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Effectiveness of High-Intensity Interval Training and Continuous Moderate-Intensity Training on Blood Pressure in Young Physically Inactive Pre-Hypertensive Adults

Short title: Aerobic Training and Blood Pressure

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Abstract

The likelihood of a pre-hypertensive young adult to develop hypertension has been steadily increasing over the past few years. Aerobic exercise training (AET) has been found to reduce high blood pressure, however, efficacy of different types of aerobic exercise is yet to be determined among the pre-hypertensive young adults. The objective of this study was to evaluate the effectiveness of high-intensity interval training (HIIT) and continuous moderate-intensity training (CMT) on blood pressure (BP) in young physically inactive pre-hypertensive adults. 32 adults (age 20.0±1.1) were randomly assigned into 3 groups; HIIT, CMT, and control (CON). HIIT and CMT groups participated in 5 weeks of AET with CON group not participating in any exercise. The HIIT protocol consisted of 1:4 minute work to rest ratio of participants 80%-85% heart rate reserve (HR-reserve) and 40%-60% HR-reserve respectively for 20 minutes, CMT group exercised at 40%-60% of HR-reserve continuously for 20 minutes. In both HIIT and CMT groups, systolic blood pressure (SBP) (3.8±2.8 mmHg, P=0.002 VS 1.6±1.5 mmHg, P=0.011) was significantly reduced. While, significant reductions were noted in the diastolic blood pressure (DBP) (2.9±2.2 mmHg, P=0.002) and mean arterial pressure (MAP) (3.1±1.6mmHg, P<0.0005) only in the HIIT group. No significant difference in SBP (-0.4±3.7 mmHg, P=0.718), DBP (0.4±3.4 mmHg, P=0.714), or MAP (0.1±2.5mmHg, P= 0.892) was observed in the CON group. Both HIIT and CMT decreased the BP in physically inactive pre-hypertensive young adults; however, HIIT yielded more beneficial results in terms of reducing the SPB, DBP, and MAP.

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1 | INTRODUCTION

Hypertension is considered as one of the main precursors of cardiovascular diseases (CVD) worldwide, which has attributed to 7.7 million deaths globally.[1,2] Seventh Joint National Committee (JNC7) report defined pre-hypertension as systolic blood pressure (SBP) of 120 mmHg to 139 mmHg and diastolic blood pressure (DBP) of 80 mmHg to 89 mmHg.[3] There is an increased risk of developing hypertension in individuals with pre-hypertension, and it has been estimated that people having blood pressure (BP) values ranging between 130–139 mmHg/80–89 mmHg are twice more likely to develop hypertension than those with lower values.[4] Modifiable risk factors of hypertension can be controlled by engaging in physical exercises.[3,5] To prevent the progressive rise in BP and cardiovascular diseases, control of pre-hypertension, and lifestyle modifications require special attention.[6]

Studies have suggested that physical exercise can cause beneficial alterations in insulin sensitivity, autonomic nervous system function and vasoconstriction which may prevent pathological increase in BP.[7,8] Physical exercise can increase blood supply to the brain, it can improve the release of growth factors from skeletal muscles into the bloodstream, stimulating angiogenesis, facilitating neurogenesis and inducing endothelial cell proliferation as well as subsequent endothelial cell membrane permeability, thus, leading to substantial reduction in BP and attenuation of hypertension symptoms.[9-11]

An estimated 9% premature mortality causing approximately 5.3 million deaths worldwide in 2008 occurred due to physical inactivity.[12] Regular physical exercise is an well-established intervention for the prevention and treatment of several chronic diseases,[13] and it has shown significant effect on reducing the BP.[14] Physical exercise has also been shown to improve several factors involved in the pathophysiology of hypertension[15-18] which can extenuate BP in both hypertensive and non-hypertensive adults.[15,19] Continuous moderate-intensity training

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(CMT) method sustained for 30 minutes or more is traditionally recommended for the prevention and treatment of high BP.[13,20]

