INTRODUCTION

Multiple Sclerosis (MS) is characterised by demyelination within the central nervous system (CNS), which may result in neurological disabilities over time, causing considerable hardship to patients and their families, in addition to being costly to treat. There are indications that vascular factors may play a role in demyelination since myelin production and maintenance in the brain is dependent on the delivery of nutrients and removal of toxic waste products by the blood. Studies have described three types of vascular dysfunction in MS: first, endothelial dysfunction due to inflammation and increased homocysteine concentrations; second, global cerebral hypoperfusion and third, impaired cerebral venous outflow with reported rapid improvement of MS symptoms with surgical correction thereof. Singh and Zamboni described altered cerebral venous drainage in patients with MS, a condition they called chronic cerebrospinal venous insufficiency (CCSVI). Their research suggested that this condition may be a major risk factor for MS. Subsequent studies have not consistently confirmed Zamboni’s original findings, and have found the prevalence of venous occlusions to differ in different populations.

In the present study, ultrasound imaging was used to determine the prevalence of abnormal extracranial venous outflow patterns and carotid artery disease in MS patients within the region of the Western Cape, South Africa. The parameters measured included intima media thickness (IMT) of the common carotid artery (CCA); the peak systolic velocity of the left external carotid artery (p=0.03) and homocysteine showed an inverse association with the cross sectional diameter of the proximal left IJV (p=0.045). No significant associations were found between ultrasound measurements and total cholesterol.

Conclusions This pilot study supports previous findings that there is no association between CCSVI and MS, but rather a detrimental effect of smoking and a sedentary lifestyle on MS disability. This may indicate that people diagnosed with MS may improve their disability status by avoiding risk factors that would adversely affect the vasculature.
et al. showed that the earliest evidence of microvascular injury in acute MS was endothelial activation with associated fibrin deposition, even in brain areas in which myelin was preserved, as well as occlusion of vessels by reticulated fibrin clots. Increased IMT of the CCA is widely accepted to be a surrogate marker for early atherosclerosis, and risk factors include increased hypertension, body mass index (BMI), LDL cholesterol, homocysteine and fibrinogen. IMT also increases with age. In contrast, a diet which is high in fruits, wholegrains, fibre and olive oil and low in saturated fat may reduce IMT and the development and progression of carotid atherosclerosis.

The aims of the present study were to investigate the effects of biochemical and lifestyle factors on vascular outcomes using ultrasound B-Mode and Doppler ultrasound imaging in patients diagnosed with MS.

METHODS

This investigation was an ethically approved collaborative study between the Cape Peninsula University of Technology, the National Health Laboratory Service (NHLS) and the University of Stellenbosch in the Western Cape, South Africa. The study was granted ethical approval by the Faculty Ethics Research Committee of the Cape Peninsula University of Technology (CPUT) and was done according to the ethical guidelines provided by the Declaration of Helsinki. Written and signed informed consent was obtained from all participants. Ultrasound examinations of these patients were performed at a private radiology practice in Cape Town.

Study participants

The study population consisted of 29 MS patients, 26 females and 3 males (Table 1). Patients were diagnosed with MS according to the criteria of McDonald et al. by their neurologists. Exclusion criteria were other neurological diseases (neuromyelitis optica and acute disseminated encephalomyelitis) as well as a previous diagnosis of carotid artery and extracranial venous disease.

Ultrasound examination

GE Logiq 9 and GE Logiq E9 ultrasound machines with Doppler software (B-mode imaging, Colour Doppler, Power Doppler and pulsed-wave Doppler) and 9-12 MHz multifrequency linear transducer were used to image the carotid arteries and extracranial venous system. B-mode imaging was used to interrogate the major neck vessels for tortuosity, anatomical variation, plaque formation in the carotid arteries, and to measure IMT of the CCA (Figure 1) and cross-sectional diameter of the internal jugular veins (Figure 2). Colour Doppler was used to assess the vessels for patency, direction of blood flow within the vessel and detect an occlusion if present. An automated average IMT, on the far side of the vessel wall, over a 2 cm segment of the mid CCA (3 cm distal to the carotid bulb) was determined in the longitudinal plane. An IMT of 0.8 mm is regarded as the upper limit of normal.

