Journal of the American Society of Hypertension 8(2) (2014) 117–126

Research Article

Accumulated brisk walking reduces arterial stiffness in overweight adults: Evidence from a randomized control trial

Thérèse M. Kearney, PhD[a], Marie H. Murphy, PhD[b], Gareth W. Davison, PhD[b], Maurice J. O'Kane, MD[c], and Alison M. Gallagher, PhD[a,*]

[a]*Northern Ireland Centre for Food and Health (University of Ulster), Coleraine, Northern Ireland;*
[b]*Sport and Exercise Sciences Research Institute (University of Ulster), Jordanstown, Northern Ireland; and*
[c]*Altnagelvin Hospital (Western Health and Social Care Trust), Londonderry, Northern Ireland*

Manuscript received June 28, 2013 and accepted October 2, 2013

Abstract

Arterial stiffness is a major contributor to the development of atherosclerosis and consequently cardiovascular disease. This study aimed to examine whether 6 months of accumulated (3 × 10 minutes, 5 days/week) brisk walking was sufficient to reduce arterial stiffness in sedentary, overweight individuals. Seventy-seven individuals (19 men, 58 women; age, 30-55 years) were randomly allocated to one of three groups; two groups completed 30 minutes of accumulated walking with either monthly or weekly telephone support; the third group (control) performed stretching exercises. The walking groups were combined and telephone support included as a covariate. Anthropometry, blood pressure (BP), blood lipids, pulse wave velocity (PWV), and NO_x (surrogate marker for nitric oxide) were measured at baseline, post-intervention and 4 months post-intervention. No changes were observed for anthropometry, BP, or lipids. However, at the end of the intervention, there was a decrease in PWV ($P < .001$) accompanied by an increase in NO_x ($P < .001$), with changes maintained 4 months post-intervention. A strong negative correlation between PWV and NO_x was also observed ($P < .001$; $r = -0.65$). A lifestyle approach to meeting current physical activity guidelines results in favorable alterations in arterial function in overweight individuals. J Am Soc Hypertens 2014;8(2):117–126.

Keywords: Pulse wave velocity; nitric oxide; exercise; moderate activity.

Introduction

In 2007, the American College of Sports Medicine suggested that healthy adults should complete at least 30 minutes of moderate intensity aerobic activity on 5 days/week, accumulated in bouts lasting 10 minutes or more.[1] In 2008, the (American) Department of Health and Human Services modified these guidelines, stating that healthy adults should attain at least 150 minutes of aerobic activity per week in bouts of not less than 10 minutes, spread throughout the week.[2]

Despite the health benefits of regular exercise, 57.3% of the adult population in Northern Ireland (NI) are currently not meeting physical activity recommendations.[3] Inactivity is estimated to cost the NI Health Service approximately £0.62 billion per year, with at least 2000 deaths per year in NI attributed to a sedentary lifestyle.[4] Although there are many contributing factors to cardiovascular disease (CVD), inactivity has been shown to be one of the major risk factor[5–7] It has been estimated that 9% of all coronary heart disease cases could be avoided if sedentary individuals became moderately active.[8]

Walking has been described as a "near perfect exercise"[9] and has been cited as the most popular physical activity within the European Union.[10] The Health Survey for England 2008 stated that both men and women spend more hours per week walking than on any other activity outside of work.[11] Although adherence to many exercise programs is often less than 50%, walking programs tend to achieve higher levels of adherence than other forms of exercise.[12–14] For most middle-aged and/or overweight individuals, brisk

Conflict of interest: none.

This work was supported by the Department of Employment and Learning, Northern Ireland.

*Corresponding author: Dr Alison M. Gallagher, PhD, Northern Ireland Centre for Food and Health, Room W2063, University of Ulster, Coleraine, Northern Ireland, BT52 1SA. Tel.: +44 28 70123178.

E-mail: am.gallagher@ulster.ac.uk

1933-1711/$ - see front matter
http://dx.doi.org/10.1016/j.jash.2013.10.001

walking at a pace of 5 km/hour (3 miles/hour) meets the requirements for moderate intensity physical activity in sedentary adults.[15,16]

Arterial stiffness is a major contributor to the development of atherosclerosis and consequently CVD.[17,18] It results in an increased after-load on the left ventricle, which can subsequently cause cardiac hypertrophy, elevated systolic pressure, reduced diastolic function, and decreased coronary perfusion.[19] When arterial stiffness is measured via pulse wave velocity (PWV),[20] it has been shown to be a strong independent predictor of cardiovascular morbidity.[21] PWV increases progressively with age, with a 2.5-fold increase between 20 and 91 years.[22] In typical middle-aged adults, normal PWV values are approximately 8 m/s in the iliac artery, 7 m/s in the brachial artery, 5 m/s in the abdominal aorta and carotid, and 4 m/s in the ascending aorta.[23] These values increase proportionally, depending on the extent and number of other CVD risk factors present.[24]

It is hypothesized that regular exercise improves arterial stiffness by altering vascular shear stress, causing increased production of the vasodilator, nitric oxide (NO).[25] The increase in hemodynamic shear stress and endothelial stretching generated through regular exercise increases endothelial nitric oxide synthase (eNOS) activity,[26,27] which enhances long-term biosynthesis of endothelial NO thereby reducing arterial stiffness. An increased release of NO in response to increased shear stress not only dilates the underlying smooth muscle of the arteries, but also maintains the concentration of NO within the vascular endothelium, despite an increase in blood flow.[28]

To date, no published work has examined the effects that brisk walking may have on arterial stiffness in overweight individuals. Therefore this study investigated whether 6 months of regular accumulated brisk walking, in line with current physical activity guidelines, was sufficient to reduce arterial stiffness in sedentary, overweight individuals, even without weight loss, and if the changes could be sustained for 4 months beyond the intervention period.

