

# Effects of Aerobic Exercise Training on Psychosocial Status and Serum Uric Acid in Men with Essential Hypertension: A Randomized Controlled Trial

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## Abstract

**Background:** Chronic psychosocial stress and serum uric acid (SUA) level have been implicated in the etiology and cardiovascular events risk factors in hypertension. Studies have reported significant benefit of exercise in the overall management of hypertension. However, studies on the effect of exercise on psychosocial stress and SUA in the management of hypertension seem scanty. **Aim:** The aim of this study was to determine the effect of continuous training program on SUA and psychosocial status of black African (Nigerian) population with hypertension. **Subjects and Methods:** Age-matched randomized controlled trial was used; subjects with diagnosis of hypertension attending the hypertensive clinic of Murtala Muhammed Specialist Hospital (MMSH), Kano, Nigeria form the population for the study. Two hundred and seventeen subjects with mild to moderate (systolic blood pressure (SBP) between 140 and 180 and diastolic blood pressure (DBP) between 90 and 109 mmHg) essential hypertension were grouped into continuous (112) and control groups (105). The continuous group involved in an 8 weeks continuous training (60%-79% HR max) of between 45 and 60 min, 3 times per week, while the controls group remain sedentary. SBP, DBP, SUA, VO<sub>2</sub> max and psychosocial status were assessed. Student *t*-test and Pearson correlation test were used in data analysis. **Results:** The study revealed significant beneficial effect of continuous training programs on VO<sub>2</sub> max, SBP, DBP, SUA, and psychosocial status ( $P < 0.05$ ). Psychosocial status and SUA was significantly and positively and negatively correlated respectively with VO<sub>2</sub> max at  $P < 0.01$ . **Conclusions:** This study concludes and supports the recommendations of moderate intensity (continuous) training program in blood pressure reduction, SUA and psychosocial stress management in hypertension.

**Keywords:** African, Blood pressure, Hypertension, Nigerian, Psychosocial stress, Serum uric acid

## Introduction

Hypertension was particularly prevalent amongst African subjects with 59% being affected.<sup>[1]</sup> In the Heart of Soweto Study, 56% of predominantly black Africans, who attended the cardiac clinic at Chris Hani Baragwanath Hospital in Soweto, were diagnosed as hypertensive.<sup>[2]</sup> Hypertension is a major global health problem and public-health challenge,

demanding a vast proportion of health care resources directly and indirectly because of its high and increasing prevalence and the concomitant risks of cardiovascular events such as stroke, kidney disease, decreased disability adjusted, and mortality.<sup>[3,4]</sup> Chronic psychosocial stress has been implicated in the etiology of hypertension.<sup>[5,6]</sup> In Africa-American, socio-environmental and psychosocial stress has been associated with higher blood pressure.<sup>[7]</sup> It has been reported that elevated serum uric acid (SUA) is an independent risk factor for hypertension and psychosocial stress.<sup>[3,4,8]</sup> Therefore, stress and or SUA reduction may be useful for treating hypertension in older African-American, yet there has been lack of controlled clinical trials of stress reducing for the management of hypertension.<sup>[9]</sup>

However, uric acid (UA) is the end-product of purine metabolism and has been associated with psychological features

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such as high energy/drive, positive effect, achievement, good performance, higher social status, and leadership. Externalized traits of temperament are associated with higher serum UA levels both in men and women.<sup>[8]</sup> Epidemiological studies suggest that psychosocial factors contribute significantly to the pathogenesis of cardiovascular disease (CVD).<sup>[10-13]</sup> Serum uric acid (SUA), a molecule which plays an important and complex role in oxidative and anti-oxidative processes has been reported to positively correlated with CVD and various measures of psychosocial stress,<sup>[12]</sup> especially in high risk patients.<sup>[13]</sup>

Epidemiological studies have shown that increased levels of physical activity reduce the incidence of all-cause mortality and cardiovascular-related deaths.<sup>[14]</sup> Although the mechanisms responsible for this benefit are not fully understood, exercise is known to have favorable effects on such traditional risk factors as elevated blood pressure (BP), hyperinsulinemia, and hyperlipidemia. Studies have also shown that exercise cannot only induce beneficial physiological adaptations, but can also improve psychological functioning.<sup>[15-19]</sup>

