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ORIGINAL ARTICLE

The effect of a short-term exercise programme on haemodynamic adaptability; a randomised controlled trial with newly diagnosed transient ischaemic attack patients

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This study assessed the effect of a short-term, 8-week exercise programme on resting and exercise blood pressure (systolic (SBP); diastolic (DBP)), and other haemodynamic responses (heart rate (HR), pulse pressure (PP), double product (DP)), of newly diagnosed transient ischaemic attack (TIA) patients. Sixty-eight TIA patients completed a continuous and incremental exercise test within 2 weeks of symptom diagnosis. HR, SBP and DBP were regularly measured at rest, during exercise and in recovery. Participants were then randomised to either an 8-week exercise programme or to a usual care control group prior to completing an identical post-intervention (PI) re-assessment. Individuals randomised to the exercise condition experienced a significantly greater reduction in resting HR ($-5.4 \pm 10.2\%$), SBP ($-6.7 \pm 8.1\%$) and DBP ($-2.8 \pm 7.2\%$) than the control group at the PI assessment (all $P<0.05$). Similar findings were demonstrated at the PI assessment when comparing haemodynamic responses during exercise ($P<0.05$), with significantly larger decrements observed for SBP and HR (both 10–14%), PP (17–24%) and DP (26–32%) for those randomised to the exercise intervention (all $P<0.05$). This study demonstrates that structured physical activity soon after TIA diagnosis will improve haemodynamic responses. The early implementation of exercise following TIA diagnosis may be an important secondary prevention strategy for this population.

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INTRODUCTION

Non-communicable diseases such as heart disease, diabetes, stroke and respiratory disease are now considered the foremost global health burden, accounting for 63% of all deaths worldwide.[1] However, the prevalence of non-communicable diseases could be significantly lessened through the reduction of risk factors, early detection and timely treatment. Hypertension, defined as chronically elevated blood pressure (BP $>140/90$ mm Hg)[2] is the leading risk factor for non-communicable diseases and contributes to 13% of all global deaths.[1]

Hypertension is present in 80% of patients with acute ischaemic stroke and is independently associated with poor health outcomes,[3] coronary artery disease (CAD) and initial or recurrent strokes.[4] The relationship between BP and the risk of cardiovascular events is continuous, consistent and independent of other risk factors.[4] For every additional increment of 20/10 mm Hg above a BP of 115/75 mm Hg, the risk of cardiovascular disease increases by 200%.[5] Other haemodynamic parameters including pulse pressure (PP), mean arterial pressure (MAP), heart rate (HR) and double product (DP) may also be associated with adverse outcomes, following stroke.[6–9]

Exercise is widely advocated to be an integral part of the multifactorial secondary prevention strategy used to improve modifiable risk factors among patients with CAD.[10–12] Many individuals who have experienced a sudden cerebrovascular event (stroke, transient ischaemic attack (TIA)) have predisposing modifiable CAD risk factors such as hypertension, tobacco use, diabetes mellitus, hyperlipidaemia, obesity and physical inactivity.[13] When considering the association between sedentary lifestyle, poor cardiovascular fitness and mortality risk,[14] a similar multifactorial approach may be an appropriate secondary prevention strategy for patients diagnosed with a cerebrovascular complication.[15,16] Indeed, a meta-analysis of randomised controlled trials has shown aerobic exercise training to have a small but clinically significant effect in reducing systolic and diastolic BP (SBP and DBP).[17] However, at present, physical activity is not universally applied or accepted in such rehabilitation programmes for cerebrovascular patients.[15,16]

A TIA is when blood flow to the brain is temporarily disrupted, usually for <24 h.[18] Recent research with non-acute ischaemic stroke (5 years post stroke)[10] and TIA patients (up to 12 months post-TIA diagnosis)[19] has demonstrated reduced CAD risk, following either a 10-week[10] or 6-month[19] exercise programme. Although these studies demonstrated a significant reduction in resting BP, the effect of regular physical activity participation on TIA patients' haemodynamic response at rest (that is, for MAP, PP and DP) and during exercise has not been examined. For example, PP can be used as a valuable cardiovascular risk assessment tool, as an increase in PP at rest may reflect an increase in large artery stiffness.[20,21] An elevated resting PP may increase the risk of major cardiovascular complications and mortality by nearly 20%.[22] In addition, DP may be used as a valuable noninvasive measure of myocardial oxygen consumption during exercise.[23] Such research has been demonstrated with coronary heart disease,[21] healthy

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adults[23] and older[22] population groups. As PP and DP are measures of BP, monitoring an individual's BP response during an acute bout of exercise is important, particularly as a large majority of cardiovascular and cerebrovascular diseases and disorders are related to systemic haemodynamic dysfunction, such as hypertension. Current guidelines for the management of hypertension provide no information about the diagnosis, management or potential clinical utility of identifying the hypertensive response to exercise.[24] It has been previously shown that SBP measured during light and moderate exercise predicts the presence of masked hypertension, particularly with individuals who elicit a hypertensive response to exercise.[25] As research has also shown that haemodynamic adaptability to exercise enhances metabolic activity within the brain due to increasing arteriovenous oxygen difference for oxygen, glucose and lactate,[26] understanding the cardiovascular and haemodynamic adaptability to physical stress in TIA patients may help to elucidate the efficacy of physical activity within secondary prevention programmes for this cohort,[27] and in combination with the knowledge of traditional vascular risk factors may ameliorate recurrent cerebro- or cardiovascular events.