Methods

Ethical approval was obtained from the institution's Research Ethics Committee, and the study was carried out in accordance with the Declaration of Helsinki (2008). Informed consent was obtained from participants prior to the onset of the intervention. Overweight (body mass index [BMI] $\geq$25 kg/m^2), sedentary (<2.5 hours moderate activity per week during previous 6 months), apparently healthy, non-smoking individuals, aged 30-55 years, were recruited from within the institution and surrounding area. Previous activity levels were assessed via 7-day recall questionnaire,[29] with individuals also being asked if their behaviors or occupations had changed within the last 6 months. A total of 102 individuals were assessed for eligibility; however, 12 did not meet the criteria and 13 withdrew prior to the study onset. This study was a randomized parallel group design. Participants were randomly allocated, by a third party, into one of three groups; a walking group with monthly telephone contact, a walking group with weekly telephone contact, and a control group. The walking groups were required to incorporate three 10-minute bouts of brisk walking into their daily routine on 5 days per week. Brisk walking was described to participants as a walk that left them slightly out of breath but still able to maintain a conversation. Participants were contacted by telephone during the intervention either monthly or weekly to provide support and encouragement. The control group were given light stretching exercises to complete twice daily on 5 days per week and were contacted on a monthly basis to control for effects of the telephone contact given to the walking groups. Telephone contact did not affect the results presented within this paper and therefore will not be discussed further. As both walking groups completed the same volume and intensity of walking, they have been amalgamated into a single group for subsequent analysis and ease of presentation. The telephone contact has been included as a covariate for statistical analyses.

Anthropometric Measures

Height was measured using a freestanding stadiometer (Holtain Ltd, Crymych, UK) to the nearest 0.1 cm, and digital scales (model TBF-410,Tanita Corp, Toyko, Japan) measured body mass to the nearest 0.1 kg. Participants wore light clothing with no shoes. BMI was calculated (kg/m^2). Body fat mass (kg) and percentage body fat was assessed via bioelectrical impedance (model TBF-410, Tanita Corp, Toyko, Japan).[30] Waist circumference was measured at the narrowest part of the waist,[31] and hip circumference was measured at the maximum buttock circumference over light clothing to the nearest 0.1 cm. Participants stood with legs parallel and shoulder-width apart. Waist-hip ratio was calculated (waist/hip). All measurements were carried out by the same researcher (TMK).

Dietary Assessment

During the study period, participants were requested not to alter their usual dietary pattern. Diets were monitored using food diaries (2 weekdays and 2 weekend days) at week one, mid-intervention (3 months), end of intervention, and 4-months post-intervention. Energy intake was analyzed using the weighed intake software program WISP for WINDOWS (version 3.0, Tinuviel Software, Warrington, Cheshire, UK). Under-reporting was calculated using the Institute of Medicine Equations.[32]

Average Daily Activity Levels

As an indication of adherence to the intervention, all participants were requested to wear a tri-axial accelerometer (RT3) (Stayhealthy, Monrovia, CA, USA) on the same

days that they filled their food diaries, during week one of the intervention, mid intervention (3 months), end of intervention (6 months), and 4 months post-intervention. Only days with at least 8 hours of recorded activity on the RT3 were included in analysis, and periods of 30 minutes or more that had excessively low RT3 counts (ie, ≤10 counts/minute) were excluded from the analysis.[33] The mean activity count over the 4 days was recorded. Results were reported in mean vector magnitude counts/minute (VM/minute) and time spent being physically active.

Aerobic Fitness

Physical fitness was evaluated using a sub-maximal incremental treadmill test, which involved walking on a treadmill (Woodway, Steinackerstrasse, Weil am Rhein, Germany) at a constant self-selected speed. The workload was progressed by increasing the incline by 2.5% at 3-minute intervals until 80% of the age-predicted maximum heart rate was reached. Oxygen uptake (VO_2; $ml.kg^{-1}.min^{-1}$) was measured via expired air analysis (Jaeger Oxycon Pro, Leibnizstrasse, Hoechberg, Germany). Blood lactate (mmol/l; Lactate Pro, Arkray Inc, Kyoto, Japan) was measured in fresh capillary blood samples, obtained from a finger prick, immediately before increasing workload. It has been established that predictions of aerobic capacity from submaximal data can be intrinsically inaccurate and that VO_2 max is not always a sensitive indicator of change in endurance fitness.[34] Therefore, although predicted VO_2 max was calculated, a more precise measure of fitness was undertaken by plotting VO_2 against blood lactate.[34,35] In this study, VO_2 was plotted against blood lactate, and the VO_2 at a reference value of 3 mmol $\times$ l^{-1} blood lactate was used as an indicator of fitness as well as predicted VO_2 max.

Blood Pressure

BP (mm Hg) was measured in the brachial artery (Omron M5-I, Milton Keynes, UK). Participants rested in a seated position for 5 minutes prior to measurements. The mean of three systolic and diastolic BP measures were recorded.

PWV Measurements

Arterial stiffness was measured using a PWV device; Labview program version 7 (Intelesens, Belfast, Northern Ireland, UK).[36,37] This device has been validated against SphygmoCor, and an excellent correlation in carotid-radial PWV has been shown for normotensive ($r^2 = 0.92$) and hypertensive ($r^2 = 0.89$) cohorts.

Prior to measurement, participants rested in a seated position for 5 minutes. The strongest pressure pulses within the radial and brachial arteries of the left arm were identified via palpation. Piezoelectric sensors[36,37] were placed over the pulsations and held in place with Velcro straps. These piezoelectric sensors were attached to the device by low weight electrical leads. The distance between the two pulse points was measured (cm) with a flexible inelastic measuring tape, and values were entered into the device's software. PWV calculations were based on the distance traveled by the pulse between the two recording sites and the pulse transit time. Simultaneous recordings of the brachial and radial pulse wave forms were recorded during a 10-second period, and the mean PWV was calculated via the automated software. PWV was calculated (PWV (m/s) = $l/\Delta t$), where l was the distance measured between the sensors and Δt was the time delay in the pulse transit time. The PWV value was based upon the time delay in peak-to-peak and cross-correlation values recorded between the two points, during the 10-second measuring period. Using cross-correlation values helped reduce the likelihood of wave distortion by reflective components in the vessel.[36] The mean of three PWV reading (m/s) at each time point was recorded. The coefficient of variation for this device, calculated within this laboratory, was 0.158.