High-intensity interval training (HIIT) has been documented as a safe and effective method of training,[21] but its efficacy in reducing BP among pre-hypertensive young adults is not well-established.[22] HIIT can be defined as a short burst of maximal effort interspersed by a few minutes of rest or active recovery, and it has been reported to be more effective than CMT for improving cardiorespiratory fitness in different populations.[16-18, 23-25] HIIT that consists of several bouts of high-intensity exercise (~85% to 95% of HRmax) lasting 1 to 4 minutes interspersed with intervals of rest or active recovery[15,17,18] has been found to improve endothelial functions and its markers[16,18] insulin sensitivity,[18] markers of sympathetic activity,[16,17] arterial stiffness,[15,16] blood glucose and lipoproteins.[18] The purpose of this study was to determine the effects of HIIT and CMT on the BP of physically inactive pre-hypertensive young adults and also to determine which type of training is more efficient in lowering the SBP and DBP of this population. This is the very first study targeting pre-hypertensive young adults and being conducted in Malaysia.

2 | MATERIALS & METHODS

2.1 | Study setting and subjects

This 5-week randomized-controlled trial was conducted in the Physiotherapy Centre at the Faculty of Medicine and Health Sciences in University Tunku Abdul Rahman, Sungai Long Kajang, Malaysia. The study subjects were reached through university portal, emails and posters for voluntary participation. Participants were recruited by convenience sampling as the study population required young adults with pre-hypertension. A total of 87 subjects were initially screened, out of which only 32 adults fit in the eligibility criteria after they were administered with the International Physical Activity Questionnaires (IPAQ) and Physical

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Activity Readiness Questionnaire (PAR-Q+). The study participants (22 males and 10 females) were randomly selected using computer generated numbers and allocated into 3 groups; high-intensity interval training (HIIT), continuous moderate-intensity training (CMT) and control group (CON).

Inclusion criteria comprised of both genders, aged between 18-25 years old, physically inactive with SBP between 120-139 mmHg and/or DBP between 80-89 mmHg. Participants with known history of respiratory illnesses (COPD, asthma), cardiovascular diseases, obesity, psychological disorders, musculoskeletal problems, taking anti-hypertensive medications, and active smokers were excluded from this study.

The protocol was based on the Helsinki Declaration Accord (World Medical Association for Human Subjects). Moreover, prior ethical clearance was obtained from the Universiti Tunku Abdul Rahman's Scientific and Ethical Review Committee (U/SERC/77/20); written informed consent was taken from each participant after debriefing them about the benefits, potential risks of muscle soreness, strict maintenance of confidentiality of the obtained information, and right to withdraw from the study at any time.

2.2 | Blood Pressure Measurement

Following the standard procedure, participants' BP from the right brachial artery was measured using an automated digital BP monitor (OMRON SEM-1) after 5 minutes of rest in a chair. Each participant's right arm was supported on the table at their heart level and both SPB and DBP was measured 3 times with 5 minutes interval between each measurement in order to obtain the most accurate result. If the difference between the BP readings were more than 5 mmHg, the measurement was taken again after a 5 minutes interval. BP was measured at the baseline before beginning the intervention and at the end of 5 weeks of intervention. Post-test measurement of BP was carried same way as recorded at the baseline. In addition,

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mean arterial pressure (MAP) was estimated also at baseline and at the end of intervention with the following formula.

MAP = DBP + 1/3(SBP – DBP)

2.3 | Exercise intervention protocol

Before the first exercise session, the subjects' heart rate (HR) was measured using a pulse oximeter (JD0486G). To calculate the exercise HR, (HRmax) of the participants in HIIT and CMT groups were calculated using the newest age-based formula, [HRmax = 211-(0.64*age)]**.** The exercise HR was then calculated using the Karvonen formula [Exercise HR = % of target intensity (HRreserve) + HRrest]. To prevent the delayed onset muscle soreness (DOMS), and to acclimatize all the physically inactive participants in both exercise groups to the exercise regimen, 1 week of familiarization period was provided with a total of 3 exercise sessions on alternate days. Participants in both the experimental groups performed a 5-minute warm-up followed by 20 minutes of continuous running on treadmill without inclination at 40% -60% of their HR-reserve. Before ending the exercise session, 5 minutes of cool-down period was performed by all the participants by walking on same treadmill at their own comfortable pace. A pulse oximeter was kept on the index finger of the participants during their exercise sessions to monitor their HR. After the familiarization period of 1 week, the HIIT group proceeded to 4 weeks of HIIT consisting of 20 minutes of treadmill running with a 1:4 minute work to rest ratio with an upper HR target at 80% - 85% of HR-reserve and a lower HR target at 40% - 60% of HR-reserve. The CMT group continued with 4 weeks of the same exercise protocol on treadmill that was carried out in the familiarization period at intensity of 40% -60% of their HR-reserve. The indication for termination of the exercise sessions was followed according to ACSM's guidelines.

