Sports Medicine	(Original articles)
เวชศาสตร์การกีฬา	(นิพนธ์ต้นฉบับ)

VASOMOTOR RESPONSES OF CIGARETTE SMOKERS TO STIMULI USED IN SEVERAL VASCULAR RESPONSE TESTINGS

Thyon CHENTANEZ[1], Yaowalak ANOTHAYONONT[2], Panya KIMUK[3] and Tossaporn YIMLAMAI[4]

[1,3]College of Sports Science and [2]Police General Hospital
and [4]Department of Physiology, Faculty of Science Mahidol University

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ABSTRACT

This study was aimed to determine the chronic effects of smoking on vasomotor responses in healthy male volunteers with 20 – 45 years of age and working at the Police General Hospital. The volunteers were divided without randomization into 2 groups of 10 smokers and 10 nonsmokers. Then, the left arm and left leg of both groups were stimulated by hot water (42^0C) , cold water (12^0C), aerobic exercise and anaerobic exercise to legs. Vasomotor responses, physical performance, and Ankle Brachial Pressure Index (ABPI) changes before and after some of the above stimulations were calculated. The results were that vasomotor responses of blood vessels of the upper and lower extremities in nonsmokers was significantly greater than in smokers after stimulation by hot water, cold water and aerobic exercise; and a significant reduction of '*Ankle Brachial Pressure Index (ABPI)'* in nonsmokers after both exercises was found, which was similar to vasomotor response found by volumeter. In conclusion, smoking is associated with reduction in many physical performances, psycho-neurological performances and vasomeotor responses. This may explain how smoking may relate to atherosclerotic changes of blood vessels and the severity may depend on duration and the amount of smoking.

(Journal of Sports Science and Technology 2012;12 (2):87 - 106)

KEY WORDS; VASOMOTOR, EXERCISE, SMOKER, CIGARETTE, ANKLE BRACHIAL PRESSURE INDEX (ABPI).

INTRODUCTION

Cigarette smoking substantially increase the risk of cardiovascular disease, including coronary heart disease, stroke, peripheral artery disease and aortic aneurysm. The products of combustion in cigarette smoke contains at least 4000 chemical constituents, that are responsible for health damage, the 2 most prominent ones being nicotine and carbon monoxide. Nicotine alters the shape of arterial endothelial cells.

(1,2) The other important substance that disturbed modulating the oxygen supply of erythrocyte to the tissue periphery is carbon monoxide. The cigarette smoking is associated with blood vessel structural changes, increase in arterial wall stiffness and immediate endothelial dysfunction of the large arteries, which are associated with coronary heart disease and ischemic stroke (3).

Quillen and co-worker (1993) showed that 5 minutes after smoking one cigarette in normotensive man, the coronary blood flow velocity decreased by 7% and coronary vascular resistance increased by 21% (4) Kool and co-worker (1993) showed that in habitual smokers, smokers, smoking one cigarette caused forearm blood flow increased 17% after wrist occlusion (5) A clinical study by Bornmyr and Svenssor (1991) showed that the maximal decrease of finger skin blood flow measured by thermography occurred 30 minutes after two 1.1 mg nicotine from cigarettes, but within 15 minutes when measured by laser-Doppler Flowmetry. (6) Gaenzer and co-worker (2001) studied in response to submaximal bicycle exercise test the diameter of the femoral artery significantly increased in both nonsmokers and smokers, with a diminish response in smokers. Flow-mediated dilation of the brachial artery induced by forearm occlusion was also reduced in smoking subjects (7).

From existing literatures, most studies were done to measure blood circulation of heart and brain in smokers by using electromagnetic flowmeter or ultrasonic Doppler shift flowmeter. However, there were few studies of peripheral vascular resistance measurement. The volumeter has rarely been used to measure indicator of change in the blood flow of extremities. Therefore, this article aims to compare an indicator of change in blood flow of upper and lower extremities before and after exercise and in warm and cold water in smokers and non-smokers.

The objectives of this study were to evaluate effects of long term smoking on physical fitness in cigarette smokers compared with general population, and assess long term effects of smoking on the indicators of responses of blood circulation in both upper and lower extremities by various stimuli, such as anaerobic exercise. aerobic exercise, warm water and cold water exposures and finally to compare blood pressure of each side of the upper and lower extremities and calculate the ankle brachial pressure index (ABPI) (8,9,10) in male smoking and nonsmoking volunteers.

MATERIALS AND METHODS

Twenty healthy males (average age 29.50 yr; range 20 – 45 yr) volunteered to serve as subjects for this study. All subjects were living in the community with a normally active life style. They were normotensive recruited from the workers of Police General Hospital, Bangkok and none were taking medications except vitamins or ergogenic aids for health. The two subject groups were matched for their average age, physical activity and body mass index (BMI). The smokers abstained from smoking for at least 4 hours before the experiment. This time interval is sufficient to reduce serum nicotine levels to nearly unmeasurable levels. (11)

All subjects gave informed consent to the experimental protocol that was approved by the Human Right Committee of Mahidol University No. 68/2005. No subjects reported skin or cardiac disease or was known to be suffering from any chronic disease. None was on any regular medication.

On the first test day, each subject was familiarized once with each test. Data collection includes anthropometric measurement such as body weight, height, waist and hip circumference vital signs and physical fitness tests. The tests were conducted at Sports Science Laboratory, College of Sports Science and Technology, Salaya Campus, Mahidol University, Bangkok, Thailand.

At least 1 day apart following the first test, all subjects was measured the left upper and lower extremity volume by water displacement method in different thermal stimulation. Subjects were tested for volume changing of extremities by four stimulus that 1) immersion the left forearm and leg in warm water at temperature 42^0C continuously, left forearm and leg were immersed at volumeter for measure volume 2) immersion the left forearm in cold water at temperature 12^0C continuously, left forearm and leg were immersed at volumeter for measure volume 3) the VO_2 max test (Astrand-Rhyming protocol test), (12) the subject was seated on the saddle which height was adjusted appropriately, started pedaling the ergometer at 0 Watt for 1 minute as a warm up period. Thereafter, the resistance was increased by 100-150 Watts (600-900 kgm/min) until heart rate (HR) more than 120 beat/min. Start recording HR every minute until 6 minutes. The left upper extremities and lower extremities were measured at volumeter for volume measurement simultaneously. The left upper extremities and lower extremities were measured at volumeter for volume measurement. Volume changed of both extremities and heart rate were recorded at four times that before each test conditions (Pre), at minute 1 – ½ (M_1), and after stimulation at minute 5 – 51½ (M_2), at minute 10 – 10½ (M_3). All data were collected for a subject on the same day while allowing for adequate rest, at least, about 30 minutes between each condition, except in VO_2 max test and Wingate test conditions were rested at least 1 day (13)

Vital signs, anthropometry, muscle strength measurements, flexibility and agility tests, psychomotor speed tests, anaerobic and aerobic capacities and powers tests were described and reported separately, owing to over length of the report (14).

Extremities volume measurement

Extremities' volume were measured by using a volumeter (made by Biomedical Equipment Technology, Mahidol University) (13). Volumeter's size was 27 cm of diameter and 83 cm of height, the out of flow's size was 3 cm of wide and 15 cm of long. The procedures for water displacement volume of the upper and lower extremity were demonstrated to and practiced by each subject after water was added to the volumeter. The volumeter was filled with water to the level of the overflow spout, and the water level was allowed to stabilize prior to reading the water temperature and beginning the immersion. Water temperature for both the upper and lower extremity measurements was maintained at room temperature 30^0C. For the

upper extremity measurements, subjects were instructed to lower the arm slowly into the volumeter and to stop when the top of the volumeter came in contact with the previously marked elbow (head of radius). At this point, a label line that determined the depth of immersion for repeated measurements was marked by a permanent magic marker. In the left hand immersion in water continuously. For the lower extremity measurements, subjects were instructed to lower the leg slowly into the volumeter and to stop when the top of the volumeter came in contact with the knee. At this point, a label line that determined the depth of immersion for accurate repetition of immersions was marked with a magic marker. The subject immersed the extremity into the volumeter, stopping at the preset label line. The displaced water was weighed on digital weight machine (AD-6201) which calibrated previously for computation which gave an accurate measurement of the water volume (liter) displaced and recorded (see reference 13)

The process began for ½ minute period of immersion at T_0 until T_3 for each part, then, next part was completed at the same cycle to finish 4 parts : left arm and left leg. First, each part was submerged into the water at 30^0C (T_0) as control. Next, this part was dipped into the water at 12^0C and 42^0C. At the first minute of submerging into specific temperature was T_1, then, it was moved and submerged into another tub for 5 minutes to maintain the same require temperature. The second tub contained water at the same temperature (12^0C or 42^0C). Volume was measured in the first tub at 6^{th} minute (T_2). After that, the target part was submerged into the second tub again for 5 minutes at the same temperature. Volume at 12^{th} minute was measured in the water at the same temperature of the first tub (T_3). Volume of each part at 30^0C after Astand exercise and Wingate exercise was measured by dipping both arm and leg at the same side into the water in each period of time. The volume of water was calculated from the weight of out flow water of each period that was measured by digital scale. The result was subtracted by plastic bag's weight, then, calculated from gram per liter (AD-6201) by using predetermined calibrated value (13).