Cross-sectional studies have shown that individuals who are more active or physically fit have lower cardiovascular responses to stress.<sup>[20]</sup> However, longitudinal studies are less consistent but generally demonstrate that heart rate (HR) and BP levels are attenuated after exercise training in healthy normotensive men and women. To the best of our knowledge, there are few large randomized controlled trials investigating the association between exercise training, SUA and psychosocial status in hypertension, and of those few studies, none has investigated these effects on pure black African population. However, heredity<sup>[21]</sup> and genetical<sup>[22]</sup> factors have been implicated in the causative of hypertension; also there is possibility that apolipoprotein (apo) E, angiotensin-converting enzyme (ACE), interleukin-6 (IL-6) genotype<sup>[23]</sup> and lipoprotein lipase (LPL) genotype effect in responses to exercise and physical activity in hypertension.<sup>[24,25]</sup> Also, SUA level is affected by age and by genetic and environmental factors.<sup>[26]</sup> These interpersonal and interracial differences clearly indicate the needs for study on pure older black African population. Therefore, the purpose of the present study was to investigate the effect of continuous training program on blood pressure, SUA, and psychosocial stress of pure black African subjects with hypertension.

## Subjects and Methods

### Subjects

Population for the study was male essential hypertensive subjects attending the hypertensive clinic of Murtala Muhammed Specialist Hospital, Kano, Nigeria. Subject were fully informed about the experimental procedures, risk and protocol, after which they gave their informed consent in accordance with the American College of Sports Medicine<sup>[27]</sup> guidelines, regarding the use of human subjects as recommended by the human subject protocol. Ethical

approval was granted by the Ethical Committee of Kano State Hospitals Management Board.

### Inclusion criteria

Only those who volunteered to participate in the study were recruited. Subjects between the age range of 50 and 70 years with chronic mild to moderate and stable (>1 year duration) hypertension (SBP between 140 and 179 and DBP between 90 and 109 mmHg) were selected. Only those who had stopped taking antihypertensive drugs or on a single antihypertensive medication were recruited.<sup>[28]</sup> They were sedentary and have no history of psychiatry or psychological disorders or abnormalities.

### Exclusion criteria

Obese or underweight (BMI between 20 and 30 kg/m<sup>2</sup>), smokers, alcoholic, diabetic, other cardiac, renal, respiratory disease patients were excluded. Those involved in vigorous physical activities and above averagely physically fit (VO<sub>2</sub> max > 27 and > 33 ml/kg min for over 60 and 50 years old, respectively) were also excluded.

A total of 323 chronic and stable, essential mild to moderate male hypertensive patients satisfied the necessary study criteria. Subjects were aged matched and randomly grouped into experimental (162) and control (161) groups.

## Procedure

Research design: In the present study, age matched randomized independent groups design was used to determine the influence of the continuous training program on cardiovascular parameters. All procedures were conducted at the physiotherapy department of MMSH, Kano, Nigeria.

### Pretest procedure

Wash out period: All subjects on antihypertensive drugs were asked to stop all forms of medication and in replaced, were given placebo tablets (consisted of mainly lactose and inert substance).<sup>[28,29]</sup> Also subjects including those not on any antihypertensive medications were placed on placebo tablets for one week (7 days); this is known as "Wash out period." The purpose of the wash out period was to get rid of the effects of previously taken antihypertensive drugs/medications. During the wash out period all subjects were on medical monitoring and were instructed to report to the hypertensive clinic for daily blood pressure monitoring and general observation. The Pretest and posttest procedures were conducted at the last day of the wash out period.

### Physiological measurement

Subjects resting heart rate (HR), SBP, and DBP were monitored from the right arm as described by Musa *et al.*,<sup>[30]</sup> using an automated digital electronic BP monitor (Omron digital BP monitor, Model 11 EM 403c; Tokyo Japan).