The CON group did not participate in any exercise program, they were instructed to follow Dietary Approaches to Stop Hypertension (DASH) diet and restrict the sodium intake

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(<100mmol/day) according to the JNV VIII guidelines. In addition to the hand-out of the guidelines given, each participant in the CON group were reminded via telephone calls once weekly about DASH diet and sodium restriction to strictly follow the guidelines.

All the participants in the 3 groups were instructed not to engage in any other form of physical activity during these 5 weeks to prevent any extraneous effect on the outcomes. In addition, to avoid the acute effects of post-exercise on BP, participants were also instructed not to perform any exercises 24 hours prior to post-test BP measurement. In accordance with the CONSORT statement, detailed description of this clinical trial is shown in the figure 1 below.

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Figure 1. CONSORT Diagram

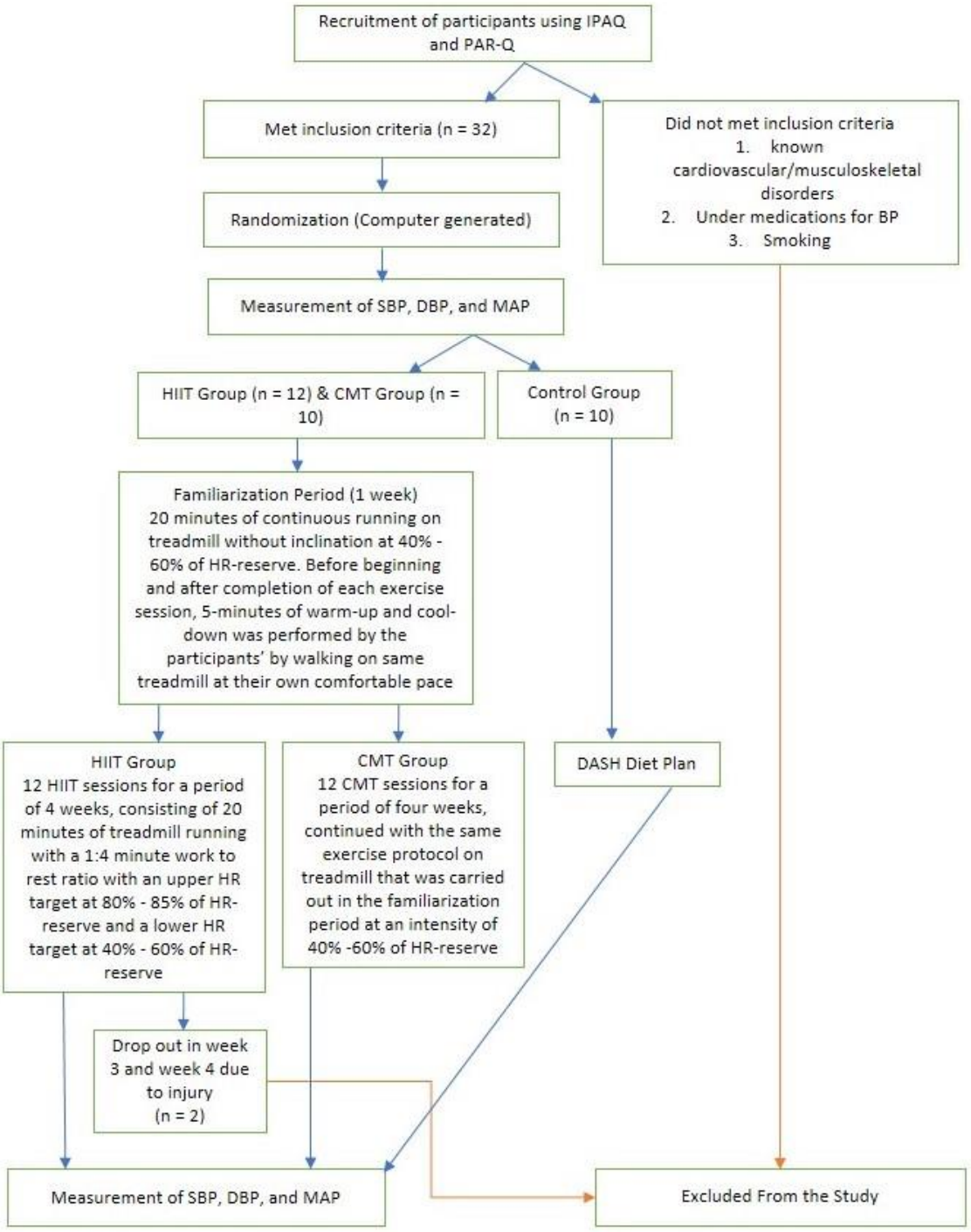

Figure 1: Flowchart on whole procedure; IPAQ = International Physical Activity Questionnaire; PAR-Q = Physical Activity Readiness Questionnaire; SPB = Systolic Blood Pressure; DBP = Diastolic Blood Presure; MAP = Mean Arterial Pressure; HIIT = High Intensity Interval Training; CMT = Continuous Moderate-Intensity Training; HR-reserve = Heart Rate Reserve

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2.4 | Statistical analysis