Volumeter made from Biomedical Equipment Technology, Mahidol University. Test reliability in 24 subjects. Forearm and leg was immersed in volumeter for measure volume two times. All data were collected for a subject on the same day while allowing adequate time of rest, at least about 30 minutes between each time. The Pearson correlation coefficient (r) equals to 0.8 ($p<0.05$) which showed that the volumeter has high reliability (13)

Tap water used in room temperature of 26^0C. Water at 42^0C was prepared by mixing 600 ml of water at 32^0C and 200 ml of water at 84^0C due to container's size availability. Water at 12^0C was prepared by mixing 300 ml of water at 32^0C and 100 ml gram of ice. Water was mixed until in one volumeter and the temperature was measured at least two times to get target temperature. One volumeter contains 37,400 ml.

In this article at temperature 3^0C, water of 1,000 ml weighed 0.975 kg. The calculation using in this experiment was done and based on 1,000 ml of water temperature of 12^0C, 30^0C and 42^0C weighed 990, 975 and 970 gram respectively.

Before and after the exercise test, all subjects were measured of supine blood pressure in both arms and ankles. Arterial blood pressure was measured using on automatic BP monitor (Dina map plus Vital signs Monitor, 73F3, Japan). The appropriate size cuff was placed over brachial artery and around each ankle, proximal to the malleolus. For each subject, systolic pressure was measured in the left brachial artery first, then in the right brachial artery, then in the left and right ankle artery (8,9,10). The Akle Brachial Pressure Index (ABPI) was calculated by the formula below:

$$\text{ABPI} = \frac{\text{Highest pressure from the ankle vessels}}{\text{Highest pressure from the brachial vessels}}$$

All data were presented as mean $\pm$ SEM and graphs were plotted. A repeated measure ANOVA was used to determine whether or not there was a statistically significant difference between the mean values obtained from before and after the conditions period within the same subject. Baseline characteristics and physical fitness were analyzed by using paired t-test. The change of blood flow during exercise was compared between study groups. All the statistical testes were performed using the SPSS for Window Versions 11 program. The level of significance for differences between groups or time intervals was set at $p<0.05$.

RESULTS

The mean values of the percent volume change of the left arm in different conditions; First, immersion in hot water (42^0C) condition (Figure 1) showed no significant difference between the two groups of subjects at all time. Second, immersion in cold water (12^0C) condition (Figure 2) showed no significant difference between the two groups of subjects at all time. Third, immersion in normal water (30^0C) condition post Astand exercise (Figure 3) showed no significant difference between the two groups of subjects at all time. Finally immersion in normal water (30^0C) condition post Wingate exercise (Figure 4) showed no significant difference between two groups of subjects at all time.

The comparison of the left arm volume pre and post test in repeated measure ANOVA method in the same conditions, the result showed that no significant difference between the two groups of subjects at all conditions.

The mean value of the percent volume change of the left leg in different conditions : First, immersion in hot water (42^0C) condition (Figure 5) values of the percent volume change showed that the smoker group was significantly lower at immediately post-test percent volume change compare to control group. Second, immersion in cold water (12^0C) condition (Figure 6) showed that the smoker group had significantly higher at immediately post-test and post-test at minute 6^{th} compare to control group. Third, immersion in normal water (30^0C) condition post Astand exercise (Figure 7) showed that the smoker group had significantly lower at immediate post-test at minute 12^{th} compare to control group. Finally, immersion in the normal water (30^0C)

condition post Wingate exercise (Figure 8) showed no significant difference between the two groups of subjects at all time.

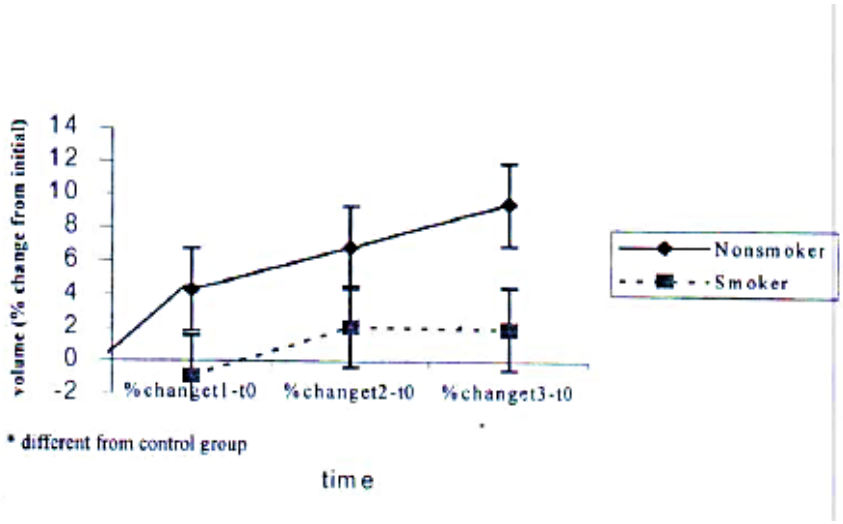


Figure 1 Comparison of the left arm percent volume change from initial of NG and SG in immersion in hot water (42^{0}C) condition and presented by mean ± SEM, statistical comparison shown was paired t-test , t0=pre-test, t1 = immediately post-test, t2 = post-test at minute 6, t3 = post – test at minute 12th. Significant value $p<0.05$, each interval = 2 minute.

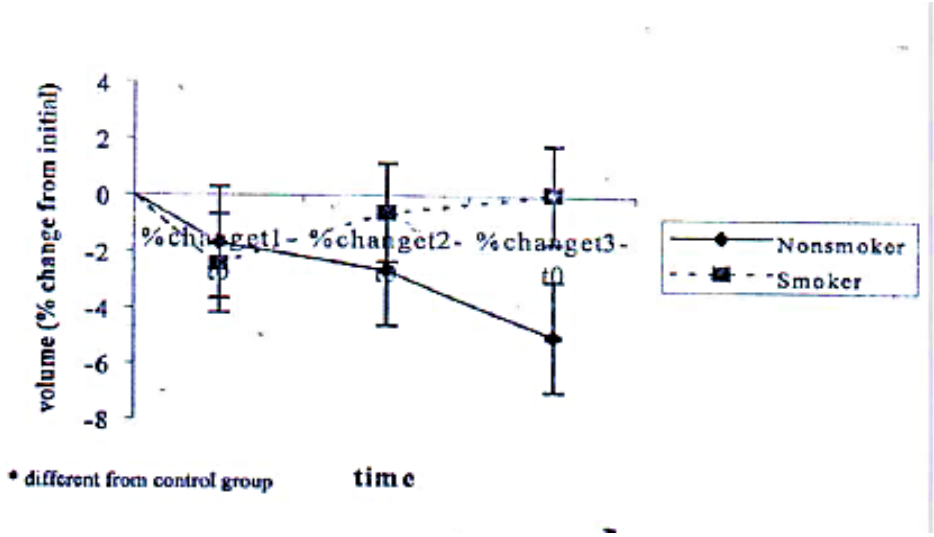


Figure 2 Comparison of the left arm percent volume change from initial of NG and SG in immersion in cold water (12^0C) condition and presented by mean ± SEM, statistical comparison shown was paired t-test , t0=pre-test, t1 = immediately post-test, t2 = post-test at minute 6^{th} , t3 = post – test at minute 12^{th}. Significant value $p<0.05$, each interval = 2 minute