Therefore, the purpose of this study was to examine the acute effect of exercise on resting and exercise BP, and other haemodynamic responses (HR, MAP, PP, DP and so on), of newly diagnosed TIA patients. It was hypothesised that regular physical activity participation soon after TIA diagnosis would lead to a greater reduction in resting and exercise BP than those individuals who did not partake.

MATERIALS AND METHODS

Participants

Sixty-eight individuals from New Zealand's Capital and Coast District Health Board catchment area participated in the study (Table 1). Participants were deemed eligible if they had been diagnosed with a TIA, as confirmed by a specialist physician at the Wellington Regional Hospital within 7 days of symptom onset, and if they did not meet exclusion criteria: unstable cardiac conditions, uncontrolled diabetes mellitus, severe claudication, oxygen dependence, febrile illness, significant dementia, inability to communicate in English or unable to take part in a cardiac rehabilitation type exercise programme. All participants were required to comply with drug treatment and standardised therapy in accordance with recommendations from the stroke physician. Informed consent was obtained after the participants were given a detailed description of the procedures.

The trial was undertaken between February 2011 and November 2012. The trial was approved by New Zealand's Central Regional Health and Disabilities Ethics Committee. Data reported in this study are registered with the Australian and New Zealand Clinical Trials Registry (ACTRN12611000630910 and ACTRN12612000567820).

Study design

The study was a single-centre, randomised, parallel-group clinical trial. Eligible subjects were contacted by telephone and invited to attend a baseline (BL) assessment. The BL assessment included a vascular risk assessment and aerobic fitness test. Subjects were randomised on completion of the BL assessment. Subjects were randomly assigned using simple randomisation procedures (computerised random numbers) to either an 8-week exercise and education intervention or to a usual care control group. Details of the allocated group were given on a piece of paper contained within sequentially numbered, opaque sealed envelopes. The randomisation procedures were prepared by an investigator with no clinical involvement in the trial. Although subjects, and the health and exercise practitioner were aware of the allocated treatment condition, outcome assessors and data analysts were kept blinded to the allocation.

The exercise programme was comprised of two sessions per week, consisting of 90-min exercise and a 30-min education session, which discussed secondary prevention and educational information. This was over and above the standard secondary prevention and educational information provided to the control group. The control group only received standard secondary prevention and educational information (that is, leaflets from the Stroke Foundation of New Zealand on understanding stroke/TIA, how to manage salt consumption, BP and healthy eating). Subjects completed an identical post-intervention (PI) assessment 2 months after BL. Emergency procedures and an automated defibrillator were in place during all assessments and exercise sessions to ensure that appropriate care was available if any adverse events were encountered during testing.

Sample size

A sample size of 30 patients per group ($n = 60$) was deemed necessary to detect a reduction in our primary outcome measure (SBP), following early engagement in exercise. This figure is in agreement with the study of Santos-Hiss *et al.*,[28] based upon acute myocardial infarction patients, using a two-sided 5% significance level and a power of 80% (mean difference 7 mm Hg; pooled s.d. 5.8 mm Hg). This included an anticipated 25% participant dropout rate between pre- and post-assessments.

BL assessment

Cardiovascular risk assessment. The BL assessment included a health history questionnaire and a cardiovascular risk stratification,[2] comprising: total cholesterol, high-density lipoproteins , total cholesterol:high-density lipoprotein ratio, fasting blood glucose, resting supine SBP and DBP, body mass index, waist and hip circumference, waist-to-hip ratio, smoking history and family history of cardiovascular disease. Resting SBP and DBP were obtained following a 15-min rest period. In accordance with the American College of Sports Medicine,[2] the measured BP was based on the average of two brachial readings. These were taken on the left side of the body, unless advised by a clinician to take the measure on the right side (that is, due to women undergoing a mastectomy of the left breast issue). Although water could be consumed, cardiovascular risk assessments were undertaken in a fasted state, and were typically conducted within the morning.

Exercise test

All participants completed a peak or symptom-limited exercise ECG treadmill stress test, using a standardised modified Bruce protocol[2] within a controlled thermo neutral laboratory environment (temperature, $21.2 \pm 1.7\,^{\circ}C$; humidity $41.2 \pm 6.0\%$; air pressure $1004 \pm 10\,Nm^2$). The modified Bruce protocol is more suitable than the Bruce protocol when testing high-risk populations[29] due to the inclusion of an additional 6 min of low-intensity exercise at the start of the test. The first stage of the test commences at 0% grade and 1.7 mph. Following 3 min of exercise, participants exercise at the same speed but at a 10% grade. Thereafter, participants exercised at 2.5 mph and a 12% gradient for the third exercise stage, and then 3.4 mph and 14% gradient for the fourth exercise stage.