Blood Biochemistry

Venous blood samples were drawn into vacutainers containing a serum clot activator. The serum was stored at -80°C until the biochemical analyses were performed.

Triglycerides, total cholesterol, and high density lipoprotein cholesterol levels were measured in serum by enzyme assay kits using the Aeroset analyser (Abbott Labs, IL, USA). Low density lipoprotein cholesterol was estimated using the Friedewald equation.[38] All biochemical indices are expressed in mg/dL.

Serum nitrite (NO_2^-) and nitrate (NO_3^-) levels were assessed using the Nitrate/Nitrite Colorimetric Assay Kit (Cayman Chemicals, Bioscience, Cambridge, UK). The final products of NO in vivo are NO_2^- and NO_3^-; however, due to the instability of NO_2^-, the relative proportions of NO_2^- and NO_3^- varies. NO_2^- has a half-life of 110 seconds in human blood,[39] whereas NO_3^- has a half-life of 5 to 8 hours.[40,41] Thus, the best index of total NO production is the sum of both NO_2^- and NO_3^- (NO_x).

To control for circadian variations, all measurements were recorded between 8:00am and 10:00am following a 12-hour fast. At the end of the intervention period, all measurements were repeated on the morning after the last walking session. To account for any "last bout effects," fasting blood samples, BP, and PWV were repeated 72 hours post-intervention (for walkers only).

Statistical Analysis

Statistical analysis was employed using SPSS version 21.0 (Surrey, UK). Data were assessed for normality using the Kolomogorov-Smirnov and Shapiro-Wilk tests. Time by group interactions were determined using repeated measures two-way analysis of covariance with telephone contact included as a covariant. Age, gender, and fitness

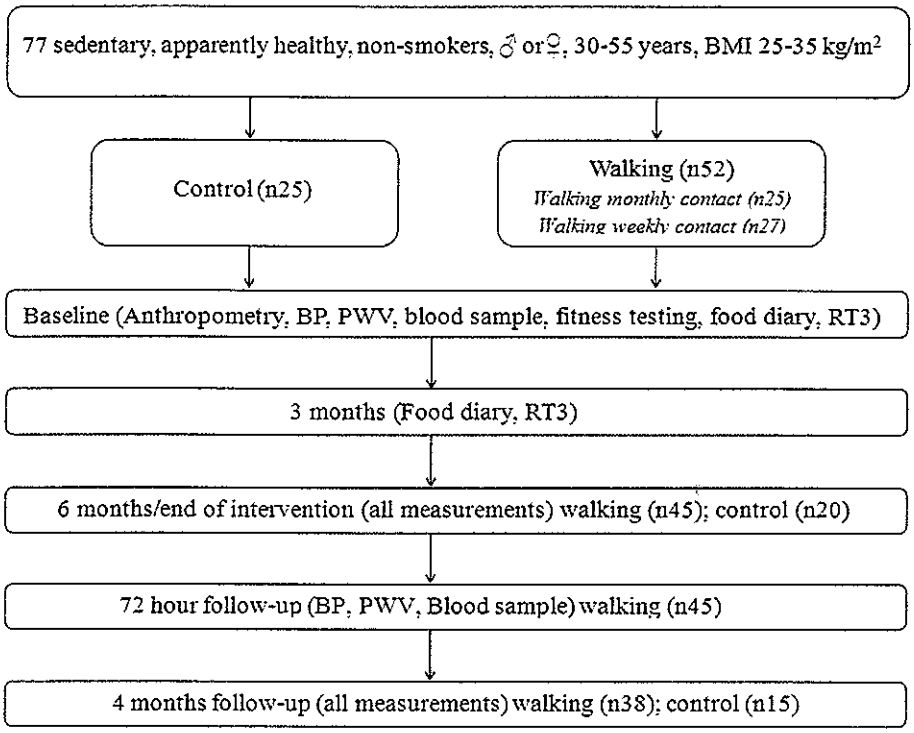

Figure 1. Overview of study methodology and flow of participants through the study. ♀, Female; ♂, male; BMI, body mass index; BP, blood pressure; PWV, pulse wave velocity.

were also included as covariants when analyzing the PWV and NO_x data. Within subject differences were analyzed using repeated measures analysis of variance, and between subject differences were analyzed using one-way analysis of variance, with posteriori Tukey Honestly Significant Difference. Amalgamated RT3 data was analyzed via independent *t*-test. Correlations were determined using Pearson's product moment correlation. The alpha level was established as $P \leq .05$; values are reported as mean ± SD unless otherwise stated. Data were analyzed on an intention-to-treat basis with only complete data sets for each measure included in the analysis.

A priori power calculation incorporating the critical difference value for arterial stiffness was completed.[42] The power was set at 0.85, indicating that a sample size of 15 per group was required. Allowing for a 50% drop-out, we sought to recruit 90 participants (ie, 30 per study group) onto the study.

Results

Following recruitment, 25 individuals were randomly assigned to the control group and 52 to the walking groups. During the intervention period, five individuals withdrew from the control group; one became pregnant, two cited lack of interest in the study, and two joined a gym. A further five individuals withdrew from the control during the 4-month follow-up period to take up alternative activities. Within the walking group, seven individuals withdrew during the intervention period, six due to lack of time and another due to bereavement. A further seven withdrew at follow-up; three due to injury, three due to lack of time, and one became pregnant. In total, 45 walkers and 20 controls completed the intervention, with 38 walkers and 15 controls returning for post-intervention measures. The flow of the participants through the study is indicated in Figure 1. Baseline characteristics of the participants are given in Table 1.

Accumulated brisk walking did not elicit any changes in resting BP, blood lipids, or body composition over the course of the intervention or during the follow-up period ($P > .05$; Table 2). There were also no differences to self-reported energy intakes between the groups or across the study period ($P > .05$).

RT3s were not issued prior to the intervention; therefore, the data collected could not be used to determine whether or not the walking group activity levels increased from baseline. Data was available for 45 walkers and 20 controls for week one of the intervention, 37 walkers and 21 controls mid-intervention (3 months), 35 walkers and 19 controls at the end of the intervention, and 34 walkers and 10 controls post-intervention.