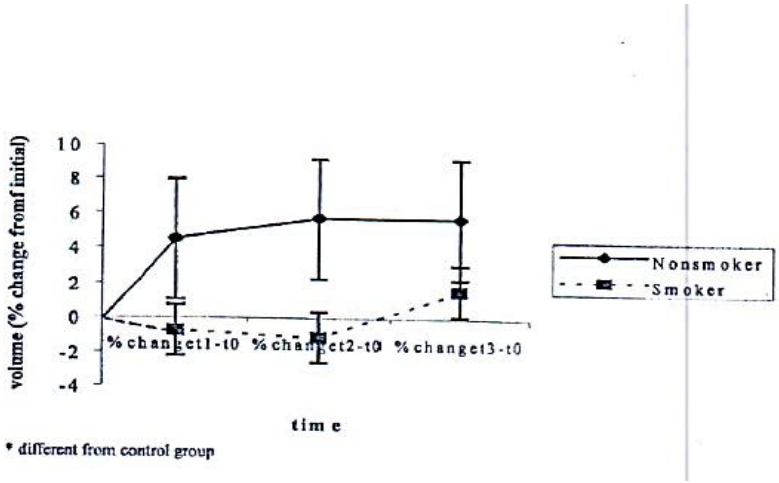


Figure 3 Comparison of the left arm percent volume change from initial of NG and SG in immersion in normal water (30^0C) at post Astand 2 minutes and presented by mean ± SEM, statistical comparison shown was paired t-test , t0=pre-test, t1 = immediately post-test, t2 = post-test at minute 6^{th} , t3 = post – test at minute 12^{th}. Significant value $p<0.05$, each interval = 2 minute.

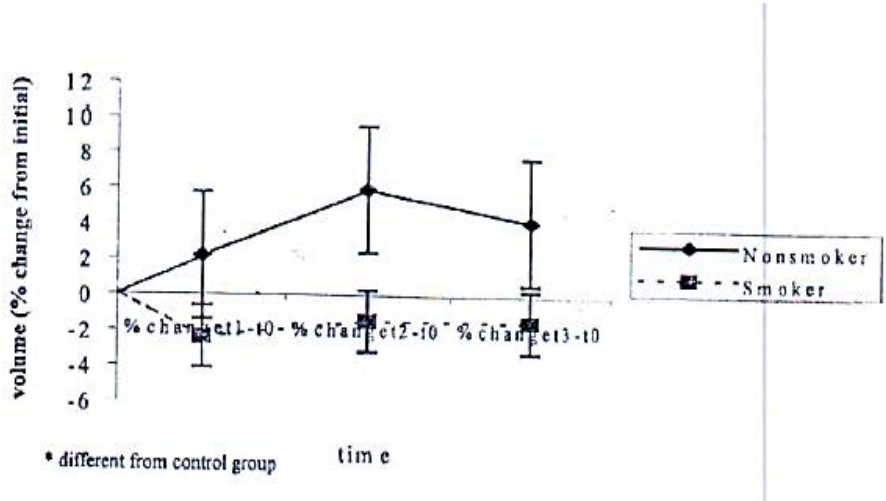


Figure 4 Comparison of the left arm percent volume change from initial of NG and SG in immersion in normal water (30^0C) at post Wingate 2 minutes and presented by mean ± SEM, statistical comparison shown was paired t-test , t0=pre-test, t1 = immediately post-test, t2 = post-test at minute 6^{th} , t3 = post – test at minute 12^{th}. Significant value $p<0.05$, each interval = 2 minute.

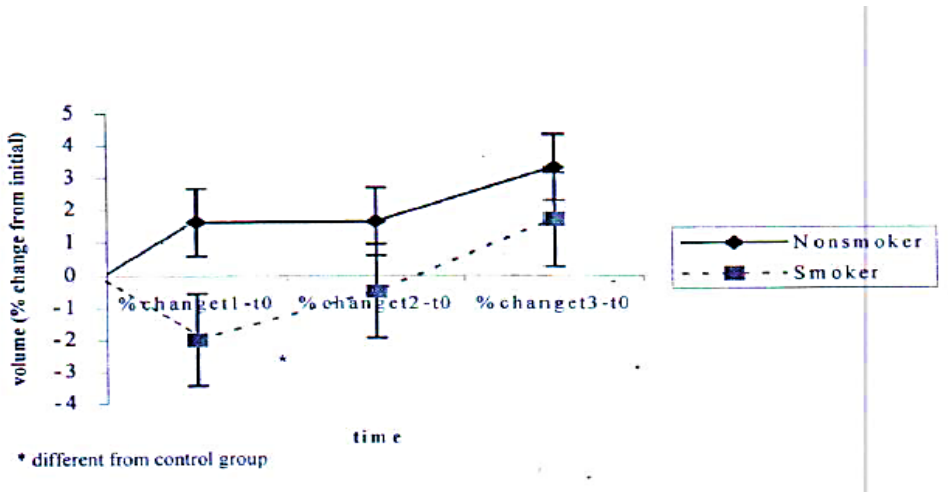


Figure 5 Comparison of the left leg percent volume change from initial of NG and SG in immersion in hot water (42^0C) and presented by mean ± SEM, statistical comparison shown was paired t-test , t0=pre-test, t1 = immediately post-test, t2 = post-test at minute 6^{th} , t3 = post – test at minute 12^{th}. Significant value $p<0.05$, each interval = 2 minute.

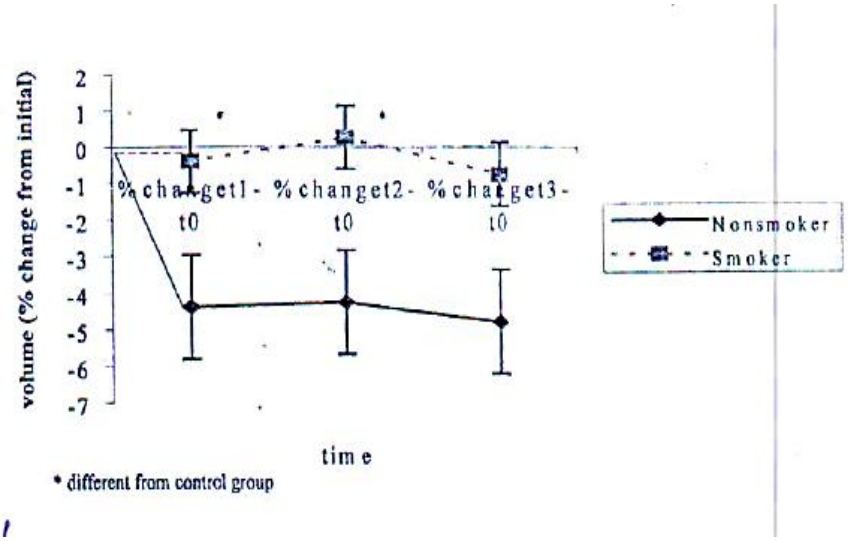


Figure 6 Comparison of the left leg percent volume change from initial of NG and SG in immersion in cold water (12^0C) and presented by mean ± SEM, statistical comparison shown was paired t-test , t0=pre-test, t1 = immediately post-test, t2 = post-test at minute 6^{th} , t3 = post – test at minute 12^{th}. Significant value $p<0.05$, each interval = 2 minute.

