherosclerosis (IMT and arterial function) between persons with MS and an age-, gender-, and body size–matched control group and then examined the possibility that PA accounted for the between-group difference in subclinical atherosclerosis and arterial function in persons with MS and controls. We hypothesized that persons with MS would exhibit increased IMT and reduced arterial function accompanied with an increase in CRP and interleukin-6 (IL-6) compared with healthy controls and that such differences would be accounted for by differences in PA levels between groups. Such an evaluation of subclinical atherosclerosis and PA may provide the opportunity for early identification of potential vascular comorbidities based, in part, on physical inactivity and provide the foundation for behavioral interventions that halt or minimize the worsening of disability by reducing CVD.

METHODS

Participants

We recruited a convenience sample of 33 persons (27 women and 6 men) with MS who resided in central Illinois. The sample of 33 persons (27 women and 6 men) without MS was recruited from the university community to be similar in age, sex, height, and weight compared with the sample of those who had MS. The inclusion criteria included (a) being ambulatory with or without single-point assistance, (b) having the visual ability to read 14-point font, (c) being 18–64 yr, (d) abstinence from smoking for a minimum of 6 months, (e) being willing to abstain from caffeine for 4 h before testing, and (f) being willing to wear an accelerometer for a 7-d period. The additional inclusion criterion for those with MS was being relapse free during the previous 30-d period. All persons who did not meet those criteria were excluded. All subjects signed informed consent, and the study was approved by the Institutional Review Board of the University of Illinois at Urbana-Champaign.

Medications. Thirteen subjects were taking blood pressure (BP) medication, 9 were taking cholesterol-lowering medications, 31 were taking multivitamins, and 25 were taking vitamin D supplements. Twenty-five of the subjects with MS were taking the following disease-modifying medications: Avonex interferon beta (n = 5; Biogen Idec, Washington, DC), Betaseron (n = 6; Bayer Healthcare Pharmaceuticals, Pinebrook, NJ), Tysabri (n = 4; Biogen Idec), Copaxone (n = 7; Teva Pharmaceutical Industries Ltd., Petah Tikva, Israel), Extavia (n = 1; Novartis Pharmaceuticals Corp., East Hanover, NJ), and Rebif (n = 2; EMD Serono, Inc., Rockland, MA). In addition, 10 of the subjects with MS were taking antispasticity medications, and seven were taking fatigue medications.

Brachial BP. After 10 min of lying in a supine position, resting systolic BP (SBP) and diastolic BP (DBP) were measured in the supine position using an automated oscillometric cuff (HEM-907XL; Omron Corporation, Kyoto, Japan). All BP measurements were made in duplicate, and the average of the two values was recorded.

IMT. The carotid artery was imaged with ultrasound (Aloka SSD-5500; Tokyo, Japan) using a 7.5-MHz linear-array probe. IMT of the common carotid artery was defined as the distance between the leading edge of the lumen–intima interface and the leading edge of the media–adventitia interface of the far wall of the carotid artery. All measurements were made at end diastole. The IMT of the common carotid artery was determined from an average of five measurements obtained 20 mm proximal to the carotid bifurcation (8,14,15).

Carotid artery stiffness. The carotid artery was imaged with ultrasound (Aloka SSD-5500) using a 7.5-MHz linear-array probe. Carotid BP was measured with applanation tonometry. HR was recorded with a single-lead ECG. The β-stiffness index (β), which adjusts arterial compliance for changes in distending pressure, was then calculated as follows:

$$\beta = \frac{\log P_f / P_0}{(D_1 - D_0)/D_0}$$ \tag{1}

where $D_1$ and $D_0$ are the maximum (systolic) and minimum (diastolic) diameters and $P_1$ and $P_0$ are the highest (systolic) and lowest (diastolic) carotid pressures. Our previous studies have used the same technique (8,9,14,15).

Wave reflection and aortic and carotid BP. Applanation tonometry was performed using a high-fidelity strain gauge transducer (SphygmoCor; AtCor Medical, Sydney, Australia) on the radial artery to obtain pressure waveforms. By using a generalized validated transfer function, a central aortic pressure waveform was reconstructed from the radial artery pressure waveform. The augmentation index (AIx) was calculated as the ratio of amplitude of the pressure wave above its systolic shoulder (i.e., the difference between the early and late systolic peaks of the arterial waveform) to the total pulse pressure and was expressed as a percentage. Because AIx is influenced by varied HR, AIx values were also normalized to an HR of 75 bpm. Carotid artery pressure waveforms were obtained using the same strain gauge transducer and calibrated against brachial mean arterial and diastolic pressure to obtain carotid BP. This technique has been used in our laboratory in previous studies (8,9,14,41).