There was no significant differences in mean daily activity levels between the control and the walking groups at the measured time points ($P > .05$); however, when the data for all time points was amalgamated, the walking group demonstrated significantly higher ($P < .001$) VM/minute than the control group (walking group $411.37 \times 10^3 \pm 0.061$ VM/min; control $268.01 \times 10^3 \pm 0.078$ VM/min) and the walking group demonstrated that they spent significantly more time over the study period ($P = .005$) being physically active compared with the

Table 1
Baseline characteristics of the study participants

	Control (n = 25)	Walking (n = 52)
	17 Women/8 Men	41 Women/11 Men
Age (years)	45 ± 7.4	45 ± 6.2
Activity counts (Mean Vector Magnitude [MVM/d])*	$4.4 \times 10^5 \pm 2.7 \times 10^5$	$5.3 \times 10^5 \pm 4.9 \times 10^5$
Energy intake (MJ/d)*	7.6 ± 1.5	7.2 ± 1.8
Height (cm)	166 ± 9.0	166 ± 8.6
Weight (kg)	80.1 ± 12.7	80.9 ± 14.1
Body fat mass (kg)	29.5 ± 12.0	29.9 ± 8.5
Body mass index (kg/m^2)	29.3 ± 4.3	29.2 ± 4.3
Body fat (%)	34.8 ± 9.3	37.5 ± 6.8
Waist circumference (cm)	94.8 ± 9.8	95.9 ± 11.0
Hip circumference (cm)	109 ± 8.7	109 ± 8.3
Waist-hip-ratio	0.9 ± 0.1	0.9 ± 0.1
Systolic blood pressure (mm Hg)	121.3 ± 12.5	122.1 ± 11.5
Diastolic blood pressure (mm Hg)	83.9 ± 8.2	85.2 ± 7.4
Pulse wave velocity (m/s)	9.2 ± 0.7	9.0 ± 1.0
Total cholesterol (mmol/L)	5.2 ± 1.0	5.6 ± 0.93
High density lipoprotein (mmol/L)	1.4 ± 0.4	1.4 ± 0.3
Low density lipoprotein (mmol/L)	3.2 ± 0.8	3.5 ± 0.3
Triglycerides (mmol/L)	1.3 ± 0.54	1.5 ± 0.72

Activity counts and energy intake were measured over four days (2 weeks days and 2 weekend days) during the first week of the intervention. The average daily activity count and energy intake from these four days has been reported.

* Activity counts and energy intakes were not assessed prior to the intervention

control group (walking group 835.99 ± 185.06 minutes daily; control 795.24 ± 153.37 minutes daily).

Aerobic fitness was measured via predicted VO_2 max as well as VO_2 at reference value of lactate (3 mmol × l^{-1}). Predicted VO_2 max did not show any significant changes across time or between groups (baseline control value 29.30 ± 6.41 mL × kg^{-1} × min^{-1}; baseline walking group values 27.64 ± 6.51 mL × kg^{-1} × min^{-1}; $P > .05$). However, the more sensitive measure, VO_2 at 3 mmol of blood lactate, indicated that the aerobic fitness of the walking group had significantly increased ($P < .001$) following the intervention and that this improvement was maintained 4-months post-intervention ($P < .001$). The control group did not show any changes in aerobic fitness over the duration of the intervention or follow-up period ($P = .458$). There was no difference between the control group and the walking group at baseline ($P = .773$); however, there was a significant difference between the walking group and the control group at the end of the intervention ($P = .044$) and at the 4-month follow-up ($P < .001$; Fig. 2).

PWV decreased ($P < .001$) within the walking group after the intervention, from 9.04 ± 0.98 m/s to 6.76 ± 1.17 m/s. This decrease was sustained at 72-hour follow-up and at 4-month follow-up (6.79 ± 1.17 m/s and 6.68 ± 1.21 m/s respectively; Fig. 3). The walking group's NO_x levels increased during the intervention from 24.15 ± 2.14 μM to 27.75 ± 1.37 μM ($P < .001$). This increase was maintained at 72-hour follow-up and at 4-months follow-up (27.23 ± 1.9 μM and 27.19 ± 1.97 μM respectively; Fig. 4). There were no changes to PWV ($P = .409$) or NO_x levels ($P = .212$) within the control group across the time points.

There were no significant differences in PWV or NO_x between the control group and walking group at baseline; however, there was a significant difference in PWV between the control and walking groups at the end of the intervention ($P < .001$) and at the 4-month follow-up ($P = .002$). There was also a significant difference in NO_x between the two groups at the end of the intervention ($P < .001$) and at the follow-up stage ($P = .004$). Age, gender, and fitness levels did not affect PWV and NO_x. There was a strong negative correlation between PWV and NO_x for the whole cohort ($r = -0.648$; Fig. 5).

Discussion

PWV was measured between the brachial and radial pulses. Although central PWV is the best indicator of general atherosclerosis, both central and peripheral measures can be indicators of atherosclerotic severity,[43] with several studies finding that increased arterial stiffness in the small peripheral arteries, as opposed to the large arteries, is an independent risk for cardiovascular events independent of age.[44,45]

It has been suggested that peripheral vessels are more sensitive to shear stress than central arteries,[46] and that NO has a

Table 2
Anthropometry, blood pressure, and lipid profiles: pre-, post-, and follow-up measures