Results are presented as mean±SD for continuous variables. Continuous variables were compared by using the paired sample t-test (within groups) and ANOVA (between groups). All reported probability values were 2-sided, and a probability value of <0.05 was considered statistically significant. The data were processed using the Statistical Package for Social Science (SPSS) version 26.0.

3 | RESULTS

3.1 | Descriptive statistics

At the beginning of this study, 32 participants were randomly assigned into HIIT (6 males and 6 females), CMT (6 males and 4 females), and the CON group (10 males). Two participants dropped out from the HIIT group (both males) during the third and fourth week of training due to musculoskeletal injury.

3.2 | Comparison within the groups

Table 1 depicts that the CON group has the highest baseline and post intervention SBP mean values of 127.93±5.09mmHg and 128.37±5.32mmHg respectively. The HIIT group has the highest baseline DBP (78.57±5.36mmHg) and CMT group has greater post-test DBP (75.73±4.26). At baseline, MAP was highest in CMT group (93.20±2.89), and greater in CON group (91.86±4.18) at post-test.

Table 1. All groups' SBP and DBP Mean (X) with standard deviation (SD)

	HIIT Group X±SD		CMT Group X±SD		CON Group X±SD	
	PRETEST	POSTTEST	PRETEST	POSTTEST	PRETEST	POSTTEST
SBP	122.76±2.	119±3.91	125.23±3.7	123.67±3.9	127.93±5	128.37±5.3

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(mmHg)	65		6	8	.09	2
DBP (mmHg)	78.57±5.36	75.63±4.86	77.23±4.54	75.73±4.26	74.00±6.23	73.60±5.78
MAP (mmHg)	93.14±3.46	90.09±2.57	93.20±2.89	91.71±3.08	91.98±4.62	91.86±4.18