Forearm blood flow. Forearm blood flow (FFB) was measured using strain gauge plethysmography (EC-4; Hokanson, Inc., Bellevue, WA). A standard BP cuff was placed around the upper arm. A strain gauge was placed around the widest part of the forearm, and an additional cuff was placed around the wrist to occlude hand circulation. Before determination of FFB, the wrist cuff was inflated and held at 250 mm Hg of pressure. FFB was determined by inflating the upper cuff to 50 mm Hg for 7 s and then deflating it for 8 s. An average of six of these 15-s plethysmographic cycles was used for FFB (8,9,14,15). FFB was
expressed as milliliters per minute per 100 mL of forearm tissue and also as flow per unit pressure (conductance) using the following equation:

\[
\text{conductance} = \left( \frac{\text{FBF}}{\text{mean arterial pressure (MAP)}} \right) \times 1000
\]  

[2]

Forearm vascular resistance was calculated using the following equation:

\[
\text{vascular resistance} = \frac{\text{MAP}}{\text{FBF}}
\]  

[3]

**Reactive hyperemia.** Reactive hyperemia (RH) of the forearm vessels was measured immediately after FBF. Arm blood flow was occluded by inflating a BP cuff on the upper arm to a pressure of 250 mm Hg for 5 min. One minute before release of the upper arm cuff, the wrist cuff was inflated to 250 mm Hg. After rapid release of the upper arm cuff, changes in forearm volume were measured, in 15-s cycles as described above, for 3 min (13 readings). The highest reading observed was recorded as the peak blood flow. All 13 measurements were plotted against time, and the area under the curve was taken as a measure of total RH (8,9,14,15).

**Blood analysis.** After an overnight fast, blood samples were collected using a butterfly needle inserted into the antecubital vein. Samples were collected into 10-mL tubes containing EDTA (anticoagulant and chelating agent). Samples were separated by centrifugation at 4°C for 15 min at 1100g and were stored at −80°C until analysis. Plasma concentrations of CRP and IL-6 and IL-6 were measured to assess systemic inflammation. Separate Quantikine enzyme-linked immunosorbent assay kits (R&D Systems, Minneapolis, MN) were used to measure plasma IL-6 and CRP. Sensitivities for the enzyme-linked immunosorbent assay kits were 0.010 ng mL\(^{-1}\) and 0.039 pg mL\(^{-1}\) for CRP and IL-6, respectively.

**PA.** PA was measured by the ActiGraph single-axis accelerometer (model 7164 version; Manufacturing Technology, Inc., Fort Walton Beach, FL). The ActiGraph accelerometer contains a single vertical axis piezoelectric bender element that generates an electrical signal proportional to the force acting on it. The acceleration/deceleration signal is digitized by an analog-to-digital converter and numerically integrated over a preprogrammed epoch interval. At the end of each interval, the integrated value of movement counts is stored in random-access memory, and the integrator is reset. In this study, the epoch was 1 min, and the accelerometers were worn during the waking hours, except while showering, bathing, and swimming, for a 7-d period. The participants recorded the time that the accelerometer was worn on a log, and this was verified by inspection of the minute-by-minute accelerometer data.

Regarding data processing, we summed the minute-by-minute counts across each of the 7 d and then averaged the total daily movement counts across the 7 d. This yielded accelerometer data in total movement counts per day with higher scores representing more PA. There is evidence that supports the reliability (34) and validity (13) of accelerometers as a measure of PA in ambulatory persons with MS.

**Type and disease severity.** Of the 33 individuals with MS, 29 had a relapse-remitting clinical course, 3 had a secondary progressive clinical course, and 1 had a primary progressive clinical course. Neurological disability was measured using the Patient Determined Disease Steps (PDDS) scale for description of the sample with MS (31). The PDDS scale contains a single item for measuring self-reported neurological impairment on an ordinal level from 0 (normal) to 8 (bedridden). This scale was developed as an inexpensive surrogate for the Expanded Disability Status Scale, and scores from the PDDS are linearly and strongly related with physician-administered Expanded Disability Status Scale scores \((r = 0.93)\) (31). This scale was included only for describing the disease severity of the sample in the present study. The median PDDS was 2 with a range of 0–6. The mean ± SD disease duration was 9.2 ± 6.7 yr.