The test was terminated when the subject reported volitional exhaustion, when their HR reached 85% of age-predicted maximum or if predetermined physiological responses were observed from the exercise ECG (for example, 2-mm ST depression). Subjects' HR and ECG were continuously recorded at rest, during exercise and during recovery. Exercise BP was based on the average of the two reading taken in the final 60 s of each exercise stage.

Exercise and education programme

Subjects completed 90-min group-based (3–5 patients) exercise sessions for 8 weeks, twice weekly. Exercise was prescribed on a one-to-one basis by health and exercise practitioners. In accordance with recommendations for moderate physical activity participation, participants completed 30 min of aerobic exercise at each exercise session.[2] This included 15 min of continuous walking and 15 min of continuous cycling. Participants exercised between 50 and 85% of age-predicted maximal HR during all aerobic exercise tasks. The exercise intensity typically increased by $\sim 5\%$ each week, although the rate of progression was dependent upon how the subject felt during each session. Participants also completed 60 min of resistance training (such as, alternate arm biceps curl and shoulder press), postural and coordination exercises using buso and Swiss balls, and flexibility exercises. Thirty minutes of resistance-type exercise occurred after the walk, and 30 min after the cycle. Exercise practitioners ensured that subjects did not exercise above 85% of their age-predicted maximal HR or beyond intensities, which may instigate cardiac abnormalities as identified from the ECG exercise test.

Once a week, a 30-min group-focused education session was held, designed to facilitate patients with a greater sense of understanding and management of their condition. The education sessions were undertaken on completion of the second exercise session of each week by a health and exercise practitioner. These sessions focused on cardiovascular disease risk factors, including BP, stroke prevention, nutrition, exercise, adherence to medication, stress management, and emotional and behavioral changes after TIA. The health and exercise practitioner would introduce some background information on a topic (that is, nutrition), and then facilitate a group discussion surrounding patient perspectives and usual practices concerning the given topic. The participants randomised to the exercise and education programme attended 95% of all available sessions.

Measures

BP measurement. Prior to completing each stage of the exercise test, BP was manually measured on the left side of the participants' body using a stethoscope and sphygmomanometer (Accosson, London, UK). To minimize inter-individual variation, BP was assessed by the same practitioner for all participants.

Data analysis

As described above, SBP, DBP and HR was obtained at rest and during exercise (stages 1–4). PP was calculated as SBP minus DBP. MAP was calculated as DBP plus one-third of PP. To provide a direct indication of the energy demand of the heart, DP was calculated at each stage of the test by multiplying SBP and HR.

Statistical analyses

Descriptive statistics and exercise duration. A series of independent samples' *t*-test were used to compare BL descriptive between the exercise and control participants. A two-factor repeated measures ANOVA: Test (BL, PI) × Condition (exercise, control) was used to compare the duration of the exercise test.

Total change in physiological responses (rest to peak values). Three-factor repeated measures ANOVAs: Test (BL, PI) × Condition (exercise, control) × Time (rest, peak value) were used to compare the change in haemodynamic responses (SBP, DBP, HR, PP and DP) between resting values and the peak values reported at the end of the exercise test. A series of two-factor repeated measures ANOVAs: Test × Condition were also used to examine the mean change in haemodynamic activity from rest to peak values. Where assumptions of sphericity were violated in the preceding analyses, the critical value of F was adjusted by the Greenhouse-Geisser epsilon value, following the Mauchly test to reduce the risk of type 1 error. Where significant interactions were located, *post hoc* analysis using a Tukey's Honestly Significant Difference test was used to calculate the minimum raw score mean difference that must be attained to declare significance between the groups.

Change in haemodynamic responses at different exercise stages. A series of independent samples' *t*-tests were conducted to examine differences in the absolute haemodynamic responses (SBP, DBP, HR, PP, MAP and DP) between the exercise and control groups during exercise (stages 1–4) at BL and PI. A similar analysis was also used to investigate the mean change in each haemodynamic marker between resting values and those reported on completion of each exercise stage. Independent samples' *t*-tests were used to examine the percentage (%) change in SBP, DBP, HR, PP and DP between BL and PI for the exercise and control groups. Levene's test was used to assess the equality of variance in the exercise and control group data. Effect sizes are also reported using Cohen's *d*. Alpha was set at 0.05 throughout. All analyses were conducted using SPSS version 20.0 (IBM Corporation, New York, NY, USA).

RESULTS

BL descriptive and exercise duration

With the exception of the number of patients with a clinical diagnosis of hypertension ($P<0.05$), there were no between-group differences in participant descriptives at the BL assessment (all $P>0.05$; Table 1). A significant Test by Condition interaction was revealed for the duration of the exercise test ($F_{(1,59)}=61.87$; $P<0.001$). *Post hoc* analysis demonstrated a significantly greater change in exercise duration between BL and PI for the exercise group (7.45 ± 2.41 vs 11.08 ± 3.16 min, respectively) compared with the control group (7.38 ± 2.58 vs 8.22 ± 2.55 min, respectively).