Pulsed-wave (PW) Doppler was used to detect carotid stenosis by measuring the speed (velocity) of blood flow in systole and diastole within the carotid vessel being sampled; as well as to detect reflux within the IJV. A value of >0.88s was considered a surrogate marker for carotid reflux. The Pulsed Repetition Frequency for this study was set as 150 cm/s for assessment of the carotid vessels. The North American Symptomatic Carotid Endarterectomy Trials (NASCET) criteria were used to grade internal carotid artery stenosis, where a stenosis ≥70% is regarded as significant.

Biochemical and lifestyle data

Of the 29 MS patients who underwent ultrasonography, biochemical and lifestyle data were available for 20 patients (17 females and 3 males). Their disability status was assessed by participating clinicians using the Expanded Disability Status Scale (EDSS). The EDSS ranges from 0 to 10, with higher scores indicating higher disability. The patients were in remission when their EDSS scores were measured, so that the scores reflected the residual disability when patients were not in a relapse.

The patients completed a questionnaire developed by a registered dietitian (Gknowmix Medical History and Lifestyle Questionnaire, available at www.gknowmix.com). Smoking status, BMI and physical activity were also recorded. The physical activity was self-reported and categorised into: 1 = Recreational sport occasionally or complete lack of exercise; 2 = Recreational sport once a week; 3 = Exercise 2-3 times a week; 4 = Exercise 4 or more times a week. Individualised reports were given to the patients with recommendations for mitigating lifestyle risk factors, including moderate exercise and dietary advice. This included intake of at least 5 portions of fruit and vegetables per day and lower intake of saturated compared to unsaturated fat, as well as a recommended nutritional program (the Rapha Regimen), which includes amino acids, vitamins, minerals, antioxidants and essential fatty acids. Iron is taken in addition if biochemical testing reveals iron deficiency. The total list of nutrients was published by van Rensburg et al. However, the original nutrient combination has been modified by the addition of 500 IU vitamin D per day.

Eight of the patients subsequently followed the recommendations of the diet and lifestyle intervention program, 6 of them for more than 5 years while the other two had been on the program for less than 5 years. Twelve patients did not follow the program of whom four were on MS medication (Interferon beta). One of the patients who opted to follow the program was on Interferon beta as well.

Biochemical determinations

Blood was drawn for biochemistry testing in the morning between 9h00 and 10h30 to standardise for diurnal variation. Plasma homocysteine was measured using a Siemens Centaur XP auto-analyser. Serum total cholesterol was determined using a Siemens Advia 1800 auto-analyser. Fibrinogen was determined by the Hemos IL-Fibrinogen C method using an ACL TOP (Beckman Coulter SA).

Statistical analysis

Mixed model repeated measures ANOVA was used to compare left and right vessel measurements. One way ANOVA was used for comparison of measurements between groups (on lifestyle/nutritional program and not on program, smoking and non-smoking). ANOVA F-test and the Mann-Whitney U test were used to test the same hypothesis. Spearman correlations were used in addition for testing relationships between biochemical variables and ultrasound measurements.
RESULTS

Twenty-nine patients with MS with a mean age of 47.72 were assessed, with a disease duration of 0.83-27 years. The clinical characteristics of the patients are shown in Table 1.

B-mode, pulsed-wave (PW) and Colour Doppler ultrasound demonstrated no thrombus within the proximal-, mid- and distal segments of the right and left IJVs. Colour and PW Doppler ultrasound imaging demonstrated reversed flow of >0.88s in IJV in (four) 13.79% of MS subjects as seen in Figure 3.

No stenosis in IJVs was demonstrated on B-mode, Colour or PW Doppler ultrasound imaging. However, significantly larger proximal and mid cross-sectional diameters (CSD) of the right IJV compared to the left were demonstrated (proximal p=0.026 and mid p=0.023). The mean CSD of the right IJV was 8.79mm +/-1.67 and the left IJV was 7.96mm +/-1.26 in the 26 female subjects. In the 3 male subjects (10.34%) the mean CSD of the right IJV was 11.05mm +/-2.27 and of the left IJV was 7.36mm +/-1.78 as seen in Figure 4. A larger CSD of the right IJV compared to the left was demonstrated in this study, which supports previous studies.[16]

The right and left CCA appeared patent and displayed no stenosis, occlusion or plaque formation on B-mode, Colour and PW Doppler ultrasound imaging. No blood flow disturbances were identified. Four (13.79%) subjects with MS displayed an increased CCA IMT of >0.8mm on B-mode ultrasound imaging. The increased IMT ranged between 0.9 -1.0mm. No evidence of vessel narrowing or increased peak systolic velocity (PSV) and end-diastolic velocity (EDV) of the ICA (PSV>125cm/s, EDV>100cm/s) and ECA (PSV>200cm/s) were identified on B-mode, Colour and PW Doppler imaging. Echogenic plaque in the ICA was identified in two (6.89%) of the 29 subjects with MS on B-mode ultrasound imaging. This small amount of plaque did not cause disturbances to blood flow. No plaque formation was noted in the External Carotid arteries (ECAs).