	Control (n = 25)	Walking (n = 52)
Body mass index (kg/m^2)		
Baseline	29.14 ± 4.25	29.19 ± 4.32
End of intervention	29.44 ± 3.81	28.70 ± 4.53
4 months post-intervention	29.08 ± 4.28	29.19 ± 4.76
Waist-hip ratio (cm)		
Baseline	0.86 ± 0.088	0.87 ± 0.78
End of intervention	0.88 ± 0.078	0.86 ± 0.83
4 months post-intervention	0.86 ± 0.070	0.84 ± 0.08
Body fat (%)		
Baseline	34.82 ± 9.32	37.50 ± 6.85
End of intervention	35.94 ± 9.37	37.49 ± 6.88
4 months post-intervention	37.61 ± 7.46	36.77 ± 6.72
Systolic blood pressure (mm Hg)		
Baseline	121.27 ± 12.54	122.12 ± 11.85
End of intervention	124.66 ± 9.55	123.60 ± 12.66
4 months post-intervention	116.68 ± 9.04	121.49 ± 10.53
Diastolic blood pressure (mm Hg)		
Baseline	83.91 ± 8.18	85.28 ± 7.43
End of intervention	84.29 ± 6.93	85.69 ± 7.33
4 months post-intervention	81.53 ± 5.44	85.09 ± 6.80
Tryglycerides (mmol/L)		
Baseline	1.30 ± 0.54	1.50 ± 0.72
End of intervention	1.37 ± 1.15	1.20 ± 0.48
4 months post-intervention	1.17 ± 0.39	1.40 ± 0.64
Total cholesterol (mmol/L)		
Baseline	5.16 ± 0.98	5.59 ± 0.93
End of intervention	5.00 ± 1.18	5.39 ± 0.94
4 months post-intervention	4.91 ± 0.93	5.43 ± 0.99
HDL (mmol/L)		
Baseline	1.38 ± 0.34	1.41 ± 0.33
End of intervention	1.35 ± 0.37	1.40 ± 0.29
4 months post-intervention	1.38 ± 0.37	1.39 ± 0.28
LDL (mmol/L)		
Baseline	3.23 ± 0.85	3.41 ± 0.86
End of intervention	3.04 ± 0.76	3.45 ± 0.66
4 months post-intervention	3.04 ± 0.77	3.41 ± 0.69

All values are mean ± SD. There were no significant changes over time or between groups.

stronger influence on thinner-walled peripheral vessels.[47] In the present study, NO_x (a surrogate marker for NO) was measured as a possible mechanism for the observed reduction in arterial stiffness resulting from brisk walking. A strong negative correlation was observed between PWV and NO_x. Furthermore, the decrease in PWV and the increase in NO_x were maintained 72 hours post-intervention, reducing the possibility that these changes were due to last bout effects.

Previous research has shown that improvement in vascular function is not restricted to the vessels of exercising musculature.[48–53] Due to the general effects of the hemodynamic variables reacting to vessel wall shear stress,[54] improvements in endothelial function may occur in vascular beds that are not directly stimulated.[55] This study involved predominantly lower limb musculature, although arm muscles are also involved in gait, particularly when walking briskly.[56]

Similar to this study, Fantin et al[57] demonstrated that 6 months of moderate intensity physical activity (1 hour/day, 2 days/week) resulted in significant reduction in PWV in elderly hypertensives. Cameron and Dart[58] observed that 4 weeks of moderate intensity cycling improved arterial stiffness independent of mean arterial pressure, while Kingwell et al[48] indicated that 4 weeks of cycling increased NO_x. Given timescale for effects of physical activity on endothelial function in these last two studies, it is possible that the results in the present study were not as a result of the 6-month walking and continued walking during the follow-up, but rather may have been achieved earlier in

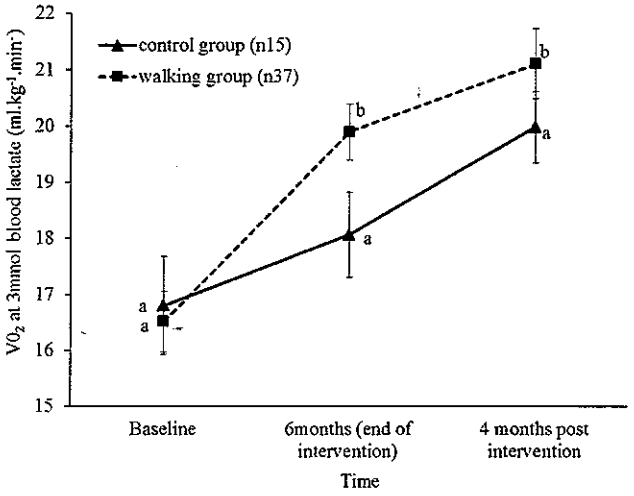

Figure 2. Oxygen uptake (VO_2) at a reference blood lactate concentration of 3 mmol/L pre-, post-, and follow-up intervention readings. Values are mean (standard error of the mean). Different superscripts ([a] or [b]) indicate significant differences between groups and within groups across time ($P < .05$).

the intervention. Sampling time points were kept to a minimum in order to minimize participant burden, thereby maximizing participant retention (overall, 84.4% completed the study, with 68.79% returning for post-intervention measures). This rate of retention was higher than expected. In hindsight, had earlier observation points been included, it may have afforded earlier detection of changes in arterial stiffness, but at the risk of increasing participant burden.

The mechanism by which exercise reduces arterial stiffness relates to changes in the arterial smooth muscle tone, which in turn alters the relative loading of collagen and elastin fibers.[59] Regular exercise results in structural adaptations of the arterial wall, including increased elastin and inhibition of collagen activity. Exercise increases blood flow

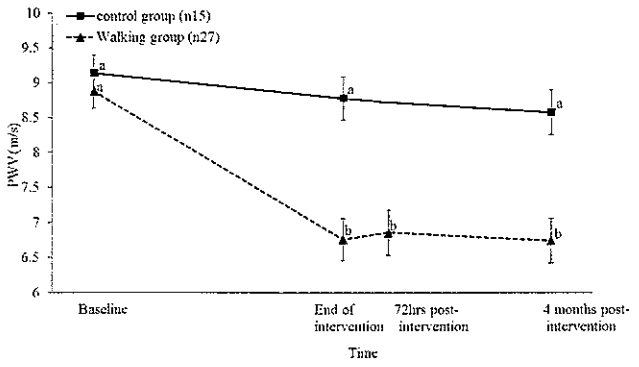

Figure 3. PWV pre-, post-, and follow-up measures (72 hours post-intervention walking group only). Values are mean (standard error of the mean). Different superscripts ([a] or [b]) indicate significant differences between groups and within groups across time ($P < .05$). PWV, Pulse wave velocity.

