Elevated myocardial oxygen consumption during cutaneous cold stress in young adult overweight and obese Africans

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Abstract

Exaggerated sympathetic-mediated cardiovascular responses to stressful stimuli (such as cold exposure) has been linked to the development of hypertension and cardiovascular disease, which in turn has been demonstrated to predict the development of future hypertension. The aim of the present study was to test the hypothesis that enhanced change in myocardial oxygen consumption (MVO2) to cutaneous cold stress may be one potential mechanism that predisposes overweight/obese individuals in Africa to developing hypertension. The Rate-Pressure-Product (a non-invasive determinant of MVO2) was measured in individuals in Africa to developing hypertension and stress. However, exaggerated sympathetic-mediated cardiovascular responses to stressful stimuli (such as exposure to cold) has been linked to the development of hypertension and other cardiovascular diseases, which in turn has been demonstrated to predict the development of future hypertension.

Theories supporting the empirical basis for the Cold Pressor Test (CPT) is anchored around the following observations: i) that normotensive persons show lesser lability of blood pressure under various forms of stress as opposed to hypertensive persons; ii) that normotensive hyper-reactors to CPT are more likely to have familial history of hypertension than less reactive normotensive persons; and iii) that hyper-reactors to CPT are highly predisposed to developing essential hypertension later in life. However, few or no studies have tested the link between responses to CPT and later development of hypertension in normotensive African population. Thus, the aim of the present study is to test the hypothesis that enhanced change in myocardial oxygen consumption (MVO2) to cutaneous cold stress (CCS) may be one potential mechanism that predisposes overweight/obese young individuals to developing hypertension in the African population. In the course of this study, the rate pressure product (RPP) is considered as the best indirect method to evaluate MVO2, as well as an indicator of myocardial stress.

Materials and Methods

Forty healthy normotensive subjects (20 males and 20 females) aged between 18 and 25 (20±0.33) years, participated in this study. The informed consent of each subject was obtained before entry into the study. All procedures followed approval of the College of Health Sciences University of Ilorin Ethical Committee standards and were in accordance to the Helsinki Declaration. Participant was also briefed of the experimental procedures and the potential benefit of the study. Furthermore, participant were given the freewill to withdraw from the study as at when deem fit by them. The subject used had a body mass index (BMI) ranging from 15.43 kg/m2 (underweight) to 40.44 kg/m2 (morbid). Thus, subjects were classified based on the median body weight of 59.50 kg, and the classification was later standardized by BMIs. All participants were advised to abstain from alcohol, caffeine containing food and strenuous exercise for at least 24 hours before the study.

Studies were carried out in the morning in the laboratory at a room temperature maintained at 25±1°C. Participants fasted overnight and were asked to urinate to avoid urinary bladder distension, which is known to affect peripheral sympathetic discharges. Baseline data were obtained during a 10 minute period of quiet rest of sitting, which was followed by measurements of anthropometric data. A second data were collected during a period of 2 minutes when the subject inserted his/her hand to the wrist level into an ice water (about 4°C). The participants were
advised to remain relaxed and breathe normally and avoid valsava-like maneuvers during hand immersion. All this was considered to avoid sympathetic activation.

Blood pressure and heart rate were initially measured trice with the digital sphygmomanometer, after which their averages were recorded. This was aimed at reducing errors during measurements. The subjects were also asked to remove their shoes for measurements of their weight and height, using a standard scale and a meter rule respectively. The respective BMI was calculated by dividing the weight (kg) by the square of the height (meter). The waist circumference was measured by a tape rule, which was curled over the umbilicus when the subject was asked to relax his/her stomach. Furthermore, the thigh and hip circumferences were measured using the tape rule. The temperature of the ice water was constantly maintained and measured by the thermometer. Finally, the MVO₂ was calculated using the RPP method, which is the product of heart rate with the systolic blood pressure.

Statistical analysis was performed using the statistical package for the social sciences (SPSS-PC Version 17). Pearson correlation analysis was used to detect associations between selected valuables. Stepwise multiple linear regression was used to determine the predictors for change in myocardial oxygen consumption following cutaneous cold stimulation. Furthermore, Student T test for unpaired data was used to assess differences between group means. Results were expressed as Mean±standard error of the mean. Two sided P values <0.05 were considered statistically significant.