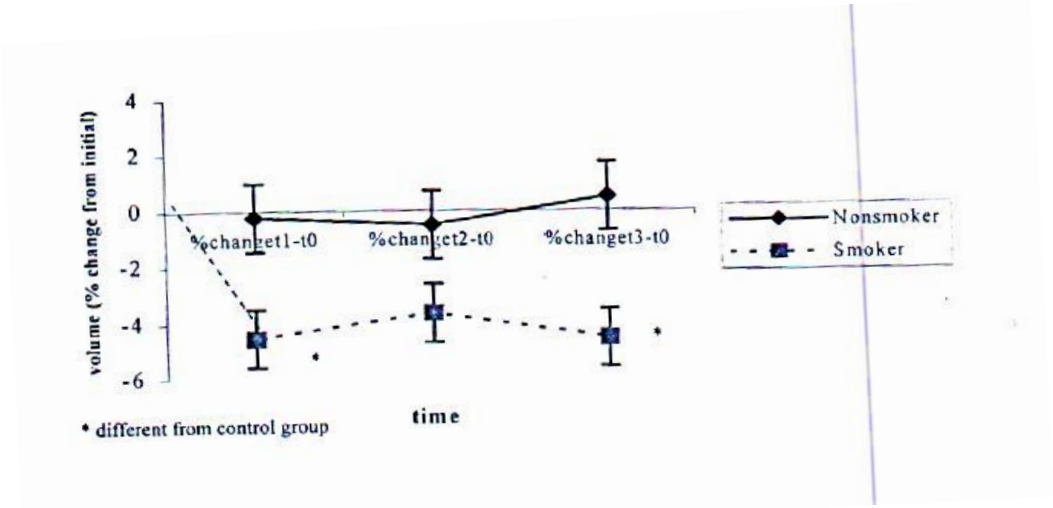


Figure 7 Comparison of the left leg percent volume change from initial of NG and SG in immersion in normal water (30^0C) at post Astand exercise 2 minutes and present by mean ± SEM, statistical comparison shown was paired t-test , t0=pre-test, t1 = immediately post-test, t2 = post-test at minute 6^{th} , t3 = post – test at minute 12^{th}. Significant value $p<0.05$, each interval = 2 minute.

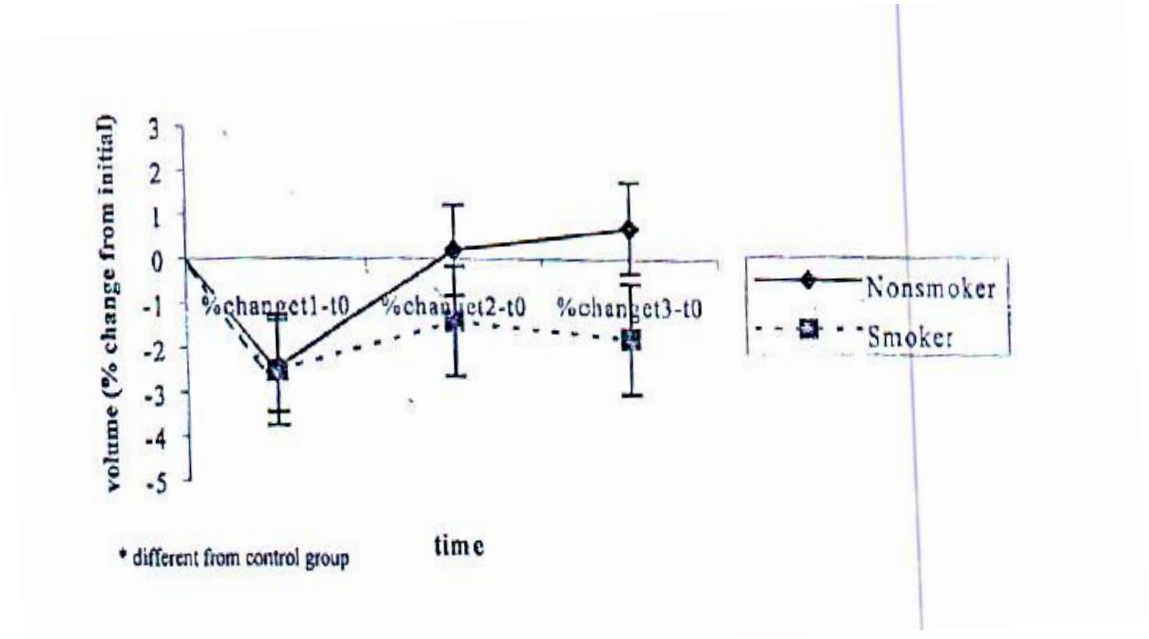


Figure 8 Comparison of the left leg percent volume change from initial of NG and SG in immersion in normal water (30^0C) at post Wingate exercise 2 minutes and present by mean $\pm$ SEM, statistical comparison shown was paired t-test , t0=pre-test, t1 = immediately post-test, t2 = post-test at minute 6^{th} , t3 = post – test at minute 12^{th}. Significant value $p<0.05$, each interval = 2 minute.

The comparison of the percent change of the heart rate between groups showed significantly differences between the two groups in immersion the left arm and left leg in normal water (30^0C) post Astand and Wingate exercise 2 minutes condition but the comparison of the percent change of the heart rate in pre and post test in repeated measure ANOVA method in the same condition, the result showed that : First, immersion the left leg in hot water (42^0C) condition; percent change values of the heart rate (Figure 9) showed that both groups showed no significant difference between pre and post test of the same subject at all time. Second condition, immersion the left leg in cold water (12^0C) condition ; percent change values of the heart rate (Figure 10) showed that both groups showed no significant difference between pre and post test of the same subject at all time. Third condition , immersion the left arm and left leg in normal water (30^0C) post Astand exercise 2 minutes condition; percent change values of the heart rate (Figure 11) showed that both groups showed significantly lower at minute 6^{th} compared to immediately post-test, significantly lower at minute 12^{th} compared to immediately post-test and minute 6^{th} ($p<0.05$). Finally condition, immersion the left arm and left leg in normal water (30^0C) post Wingate exercise 2 minutes condition percent change values of the heart rate (Figure 12) showed that nonsmoker groups found significantly lower at minute 6^{th} compared to immediately post-test, significantly lower at minute 12^{th} compared to immediately post – test ($p<0.05$), in smoker group showed significantly lower at minute 6^{th} compared to immediately post-test, significantly lower at minute 12^{th} compared to immediately post-test minute 6^{th} ($p<0.05$)

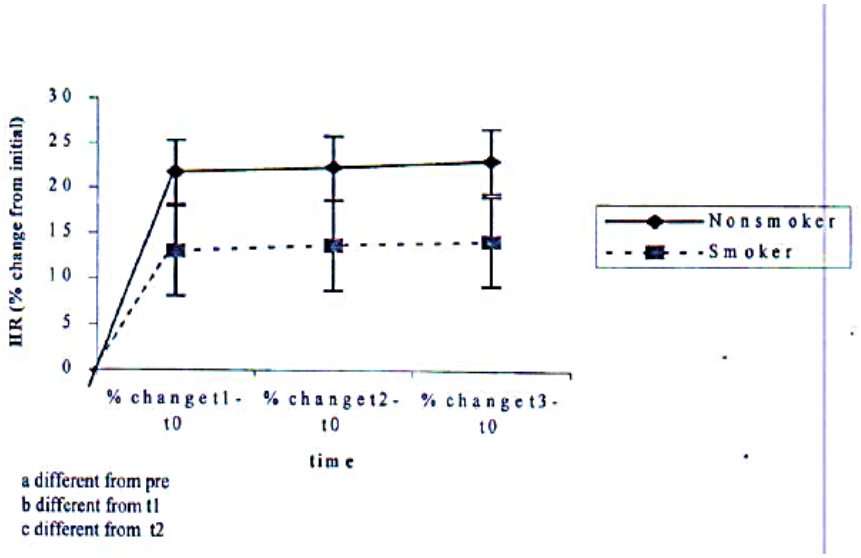


Figure 9 Comparison of percent change of heart rate of NG and SG pre-post test in immersion of the left leg in hot water (42^0C) condition and presented by mean ± SEM, statistical comparison shown was repeated measure ANOVA. Pre = pre-test, t1 = immediately post-test, t2 = post-test at minute 6^{th}, t3 = post – test at minute 12^{th}. Significant value $p<0.05$, each interval = 2 minute.