**Data Analysis**

Descriptive statistics are presented in text and tables as mean ± SEM. Groups were compared for initial differences in study variables using independent-samples t-tests, and we expressed the magnitude of differences using the Cohen \(d\) (i.e., difference in mean scores between groups divided by pooled SD). Linear regression analysis with direct entry was used to examine if PA accounted for potential differences in arterial function and structure between groups. This analysis involved regressing arterial function or structure measures on a dichotomous grouping variable \((0 = \text{MS}, 1 = \text{control})\) in step 1 and then directly adding PA in step 2. If the effect of the grouping variable became nonsignificant and approached zero in step 2, this would provide evidence that PA accounted for the association between group and arterial function/structure measures. The proportion of explained variance in the outcome from the regression analysis was based on the adjusted \(R^2\).

**RESULTS**

Participant characteristics are presented in Table 1. There were no group differences in participant characteristics \((P \text{ values } > 0.05)\) with the exception of a large difference in PA \((P < 0.001)\) with an effect size of \(d = 1.02\). All BP

<table>
<thead>
<tr>
<th>TABLE 1. Descriptive variables.</th>
<th>MS ((n = 33))</th>
<th>Controls ((n = 33))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>47 ± 1.83</td>
<td>47 ± 1.97</td>
</tr>
<tr>
<td>Height (inches)</td>
<td>65.39 ± 0.68</td>
<td>65.71 ± 0.62</td>
</tr>
<tr>
<td>Weight (lb)</td>
<td>164.65 ± 7.86</td>
<td>161.89 ± 6.63</td>
</tr>
<tr>
<td>BMI (kg m(^{-2}))</td>
<td>27.13 ± 1.25</td>
<td>26.44 ± 1.13</td>
</tr>
<tr>
<td>PA (counts day(^{-1}))</td>
<td>179,299.48 ± 19,192.23</td>
<td>342,551.8053 ± 36,356.02</td>
</tr>
<tr>
<td>CRP (mg L(^{-1}))</td>
<td>1.87 ± 0.32</td>
<td>1.61 ± 0.27</td>
</tr>
<tr>
<td>IL-6 (pg mL(^{-1}))</td>
<td>0.81 ± 0.12</td>
<td>0.88 ± 0.23</td>
</tr>
<tr>
<td>DMD (%)</td>
<td>75</td>
<td>—</td>
</tr>
<tr>
<td>Antispasticity</td>
<td>30</td>
<td>—</td>
</tr>
<tr>
<td>medications (%)</td>
<td>21</td>
<td>—</td>
</tr>
<tr>
<td>Fatigue</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values are mean ± SEM.

BMI, body mass index; DMD, disease-modifying drugs.
variables are presented in Table 2. There were no significant differences between subjects with MS and the controls (P values > 0.05). The arterial structure and function variables are presented in Table 3. Resting FBF (P < 0.05), peak FBF (P < 0.01), and carotid arterial compliance (P < 0.05) were significantly lower in subjects with MS, whereas central pulse wave velocity (cPWV) was significantly higher (P < 0.05) compared with the control group. The effect sizes, all moderate in magnitude, were -0.61, -0.64, -0.51, and 0.45 for resting FBF, peak FBF, carotid arterial compliance, and cPWV, respectively. The change from resting to peak FBF after RH is shown in Figure 1.

Initial bivariate correlation analyses indicated that PA was significantly correlated with peak FBF (r = 0.38, P < 0.05) and cPWV (r = -0.33, P < 0.05) but not resting FBF (r = -0.02, P > 0.05) and carotid arterial compliance (r = 0.15, P > 0.05). We then performed hierarchical regression analyses for the variables that differed significantly between groups on the basis of the t-tests, namely, resting and peak FBF, carotid arterial compliance, and cPWV. The first regression analysis indicated that group accounted for a significant amount of the variance in FBF (P < 0.05), and the group effect remained unchanged (P < 0.05) even after controlling for PA (P > 0.05). The second regression analysis indicated that group accounted for a significant amount of the variance in peak FBF (P < 0.05), but the group effect was nonsignificant (P > 0.05) and accounted for by PA (P < 0.05). The final regression analysis indicated that group accounted for a significant amount of the variance in cPWV (P = 0.05), but the group effect was nonsignificant (P > 0.05) and accounted for by PA (P < 0.05). This series of analyses provided evidence that PA accounted for the relationship between group and peak FBF and cPWV as measures of arterial function.