**Results**

The study population was composed of 40 normotensive subjects, whose physical and clinical characteristics showing the resting systolic blood pressure, diastolic blood pressure and heart rate were classified by the median weight of 59.50 kg (Table 1). Their characteristics were also classified based on BMIs (Table 2). However, multiple linear regression was used to check the predictors for change in myocardial oxygen consumption following cutaneous cold stimulation. BMI predicted strongly (r=0.480, P=0.002) in the first model. BMI together with body weight were also a predictor in the second model. Table 3 shows the predictive strengths of each variable in the model.

The resting MVO₂ when classified by the median body weight (59.50 kg) is 8880.15±345.64 for body weight greater than 59.50 kg and 8631.15±377.19 for body weight less than 59.50 kg. The resting MVO₂, classified with body mass indices is 8340.89±432.98 for underweight (≤17.9 kg/m²), 8845.07±482.95 for normal weight (18-25 kg/m²), 9581.71±500.45 for overweight (25.1-30 kg/m²) and 9581.7±300.45 for obese/morbid subject (≥30.1 kg/m²). There was an increase of 2578.15±477.24 in MVO₂ in subject with body weight (≤59.50 kg) and an increase of 1029.40±411.82 in subject with body weight >59.50 kg.

**Table 1. Physical and clinical characteristics of the study population classified with weight ≥59.50 and <59.50 kg.**

| Variables     | Weight (≥59.50 kg) (n=20) | Weight (<59.50 kg) (n=20) |
|---------------|---------------------------|---------------------------|
| Age, years    | 21.50±0.60                | 20.40±0.24                |
| Waist circumference (cm) | 88.24±1.75               | 65.94±0.87                |
| Hip circumference (cm) | 108.88±2.03              | 82.79±1.02                |
| Waist to hip ratio | 0.82±0.12                 | 0.80±0.01                 |
| BMI (kg/m²)   | 28.47±0.93                | 17.87±0.32                |
| Baseline SBP (mmHg) | 119.45±2.22              | 111.55±2.61               |
| Baseline DBP (mmHg) | 79.10±1.51               | 70.65±1.17                |
| Baseline HR (bpm) | 74.25±2.40                | 77.00±2.16                |

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate.

**Table 2. Physical and clinical characteristics of the study population classified with different body mass indices.**

| Variables     | Underweight (≤17.9 kg/m²) (n=9) | Normal weight (18-25 kg/m²) (n=14) | Overweight (25.1-30 kg/m²) (n=10) | Obese/morbid (≥30.1 kg/m²) (n=7) |
|---------------|---------------------------------|-----------------------------------|-----------------------------------|----------------------------------|
| Age, years    | 20.22±0.36                      | 20.64±0.27                        | 22.30±1.12                        | 20.51±0.48                       |
| Waist circumference (cm) | 63.19±0.62                 | 71.55±2.15                        | 86.16±2.24                        | 95.94±1.47                       |
| Hip circumference (cm) | 80.33±1.81                  | 88.84±2.32                        | 104.15±2.42                       | 117.88±3.67                      |
| Waist-hip ratio | 0.79±0.13                     | 0.81±0.11                         | 0.85±0.23                         | 0.82±0.11                        |
| Weight (kg)   | 43.67±0.97                      | 53.21±2.69                        | 78.10±2.01                        | 87.86±1.74                       |
| Height (m)    | 1.62±0.01                       | 1.63±0.23                         | 1.70±0.20                         | 1.64±0.29                        |
| BMI (kg/m²)   | 16.54±0.24                      | 19.89±0.55                        | 26.98±0.51                        | 32.82±1.28                       |
| Baseline SBP (mmHg) | 112.11±3.29               | 114.71±4.08                       | 116.20±2.84                       | 120.43±2.47                      |
| Baseline DBP (mmHg) | 69.78±2.91                 | 73.79±2.39                        | 77.10±2.07                        | 81.00±2.05                       |
| Baseline HR (bpm) | 74.22±2.47                | 76.93±2.39                        | 72.30±3.67                        | 79.57±3.86                       |