Table 2 illustrates the results of paired sample t-test. In CON group, a mean difference of -0.43 (p-value = 0.718 > 0.05) for the SPB was seen, indicating non-significant difference between the pre-SBP and post-SBP. For the DBP, the mean difference of 0.40 (p-value = 0.714 > 0.05) was found, showing no significant difference between the pre-DBP and post-DBP for CON group. Similarly, MAP did not exhibit any significant difference (mean = 0.11, p-value = 0.892). For CMT group, a mean difference of 1.57 (p-value = 0.011 < 0.05) was observed in terms of SBP which was statistically significant. However, for the DBP, the mean difference between the pre-test and post-test was 1.50 (p-value = 0.161 > 0.05), depicting a non-significant difference between the pre-DBP and post-DBP in the CMT group. MAP in CMT group showed an insignificant reduction of mean (1.49, p-value = 0.054). A mean difference of 3.76 (p-value = 0.002 < 0.05) was found in HIIT group for the SBP, and 2.93 (p-value = 0.002 < 0.05) for DBP, inferring a statistically significant difference between the pre-test and post-test of both SPB and DPB respectively in the HIIT group. Similar result was noticed in MAP with a significant mean difference of 3.05 (p-value < 0.0005)

Table 2. Paired Sample t-Tests for SBP and DBP in the CON Group, CMT Group and HIIT Group

	Paired Differences				
Groups	Mean	Std. Deviation	t	df	p-value

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CON Group						
Pair 1	Pre-SBP mean - Post-SBP mean	-0.43	3.68	-0.37	9	0.718
Pair 2	Pre-DBP mean - Post-DBP mean	0.40	3.35	0.38	9	0.714
Pair 3	Pre-MAP mean - Post-MAP mean	0.11	2.50	0.14	9	0.892
CMT Group						
Pair 1	Pre-SBP mean - Post-SBP mean	1.57	1.54	3.22	9	0.011
Pair 2	Pre-DBP mean - Post-DBP mean	1.50	3.10	1.53	9	0.161
Pair 3	Pre-MAP mean - Post-MAP mean	1.49	2.12	2.22	9	0.054
HIIT Group						
Pair 1	Pre-SBP mean - Post-SBP mean	3.76	2.83	4.20	9	0.002
Pair 2	Pre-DBP mean - Post-DBP mean	2.93	2.23	4.16	9	0.002
Pair 3	Pre-MAP mean - Post-MAP mean	3.05	1.64	5.90*	9	<0.0005

Paired sample t test was performed, level of significance at $P < .05$

3.3 | Comparison between the groups

For the SBP, the F-test (ANOVA) result is 5.02 (p-value = 0.014 < 0.05) (Table 3). Therefore, it can be concluded that there are significant differences in the mean SBP across

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the 3 groups. However, for the DBP, the F-test statistics is 1.87 (p-value = 0.173 > 0.05) indicating a non-significant difference among the 3 groups. MAP F-test was 4.76 (p-value = 0.017 < 0.05), showing a significant difference between 3 groups.

Table 3. Comparison of SBP mean difference and DBP mean difference across the three groups

ANOVA						
		Sum of Squares	df	Mean Square	F	p-value
SBP	Between Groups	69.72	2	34.86	5.02*	0.014
	Within Groups	187.53	27	6.95		
	Total	257.25	29			
DBP	Between Groups	32.25	2	16.12	1.87	0.173
	Within Groups	232.47	27	8.61		
	Total	264.71	29			
MAP	Between Groups	43.08	2	21.54	4.76*	0.017
	Within Groups	122.13	27	4.52		
	Total	165.21	29			

One-way ANOVA was performed, level of significance at $P < .05$

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Since ANOVA showed significant difference in SBP and MAP across the 3 groups, a post-hoc test (Tukey test) was performed to investigate which pairs of the groups are different in terms of the mean SBP and mean MAP. We found that SBP mean difference of HIIT and CMT group is statistically insignificant (p-value = 0.282 > 0.05) (Table 4). However, we noticed a significant SBP mean difference between the HIIT group and the CON group (p-value = 0.010 < 0.05), but, SBP mean difference between CMT and CON group is statistically insignificant (p-value = 0.258 > 0.05). MAP did not show any significant mean difference between HIIT and CMT groups (p-value = 0.244 > 0.05), and between CMT and CON groups (p-value = 0.337 > 0.05). However, a significant mean difference in MAP was seen between HIIT and CON groups (p-value = 0.013 < 0.05). Hence, we can conclude that HIIT is more effective in reducing the SBP, DBP, and MAP as compared to CMT.