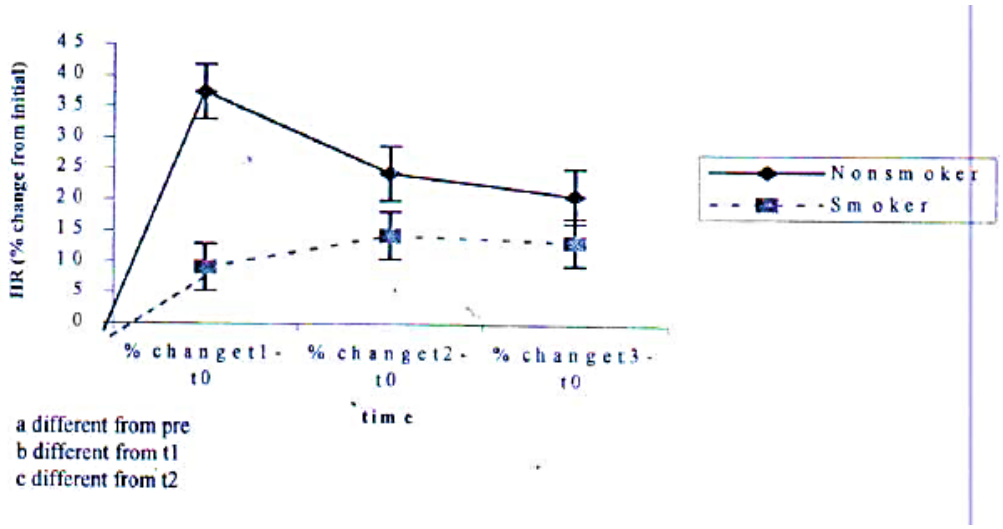


Figure 10 Comparison of percent change of heart rate of NG and SG pre-post test in immersion of the left arm and left leg in cold water (12^0C) condition and presented by mean ± SEM, statistical comparison shown was repeated measure ANOVA. Pre = pre-test, t1 = immediately post-test, t2 = post-test at minute 6^{th}, t3 = post – test at minute 12^{th}. Significant value $p<0.05$, each interval = 2 minute.

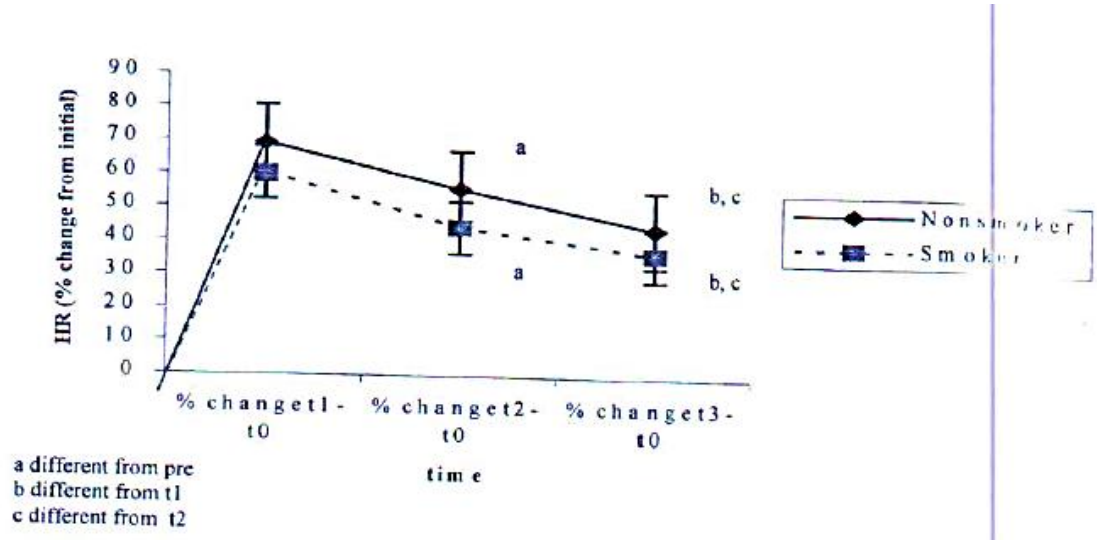


Figure 11 Comparison of percent change of heart rate of NG and SG pre-post test in immersion of the left arm and left leg in normal water (30^0C) Post Astand exercise 2 minutes condition and presented by mean ± SEM, statistical comparison shown was repeated measure ANOVA. Pre = pre-test, t1 = immediately post-test, t2 = post-test at minute 6^{th}, t3 = post – test at minute 12^{th}. Significant value $p<0.05$, each interval = 2 minute.

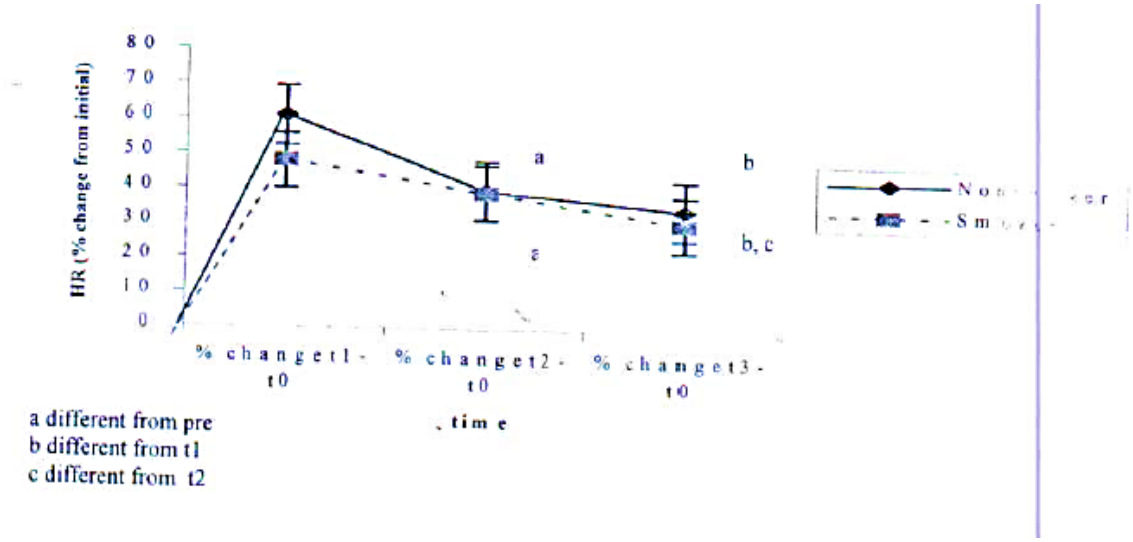


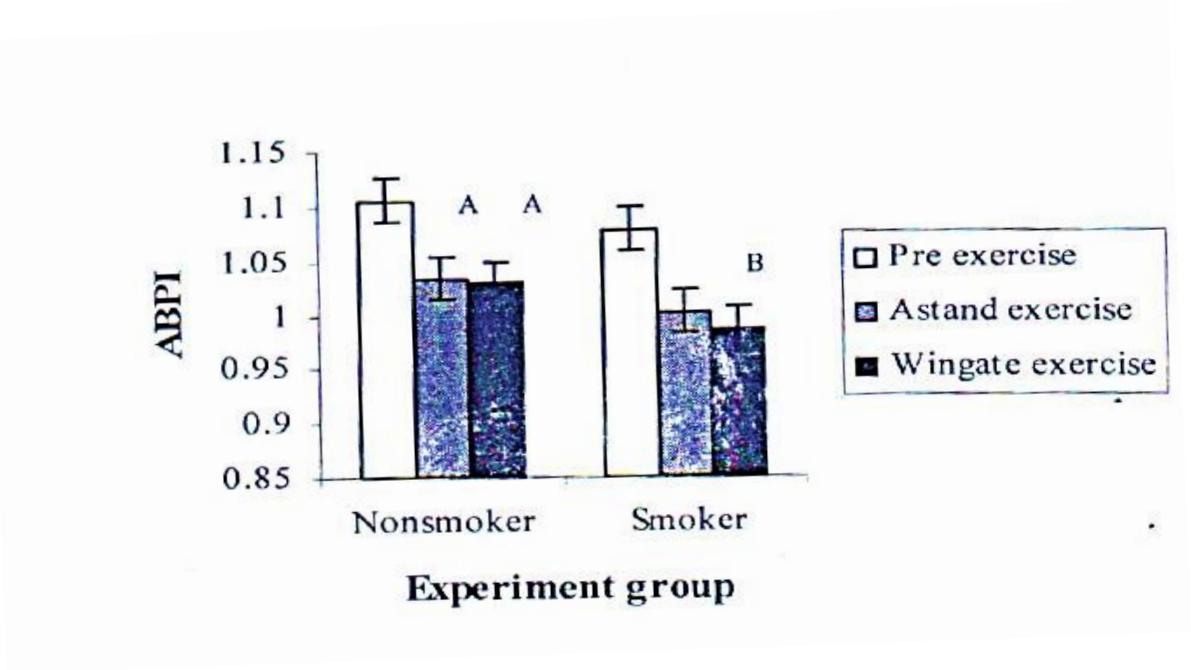
Figure 12 Comparison of percent change of heart rate of NG and SG pre-post test in immersion of the left arm and left leg in normal water (30^0C) Post Wingate exercise 2 minutes condition and presented by mean ± SEM, statistical comparison shown was repeated measure ANOVA. Pre = pre-test, t1 = immediately post-test, t2 = post-test at minute 6^{th}, t3 = post – test at minute 12^{th}. Significant value $p<0.05$, each interval = 2 minute.