Biochemical and lifestyle assessments, available for 20 subjects with MS, were evaluated statistically for associations with ultrasound measurements.

Significant differences were found between smokers and non-smokers in the CSD of the mid left IJV (Mann-Whitney U test; p=0.02; Figure 5a) and proximal left IJV (p=0.03; Fig 5b). Smokers had significantly smaller IJV diameters than non-smokers. The maximum CSD of the proximal mid IJV was 1.00 cm in non-smoking MS patients, and 0.80 cm in smoking MS patients. The maximum CSD of the proximal left IJV was 1.20 cm in non-smoking MS patients, and 0.95 cm in smoking MS patients. Homocysteine concentration also had an inverse association with the CSD of the proximal left IJV (p=0.045). Inverse non-significant associations were also seen between homocysteine and the CSDs of the proximal-, mid- and distal right IJVs.
A significant direct association was seen between fibrinogen and the left ECA PSV (p=0.03). No associations of fibrinogen with CSDs of the carotid arteries or the IMT were recorded; however, a trend towards associations of fibrinogen with diameters of the IJVs could be detected, although these effects were not significant (PROX R IJV CSD r=-0.38, p=0.08; MID R IJV CSD r=-0.36, p=0.08; DIST L IJV CSD r=-0.19, p=0.05). A significant inverse association between homocysteine and the right ECA PSV was found (p<0.01); however, similar inverse associations were not observed for homocysteine with PSV measurements in other vessels. No significant associations were found between ultrasound measurements and total cholesterol.

A novel finding of this study was that the disability status, assessed with the EDSS, correlated significantly with the IMT of the R CCA (p<0.0001; Figure 6). A similar direct association was found with the IMT of the L CCA (p=0.02; Spearman p=0.09). Age also correlated significantly with IMT of the L and R CCA (p<0.001 in both cases). The Sobel test for mediation was used to test the hypothesis that age was a mediator between the IMT and the EDSS. The test was not significant (p=0.58 for the L CCA, and p=0.82 for the R CCA), indicating that a direct relationship between the IMT and the EDSS was found. Age was not significantly associated with the EDSS: of people over 50 years of age, 5 had an EDSS of 1.5 - 3 (considered a benign outcome) while 5 had an EDSS of 4 - 7.5 (more disabled).

Figure 7 demonstrates a significant inverse association (Spearman p=0.03) between physical activity and the IMT of the L CCA. The IMT of the R CCA was inversely related to physical activity, and was thicker in smokers compared to non-smokers; however the differences were not significant. The EDSS did not correlate with physical activity (Spearman R=-0.32; p=0.20). Patients on the dietary and lifestyle program had a lower mean BMI (26.1 ± 2.8; 95% CI 19.9 - 32.3) than patients not on the program (31.6 ± 2.1; 95% CI 27.0 - 36.2). However, the BMI did not correlate with the R CCA IMT (p=0.5) or the L CCA IMT (p=0.8).

Figures 8a and 8b illustrate significant differences (Mann-Whitney U test, p=0.03 and p<0.01) respectively for the PSV and the EDV of the R CCA in subjects with MS on the dietary and lifestyle program (NUTR PROG) versus those not on the program, which may indicate narrower carotid arteries in the latter group. Figure 8c shows significantly lower EDSS scores in patients on the program versus those not on the program (p=0.03). The EDSS was not associated with disease duration (p=0.46) or medication use (p=0.52).

**DISCUSSION**

The internal jugular veins (IJV) are considered to be the main outflow pathway for intracranial venous blood. The present study demonstrated patency of the IJVs in 29 subjects with MS.