Table 4. Post-hoc test (Tukey test)

Dependent Variable	(I) Group	(J) Group	Mean Difference (I-J)	p-value
SBP	HIIT	CMT	-1.83	0.282
		CON	-3.73*	0.010
	CMT	HIIT	1.83	0.282
		CON	-1.90	0.258
	CON	HIIT	3.73*	0.010
		CMT	1.90	0.258
MAP	HIIT	CT	-1.57	0.244
		CON	-2.93*	0.013
	CMT	HIIT	1.56	0.244

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		CON	-1.37	0.337
	CON	HIIT	2.93*	0.013
		CMT	1.37	0.337

Post-hoc (Tukey) test was performed, level of significance at $P < .05$

4 | DISCUSSION

This study showed beneficial effects of HIIT and CMT on the resting BP of physically inactive young adults with pre-hypertension. It is evident from the findings of the current study that both HIIT and CMT can reduce SBP significantly among pre-hypertensive young adults. Previous meta-analysis revealed that two most prominent intervention protocols HIIT and CMT were effective in reducing SBP in adults with pre- to established hypertension.[22] Our findings correlate with a study that compared the effects of continuous and interval training in the management of hypertension, where researchers found SBP reduction in both experimental groups (-16.4±13.2 mmHg and -13.9±12.6 mmHg respectively).[26] Similar results were derived from the systematic review by Punia S et al in 2016.[27] Our study revealed significant reductions in SBP after conducting 5 weeks of HIIT and CMT programs. Therefore, in addition to lowering SBP among the hypertensive population, HIIT and CMT can be useful tools in reducing the SBP among pre-hypertensive young adults.

Current study demonstrates significant reduction of DBP among the participants undergoing HIIT exercise protocol whereas non-significant reduction of DBP was observed among the CMT and control group. Previous literature[28] suggests that HIIT demonstrated greater improvements in the endothelial function and arterial stiffness as compared to CMT. This explains the increased BP reduction in the HIIT group as endothelium plays a pivotal role in homeostasis and maintenance of vascular tonus which can be a contributing factor in BP reduction. A recent randomized clinical trial also revealed similar results where the authors

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found a significant reduction in SBP but non-significant reduction in DBP.[29] Although the decrease in DBP of the CMT group was statistically non-significant in this study, if given a longer intervention period there would be a more obvious result as most studies have confirmed a significant reduction in DBP following 8 weeks or more of continuous exercise in hypertensive and normotensive adults.[30,31] Interestingly in the current study, within a time frame of 5 weeks, HIIT showed efficacy to reduce DBP significantly. Therefore, HIIT could be a better option to control DBP among pre-hypertensive young adults.

MAP measures the pressure necessary for adequate perfusion of the organs of the whole body. Therefore, it could be a better indicator of perfusion than SBP. High MAP can be detrimental leading towards morbid conditions like ventricular hypertrophy, myocardial infarction and stroke. HIIT intervention in this current study also demonstrated significantly greater reductions in the MAP as compared to CMT (3.05 vs. 1.49 respectively). Similar findings were reported in past studies, whereof, HIIT led to notable reductions in the MAP among pre-hypertensive subjects[32] and sedentary individuals.[33,34] Overall, the HIIT exercise resulted in significant BP reduction and favorable alteration in MAP, thus showing positive cardiovascular response post intervention. However, further studies are required to evaluate the potential mechanisms contributing to these physiological responses and changes in the pre-hypertensive population.

HIIT interventions are considered to be more effective and time-efficient interventions for BP and aerobic capacity level improvements as compared to other exercises.[35] Wahl P et al in 2013 found that HIIT stimulated a transient increase in the circulating levels of vascular endothelial growth factor and hepatocyte growth factor.[36] Thus, it can be postulated that HIIT intervention reduces BP by actively promoting and stimulating the angiogenic factors. Study by Ciolac et al showed that HIIT is far more superior in lowering the BP compared to CMT due to 3 factors; improving cardiorespiratory fitness, hormonal response and nitric oxide