Table 1. Participant descriptives at the baseline assessment for participants randomised to the exercise and control group

	Exercise (n = *36*)	*Control* (n = *32*)
Age (years)	65.4 ± 10.4	68.1 ± 9.5
Gender (*n*)	23 M (63%)	19 M (60%)
Ethnicity (n)		
NZ European	32 (88%)	27 (84%)
Maori	1 (3%)	2 (6%)
Pacific Islander	2 (6%)	1 (3%)
Asian	1 (3%)	1 (3%)
Indian	0	1 (3%)
Height (cm)	1.67 ± 0.10	1.68 ± 0.09
Weight (kg)	79.5 ± 14.1	79.7 ± 16.2
BMI (kg min^{-1})	28.5 ± 3.6	28.0 ± 4.9
Waist (cm)	95.4 ± 13.3	96.8 ± 12.9
Hip (cm)	96.2 ± 17.2	101.1 ± 12.3
Waist-to-hip ratio	0.96 ± 0.09	0.95 ± 0.08
Blood pressure (mm Hg)		
Seated SBP	141 ± 16	136 ± 16
Seated DBP	82 ± 9	80 ± 9
Standing SBP	141 ± 20	135 ± 19
Standing DBP	83 ± 10	81 ± 9
Supine SBP	141 ± 15	136 ± 14
Standing DBP	83 ± 8	79 ± 9
Clinical diagnosis of hypertension (⩾140/90 mm Hg)	12 (33%)	7 (22%)[a]
Total cholesterol	3.81 ± 1.16	4.10 ± 0.99
HDL	1.21 ± 0.49	1.33 ± 0.49
Total cholesterol: HDL ratio	3.00 ± 1.33	2.93 ± 0.93
Fasting blood glucose	5.81 ± 2.22	5.70 ± 1.23
Prescribed medication		
Statins	30 (84%)	28 (87%)
Antithrombotic	31 (87%)	27 (84%)
ACEI	11 (30%)	13 (42%)
Diuretics	12 (32%)	12 (37%)
Calcium blockers	11 (30%)	8 (26%)
Beta blockers	9 (26%)	7 (21%)
Anticoagulants	3 (8%)	4 (13%)
Other anti-hypertensives	3 (8%)	3 (8%)
Mean medication use	2.90 ± 1.04	2.92 ± 1.07

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; HDL high-density lipoproteins; SBP, systolic blood pressure. [a]Significant difference between exercise and control groups at BL ($P<0.05$).

Total change in physiological responses (rest to peak values)

There was a significant Test by Condition by Time interaction for HR, SBP and DBP (all $P<0.05$). As demonstrated in Table 2, *post hoc* analysis revealed a significant decrease in resting HR ($P<0.05$), SBP ($P<0.01$) and DBP ($P<0.05$), and a significant increase in peak HR ($P<0.05$) for the exercise group between BL and PI. *Post hoc* analysis also revealed a significant decrease in DBP at peak exertion for the control group ($P<0.05$; Table 2). There were no Test by Condition by Time interactions for DP or PP (both $P>0.05$). Similar findings were observed when comparing the mean change

in haemodynamic activity between resting and peak values, with significant interactions observed for HR ($P<0.05$) and SBP ($P<0.01$) for the exercise group (Table 2).

Table 2. Mean (± s.d.) HR, SBP, DBP, PP and DP for exercise and control participants at rest and at peak exertion for both BL and PI

	Exercise		*Control*	
	BL	*PI*	*BL*	*PI*
HR (b min^{-1})				
Rest	67 ± 13	64 ± 12[a]	67 ± 12	65 ± 8
Peak	124 ± 19	130 ± 18[b]	125 ± 17	126 ± 19
Change	57 ± 17	66 ± 19[a]	59 ± 17	61 ± 18
SBP (mm Hg)				
Rest	141 ± 15	131 ± 14[b,c]	136 ± 14	134 ± 17
Peak	180 ± 22	184 ± 20	173 ± 19	173 ± 18
Change	39 ± 15	53 ± 18[b]	37 ± 16	38 ± 17
DBP (mm Hg)				
Rest	83 ± 8	80 ± 9[a]	79 ± 9	79 ± 10
Peak	84 ± 8	82 ± 11	82 ± 11	79 ± 10[b]
Change	1.2 ± 7.0	2.1 ± 6.8	3.5 ± 8.5	− 0.1 ± 5.9[a]
PP (mm Hg)				
Rest	58 ± 12	51 ± 12[c]	57 ± 13	55 ± 15
Peak	95 ± 20	98 ± 20	90 ± 20	93 ± 16
Change	37 ± 17	47 ± 18	34 ± 16	38 ± 16
DP (b min^{-1} mm Hg)				
Rest	9.4 ± 2.1	8.3 ± 2.0[c]	9.1 ± 1.9	8.7 ± 1.6
Peak	22.3 ± 4.6	22.6 ± 4.3	21.4 ± 4.3	21.5 ± 4.4
Change	12.9 ± 4.0	14.2 ± 3.6	12.4 ± 4.0	12.8 ± 4.3

Abbreviations: BL, baseline; DBP, diastolic blood pressure; DP, double product; HR, heart rate; MAP, mean arterial pressure; PP, pulse pressure; SBP, systolic blood pressure.
Data are also reported as the mean change between rest and peak values (grey rows). DP is reported as HR (b min^{-1}) multiplied by pressure (mm Hg), divided by 1000. [a]Significant difference between BL and PI ($P<0.05$). [b]Significant difference between BL and PI ($P<0.01$). [c]Medium to large effect (Cohen's $d=0.5$–0.8).