**TABLE 1. Description of Clinical Characteristics**

<table>
<thead>
<tr>
<th>Age, years (Range)</th>
<th>28-64</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Females n=26, males n=3</td>
</tr>
<tr>
<td>Race</td>
<td>Caucasian n=22, Mixed ancestry n=7</td>
</tr>
</tbody>
</table>

**MS Patients with Biochemical and Lifestyle data n=20**

<table>
<thead>
<tr>
<th>Number (%)</th>
<th>On Nutritional program (n=8)</th>
<th>Not on program (n=12)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current Smokers</td>
<td>0 (0)</td>
<td>4 (33)</td>
<td></td>
</tr>
<tr>
<td>Females</td>
<td>6 (75)</td>
<td>11 (92)</td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>2 (33)</td>
<td>1 (8)</td>
<td></td>
</tr>
</tbody>
</table>

**Mean; std err (± 95% CI)**

| Age, years | 49; 2.6 (43-55) | 49; 3.4 (41-56) | 0.97 |
| Age of Symptoms, years | 37.4 ± 2.6 (31.3-43.5) | 31.7 ± 4.0 (22.8 - 40.5) | 0.22 |
| Age of Diagnosis, years | 41.8 ± 1.7 (37.7-45.8) | 37.0 ± 3.3 (29.8-44.2) | 0.22 |
| Disease duration, years | 7.9 ± 1.4 (4.5-11.2) | 9.3 ± 2.3 (4.3-14.3) | 1.0 |
| Body Mass Index (kg/m²) | 26.1 ± 1.5 (22.0-30.3) | 31.6 ± 2.5 (25.9-37.3) | 0.18 |
| Cholesterol, total (mmol/L) | 5.6 ± 0.4 (4.7-6.6) | 5.1 ± 0.3 (4.5-5.6) | 0.21 |
| Homocysteine (µmol/L) | 8.5 ± 1.1 (5.9-11.1) | 10.0 ± 0.7 (8.5-11.6) | 0.37 |
| Serum Folate (µg/L) | 15.3 ± 2.8 (8.5-22.0) | 11.8 ± 2.0 (7.3-16.3) | 0.26 |
| CRP (mg/L) | 3.5 ± 0.4 (2.5-4.5) | 8.7 ± 3.1 (1.8-15.6) | 0.14 |
| Fibrinogen (µg/L) | 3.4 ± 0.2 (2.8-3.9) | 3.4 ± 0.18 (3.0-3.8) | 0.78 |
| Physical activity | 2.4 ± 0.4 (1.4-3.5) | 1.8 ± 0.3 (1.0-2.5) | 0.25 |

Data is given as Mean; Standard error, ± 95% Confidence Interval
sampled with no evidence of thrombus on B-mode and Colour Doppler ultrasound imaging. This can be regarded as a new finding as no literature is available on the prevalence of internal jugular vein thrombus in subjects with MS. Previous research studies, however, have demonstrated IJV intraluminal defects such as webs, septa and/or malformed valves which affects the venous outflow patterns. No IJV intraluminal defects were demonstrated in this study. According to Zamboni et al., reflux of flow directed towards the brain for a duration of >0.88s is regarded as significant. They defined this abnormal cerebrospinal venous drainage in subjects with MS as chronic cerebrospinal venous insufficiency (CCSVI) and hypothesised that CCSVI is strongly associated with MS and could play a causative role in the development of the disease. Zamboni’s theory generated great interest in patients with MS, who have

**Figure 5a:** Cross-sectional diameter (CSD) of the mid left internal jugular vein (IJV) of smoking MS patients versus non-smoking MS patients. IJV=internal Jugular Vein, L=left, CSD=cross-sectional diameter, no=non-smoking MS patients, yes=smoking MS patients. There is a significant difference between the 2 groups (Mann-Whitney U test, p=0.02). The maximum CSD of the left mid IJV in non-smoking MS patients (n=16) is ~10mm (1.00cm). The maximum CSD of the left mid IJV in smoking MS patients (n=4) is <8mm (0.80cm).

**Figure 5b:** Cross-sectional diameter (CSD) of the proximal left internal jugular vein (IJV) of smoking MS patients versus non-smoking MS patients. IJV=internal Jugular Vein, L=left, CSD=cross-sectional diameter, no=non-smoking MS patients, yes=smoking MS patients. There is a significant difference between the 2 groups (Mann-Whitney U test, p=0.03). The maximum CSD of the left proximal IJV in non-smoking MS (n=16) patients is ~12mm (1.20cm). The maximum CSD of the left proximal IJV in smoking MS patients (n=4) is ~9.5mm (0.95cm).

**Figure 6:** Significant association between the EDSS and the IMT of the R CCA (p<0.0001). R CCA=right common carotid artery, IMT=intima media thickness. EDSS=Expanded Disability Status Scale.