## Anthropometric measurement

Subjects' physical characteristics (weight [kg] and height [m]) and body composition (body mass index [BMI] ( $\text{kg}/\text{m}^2$ )) assessment was done in accordance with standardized anthropometric protocol.<sup>[31,32]</sup>

Blood sample collection (venipuncture method): Both pre- and post-treatment venous blood samples were obtained after about 12 h overnight fast (fasting blood sample). Five milliliter syringe was used for blood sample collection, using the procedure described by Bachorik.<sup>[33]</sup> All samples were stored in a refrigerator at  $-80^\circ\text{C}$  until analysis.<sup>[34]</sup>

Uric acid analysis: Uric acid analysis was determined using commercial enzymatic colorimetry method (PAP-Method) using the Human Kit (Human Gesellschaft Biochemical Diagnostic mbH, Germany) as recommended by the manufacturer.

## Psychosocial assessment

Subjects were in a comfortable sitting position and were presented with a questionnaire tagged the General Well Being Schedule (GWBS). Subjects were instructed to respond to the subscales of the 18 items questions. Subjects were timed for a maximum of 20 min and the questionnaire collected immediately. High values indicate high psychosocial well-being or decrease psychosocial stress. The questionnaire was developed and validated by the National Centre for Health Statistics.<sup>[35]</sup>

## Stress test

The Young Men Christian Association (YMCA) submaximal cycle ergometry test protocol was used to assess subject's aerobic power ( $\text{VO}_2$  max) as described by ACSM.<sup>[36]</sup> The stress test (pre and post training) was conducted under the supervision of experts in basic life support care and the emergency unit of the hospital was made ready to accommodate any incident that might occur during the stress test.

## Test procedure

### Training program

Following stress test and prior to the exercise training, all subjects in both control and continuous groups were reassessed by the physician and were prescribed with antihypertensive drug; methyldopa as necessary. Methyldopa was preferred because it does not alter normal hemodynamic responses to exercise<sup>[37]</sup> and it is a well-tolerated antihypertensive drug in the Africa<sup>[38]</sup> and mostly prescribed in the northern part (Kano) of Nigeria where the study was conducted and useful in the treatment of mild to moderately severe hypertension.<sup>[39]</sup> Subjects maintain these prescriptions with regular medical consultation and observation throughout the period of exercise training.

### The continuous group (group 1)

Subjects in the continuous group exercised on a bicycle ergometer at a low intensity of between 60% and 79% of

their HR max as recommended by ACSM.<sup>[27]</sup> The starting workload was 100 kg (17 W) which was increased at a pedal speed of 50 r/min to obtain a HR max reserve 35% was increased in the first two weeks to and level up at 59% HR max reserve throughout the remaining part of the training period. The initial of exercise session was increased from 45 minutes in the first two weeks of training to and leveled up at 60 min throughout the remaining part of the training. Exercise session of three times per week was maintained throughout the 8 weeks training period for continuous group.

### The control group (group 2)

Subjects in the control group were instructed not to undertake any vigorous physical activity during the 8 weeks period of study.

## Posttest procedure

Wash out Period: At the end of the 8 weeks training period, all subjects were asked to stop methyldopa and subjects were prescribed with placebo tablets for one week as in pretest procedure.

Post training SBP, DBP, psychosocial status assessment and stress test were conducted as earlier described in the pretest procedures using standardized protocols, techniques and methods.

All pre- and post-test measurements were recorded on a data sheet. Two hundred and seventeen subjects (112 from continuous, and 105 from control group) completed the eight weeks training program. One hundred and six subjects (50 from continuous, and 56 from control group) had dropped out because of noncompliance, unfavorable responses to methyldopa, and exercise training or had incomplete data; therefore, the data of 217 subjects were used in the statistical analysis [Figure 1].