Ankle Brachial Pressure Index (ABPI)

The Ankle Brachial Pressure Index of NG and SG calculated from measure the brachial systolic blood pressure and the ankle systolic blood pressure. Calculate the ABPI using the formula below.

$$ABPI = \frac{\text{Highest pressure from the ankle vessels}}{\text{Highest pressure from the brachial vessels}}$$

The two sessions of the ABPI in pre and post exercise were shown in Figure 13 firstly, the descriptive values at ABPI in the first evaluation showed no significant difference of two groups of subjects ($p<0.05$). The repeated measure ANOVA test within groups had showed that; nonsmoker had significantly lesser in post Astand and Wingate exercise when compare to the pre exercise ($p<0.05$) but smoker had significantly lesser only in post Wingate exercise when compare to the pre exercise ($p<0.05$)



Fingure 13 Comparison of the three sessions of the ABPI of NG and SG presented by mean ± SEM, statistical shown as repeated ANOVA, Pre exercise, Post Astand exercise and Post Wingate exercise 15 minutes, Significant value $p<0.05$, A; different from Pre exercise nonsmoker, B; different from Pre exercise smoker.

DISCUSSION

Acute volume changes of extremities were previously recognized as indicator of alteration of vasomotor by many investigators (15,16,17). Alterations of volume of extremities can be resulted from different stimulations such as exercise training and thermal exposure. During exercise, the resistance vessels relax, and the muscle blood flow may increase many folds; the magnitude of the increase depends on largely the severity of the exercise. In this present study, we found that immersion of the left arm in hot water 42^{0}C condition, the nonsmoker had greater left arm volume vasodilatation than smoker in every periods. In immersion of the left arm in cold water 12^{0}C condition, the smoker group also had left arm volume vasoconstriction lesser than nonsmoker as usual in every periods. In immersion in normal water 30^{0}C condition post Astand exercise 2 minutes, the smoker had left leg volume vasoconstriction lesser than the nonsmoker in every periods. In immersion in normal water 30^{0}C condition post Wingate exercise 2 minutes,

the smoker had left leg volume vasodilatation nearly the same as nonsmoker in every periods. In this study the blood vessels of the left arm in the smoker group did not show higher vasodilator than the nonsmoker group. This may imply that the smoker group in this study were not heavy smoker (they smoked, Mean = 10 cigarette/day) and not long term smoker (Mean = 12.8 year). This characteristic may be due to effects of smoking on blood vessel dysfunction. This finding was supported by Jacobs et al. (1993) who investigated the endothelium-dependent vasorelaxation in the forearm, no difference was observe between chronic smokers and nonsmokers (18). Pellaton and co-worker (2002) investigated chronic smoking alters the vasodilatory capacity in the microcirculation. They found that the vasodilatory response of the skin microvasculature is impaired in subjects who have smoked cigarette for many years (19). Celermajer and co-worker (1992) used high – resolution ultrasound measured vessel diameter at rest, during absence in the smokers and inversely related to lifetime smoking (20). Lekakis and co-worker (1997) studied the effects of acute cigarette smoking on endothelium dependent brachial artery dilation in healthy individuals. They suggested that short-term smoking did not have much effect to arterial smooth muscle but there may be mildly impairment in adults who are long –term smokers (21). The other reason of not seeing significant changes in term of arm or leg volume in this study may be the method of volumetry used here is not sensitive enough to detect the changes.

Immersion of the left leg in hot water 42^{0}C condition, the nonsmoker had greater left leg extremities volume vasodilatation than smoker in every periods. Immersion of the left leg in cold water 12^{0}C condition the nonsmoker had grater left leg extremities volume vasoconstriction than smoker in every periods. In immersion in normal water 30^{0}C condition post Astand exercise 2 minutes the nonsmoker had left leg extremities volume vasodilatation more than smoker in at immediately period and minute 12th. In immersion in normal water 30^{0}C condition post Wingate exercise 2 minutes, the nonsmoker had left leg extremities volume similar degree to smoker in every periods. In this results showed that blood circulation of the left leg of the smoker group had not vasoconstriction in cold water and had lesser vasodilatation than the nonsmoker when response by hot water and exercise. This may imply that the smoker group may have already vasoconstriction since it was found that smoking caused an enhanced endothelial induced vasoconstriction and a decreased norepinephrine induced vasoconstriction. This finding supports by Haustein (1999) has suggested that habitual smoking reduces the dilatation reserves of the smallest vessels (2) Gaenzer and co-worker (2000) studied diameter and blood flow of the femoral and brachial arteries in response to a submaximal bicycle exercise test. They found that in response to exercise the diameter of the femoral artery significantly increased in both nonsmoker and smoker, with a diminished response in smokers (7)

In percent volume changes, we found that immersion of the left arm in hot water 42^{0}C condition (Figure 1), values of the left arm of the nonsmoker had greater vasodilatation than smoker in every periods. When compare with heart rate which is an net result of balance of sympathetic and parasympathetic nervous system activity at the same time it can be seen that the smoker had greater heart rate increase than

nonsmoker in every periods, and at minute 12th the heart rate which is the highest. Values of the left leg of nonsmoker had greater vasodilatation than smoker in every periods and significantly at immediately post test. This results showed that the smoker groups may have impairment of the endothelium dependent dilation of the brachial arteries. Therefore, the increase in sympathetic activity of the smoker group can be partially used to explain greater vasoconstriction in the left arm and left leg than the nonsmoker group. This may imply that the degree of vasoconstriction of arm and leg may be controlled by other unclear factors other than norepinephrine such as nitric oxide (22,23,24)

Immersion of the left arm in cold water 12^0C condition (Figure 2) values percent volume change of the left arm of the nonsmoker had greater degree of vasoconstriction than smoker in every periods. When compare to the heart rate changes at the same time period, the smoker had greater heart rate increase than the nonsmoker in all period investigated but have trend to decrease continuously at minute 6th and 12th. Values of the percent volume change of the left leg of the smoker group had lesser degree of vasoconstriction than nonsmoker group at all periods. These results may have some pathological changes in the blood vessels. The increase in sympathetic activity of nonsmoker group could be partially used to explain greater degree of vasoconstriction in the left arm and left leg. This may imply that the degree of vasoconstriction of the arm and leg may be controlled by other factors such as nitric oxide. (22,23,24)

In immersion in normal water 30^0C condition post Astand exercise 2 minutes (Figure 3), values percent change of the left arm of nonsmoker group had greater degree of vasodilatation than smoker group in every periods. When relate the above data with heart rate change which is a net result of balance of sympathetic and parasympathetic nervous system activity at the same time it can be seen that smoker had slightly greater heart rate increase than nonsmoker in every periods but not statistically significant different.

In immersion in normal water 30^0C condition post Wingate exercise 2 minutes (Figure 4), Values of percent change of the left arm of smoker group had lesser degree of vasodilatation than nonsmoker group in every period. When relate the above data with heart rate change which is a net result of balance of sympathetic and parasympathetic nervous system activity at the same time it can be seen that nonsmoker had slightly greater heart rate increase than smoker in every period but not significant.