**DISCUSSION**

One of the primary novel findings of this study was that arterial function but not structure was significantly altered in persons with MS compared with control subjects matched for age, sex, height, and weight. This finding was consistent with our hypothesis that persons with MS would exhibit reduced arterial function compared with healthy controls. The second novel finding was that the much lower PA levels in persons with MS accounted for differences in arterial function between groups. Such results indicate that subclinical markers of atherosclerosis are capable of identifying early risk for CVD in MS and that physical inactivity might be associated with an increased risk of CVD in MS based on its association with measures of arterial function. Those observations are important from a public health perspective considering that persons with MS have a similar or higher risk of CVD than the general population and that this risk is associated with worsening disease prognosis and progression. Perhaps, the risk is modifiable with PA interventions, which would be paramount considering the rates of CVD and physical inactivity in the MS population.

Vascular comorbidity is common in MS and is associated with poor CVD outcomes and increased risk of disease progression (25). Indeed, the risk of early gait disability progression increases by more than 200% with the presence of two or more comorbidities (25). To date, we are not aware of previous evidence documenting differential subclinical atherosclerotic development in persons with MS compared with controls. Accordingly, this study provides novel evidence for differential levels of subclinical atherosclerosis in persons with MS compared with controls without MS. Age,

---

**TABLE 2. BP variables reported as millimeters of mercury.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>MS (n = 33)</th>
<th>Controls (n = 33)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP (mmHg)</td>
<td>120.48 ± 2.92</td>
<td>121.63 ± 2.14</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>74.18 ± 1.87</td>
<td>75.69 ± 1.50</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>89.39 ± 2.10</td>
<td>91.00 ± 1.62</td>
</tr>
<tr>
<td>Pulse pressure</td>
<td>46.30 ± 1.75</td>
<td>45.93 ± 1.28</td>
</tr>
<tr>
<td>Carotid SBP</td>
<td>111.54 ± 2.83</td>
<td>115.45 ± 2.31</td>
</tr>
<tr>
<td>Carotid DBP</td>
<td>73.96 ± 1.86</td>
<td>75.63 ± 1.50</td>
</tr>
<tr>
<td>Carotid MAP</td>
<td>89.36 ± 2.10</td>
<td>91.00 ± 1.62</td>
</tr>
<tr>
<td>Carotid PP</td>
<td>37.51 ± 1.69</td>
<td>39.81 ± 1.79</td>
</tr>
<tr>
<td>Aortic SBP</td>
<td>113.21 ± 2.81</td>
<td>112.25 ± 2.21</td>
</tr>
<tr>
<td>Aortic DBP</td>
<td>75.56 ± 1.88</td>
<td>76.28 ± 1.53</td>
</tr>
<tr>
<td>Aortic MAP</td>
<td>95.12 ± 2.17</td>
<td>91.81 ± 1.71</td>
</tr>
<tr>
<td>Aortic pulse pressure</td>
<td>37.87 ± 1.80</td>
<td>36.00 ± 1.26</td>
</tr>
</tbody>
</table>

Values are mean ± SEM.

**TABLE 3. Arterial structure and function variable.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>MS (n = 33)</th>
<th>Controls (n = 33)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak FBF* (mL/min-100 mL-1)</td>
<td>16.50 ± 1.10</td>
<td>21.01 ± 1.51</td>
</tr>
<tr>
<td>Resting FBF* (mL/min-100 mL-1)</td>
<td>2.49 ± 0.18</td>
<td>3.17 ± 0.22</td>
</tr>
<tr>
<td>Ax (% of forearm tissue)</td>
<td>28.62 ± 2.05</td>
<td>25.50 ± 2.73</td>
</tr>
<tr>
<td>Ax (% of forearm tissue)</td>
<td>22.81 ± 2.01</td>
<td>17.53 ± 2.76</td>
</tr>
<tr>
<td>cPWV* (m/s-1)</td>
<td>7.06 ± 0.25</td>
<td>6.5 ± 0.18</td>
</tr>
<tr>
<td>IMT (mm)</td>
<td>0.49 ± 0.02</td>
<td>0.45 ± 0.01</td>
</tr>
<tr>
<td>AC- (mm²/kPa-1)</td>
<td>0.81 ± 0.04</td>
<td>0.96 ± 0.05</td>
</tr>
</tbody>
</table>

Values are mean ± SEM.