## Statistical analysis

Following data collection, the measured and derived variables were statistically analyzed. The descriptive statistics (means and standard deviations) of the subjects physical characteristics, estimated  $\text{VO}_2$  max, psychosocial status, and cardiovascular parameters were determined. Student's *t*-test and Pearson product moment correlation test were computed for the variables of interest. In the *t* and correlation tests, the difference between subjects post-training and pre-training measurements (changed score) were used as dependent measures. The score changed was the difference between the posttest and pretest values. All statistical analysis was performed on a Toshiba compatible microcomputer using the statistical package for the social science (SPSS) Version 16.0, (Chicago IL, USA). The probability level for all the above tests was set at 0.05 to indicate significance.

## Results

The subject's age ranged between 50 and 70 years. Mean age, height, weight, and BMI of subjects in continuous exercise group were (58.63 (7.22) years, 1.73 (6.97) m, 67.49 (10.16) kg, 22.48 (2.89) kg m<sup>-2</sup>), respectively, while for the control group mean age, height, weight and BMI were (58.27 (6.24) years, 1.68 (5.31) m, 68.47 (17.07) kg, 23.37 (5.31) kg m<sup>-2</sup>, respectively). There was no significant difference in age ( $P = .697$ ), baseline SBP ( $P = 0.597$ ), baseline DBP ( $P = 0.597$ ), baseline SUA ( $P = 0.969$ ) and baseline VO<sub>2</sub> max ( $P = 0.685$ ) between groups. The physical characteristics of the subjects are comparable [Table 1].

Groups pre and post treatment mean BP (SD) mmHg; psychosocial status, SUA (mg/dl) and VO<sub>2</sub> max ml kg<sup>-1</sup> min<sup>-1</sup> are depicted in Table 2. Changed score values and Student's *t*-test results [Table 3] indicated a significant effect in the exercise groups over control in SBP ( $P < 0.001$ ), DBP ( $P = 0.040$ ), psychosocial status ( $P < 0.001$ ), SUA ( $P < 0.001$ ) and VO<sub>2</sub> max ( $P < 0.001$ ) at  $P < 0.05$ .

There was a significant positive and negative correlation between changes between VO<sub>2</sub> max and psychosocial status ( $r = 0.399$ ) and SUA ( $-0.266$ ), respectively, at  $P < 0.01$  [Figure 2].