The above findings that post of Astand and Wingate exercise may imply that the smoker group can have lesser degree of vasodilatation in arm than nonsmoker group but smoker group will have lesser degree of vasodilatation in the leg than nonsmoker group. This results may suggested that the activity of endothelial nitric oxide may be impaired in the smoker group. This finding supports by Hautein (1999) has suggested that habitual smoking reduces the dilatation reserves of the smallest vessels (2) Celermajer and co-worker (1993) and Czemin and co-worker (1995) suggested that in healthy individuals, long-term smoking will have primary affects on coronary and peripheral arterial endothelial function (20,25). The primary vasodilatation mechanism can be caused by metabolic change in nature such as adenosine release from active muscle and endothelial dependent vasodilatation would be secondary to the primary dilatory event and ensuring increase in blood

flow. Exercise is associated with increases in plasma catecholamine levels that are intensity related (1). Thus, increased plasma and varicosity level and release of catecholamine would be predicted to induce endothelium derived nitric oxide release. Role of endothelium derived nitric oxide in dilation of skeletal muscle vasculature was extensively demonstrated (26) Other endothelial deriving relaxing factors such as vasoactive prostaglandins also seem to be involved in endothelium dependent flow induced dilation of skeletal muscle arterioles (27). Joanides and co-worker (1995) and Meredith and co-worker (1996) have suggested that the effects of exercise may be by induction of nitric oxide (28,29). Gaenzer and co-worker (2000) studied diameter and blood flow of the femoral and brachial arteries in response to a submaximal bicycle exercise test. They found that in response to exercise the diameter of the femoral artery significantly increased in both nonsmoker and smoker, with a diminished response in smokers. Flow-mediated dilation (FMD) of the brachial artery induced by forearm occlusion was also reduced in smoking subjects. They suggested that an impaired FMD in smokers as evidence for endothelial dysfunction (7). Zeiher and co-worker (1995) used coronary angiography measure epicardial artery diameter at baseline, after maximal increases in coronary blood flow that caused FMD (which is strictly endothelium – independent) and after intracoronary injection of nitroglycerine (an endothelium – independent dilator) in 96 patients. They found that the blunted dilator response to increased blood flow was out of proportion to the mildly impaired dilator response to nitroglycerine in smoker, so long – term cigarette smoking may be associated with impaired endothelium independent coronary vasodilatation (30)

The difference of heart rate of nonsmoker and smoker may imply the difference in sympathetic response of nonsmoker and smoker which parallel to degree of vasoconstriction and vasodilatation of each group. Therefore, the differences of vasoconstriction of arm and leg of smoker may be partly due to toxic substances in cigarette such as; nicotine which may cause sympathetic activation induce norepinephrine release from postganglionic sympathetic nerves innervating blood vessels through a direction on the nerve terminals , inhibit the activity of nitric oxide synthase (31). Goldbarge and co-worker (1971) examined the circulatory effects of smoking a single cigarette in healthy young subjects during moderately severe exercise. They found that smoking decreased the efficiency of the heart, causing a smaller stroke volume and higher heart rate during exercise (32). Cooper and co-worker (1968) demonstrated a lower level of endurance to exercise in moderate or heavy smokers. They studied airman and found that performance on a 12-minute field test was inversely related to the number of cigarette smoked per day and the duration of smoking (1). Baer and Radichevich (1985) suggested that cigarette smoking is associated with an increase in blood pressure, pulse rate and plasma ACTH, cortisol, aldosterone and catecholamine levels in hypertensive smokers (33)

The Ankle Brachial Pressure Index (ABPI)

The Ankle Brachial Pressure Index (ABPI) was a quick noninvasive measure of peripheral arterial occlusive disease. It developed as an indicator for peripheral vascular disease. It was used as an indicator of

generalized artherosclerosis and to predict risk of future cardiovascular events (34,35). In this study it was found that the smoker had lesser ABPI value than the nonsmoker in pre-exercise, post-Astand exercise and post-Wingate exercise. The results of this study may show that the smoker had a lower calf blood flow than the nonsmoker during resting, reactive hyperemic, and maximal hyperemic condition. The results demonstrated that the effects of long term cigarette smoking lowers the ABPI and the index number drops after exercise, the smoker had the ABPI lower than nonsmoker group, this may indicate that significant peripheral arterial disease may be present. This finding was supported by Yataco and co-worker (1999) who examined the acute effects of cigarette smoking on ABPI and the peripheral circulation in 10 older chronic smokers with peripheral arterial occlusive disease. They found that the ABPI on the smoking day was lower than on the nonsmoking day owing to a lower ankle systolic blood pressure (36). Gardner and co-worker (2004) suggested that cigarette smoking may cause peripheral vasoconstriction in the lower extremities. Furthermore, the greater impairment in perfusion of the calf musculature in the smokers at baseline may be a potential explanation for the lower claudication distance and lower overall physical functions than those in the nonsmoking patients (37)

In conclusion; the oxygen consumption and agility of nonsmoker was significantly higher than in smoker. Vasomotor responses of blood vessels of upper and lower extremities in nonsmoker was significantly higher than in smoker after stimulation by hot water, cold water and aerobic exercise. A statistical significant reduction of Ankle Brachial Pressure Index (ABPI) in nonsmoker after both exercises was found, which are consistent to the above data on vasomotor responses. These findings may further demonstrate the usefulness of volumetric method and ABPI index determination in helping in diagnosis of vascular diseases.

REFERENCE

1. Hawkins BT, Brown RC, Davis TP. Smoking and ischemic stroke : a role for nicotine. *TRENDS in Pharmacological Science.* 2002;23(2):78-82.
2. Houstein KO. Smoking tobacco microcirculatory changes and the role of nicotine. *International Journal of Clinical Pharmacology and Therapeutics.* 1999;33(2):76-85.
3. Holbrook JH. Tobacco In *Principle of Internal Medicine.* 11th ed. 1987;1:855-856.
4. Quillen JE. Rossen JD, Oskarsson HJ, Minor RL, Lopez JAG, Winniford MD. Acute effect of cigarette smoking on the coronary circulation ; constriction of epicardial and resistance vessels. *J Am Coll Cardiol.* 1993;22:642-647.
5. Kool MJF, Hoeks APG, Struijker Boudier HAJ, Reneman RS, Van Bortel LMAB. Short and long – term effects of smoking on arterial wall properties in habitual smokers. *J Am coll cardiol.* 1993;22:1881-1886.
6. Bornmyr S, Svensson H. Thermography and Laser-Doppler flowmetry for monitoring changes in finger skin blood flow upon cigarette smoking. *Clin Physiol.* 1991;11:135-141.