BL: change in haemodynamic responses at different exercise stages

Participants randomised to the exercise group demonstrated a significantly greater SBP during all exercise stages (stages 1–4) throughout the BL assessment (all $P<0.05$; Table 3). These findings were evident despite exercise, and control participants reporting a similar HR and DP response at rest and during exercise (stages 1–3). Significant differences in DBP and PP were only observed on completion of the first and third exercise stages, respectively (both $P<0.05$; Table 3).

When comparing the mean change in haemodynamic values between resting and each exercise stage from the BL assessment, significant differences were only observed for DBP between rest and stage 4 of the exercise test ($P<0.05$; Table 3). No statistical differences were observed between groups for SBP, HR, DP and PP (all $P>0.05$).

PI: change in haemodynamic responses at different exercise stages

During PI, although no differences in SBP, DBP, PP or MAP were noted between the groups, a significantly lower HR (rest to stage 4) and DP (rest to stage 3) was observed for the exercise group (all $P<0.05$; Table 4). When considering the mean change in the haemodynamic response between the resting values and each exercise stage from the PI assessment, significant differences were only observed for HR (rest to stages 1, 2 and 3; all $P<0.01$) and DP (rest to stages 1 and 2; both $P<0.05$). *Post hoc* analysis revealed a significantly lower HR and DP response for the exercise group at each of the aforementioned time points (Table 4).

Percentage change in haemodynamic values from BL to PI

When investigating the percentage change between BL and PI, individuals randomised to the exercise group experienced a significantly greater reduction in SBP, PP, HR and DP at rest and during exercise (stages 1–3) than the control group (all $P<0.05$; Figures 1 and 2). There were no statistical differences in each of

Table 3. Haemodynamic responses from the baseline assessment at rest and during exercise (stages 1–4)

	Rest	*Stage 1*		*Stage 2*		*Stage 3*		*Stage 4*	
n									
Exercise	36	36		33		24		6	
Control	32	30		28		19		9	
SBP (mm Hg)									
Exercise	141 ± 15	160 ± 18[a,b]	19 ± 16	173 ± 17[a,b]	32 ± 15	182 ± 16[a,b]	41 ± 13	192 ± 5[a,c]	51 ± 13
Control	136 ± 14	149 ± 19	13 ± 16	161 ± 20	25 ± 16	168 ± 23	32 ± 16	170 ± 20	34 ± 19
DBP (mm Hg)									
Exercise	83 ± 8	85 ± 6[a]	2 ± 5	85 ± 6	2 ± 5	84 ± 8	1 ± 7	85 ± 11	2 ± 8
Control	79 ± 9	81 ± 10	2 ± 6	82 ± 10	3 ± 7	83 ± 11	4 ± 8	82 ± 12	3 ± 8[a]
PP (mm Hg)									
Exercise	58 ± 12	75 ± 16	17 ± 16	87 ± 15	29 ± 13	98 ± 15[a,b]	40 ± 13	108 ± 11	50 ± 19
Control	57 ± 13	68 ± 19	11 ± 16	79 ± 20	22 ± 16	85 ± 21	28 ± 18	87 ± 24	30 ± 19
MAP (mm Hg)									
Exercise	102 ± 9								
Control	98 ± 9								
HR (b min^{-1})									
Exercise	67 ± 13	95 ± 19	28 ± 13	110 ± 22	43 ± 15	120 ± 19	53 ± 15	124 ± 15[c]	57 ± 14
Control	67 ± 12	96 ± 14	29 ± 12	111 ± 16	44 ± 15	122 ± 14	55 ± 13	138 ± 8	71 ± 6
DP (b min^{-1} · mm Hg)									
Exercise	9.4 ± 2.1	15.4 ± 3.6	6.0 ± 2.9	19.1 ± 4.3	9.7 ± 3.4	21.9 ± 4.4	12.5 ± 3.6	23.7 ± 2.7	14.3 ± 2.5
Control	9.1 ± 1.9	14.1 ± 3.1	5.0 ± 2.4	17.9 ± 4.0	8.8 ± 3.2	21.2 ± 4.1	12.1 ± 2.9	23.4 ± 3.1	14.3 ± 2.5

Abbreviations: DBP, diastolic blood pressure; DP, double product; HR, heart rate; MAP, mean arterial pressure; PP, pulse pressure; SBP, systolic blood pressure.
Data are reported as mean ± s.d. for absolute values (white columns) and when representing the mean change between each exercise stage and the resting values (grey columns). DP is reported as HR (b min^{-1}) multiplied by pressure (mm Hg), divided by 1000. [a]Significant difference in haemodynamic response between exercise and control groups ($P<0.05$). [b]Medium-to-large effect size (cohen $d>0.5$–0.8). [c]Large effect size (cohen $d>0.8$).