**Figure 7:** Significant inverse association between Physical Activity and the IMT of the L CCA (Spearman p=0.03). L CCA=left common carotid artery, IMT=intima media thickness.
communicated on social media, expressing their desire to have ultrasound tests done. This enhanced interest was also experienced by the researchers during this study.

A larger CSD of the right IJV compared to the left was demonstrated, which supports previous studies.[16] Reversed flow in the internal jugular veins during valsalva was demonstrated in 13.8% of subjects with MS. Reflux in the IJV could be due to valve incompetence or stenosis. A reduction of ≥50% of the CSD of the IJV was considered stenotic. However, no stenosis of the IJV was identified. The reflux identified in the 13.8% of subjects with MS was due to valve incompetence and not stenosis. Thus, this study does not support Zamboni’s CCSVI theory. Other published studies could also not reproduce the findings published by Zamboni and his colleagues.

**Figure 8a:** Higher PSV in the right CCA in MS patients not on the lifestyle/nutritional program versus those on the program.

NO=MS patients not on nutritional program (n=12), YES=MS patients on the nutritional program (n=6), NUTR PROG=nutritional program, CCA=common carotid artery, R=right, PSV=peak systolic velocity. There was a significant difference between the 2 groups (p=0.03). Maximum PSV of those not on the programme ~118 cm/s, Maximum PSV of those on the programme ~105 cm/s.

**Figure 8b:** Higher EDV in the right CCA in MS patients not on the lifestyle/nutritional program versus those on the program.

NO=MS patients not on nutritional program (n=12), YES=MS patients on the nutritional program (n=6), NUTR PROG=nutritional program, CCA=common carotid artery, EDV=end-diastolic velocity, R=right. There was a significant difference between the 2 groups (p<0.01). Maximum EDV of those not on the programme ~35 cm/s, Maximum EDV of those on the programme ~28.5 cm/s.

**Figure 8c:** Higher EDSS in MS patients not on the Lifestyle/Nutritional program versus those on the program.

NO=MS patients not on nutritional program (n=12), YES=MS patients on the nutritional program (n=6), NUTR PROG=nutritional programme, EDSS=Expanded Disability Status Scale. There was a significant difference between the 2 groups (p<0.03). Maximum EDSS of those not on the programme 7.5, Maximum EDSS of those on the programme 3.5.

Mayer et al.[21] found no supportive evidence for the presence of CCSVI in patients with MS. Awad et al.[22] also states that there is no conclusive evidence to support CCSVI and its association with MS. Gever[23] wrote a report on the “Largest CCSVI study fails to support theory” where approximately 2000 subjects with blinded central imaging analysis found CCSVI in approximately 3% of subjects with MS. Based on this finding, the Italian group AISM (Associazione Italiana Sclerosi Multipla) declared that CCSVI is not a disease connected to MS. Baracchini et al.[24] state that CCSVI appears to be an alien condition and its existence should be questioned.

To our knowledge, no literature has been published on ultrasound investigation of carotid artery disease in subjects with MS. In this study, the carotid arteries in all subjects with MS (n=29) appeared patent with no evidence of stenosis or occlusions. The intima media of the CCA was thickened (0.9 and 1.0mm) in 13.8% of subjects with MS. An IMT >0.8mm is regarded as a marker for early atherosclerotic disease. An evidence-based review found that MS was associated with an increased risk of cerebrovascular diseases compared with the general population.[25]

No plaque was identified in the external carotid arteries (ECAs). Echogenic plaque in the internal carotid artery (ICA) was identified in two of the subjects with MS (n=29). This small amount of plaque did not cause disturbances to blood flow nor significant intraluminal reduction. This study however demonstrated several features of vascular abnormalities in the subjects with MS, and associations of ultrasound results were found with lifestyle factors such as physical activity, smoking and biochemistry. To our knowledge, these effects have not been investigated in relation to ultrasound before.

Effects of smoking on the vasculature could be demonstrated. The L CCA and R CCA IMT in current smokers was thicker than in non-smokers, but not significantly. However, the CSD of the PROX and MID IJVs were significantly smaller in current smokers (p=0.03 and p=0.02 respectively; Figures 5a and 5b). To our knowledge, no literature has been published on ultrasound investigation of carotid artery disease in subjects with MS. In this study, the carotid arteries in all subjects with MS (n=29) appeared patent with no evidence of stenosis or occlusions. The intima media of the CCA was thickened (0.9 and 1.0mm) in 13.8% of subjects with MS. An IMT >0.8mm is regarded as a marker for early atherosclerotic disease. An evidence-based review found that MS was associated with an increased risk of cerebrovascular diseases compared with the general population.[25]
knowledge, this is the first time significant effects of smoking on the diameter of IJVs were reported. Dolic et al. reported that current or previous smoking was more frequently associated with CCSVI diagnosis in 252 subjects with MS.