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate.
weight, 438.00±521.55 in normal weight, greater increase in MVO2 compared to those weight greater than 59.50 kg had significantly stimulation. It was seen that subject with body
gen consumption following cutaneous cold
was a significant increase in myocardial oxy-
...change in myocardial oxygen consumption following cutaneous cold stimulation, due
to dilatation of coronary resistance vessels resulting from increased sympathetic activity.17,18 The increased sympathetic activity was more in overweight and obese/morbid individuals. These probably suggest the increase blood flow seen after cutaneous cold stimulation. Another plausible mechanism explaining this changes can be attributed to the high plasma levels of leptin found in overweight and obese/morbid people.19 Hyperleptinemia increases sympathetic activity, which stimulates increase blood flow.20,21 Leptin also have direct vasodilatory effects on the coronary arteries by inducing nitric oxide (NO) production.22 The vasodilatory effect of NO thus increases myocardial blood flow and increases myocardial oxygen consumption.15-18

However, this research is not without some flaws, and more research is needed in strengthening this association. The following limitations were encountered and exceedingly difficult to study in the course of the research because most of the new techniques are very elaborate, invasive, time consuming and expensive. These limitations include; measurements of blood flow by intravascular doppler catheter; determination of regional oxygen consumption of the heart by combining quick-freeze techniques with microspectroscopic determinations of arterial and venous hemoglobin saturation; estimation of regional cardiac oxygen consumption and regional measurements of blood pressure by15 O-Oxygen Positron-Emission Technique and Carbon-Nitrogen magnetic resonance;13 direct indication of the oxygen supply- consumption ratio by regional reduced nicotinamide adenine dinucleotide videofluorimetry and microvascular oxygen pressures measured by Pd-porphyrin phosphorescence; measurements of blood catecholamines level before and after stimulation; measurements of blood leptin levels and measurements of blood lipids profiles (triglycerides, low-density lipoprotein, high-density lipoprotein, and cholesterol).

**Conclusions**

The data of the present study shows that both body weight and BMI strongly predict change in myocardial oxygen consumption following CCS. This suggests that both body weight and BMI is associated with sympathetic activation following CSS. In addition, the findings also suggested that cardiac muscles of people who are overweight or obese, requires more oxygen during cold exposure. The cold exposure in this study was simulated by CCS. Thus, it can be concluded that normotensive overweight or obese individuals have an exaggerated RPP response to the CCS. However, exposure to cold may augment sympathetic reactivity in overweight/obese individuals, which may contribute to increased risk of developing myocardial dysfunction, even in young normotensive individuals. Furthermore, RPP changes to CCS could be a useful simple measure for early detection of cardiac complications, particularly in low/middle income countries.

The findings of this study suggest that, during cold exposure, people who are overweight or obese, are at high risk of developing myocardial ischemia, if there is any alteration in coronary blood flow (e.g. coronary artery disease). This is so because, the cardiomyocyte of these group of people, demands more oxygen.18,19 An imbalance between oxygen demand and supply translates into ischemia,20,21 Hence, in therapy of coronary artery disease, attention should be directed to directional changes in factors influencing supply and demand of oxygen, to improve blood flow to the myocardium.

**Discussion**

The result of the present study shows there was a significant increase in myocardial oxygen consumption following cutaneous cold stimulation. It was seen that subject with body weight greater than 59.50 kg had significantly greater increase in MVO2 compared to those with body weight less than 59.50 kg. The findings of the study suggest that oxygen consumption following cutaneous cold stimulation was higher in underweight, overweight and obese participants, but was relatively moderate in normal weight subjects. Thus, there was a U-shaped relationship within the groups classified with BMI. This finding is comparable with the result of other studies that reported an increase in myocardial oxygen consumption following cutaneous cold stimulation, due to dilatation of coronary resistance vessels resulting from increased sympathetic activity.17,18 The increased sympathetic activity was more in overweight and obese/morbid individuals. These probably suggest the increase blood flow seen after cutaneous cold stimulation. Another plausible mechanism explaining this changes can be attributed to the high plasma levels of leptin found in overweight and obese/morbid people.19 Hyperleptinemia increases sympathetic activity, which stimulates increase blood flow.20,21 Leptin also have direct vasodilatory effects on the coronary arteries by inducing nitric oxide (NO) production.22 The vasodilatory effect of NO thus increases myocardial blood flow and increases myocardial oxygen consumption.15-18

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