Table 4. Haemodynamic responses from the post-intervention assessment at rest and during exercise (stages 1–4)

	Rest	*Stage 1*		*Stage 2*		*Stage 3*		*Stage 4*	
n									
Exercise	36	36		31		28		23	
Control	32	30		29		21		11	
SBP (mm Hg)									
Exercise	131 ± 14	143 ± 12	12 ± 9	156 ± 19	25 ± 16	167 ± 18	36 ± 14	178 ± 18	47 ± 14
Control	134 ± 17	146 ± 17	12 ± 15	158 ± 19	24 ± 15	166 ± 19	32 ± 16	173 ± 19	39 ± 19
Exercise	80 ± 9	80 ± 9	0 ± 4	79 ± 10	−1 ± 5	80 ± 9	0 ± 5	80 ± 9	0 ± 8
Control	79 ± 10	79 ± 9	0 ± 5	78 ± 9	−1 ± 5	81 ± 9	2 ± 6	79 ± 10	0 ± 6
PP (mm Hg)									
Exercise	51 ± 12	75 ± 16	24 ± 10	77 ± 19	26 ± 15	87 ± 18	36 ± 15	99 ± 17	48 ± 16
Control	54 ± 15	67 ± 19	13 ± 15	80 ± 18	26 ± 17	85 ± 15	31 ± 16	93 ± 13	39 ± 15
MAP (mm Hg)									
Exercise	97 ± 9								
Control	98 ± 10								
HR (b min^{-1})									
Exercise	64 ± 7	81 ± 13[a,b]	17 ± 8	95 ± 13[a,b]	31 ± 9	110 ± 14[a,b]	46 ± 9	127 ± 13[a,b]	63 ± 8
Control	65 ± 8	93 ± 14	28 ± 12[a]	107 ± 15	42 ± 14[a]	124 ± 16	59 ± 16[a]	136 ± 10	71 ± 9
DP (b min^{-1} · mm Hg)									
Exercise	8.3 ± 2.0	11.5 ± 2.3[a,b]	3.2 ± 1.7	14.7 ± 3.3[a,c]	6.4 ± 2.8	18.5 ± 3.6[a,c]	10.2 ± 2.8	22.7 ± 3.3	14.4 ± 2.8
Control	8.7 ± 1.6	13.7 ± 3.2	4.0 ± 2.4[a]	17.1 ± 3.9	8.4 ± 3.1[a]	20.9 ± 4.3	12.2 ± 3.9	23.4 ± 3.1	14.7 ± 2.7

Abbreviations: DBP, diastolic blood pressure; DP, double product; HR, heart rate; MAP, mean arterial pressure; PP, pulse pressure; SBP, systolic blood pressure. Data are reported as mean ± s.d. for absolute values (white columns), and when representing the mean change between each exercise stage and the resting values (grey columns). DP is reported as HR (b min^{-1}) multiplied by pressure (mm Hg), divided by 1000. [a]Significant difference in haemodynamic response between exercise and control groups ($P<0.05$). [b]Large effect size (cohen $d>0.8$). [c]Medium-to-large effect size (cohen $d>0.5$–0.8).

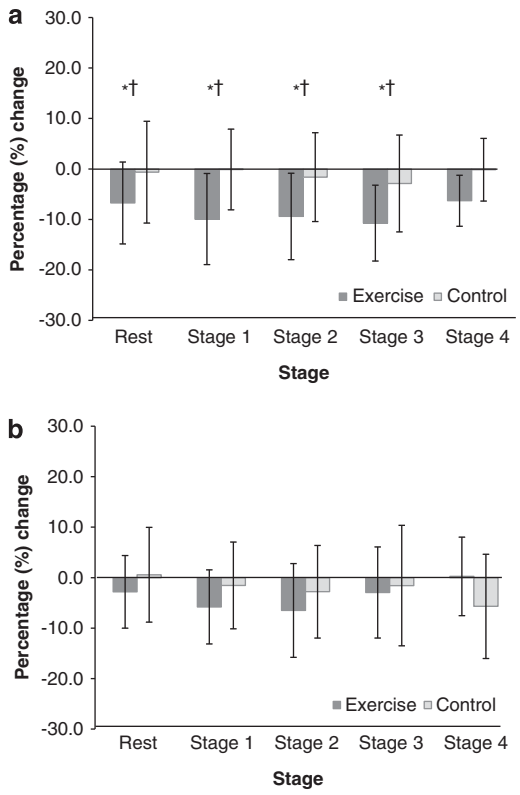

Figure 1. Mean (± s.d.) percentage change in SBP (**a**), and DBP (**b**) between BL and PI for exercise and control groups at rest and during exercise (stages 1–4). Details of participant numbers (*n*) are identical to those reported in Table 3 for each condition and stage. *Significant difference between exercise and control groups ($P<0.05$). †Large effect size (cohen $d>0.8$).

these physiological markers at the higher exercise intensity (stage 4). There were no statistical differences in DBP between groups at rest or during exercise (all $P>0.05$; Figure 1).

DISCUSSION

The purpose of this study was to examine the effects of an 8-week exercise intervention on the haemodynamic adaptability to an acute exercise test of newly diagnosed TIA patients. In this study, 68 TIA patients completed a BL health and fitness assessment within 2 weeks of TIA symptom onset, and a follow-up assessment 8 weeks later. The study hypothesis was accepted, as the early engagement in exercise had a positive effect on resting and exercise BP, and other haemodynamic responses, in newly diagnosed TIA patients.