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response which is a mediator of vasodilation in blood vessels that plays a major role in BP control.[37] It has been stated that HIIT interventions that lasts for 4-12 weeks duration are able to produce a larger decrease in SPB (-3.63mmHg) than other forms of exercise.[35] Previous studies also support that HIIT is superior to CMT in improving cardiorespiratory fitness and reducing BP among normotensive and hypertensive individuals,[16-18] but its efficacy in reducing BP among pre-hypertensive population needed further investigation. In the current study, there was a significant difference in the mean SBP across the three groups; HIIT, CMT and CON as revealed by ANOVA test. Further analysis by post-hoc test demonstrated a significant mean difference in the SBP between the HIIT group and CON group (p-value = 0. 010 < 0.05). However, there was an insignificant mean difference in the SBP between the CMT and CON group participants (p-value = 0.282 > 0.05). Additionally, HIIT was found to be effective in reducing the DBP significantly (p-value = 0.002 < 0.05). Although physical activity has been associated with reduced BP but there can be some variations due to different training modality, exercise prescription, intensity, frequency and the duration of intervention.[28] Nevertheless, the current study clearly demonstrates that HIIT is superior to CMT in controlling the progression of pre-hypertension towards hypertension in Malaysian young adults.

Studies by Stephen PJ et al and Paula TP et al revealed that the DASH diet and sodium restriction have significant effect on the reduction of SBP, DBP, and HR among hypertensive patients.[38,39] A recent meta-analysis also revealed similar observations.[40] Therefore, a possible reason why there was no reduction in SPB and DBP in the CON group could be due to non-adherence to the diet protocol, even after weekly reminders via phone calls to the participants for strict follow of the regimen. Although HIIT and CMT groups were not instructed to follow DASH diet and sodium restriction as the researchers aimed to determine the effectiveness of HIIT and CMT solely, however, a significant SBP reduction and non-

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significant DBP reduction was observed among the participants of CMT group. Whereas in the HIIT group, both SBP and DBP were significantly reduced after 5 weeks. This result suggests the efficacy of HIIT and CMT over DASH diet and sodium restriction only to control resting BP. Therefore, HIIT collectively with DASH diet and sodium restriction could be a better approach towards controlling pre-hypertension in a short frame of time.

5 | STUDY LIMITATIONS

Due to the time constraint and limited resources; the researchers were able to recruit only 32 participants for this research. Secondly, the HIIT and CMT groups, each consisted of 4 and 6 females in the respective groups; whereas the CON group consisted of all males due to the fact that many females were under hypotensive or normotensive categories. Dietary intake of the participants may also play a significant role when it comes to controlling the BP, since it was not possible to directly observe the participants in CON group and monitor their adherence to the DASH diet and sodium restriction. Therefore, future studies with bigger sample size, longer duration, and stringent control of the DASH diet and sodium restriction plan is highly recommended.

6 | CONCLUSION

HIIT is able to effectively reduce both SBP and DBP of the healthy physically inactive pre-hypertensive young adults but CMT reduced only the SBP in this study. Therefore, HIIT could be a promising alternative intervention to reduce BP and thus could be useful to prevent the progression of pre-hypertension towards hypertension among physically inactive young adults.

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CONFLICT OF INTEREST

The authors have no conflicts of interest.

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AUTHOR CONTRIBUTIONS

The conceptualization process involved Imtiyaz Ali Mir and Anil T John. Study design was carried out by Imtiyaz Ali Mir, Moniruddin Chowdhury, and Anil T John. Data collection was performed by Chao Yi Chong and Imtiyaz Ali Mir. Data analyses and interpretation was done by Imtiyaz Ali Mir, Moniruddin Chowdhury, Md. Rabiul Islam, Md Zobaer Hasan, and Yukihito Higashi. Manuscript drafting and critical review were performed by Anil T John, Imtiyaz Ali Mir, Moniruddin Chowdhury, Md. Rabiul Islam, Md Zobaer Hasan, Syeda Humayra, and Yukihito Higashi.

ETHICS STATEMENT

This study was conducted according to the Helsinki Declaration Accord. In addition, prior ethical clearance was obtained from the Universiti Tunku Abdul Rahman's Scientific and Ethical Review Committee (U/SERC/77/20), and written informed consent was taken from each participant.

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