7. Gaenzer H, Neumayr G, Marschang P, Sturm W, Kirchmair R, Patsch JR. Flow-mediated vasodilation of the femoral and brachial artery induced by exercise in healthy nonsmoking and smoking men. *Journal of the American College of Cardilogy.* 2001;38(5):1313-1319.
8. Yataco AR and Gardner AW. Acute reduction in ankle / brachial index following smoking in chronic smokers with peripheral arterial occlusive disease. *Angiology.* 1999;50(5):355-360.
9. Woo J, Lynn H, Wong SY, Hong A, Tong YN, Lau WY, Lau E, Orwall E and Kwok TCY. Correlates for a low ankle-brachial index in elderly Chinese. *Atherosclerosis*. 2005;7(2):1-7.
10. Resnick HE, Lindsay RS, McDermott MM. Relationship of high and low ankle – brachial index to all – course and cardiovascular disease mortality; The Strong Heart Study. *Circulation.* 2004;109:733-738.
11. Benowitz NL. Drug therapy: pharmacologic aspects of cigarette smoking and nicotine addition. *N Engl J Med.* 1988;319:1318-1330.
12. Exercise Physiology Laboratory Techniques. Department of Physiology, Faculty of Science, Mahidol University, 2003.
13. Phumchai U. Alterations of vasomotor responses to exercise stimulation of arms and legs during aerobic and anaerobic training. *Thesis, Mahidol Research* . Faculty of Science. Mahidol University. 2004.
14. Chentanez T, Anothayanont Y, Kaimuk P and Yimlamai T. Psychophysiological changes of cigarette smokers to stimuli of aerobic and anaerobic exercises J.Sports Sci Technol. 2012;12(1): (In Press).
15. Johnson JM, Brengelmann GL. and Rowell LB. Interactions between local and reflex influences on human forearm skin blood flow. *J. Appl. Physiol.* 1976;41(6):826-831.
16. Radegran G and Saltin B. Nitric oxide in the regulation of vasomotor tone in human skeletal muscle. *Am.J.Physiol Heart Circ Physiol.* 1999;276:H1951-1969.
17. Johnson JM and Park MK. Effect of heat stress on cutaneous vascular response to the initiation of exercise in man. *J.App. Physiol : Respirat. Environ. Exercise Physiol* . 1982;53(3):744-749.
18. Jocobs MC, Lenders JWM, Kapma JA, Smith P, Thien T. Effect of chronic smoking on endothelium – dependent vascular relaxation in humans. *Clin sci.* 1993;85:51-55.
19. Pellaton C, Kubli S, Feihl F, Waeber B. Blunted vasodilatory responses in the cutaneous microcirculation of cigarette smokers. *Am Heart Jounal.* 2002;144:269-674.
20. Celemajer DS, Sorensen KE, Georgakopoulos D, Bull C, Thomas O, Robinson J and Deanfield JE. Cigarette smoking is associated with dose-related and potentially reversible impairment of endothelium-dependent dilation in healthy young adults. *Circulation.* 1993:88(5):2149-2155.
21. Lekakis J. Papamichael C, Vemmos C, Nanas J, Kontoyannis D, Stamatelopoulos S, Moulopoulos S. Effect of acute cigarette smoking on endothelium dependent brancial artery dilation in healthy individuals. *The American Journal of Cardiology* . 1997;79(15):529-531.

22. Christman JV and Gisolfi CV. Heat acclimation : role of norepinephrine in the anterior hypothalamus. *J. Appl, Physiol.* 1985;58(6): 1923-1928.
23. Kellogg DL, Johnson JM, and Kosiba WA. Control of internal temperature threshold for active cutaneous vasodilation by dynamic exercise. *J. Appl. Physiol.* 1991;71(6): 2476-2482.
24. Redergan G, and Saltin Bl. Nitric oxide in the regulation of vasomotor tone in human skeletal muscle. *Am.J.Physiol Heart Circ Physiol.* 1999;276:H1951-1969.
25. Elizabeth F, Bernstein GM, Scott BW, Benett PJ and Mendelson JR. Critical flicker \frequency responses in visual cortex. *Exp Brain Res.* 2001;139:106-110.
26. Frost PH, Davis BR, Burlando AJ., Guithrie GP, Isaacsohn JL, Coronary heart disease risk factors in men and woman aged 60 years : findings from the systolic hypertension in the elderly program. *Circulation*.1996;94:26-34.
27. Grote L, Zou D, Kraiczi H, Hedner J. Finger plethysmography – a method for monitoring finger blood flow during sleep disorder breathing . *Respiratory Physiology & Neurobiology*.2003;136:141-152.
28. Joannides R, Haefeli WE. Lindner L, Nitric oxide is responsible for flow-dependent dilatation of human peripheral conduit arteries *in vivo. Circulation.* 1995;91:1314-1319.
29. Meredith IT, Currie KE, Anderson TJ. Post ischemic vasodilation in human forearm is dependent on endothelium-derived nitric oxide. *Am J Physiol.* 1996;270:H1435-1440.
30. Zeiher AM, Schaechinger V, Minners J. Long – term cigarette smoking impairs endothelium-dependent coronary arterial vasodilator function. *Circulation.* 1995;92:1094-1100.
31. Terborg C, Birkner T, Schack B, and Witte OW. Acute effects of smoking on cerebral oxygenation and hemodynamics : A combined study with near-infrared spectroscopy and transcranial doppler sonography. *Journal of Neurological Sciences.* 2002;205:71-75.
32. Goldbarge AN, Krone RJ, and Resnekiv L. Effects of cigarette smoking on hemodynamics of resting and during exercise in normal subjects. *Chest.* 1971;60(6): 531-536.
33. Baer L and Radichevich I. Cigarette smoking in hypertensive patiants, blood pressure and endocrine response. *The American Journal of Medicine.* 1985;78:564-568.
34. Woo J, Lynn H, Wong SY, Hong A, Tong YN, Lau WY, Lau E, Orwall E and Kwok TCY. Correlates for a low ankle-brachial index in elderly Chinese. *Atherosclerosis.* 2005;7(2): 1-7.
35. Resnic HE, Linsay RS, McDermott MM. Relationship of high and low ankle-brachial index to all-course and cardiovascular disease mortality: The Strong Heart Study. *Circulation.* 2004;109: 733-738.
36. Yataco AR and Gardner AW. Acute reduction in ankle/brachial index following smoking in chronic smokers with peripheral arterial occlusive disease. *Angiology.* 1999;50(5):355-360.

37. Gardner AW,Killewich LA, Montgomery PS and Katzel LI. Response to exercise rehabilitation in smoking and nonsmoking patients with intermittent claudication. *Journal of Vascular Surgery.* 2004;39(3):531-538.

Sportsl Medicine	(Original articles)
เวชศาสตร์การกีฬา	(นิพนธ์ต้นฉบับ)

การตอบสนองของเส้นโลหิตแขนและขา ในผู้สูบบุหรี่ต่อสิ่งกระตุ้นต่อระบบเส้นโลหิตบางอย่าง

ไถ้ออน ชินธเนศ, เยาวลักษณ์ อโณทยานนท์, ปัญญา ไข่มุก และทศพร ยิ้มลมัย
วิทยาลัยวิทยาศาสตร์และเทคโนโลยีการกีฬา และ โรงพยาบาลตำรวจ และ ภาควิชาสรีรวิทยา คณะวิทยาศาสตร์ มหาวิทยาลัยมหิดล

บทคัดย่อ

การศึกษาผลของการสูบบุหรี่ต่อการตอบสนองของเส้นโลหิตแขนและขาในอาสาสมัครชายที่มีสุขภาพดีอายุระหว่าง 20 – 45 ปี และปฏิบัติงานที่โรงพยาบาลตำรวจ จำนวน 2 กลุ่ม คือ กลุ่มไม่สูบบุหรี่ และกลุ่มสูบบุหรี่ กลุ่มละ 10 คน โดยแขนซ้ายและขาซ้ายทั้งสองกลุ่มได้รับการกระตุ้นด้วย การออกกำลังกายแบบใช้ออกซิเจน และไม่ใช้ออกซิเจน ที่ขาทั้งสองข้าง ผลการประเมินพบว่า การตอบสนองของเส้นโลหิตแขนและขาต่อสิ่งกระตุ้นมาตรฐาน พบว่า เส้นโลหิตที่ขาของผู้ไม่สูบบุหรี่ตอบสนองต่อการกระตุ้นด้วยน้ำร้อน น้ำเย็น และการออกกำลังกายแบบใช้ออกซิเจน มากกว่าผู้สูบบุหรี่อย่างมีนัยสำคัญทางสถิติ ค่า Ankle Brachial Pressure Index (ABPI) ลดลงอย่างมีนัยสำคัญทางสถิติ ภายหลังการออกำลังกายทั้ง 2 แบบในผู้ไม่สูบบุหรี่ สอดคล้องกับผลการตอบสนองของเส้นโลหิตแขนและขาที่วัดได้จากการใช้โวลุมมิเตอร์ และวิธีอื่น ๆ การศึกษาครั้งนี้แสดงให้เห็นว่า การสูบบุหรี่ทำให้สมรรถภาพทางกาย การตอบสนองทางจิตประสาท และการตอบสนองของเส้นโลหิตแขนและขาลดลงนำมาซึ่งความเสี่ยงต่อการเกิดเส้นเลือดตีบแข็งได้ ทั้งนี้ขึ้นอยู่กับปริมาณและระยะเวลาในการสูบบุหรี่

คำสำคัญ : การตอบสนองของเส้นโลหิตต่อสิ่งกระตุ้น, การออกกำลังกาย, ผู้สูบบุหรี่, บุหรี่, นิโคติน, Ankle brachial pressure index (ABPI)