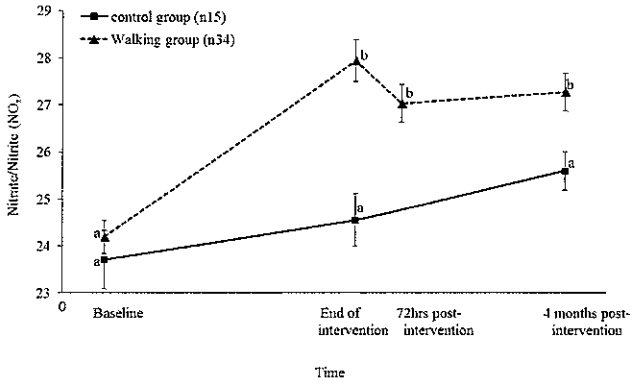

Figure 4. Nitrate and nitrate (NO_x) pre-, post-, and follow-up measures (72 hours post-intervention walking group only). Values are mean (standard error of the mean). Different superscripts ([a] or [b]) indicate significant differences between groups and within groups across time ($P < .05$). NO_x; the sum of NO_2^- and NO_3^- (acts as a surrogate marker for nitric oxide).

velocity and the associated shear, and cyclic stretching of the endothelium increases eNOS activity, thereby increasing NO.[27,60] Vascular shear stress is now a well-established stimulus for the elevation of intra-endothelial Ca^{2+} levels and subsequent release of NO from the endothelium.[61] NO induces relaxation of the vascular smooth muscle; the stress is then transferred from the stiffer collagen fibers to the more extensible elastin fibers, thereby improving arterial compliance.

Although there were no changes to systolic or diastolic BP, this was perhaps unsurprising, since at baseline all participants were within the normal range.[20] These results

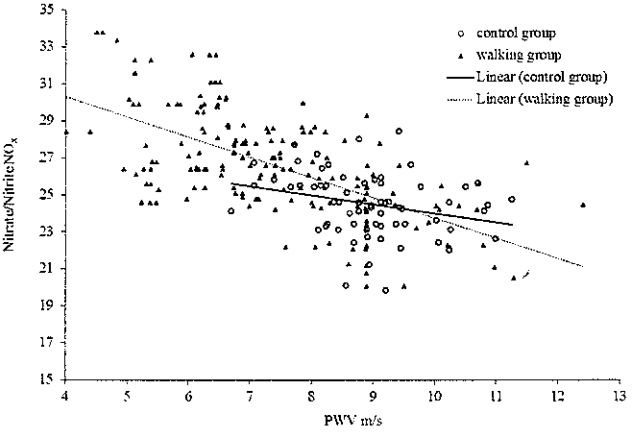

Figure 5. Correlation between NO_x and PWW using data collected from all the study time points within the 6-month brisk walking intervention and follow-up period. R^2 for control and walking group data combined, −0.648. R^2 for control group, −0.248. R^2 for walking group, −0.0617. NO_x, The sum of NO_2 and NO_3^- (acts as a surrogate marker for nitric oxide); PWV, pulse wave velocity.

concur with others who reported no change in BP after a 3-month brisk walking intervention[62,63] and 6-month brisk walking intervention.[64] Exercise training generally results in a greater lowering of BP when the participants are hypertensive rather than normotensive at baseline.[65]

Although VO_2 max is the traditional index of endurance fitness, this measure is less sensitive to change when dealing with low intensity training and can prove difficult to determine in previously sedentary, middle-aged individuals.[35] A more sensitive assessment of fitness can be determined by plotting VO_2 against blood lactate.[34,35] Using VO_2 at 3 mmol $\times$ l^{-1} blood lactate as an indicator of cardiorespiratory fitness, there was an increase in fitness in the walking group from 16.51 $\pm$ 3.89 mL $\times$ kg^{-1} $\times$ min to 19.89 $\pm$ 3.61 mL $\times$ kg^{-1} $\times$ min. At 4 months post-intervention, fitness had further increased to 21.11 $\pm$ 4.48 mL $\times$ kg^{-1} $\times$ min $\times$ 1, although this did not differ from fitness levels at the end of the 6-month intervention. There were no changes to the control group during the study period.

The limited RT3 data available on adherence in relation to walking intensity and duration is a recognized weakness of the study. The researchers did, however, make regular telephone contact with the participants to encourage regular walking. This study reflects the resources available in primary health care, where provision of supervised walks or compliance indicators is often unavailable. Despite no observed changes in anthropometry, BP, or fasting blood lipids, the results from this study indicate that 6 months of brisk walking in line with physical activity guidelines, in overweight individuals, is effective at reducing arterial stiffness, a recognized contributor to the development of atherosclerosis and consequently to CVD. Furthermore, the walking group maintained their fitness levels 4 months post-intervention, and the beneficial effects on arterial stiffness that appear to be associated with concomitant increases in NO were also sustained 4 months post-intervention. Thus, a lifestyle approach to fulfilling current physical activity guidelines may result in favorable alterations in arterial function in overweight individuals with improvements sustained beyond the intervention period.

Acknowledgments

The authors are grateful to Dr Mark Lynch for his assistance in biochemical bloods analysis.