Another novel finding of the study is that the IMT of the R CCA correlated highly significantly with disability as measured by the EDSS (p<0.0001), while the IMT of the L CCA showed a similar association with the EDSS (p=0.02; Spearman p=0.09). The right and left CCAs have different anatomical origins. The R CCA originates from the brachiocephalic trunk, while the L CCA originates from the aortic arch. Plaque often accumulates at the bifurcation of the R CCA. The left and right CCA may show different prognostic values.

The IMT is a validated predictor of early atherosclerosis, while the thickness and textural characteristics may be associated with the risk of developing stroke. The present study demonstrated a significant inverse association (p=0.03) between physical activity and the IMT of the L CCA, confirming previous findings. The IMT of the R CCA was also inversely related to physical activity, and was thicker in smokers compared to non-smokers; however the differences were not significant.

IMT has also been found to be a predictor of executive cognitive function, indicating that the IMT has an important influence on brain function. Arterial wall thickening is associated with inflammation and activation of endothelial cells and increases hypertension due to cell adhesion and macrophage infiltration, while a diet promoting scavenging of superoxide free radicals was associated with improved endothelial-dependent relaxation of the aorta and lowered hypertension.

In the present study, a dietary and lifestyle intervention program influenced the PSV and EDV in the R CCA. Patients who were on the program displayed significantly lower PSV and EDV values than patients not on the program (Figures 8a and 8b). According to Alexandrov et al. measuring PSV is the most important component of the carotid Doppler examination since it gives information about the diameter of the vessels. As a function of the area of the residual lumen, PSV increases with the narrowing of an artery. This may indicate that the patients following the lifestyle/nutritional program had greater potency of arterial function than the patients not following the program. In this study, the EDSS was also significantly higher in patients not following the program, confirming a previous finding. This may indicate that vascular insufficiencies may lead to reduced delivery of oxygen and nutrients to oligodendrocytes (the cells that produce myelin) and removal of toxic waste products from these cells. To our knowledge, no literature on ultrasound of carotid artery blood flow velocity patterns in subjects with MS has been published to date. However, the use of dietary supplements was associated with a less frequent CCSVI diagnosis. A significant correlation between fibrinogen and the PSV of the left ECA (Spearman r=0.54, p=0.03) was also demonstrated in this study, while homocysteine concentration was inversely associated with the CSD of the proximal left IJV (p=0.045). Homocysteine has an association with carotid artery stenosis. Elevated fibrinogen levels are associated with the severity of peripheral arterial disease and fibrinogen accumulates in atherosclerotic plaques. Fibrinogen was also found to cross the blood-brain barrier in patients with MS and activate the microglia (the immune cells resident in the brain). Although no plaque lesions were identified in the ECAs in this study or in the IJVs, further research in this field needs to be undertaken to ascertain the clinical significance of the association between fibrinogen and increased blood flow rates, which could indicate shear stress within the vessels.

LIMITATIONS OF THE STUDY

Limitations of this pilot study are a small sample size, the absence of a control group, the preponderance of females taking part in the study, and that objective blood pressure assessments were not available (although hypertension was assessed on medical history). Another limitation is that the study was not a prospective clinical trial, but rather retrospectively assessed the effects of biochemical, dietary and lifestyle factors on the vasculature with ultrasound techniques. Future studies should address these limitations by comparing baseline ultrasound values with outcomes over time in a larger cohort of patients and controls.

CONCLUSION

This pilot study supports findings of other studies that found no significant correlation between CCSVI and MS. However, lifestyle factors such as smoking and a sedentary lifestyle were found to affect the patency of the vasculature, which over time, could lead to significant stenosis of the major neck veins or to earlier atherosclerosis. The new finding of the study that smoking caused a significant reduction in the cross-sectional diameter of the internal jugular veins is a further indication of the detrimental effect of smoking on MS. Furthermore, the finding that the EDSS was associated with the thickness of the intima media of the CCA and was inversely associated with adherence to a dietary and lifestyle program, may indicate that people diagnosed with MS are not destined to a life of disability, but can improve their disease outcome by avoiding risk factors that would have adverse effects on the vasculature.

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