Improvements in resting haemodynamic responses between BL and PI were observed for those individuals randomised to the exercise group. A greater change in resting HR, SBP and DBP were observed for the exercise participants (Table 2). For example, for those TIA patients who had completed 8 weeks of regular physical activity, the PI assessment demonstrated a −5.4 ± 10.2% (HR), −6.7 ± 8.1% (SBP) and −2.8 ± 7.2% (DBP) reduction in each of the aforementioned resting haemodynamic responses (Figures 1 and 2). This was significantly greater than the changes observed between BL and PI for the control group (−0.2 ± 10.6, 0.6 ± 10.0 and 0.6 ± 9.4% for HR, SBP and DBP, respectively). Although the observed changes in resting SBP equated to a medium to large effect (Cohen's $d=0.68$), only a small to moderate effect was observed for both HR (Cohen's $d=0.24$) and DBP (Cohen's $d=0.35$). The weaker relationships for HR and DBP may be attributed to the smaller mean change in values between BL and PI, and the larger inter- and intra-individual variations in participant responses (see Table 2 and Figures 1 and 2). Interestingly, there were no statistical differences in resting PP and DP between BL and PI for the exercise group (Table 2),

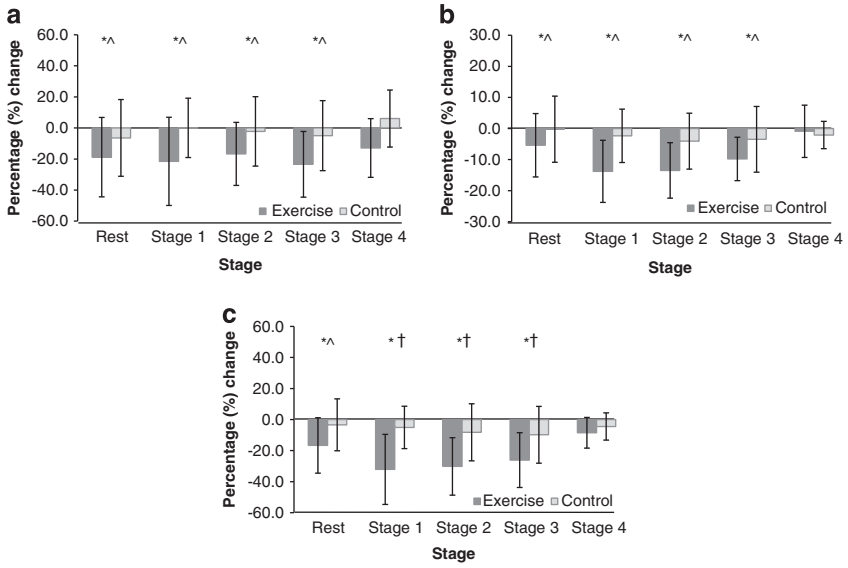

Figure 2. Mean (± s.d.) percentage change in PP (**a**), HR (**b**) and DP (**c**) between BL and PI for exercise and control groups at rest and during exercise (stages 1–4). Details of participant numbers (*n*) are identical to those reported in Table 3 for each condition and stage. *Significant difference between exercise and control groups ($P < 0.05$). †Large effect size (Cohen $d > 0.8$). ^Medium effect size (Cohen $d > 0.5$).

however, medium effect sizes were observed (Cohen's $d = 0.58$ and 0.54, respectively). A high SBP before exercise and a steep rise in SBP over time represents a higher risk of developing hypertension.[30] As high BP is considered one of the most pertinent risk factors for initial or recurrent strokes or TIAs, a reduction in resting BP is of paramount importance post-TIA diagnosis. As such, the results observed in this study are of pragmatic interest, with regards to the early exercise engagement of newly diagnosed TIA patients. As demonstrated in Table 1, TIA patients are typically prescribed medication (stations and antithrombotic) to help reduce the severity of high BP and blocked arteries as risk factors for recurrent cerebro- or cardiovascular events. The present study demonstrates that the inclusion of regular physical activity participation (in conjunction with medicinal management) in the secondary prevention treatment paradigm, soon after initial TIA diagnosis, is of value for this population group.

Current guidelines for the management of hypertension provide no information about the diagnosis, management or potential clinical utility of identifying the hypertensive response to exercise.[24] SBP measured during light and moderate exercise has been shown to predict the presence of masked hypertension, particularly in individuals who elicit a hypertensive response to exercise.[25] Accordingly, the importance of regular physical activity for this population group is further demonstrated when considering the SBP, DBP and the corresponding PP response during exercise. This study demonstrated that on completion of the first, second and third exercise stage, a 10–14% reduction in SBP was observed for the exercise group (Figure 1). This equated to a large effect (Cohen's $d > 0.80$) and a 15–17-mm Hg mean change in SBP for each of these exercise stages (see Tables 3 and 4). Although a natural decrement in SBP was observed in the control group (~1–3% or 2–3 mm Hg), this change was statistically inferior to that observed with the exercise group. When considering the changes in DBP, there were no statistical differences between conditions, yet there was a general trend for a reduced DBP throughout the exercise test. In addition, an encouraging 17–24% decrease in PP was observed for the exercise condition (Figure 2). Such changes in SBP and PP should be of interest for health and exercise practitioners, with regards to the prescription of low to moderate exercise intensities for patients diagnosed with a TIA. A high PP has been shown to be an important risk factor and strong predictor of heart disease.[21,22,31] A 10-mm Hg increase in resting PP, for example, may increase the risk of major cardiovascular complications and mortality by nearly 20%.[22] An increase in large artery stiffness and peripheral vascular resistance are the most likely reason for an increase in PP.[21,31] The greater the PP, the stiffer and more damaged the vessels are thought to be. Thus, the greater change in PP for those who took part in the exercise programme is likely due to decreases in SBP and a reduction in large artery stiffness. Further research is necessary with regards to the physiological effect of regular physical activity participation on large artery (that is, aortic and carotid) stiffness in TIA patients.