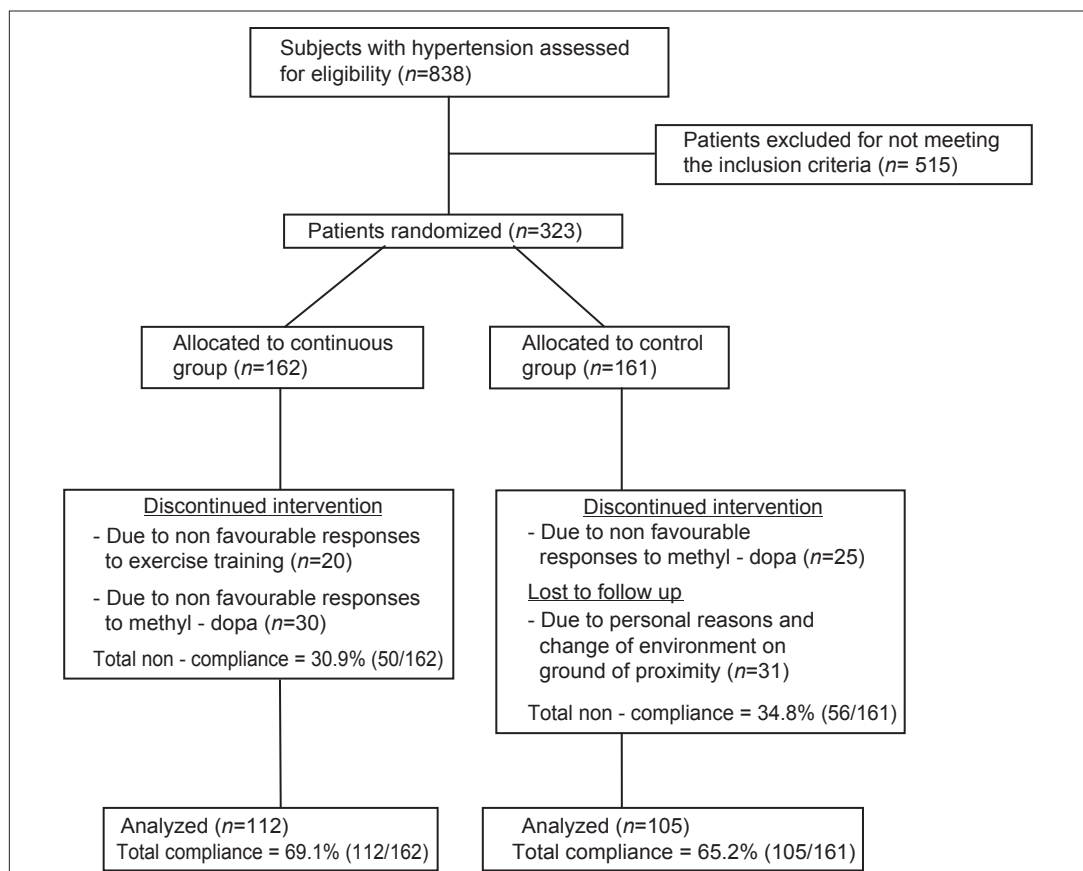
## Discussion

Findings from the present study revealed a significant decrease in SBP, DBP, SUA and increase in VO<sub>2</sub> max in the continuous group over control group. The favorable changes resulting from aerobic training in both SBP and DBP demonstrated in the present study is consistent with several other studies.<sup>[40-43]</sup> Also, result of the present study indicated a significant increase in psychosocial wellbeing (reduction in psychosocial stress) and significant decrease in SUA in the continuous group over control group.

### Psychosocial status

The favorable changes resulting from aerobic training on psychosocial status as demonstrated in the present study is consistent with the study of Smith *et al.*,<sup>[44]</sup> they investigated the effect of aerobic exercise on 133 sedentary hypertensive (SBP:130-180 mmHg; DBP:85-110 mmHg) males and females. Participants were grouped into aerobic group, aerobic with weight reduction group and control group, participants engaged in 6 months treatment period. They reported a significant decreased in self-reported depressive syndrome in the treatment groups compare to the placebo group.

The observation in the present study is also in line with a study by Ulrik *et al.*,<sup>[45]</sup> and Kloczek *et al.*,<sup>[46]</sup> though on heart failure



**Figure 1:** Study design flow chart.

Psychosocial  $r = 0.399^{**}$  SUA  $r = -0.266^{**}$  significant at 0.01\*\*

**Table 1: Groups mean (SD) base line characteristics and independent t-test (n = 217)**

Variables	Continuous group (n = 112) X (SD)	Control group (n = 105) X (SD)	t values	P values
Age (years)	58.63 (7.22)	58.27 (6.24)	0.390	0.697
SBP (mmHg)	170.45 (15.57)	160.87 (13.23)	0.540	0.597
DBP (mmHg)	97.56 (7.53)	97.17 (1.43)	0.530	0.597
VO <sub>2</sub> max (ml/kg/min)	20.69 (12.49)	21.23 (5.76)	0.406	0.685
SUA (mg/dl)	4.69 (1.56)	4.68 (1.29)	0.038	0.969
Weight (kg)	67.48 (10.16)	68.47 (17.07)	-0.514	0.608
BMI (kg/m <sup>2</sup> )	22.92 (2.20)	23.37 (3.87)	-1.060	0.290