References

1. Haskell WL, Lee IM, Russell R, Pate RR, Powell KE, Blair SN, et al. Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. Circulation 2007;116: 1081–93.
2. Pate RR, Yancey AK, Kraus WE. The 2008 Physical Activity Guidelines for Americans: implications for clinical and public health practice. Am J Lifestyle Med 2010:4:209–17.
3. Murphy MH, Donnelly P, Shibli S, Foster C, Nevill A. Physical activity, walking and leanness: an analysis of the Northern Ireland Sport and Physical Activity Survey (SAPAS). Prev Med 2012;54:140–1.
4. Health Promotion Agency: a health economics model. The cost benefits of the Physical Activity Strategy for Northern Ireland - a summary of key findings. Belfast: Health Promotion Agency; 2001. P. 1–16.
5. Howard RA, Freedman DM, Park Y, Hollenbeck A, Schatzkin A, Leitzman MF. Physical activity, sedentary behaviour, and the risk of colon and rectal cancer in the NIH-AARP Diet and Health Study. Cancer Causes Control 2008;19:939–53.
6. Owens N, Healy GN, Matthews CE, Dunstan DW. Too much sitting: the population health science of sedentary behaviour. Exercise Sport Sci Rev 2010;38: 105–13.
7. Hamer M, Chida Y. Walking and primary prevention: a meta-analysis of prospective cohort studies. Br J Sports Med 2008;42:238–43.
8. Britton A, McPherson K. Monitoring the progress of the 2010 target for CHD Mortality: Estimated consequences on CHD incidence and mortality from changing prevalence of risk factors. London: National Heart Forum; 2002.
9. Morris J, Hardman A. Walking to health. Sports Med 1997;23:306–32.
10. Vaz De Almeida MD, Graca P, Alfonso C, D'amicis A, Lappalainen R, Damkjaer S. Physical activity levels and body weight in a nationally representative sample in the European Union. Public Health Nutr 1999;2: 105–13.
11. Craig R, Mindell J, Hirani V. Health Survey for England 2008-Volume 1: Physical activity and fitness. London: National Centre for Social Research; 2010.
12. Martin JE, Dubbert PM. Adherence to exercise. Exercise Sport Sci Rev 1995;13:137–67.
13. Perri MG, Martin AD, Leermakers EA, Sears SF, Notelovitz M. Effects of group versus home-based exercise in the treatment of obesity. J Consult Clin Psychol 1997;65:278–85.
14. Siegel PZ, Brackbill RM, Heath GW. The epidemiology of walking for exercise: implications for promoting activity among sedentary groups. Am J Public Health 1995;85:706–71.
15. Ainsworth BE, Haskell WL, Whitt MC, Irwin ML, Swartz AM, Strath SJ, et al. Compendium of physical

activities: an update of activity codes and MET intensities. Med Sci Sport Exer 2000;32:S498–516.
16. Murtagh EM, Boreham CAG, Murphy MH. Speed and exercise intensity of recreational walkers. Prev Med 2002;35:397–400.
17. Laurent S, Cockcroft J, Bortel LV, Boutouyrie P, Giannattasio C, Hayoz D, et al. Expert consensus document on arterial stiffness: methodological issues and clinical applications. Eur Heart J 2006;27: 2588–605.
18. Naka KK, Tweddel AC, Doshi SN, Goodfellow J, Henderson AH. Flow-mediated changes in pulse wave velocity: a new clinical measure of endothelial function. Eur Heart J 2006:27:302–9.
19. Parrinello G, Colomba D, Bologna P, Licata A, Pinto A, Paterna S, et al. Early carotid atherosclerosis and cardiac diastolic abnormalities in hypertensive subjects. J Hum Hypertens 2004;18:201–5.
20. Mancia G, De Backer G, Dominiczak A, Cifkova R, Fagard R, Germano G, et al. 2007 Guidelines for the management of arterial hypertension: the Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). J Hypertens 2007; 25:1105–87.
21. Noor A, Mahmud JA, Bennett K, Feely J. Assessment of arterial stiffness in hypertension: comparison of oscillometric (Arteriograph), piezoelectronic (Complior) and tonometric (SphygmoCor) techniques. J Hypertens 2009;27:2186–91.
22. Vaitkevicius PV, Fleg JL, Engel JH, O'Connor FC, Wright JG, Lakatta LE, et al. Effects of age and aerobic capacity on arterial stiffness in healthy adults. Circulation 1993;88:1456–62.
23. Zambanini A, Cunningham SL, Parker KH, Khir AW, McG Thom SA, Hughes AD. Wave energy patterns in carotid, brachial and reduial arteries: a non-invasive approach using wave-intensity analysis. Am J Physiol-Heart Circ 2005;289:H270–6.
24. Lehmann ED, Hopkins KD, Rawesh A, Joseph RC, Kongola K, Coppack SW, et al. Relation between number of cardiovascular risk factors/events and noninvasive Doppler ultrasound assessments of aortic compliance. Hypertension 1998;32:565–9.
25. Hambrecht R, Wolf A, Gielen S, Linke A, Hofer J, Erbs S, et al. Effect of exercise on coronary endothelial function in patients with coronary artery disease. New Engl J Med 2000;342:454–60.
26. Sessa WC. Regulation of endothelial derived nitric oxide in health and disease. Mem Inst Oswaldo Cruz 2005;100:15–8.
27. Tanabe T, Maeda S, Miyauchi T, Lemitsu M, Takanashi M, Irukayama-Tomobe Y, et al. Exercise training improves aging-induced decrease in eNOS expression in the aorta. Acta Physiol 2003;78:3–10.
28. Kelm M, Feelisch M, Deussen A, Strauer BE, Schrader J. Release of endothelium derived nitric oxide in relation to pressure and flow. Cardiovasc Res 1991; 25:831–6.
29. Lowther M, Mutrie N, Loughlan C, McFarlane C. Development of a Scottish physical activity questionnaire: a tool for use in physical activity interventions. Br J Sports Med 1999;33:244–9.
30. Ritchie JD, Miller CK, Smiciklas-Wright H. Tanita foot-to-foot bioelectrical impedance analysis system validated in older adults. J Am Diet Assoc 2005;105: 1617–9.
31. Willis LH, Slentz CA, Houmand JA, Johnson JL, Duscha BD, Aiken LB, et al. Minimal versus umbilical waist circumference measures as indicators of cardiovascular disease risk. Obesity 2007;15:753–9.
32. Institute of Medicine of the National Academies. Dietary Reference Intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein, and amino Acids. Washington, DC: National Academies Press; 2002.
33. Chen C, Jerome GJ, LaFerriere D, Young DR, Vollmer VM. Procedures used to standardize data collected by RT3 triaxial accelerometers in a large-scale weight-loss trial. J Physl Act Health 2009;6: 354–9.
34. Stensel DJ, Brookewavell J, Hardman AE, Jones PR, Norgan NG. The influence of a 1-year program of brisk walking on endurance fitness and body composition in previously sedentary men aged 42-59 years. Eur J Appl Physiol Occup Physiol 1994;68:531–7.
35. Åstrand PO, Rodahl K. Textbook of work physiology. New York: McGraw Hill Book Company; 1986.
36. McLaughlin J, McNeill M, Braun B, McCormack PD. Piezoelectric sensor determiniation of aterial pulse wave velocity. Physiol Meas 2003;24:693–702.
37. Murphy JC, Morrison K, McLauglin J, Manoharan G, Adgey J. An innovative piezoelectric-based method for measuring pulse wave velocity in patients with hypertension. J Clin Hypertens 2011;13(7):497–505.
38. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 1972;18:499–502.
39. Kelm M, Preik-Steinhoff H, Preik M, Strauer BE. Serum nitrite sensitively reflects endothelial NO formation in human forearm vasculature: evidence for biochemical assessment of the endothelial -arginine-NO pathway. Cardiovasc Res 1999;41:765–72.
40. Tannenbaum SR. Nitrate and nitrite; origin in humans. Science 1979;205:1333–5.
41. Kelm M, Yoshida K. The biology of nitric oxide. In: Moncada S, Marletta MA, Hibbs JB, Higgs EA, editors. Physiological and clinical aspects. London: Portland Press; 1996. P. 319–22.