Although there were no differences in the change in HR and DP from rest to each exercise stage at BL (Table 3), significant differences were observed at the PI assessment (Table 4), with a smaller change in HR and DP typically observed for the exercise group compared with the control group at each exercise stage (stages 1–3). The changes observed between BL and PI for the exercise group typically equated to, on average, a 10–14% and a 26–32% decrease in HR and DP, respectively (Figure 2), for stages 1–3. DP is a surrogate measure of myocardial oxygen demand and cardiac workload. It is a measure of the stress put on the cardiac muscle based on the number of times it needs to beat per minute (HR), and the arterial BP (SBP) that it is pumping against. DP provides a direct indication of the energy demand of the heart, and thus is a good measure of the energy consumption of the heart. As such, the greater statistical decrease in DP between BL and PI for the various stages of the exercise test demonstrates improved exercise efficiency due to a lower HR and SBP being reported at each stage of the test.

Our study has several limitations. Although not statistically different, the 6-mm Hg difference in resting SBP at the BL assessment between groups (Tables 1 and 2) was most likely a manifestation of randomizing more hypertensive participants to the exercise group ($n = 12$) than the control group ($n = 7$). As such, this is most likely the primary reason to why a significantly higher SBP was observed at the BL assessment and for each of the four exercise stages for those individuals randomised to the exercise intervention (Table 3). On completion of the study, despite no changes in the number of hypertensive patients observed within the control group, there was a substantial decrease in the number of clinically diagnosed hypertensive patients involved in the exercise group ($n = 7$). In hindsight, the inclusion of minimization

randomisation procedures may have removed such bias from the study. It should also be noted that due to differences in participant fitness, the number of participants included in some of the analyses varied, depending upon the assessment session (BL and PI) and how many exercise stages were completed by the participant. Owing to differences in physical fitness at BL, fewer participants completed the higher exercise intensities (that is, fourth exercise stage, Table 3, $n = 15$). This is the primary reason as to why independent sample *t*-tests were used to assess changes in absolute and relative (% change) markers, rather than repeated measures ANOVAs. Nevertheless, with significant improvements in fitness, as demonstrated by an increase in exercise duration, particularly for the exercise group (33 and 8% improvement for the exercise and control conditions, respectively), more participants were included in the higher exercise-intensity PI analysis (stage 4, Table 4, $n = 34$). Furthermore, although medication use was similar between the groups at BL (Table 1), it was decided not to include medication as a covariate in any ANOVA analysis due to the limited sample size, and wide range of medications and dosages. Further research is therefore necessary to determine the effect of medication usage on the haemodynamic responses of TIA patients during exercise. Future research should also consider the effect of a long-term intervention on acute TIA and stroke patients' haemodynamic adaptability, and whether the magnitude of the changes observed in this study is demonstrated on other aerobic modes of exercise (cycle aerometry and elliptical cross trainer) at differing exercise intensities (moderate- cf. high-intensity), and using different exercise protocols (continuous cf. intermittent).

In conclusion, the present study supports the efficacy of a structured physical activity intervention soon after TIA diagnosis. This study has shown significant changes in resting and exercise SBP, PP, HR and DP following a 8-week exercise programme twice weekly. With an ageing population and increased life expectancy, the number of stroke and TIA survivors in our society is likely to increase. As such, the implementation of structured physical activity programmes could be a beneficial lifestyle strategy in the prevention of hypertension, and an important component of the secondary prevention strategy for TIA patients.

What is known about the topic

- Hypertension is a prevalent risk factor for individuals diagnosed with cardiovascular or cerebrovascular disease.
- Regular physical activity participation has a beneficial effect on fitness and cardiovascular risk in CAD and TIA patients.
- Exercise can help to improve the resting BP profile of non-acute stroke and TIA patients.[10,19] However, the effect of exercise on BP and other haemodynamic responses during exercise with this population group is yet to be assessed.

What this study adds

- Regular physical activity participation soon after TIA diagnosis significantly improves resting and exercise BP. No changes in BP were observed for the control subjects.
- The haemodynamic adaptability of taking part in structured exercise was evident when analysing the percentage change in PP, HR and DP at rest and during exercise. A significantly greater change in each of these responses were observed in the subjects who completed the 8-week exercise programme.
- The early engagement in exercise within 2 weeks of TIA symptom diagnosis may be a beneficial secondary prevention strategy for TIA patients.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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