\*Significant, P &lt; 0.05

**Table 2: Groups mean (SD) pretest and posttest values (n = 217)**

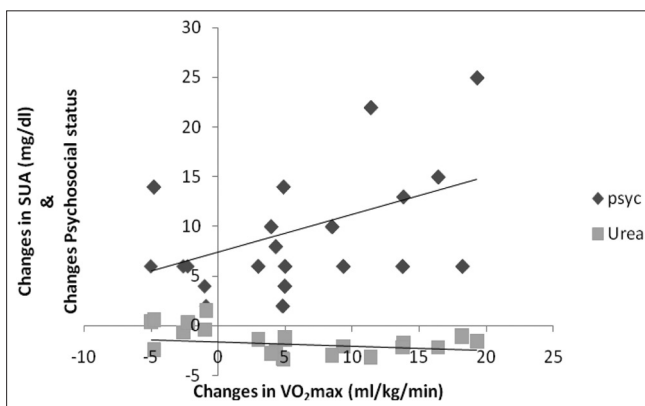
Variables	continuous pretest X (SD)	continuous posttest X (SD)	control pretest X (SD)	control posttest X (SD)
SBP (mmHg)	170.45 (15.57)	157.82 (23.91)	160.87 (13.23)	163.47 (14.88)
DBP (mmHg)	97.56 (7.53)	94.83 (7.21)	97.17 (1.43)	96.10 (2.61)
VO <sub>2</sub> max (ml/kg/min)	20.69 (12.49)	28.68 (13.60)	21.23 (5.76)	22.82 (7.44)
Psychosocial status	59.94 (9.09)	71.69 (5.95)	63.93 (10.28)	65.27 (10.47)
SUA (mg/dl)	4.69 (1.56)	2.73 (1.29)	4.68 (1.29)	3.99 (1.75)

\*Significant, P &lt; 0.05

**Table 3: Independent t-test between groups changed score (pretest–post-test values) values (n= 217)**

Variables	Continuous changed score X (SD)	Control changed score X (SD)	P values
SBP (mmHg)	-13.41 (6.95)	2.61 (7.85)	<0.001*
DBP (mmHg)	-7.41 (6.26)	-1.07 (1.76)	0.040*
VO <sub>2</sub> max (ml/kg/min)	7.99 (6.23)	1.59 (3.54)	<0.001*
Psychosocial status	10.44 (6.23)	1.33 (3.15)	<0.001*
SUA (mg/dl)	-1.96 (1.09)	4.68 (1.29)	<0.001*

\*Significant, P &lt; 0.05

**Figure 2:** Correlation between training changes in VO<sub>2</sub> max, SUA, and psychosocial status (n = 112)

and CHD patients, respectively. Both studies demonstrated significant improvement in the quality of life in the interval training over continuous. The mechanism of the superior effect of intensive physical training on the quality of life is not presently known, but it is reasonable to suggest that it is due to greater physiological adaptation and thereby improved capacity for activity in interval group.

Another similar result was reported by Georgiades *et al.*<sup>[47]</sup> in their study, they investigated the effects of exercise and

weight loss on cardiovascular responses during mental stress in mildly to moderately overweight patients with elevated blood pressure. Ninety-nine men and women with high normal or unmedicated stage 1 to stage 2 hypertension; (systolic blood pressure 130-179 mm×Hg, diastolic blood pressure 85-109 mm Hg), underwent a battery of mental stress tests, including simulated public speaking, anger recall interview, mirror trace, and cold pressor, before and after a 6-month treatment program. Subjects were randomly assigned to 1 of 3 treatments: (1) aerobic exercise, (2) weight management combining aerobic exercise with a behavioral weight loss program, or (3) waiting list control group. Their results demonstrated that exercise, particularly when combined with a weight loss program, can lower both resting and stress-induced blood pressure levels and hemodynamic pattern resembling that targeted for antihypertensive therapy.

However, a contradictory finding to the present study was reported by Pierce *et al.*<sup>[48]</sup> they investigated the effects of 16 weeks of physical exercise training on the psychological functioning of patients with mild hypertension. Ninety patients were examined at baseline and after 16 weeks of training, patients completed a psychometric test battery that included objective measures of neuropsychological performance and standardized self-report measures of psychosocial functioning. Patients were randomly assigned to 1 of 3 groups: aerobic

exercise, strength training and flexibility exercise, or a waiting list control group. After training, there were no group differences on any of the psychological measures. Another contradictory finding, though, on healthy subjects was reported by Kohut *et al.*<sup>[49]</sup> They investigated the effect of aerobic exercise on psychosocial scores (depression, optimism, sense of coherence), sixty four years healthy old adults, also subgroup of subjects treated with non selective beta (1) beta (2) adrenergic antagonist were assigned to either aerobic exercise or control for 3 days /week, 45 min for 10 months. They reported non-significant effect of aerobic exercise compared to control on psychosocial scores.