42. Altman DG. Statistics and ethics in medical research. III: How large a sample? Br Med J 1980;281:1336–8.
43. Lacroix V, Willemet M, Verhelst R, Beauloye C, Jacquet L, Astarci P, et al. Central and peripheral pulse wave velocities are associated with ankle–brachial pressure index. Artery Res 2012;6:28–33.
44. Grey E, Bratteli C, Glasser SP, Alinder C, Finkelstein SM, Lindgren BR, et al. Reduced small artery but not large artery elasticity is an independent risk marker for cardiovascular events. Am J Hypertens 2003;16:265–9.
45. Woodman RJ, Kingwell BA, Beilin LJ, Hamilton SE, Dart AM, Watts GF. Assessment of central and peripheral arterial stiffness. Am J Hypertens 2005;18:249–60.
46. Kuo L, Chancellor JD. Adenosine potentiates flow-induced dilation of coronary arterioles by activating K_{ATP} channels in endothelium. Am J Physiol-Heart Circ 1995;269:H541–9.
47. McVeigh G, Brennan G, Hayes R, Cohn J, Finkelstein S, Johnston D. Vascular abnormalities in non-insulin-dependent diabetes mellitus identified by arterial waveform analysis. Am J Med 1993;95:424–30.
48. Kingwell BA, Berry KL, Carmeron JD, Jennings GL, Dart AM. Arterial compliance increases after moderate intensity cycling. Am J Physiol-Heart Circ 1997;273: H2186–91.
49. Maiorana A, O'Driscoll G, Dembo L, Cheetham C, Goodman C, Taylor R, et al. Effect of aerobic and resistance exercise training on vascular function in heart failure. Am J Physiol-Heart Circ 2000;279:H1999–2005.
50. Maiorana A, O'Driscoll G, Dembo L, Goodman C, Taylor R, Green D. Exercise training, vascular function and functional capacity in middle-aged subjects. Med Sci Sport Exer 2001;33:2022–8.
51. Silber D, McLaughlin D, Sinoway L. Leg exercise conditioning increases peak forearm blood flow. J Appl Physiol 1991;71:1568–73.
52. Walsh JH, Best M, Maiorana AJ, Taylor RR, O'Driscoll GJ, Green DJ. Exercise improves conduit function in CAD patients. J Appl Physiol 2003;285:20–5.
53. Watts K, Beye P, Siafarikas A, Davis EA, Jones TW, O'Driscoll G, et al. Exercise training normalises vascular dysfunction and improves central adiposity in obese adolescents. J Am Coll Cardiol 2004;43:1823–7.
54. Neibauer J, Cooke JP. Cardiovascular effects of exercise: role of endothelial shear stress. J Am Coll Cardiol 1996;28:1652–60.
55. Green DJ, Maiorana A, O'Driscoll G, Taylor R. Effect of exercise training on endothelium derived nitric oxide functions in humans. J. Physiol 2004;561:1–25.
56. Webb D, Tuttle RH, Baksh M. Pendular activity of human upper limbs during slow and normal walking. Am J Phys Anthropol 1994;93:477–89.
57. Fantin F, Rossi A, Morgante S, Soave D, Bissoli L, Cazzadori M, et al. Supervised walking groups to increase physical activity in elderly women with and without hypertension: effect on pulse wave velocity. Hypertens Res 2012;35:988–93.
58. Cameron JD, Dart AM. Exercise training increases total systemic arterial compliance in humans. Am J Physiol- Heart Circ 1994;266:H693–701.
59. Belz GG. Elastic properties and windkessel function of the human aorta. Cardiovasc Drugs Ther 1995;9: 73–83.
60. Tinken TM, Thijssen DHJ, Hopkins N, Dawson EA, Cable NT, Green DJ. Shear stress mediates endothelial adaptations to exercise training in humans. Hypertension 2010;55:312–8.
61. Edwards G, Félétou M, Weston AH. Endothelium-derived hyperpolarising factors and associated pathways: a synopsis. Pflugers Arch- Eur J Physiol 2010; 459:863–79.
62. Moreau KL, Donato AJ, Seals DR, DeSouza CA, Tanaka H. Regular exercise, hormone replacement therapy and the age-related decline in carotid arterial compliance in healthy women. Cardiovasc Res 2003; 57:861–8.
63. Tanaka H, Dinenno FA, Monahan KD, Clevenger CM, DeSouza CA, Seals DR. Aging, habitual exercise, and dynamic arterial compliance. Circulation 2000;102: 1270–5.
64. Kobayashi Y, Hosoi T, Takeuchi T, Aoki S. Benefits of a convenient, self-regulated 6 month walking program in sedentary, middle-aged women. Jpn J Phys Fit Sport 2001;50:313–24.
65. Bertrand EA, Frances Y, Lafay V. Exercise training and blood pressure. B Acad Nat Méd Paris, 1995;179: 1471–81.