* P < 0.05 from controls.

Ax (HR 75), Ax at HR of 75 bpm; AC, carotid arterial compliance.
Sex, and body size are strongly associated with subclinical atherosclerosis (16,22,38,43), but such factors cannot explain our findings because participants were matched for these variables. This might suggest that MS per se is associated with the differential development of subclinical atherosclerosis. Our data are not consistent with this notion but rather support the idea that subclinical atherosclerosis in relation to MS is accounted for by PA. This would implicate physical inactivity as a primary contributor to the differential levels of subclinical atherosclerosis in MS versus controls. Indeed, previous investigations have shown that persons with MS exhibit reduced levels of PA (30,35), and these reductions may be as dramatic as the 1 SD difference in PA reported in the present study. Furthermore, we have shown in a series of studies that low levels of PA in people with MS are associated with symptoms such as fatigue, ataxia, pain, and depression (27,31–33). As MS-related symptoms worsen, PA continues to decline (27). Our current data are consistent with these findings showing that PA is much and significantly lower in individuals with MS compared with controls. Furthermore, we measured PA using accelerometry, which is considered an excellent objective measure of PA (26), eliminating concerns regarding self-reported levels of PA. It is well established that PA is related to the development of CVD and to both baseline values and progression of subclinical atherosclerosis in the general population (19,39,40). Consequently, it may not be surprising that PA accounted for the relationship between subclinical atherosclerosis and MS in our study.

Inflammation plays a key role in atherosclerosis, particularly in plaque development (37). CRP, a common inflammatory marker, is a predictor of morbidity and mortality in the general population (6,21). CRP is further associated with subclinical atherosclerosis (12,17,18). Among persons with MS, CRP is elevated during relapses and has been associated with disease progression (42). However, similar to our findings, CRP does not necessarily differ between patients and controls (42), and CRP was unrelated to PA or MS in our study (data not shown). This may be explained by the low CRP levels resulting in a mean CRP well within an acceptable clinical range for both groups. Chronic inflammation has been linked to all measures of subclinical atherosclerosis measured in our study (6,12,18,21), but neither CRP nor IL-6 differed between individuals with MS and control; thus, inflammation per se does not seem to influence our findings. This may have been influenced by the large number of individuals with MS who were taking disease-modifying agents, most of which are immune suppressors and likely influence systemic inflammation.

Although there was an increase in conduit and resistance arterial stiffness in subjects with MS, no differences were observed in central or aortic BP. Although chronically elevated arterial stiffness has been shown to increase SBP and aortic pulse pressure and, in turn, increase myocardial work and reduce coronary perfusion (36), the clinical significance of the current findings is unclear. However, this finding is in agreement with Fjeldstad et al. (10), who found no significant differences in the SBP and DBP of subjects with MS and controls, although the arterial compliance was significantly compromised in subjects with MS.

This study included a cross-sectional design, and although we reported that PA was associated with arterial function, we could not infer causation among variables. The sample had minimal disability on the basis of the inclusion criteria of being ambulatory with or without single-point assistance, and such results might not generalize among those with advanced MS.

In conclusion, we provide novel evidence that resting FBF, peak FBF, carotid arterial compliance, and cpPWV, all markers of arterial functioning, were significantly different in persons with MS as compared with the controls. These differences in arterial dysfunction seem to be occurring in absence of clinical blood markers for inflammation and any significant changes in the BP. In addition, PA was significantly reduced in persons with MS compared with controls, and this accounted for some of the arterial dysfunction between groups. Thus, our findings suggest that increasing PA in persons with MS may be of considerable importance because this may affect both CVD risk and disease progression.

This study was partially funded by the University of Illinois at Urbana-Champaign Research Board. The authors declare no conflict of interests. The results of the present study do not constitute endorsement by the American College of Sports Medicine.

REFERENCES