The reasons for discrepancies in findings between the present study and others might not be unconnected to the type, mode, frequency, duration of intervention, condition of subjects that varied across studies. The mechanisms responsible for exercise-related improvements in psychosocial status are not known. However, a number of psychological factors have been proposed to explain the effect that exercise has on depressed mood including increased self-efficacy, a sense of mastery, positive thoughts, distraction from negative thoughts, and enhanced self-concept. Also a number of biologic pathways also have been suggested including increased central norepinephrine neurotransmission,<sup>[50,51]</sup> alterations in the hypothalamo-pituitary-adrenocortical axis,<sup>[52]</sup> and increased secretion of amine metabolites as well as serotonin synthesis and metabolism.<sup>[53-55]</sup>

### Serum uric acid

The present study also demonstrated a significant reduction in exercise group serum uric acid level over control. This finding is in line with the report of Filipovsky *et al.*,<sup>[56]</sup> who investigated the effect of 5 weeks aerobic physical training course on uricaemia levels of 77 sedentary subjects with hypertension. They reported significant decrease in uric acid level at  $P < 0.001$ . This significant change persisted up to between 3 and 7 months after the intervention of exercise training. They concluded that 5-week intensive physical training had a favorable on both short and long-term effect on uricaemia levels in hypertension. Langlois *et al.*,<sup>[57]</sup> reported a contrary notion; they investigated whether uric acid (UA) status is related to lower limb function in hypertensive with peripheral arterial disease (PAD). One hundred and forty five nonhypertensive subjects with PAD and 166 subjects with hypertension and PAD participated. Subjects involved in aerobic exercise on treadmill. They reported a significant increased in serum uric acid concentration in PAD hypertensive (404 (101) versus 347 (80)  $\mu\text{mol/l}$ ,  $P < 0.001$ ).

Leyver *et al.*,<sup>[58]</sup> investigated the relationship between SUA concentrations and the measures of functional capacity. Fifty nine patients with a diagnosis of chronic heart failure due to coronary heart disease ( $n = 34$ ) or idiopathic dilated cardiomyopathy ( $n = 25$ ) and 20 healthy controls underwent

assessment of functional capacity. Maximal oxygen uptake ( $\text{VO}_2 \text{ max}$ ) and SUA were measured during a maximal treadmill exercise test. They reported an inverse relationship between SUA concentrations and measures of functional capacity in patients with cardiac failure. They concluded that the strong correlation between SUA and  $\text{VO}_2 \text{ max}$  suggests that in chronic heart failure increased SUA concentrations reflect an impairment of oxidative metabolism.

## Conclusion

The present study supports the recommendations of moderate intensity (continuous) training program in blood pressure reduction and dual therapeutic effects on psychosocial stress reduction and SUA in the management of hypertension.

### Clinical rehabilitation impact

The study demonstrated a rationale for the adjunct therapeutic role of moderate intensity training in the down regulation of blood pressure, SUA and psychosocial stress management. Therefore, exercise specialists and other professionals in rehabilitation should feel confident in the use of this mode of training in the non-pharmacological adjunct multipurpose management of hypertension.

### Limitation

The present study demonstrated a rationale bases for the role of continuous exercise training in the down regulation of the blood pressure, SUA and psychosocial stress. However, the limitation of the study includes failure to perform the intension-to-treat analysis (ITTA) in the randomized controlled trial. Though, it has been reported that ITTA provides unbiased assessments of treatment efficacy,<sup>[59]</sup> however, on-treatment analysis (per protocol analysis) has the advantage that it provides for a new treatment to show additional efficacy and it most closely reflects the scientific model underlined in the protocol.<sup>[60]</sup> These limitation however, warrants attention in future studies.

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