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Myocardial oxygen consumption at rest and during submaximal exercise: effects of increased adiposity

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Summary: Overweight and obesity are major risk factors for cardiovascular diseases. The objective of this study was to determine the effect of increased adiposity on myocardial oxygen consumption at rest and during submaximal exercise in young adults. The study consisted of 85 young adults (18-22years) grouped into 3 based on their body mass index as normal (NW, n=30), overweight (OW, n=25) and obese (OB, n=30). Steady dynamic exercise test equivalent to Grade 2 Bruce protocol was carried out on treadmill for 5min. Blood pressure and heart rate were recorded before, during 3rd min of exercise, immediately after cessation of exercise and during 5th min of recovery. MVO_2 was measured by the Rate Pressure Product (RPP) calculated as product of heart rate and systolic blood pressure. Statistical analysis was done using ANOVA and regression analysis. The mean resting RPP was significantly higher in overweight and obese groups when compared with the normal weight group ($p<0.05$). There was significant increase in RPP changes to exercise [mean difference in NW-8270.93 bpm.mmHg (99.61%), OW-10593.12 bpm.mmHg (118.39%) and OB-10897.33 bpm.mmHg (118.10%), $p< 0.05$] and the value did not return to baseline after 5 mins of recovery in study groups ($p< 0.05$). BMI and Waist stature ratio were the most important independent parameters in prediction of RPP. The study shows that overweight and obese young adults have elevated resting RPP and much higher RPP response to exercise indicating increased (MVO_2) at rest and during exercise suggesting higher hemodynamic stress to the heart.

Keywords*:* Overweight, Obesity, Steady exercise, MVO_2

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INTRODUCTION

Obesity is a common condition that develops from the interaction between the genotype and the environment and involves social, behavioral, cultural, physiological, metabolic and genetic factors (Kotsis et al., 2010). Obesity has an important negative impact on health in a population and is characterized by hemodynamic and metabolic alterations. Overweight and obesity are major risk factors for cardiovascular diseases. These individuals have higher prevalence for many diseases like coronary heart disease, hypertension, hyperlipidemia and diabetes mellitus (Must et al., 1999). All these diseases are preventable by changes in lifestyle of a person.

Myocardial oxygen consumption (MVO_2) is a good indicator of the response of the coronary circulation to increased myocardial oxygen demand. Because of the essentially aerobic metabolism of the myocardium, changes in MVO_2 correlate highly with work of the heart. Measuring changes in MVO_2 allow study of various medical, surgical, and physical interventions on the ability of the heart to perform work (McArdle et al., 2005). MVO_2 can be easily calculated by indirect methods like Stroke work, Fick's Principle, the tension time index and Rate Pressure Product (RPP) (Sarnoff et al., 1958).

RPP, also known as Cardiovascular Product or Double Product, is the product of heart rate and systolic blood pressure which is used in cardiology and exercise physiology to indirectly determine the MVO_2 and thus cardiovascular risk of subjects. RPP is a correlate of myocardial oxygen consumption, and hence of work load of the heart. It is considered a determinant of cardiovascular risk, since its increase precedes ischemic events (White. 1999). Thus RPP is used to measure the workload or oxygen demand of the heart, and reflects hemodynamic stress. RPP is said to be raised in obesity due to cardiac remodelling or sympathovagal imbalance (White. 1999; Martin et al., 2005; Ikonomidis et al., 2007).

Exercise stress testing is an accepted mode of evaluating the peak oxygen consumption and

cardiopulmonary status. RPP increases with the increased workload on the heart to provide the adequate blood supply to the myocardium during exercise. In healthy people, RPP changes in accordance with increased myocardial blood flow and oxygen consumption during exercise. Any total value greater than 10,000 indicates an increased risk for heart disease (McArdle et al., 2005). In obese people there is exaggerated response of systolic blood pressure to exercise stress. There are not many studies on RPP changes to submaximal exercise in overweight and obese young adults. Hence the present study was under taken with the aim of evaluating the effect of overweight and obesity on RPP and the effect of submaximal steady exercise on the RPP in apparently healthy overweight and obese young adults.

The objectives of this study were to determine the effect of increased adiposity on RPP in healthy young adults at rest; to evaluate the association between RPP and different obesity variables at rest and to study the effect of submaximal steady exercise on the RPP in healthy overweight and obese young adults.

MATERIALS AND METHODS

The first year medical students of Jagadguru Sri Shivarathreeshwara Medical College (JSSMC), Mysore, India were screened for their age, history of hypertension, cardiac or pulmonary diseases, smoking and consumption of alcohols. Clinical examination was conducted on all subjects to rule out any systemic disorders. The height and weight of each student was recorded and body mass index (BMI) was calculated as the weight in kilogram divided by the square of the height in meter.

Those in the age group of <18 yr and > 22 yr, with the history of hypertension, cardiac or pulmonary diseases were excluded from the study. Thus subjects satisfying the inclusion criteria's were divided into three groups depending on BMI cut off point for Indian population (i goveronment_in .mht, 2008). All obese with BMI $\geq$ 25 Kg/m^2 (n = 30) (male = 16 & female = 14) and overweight with BMI $\geq$ 23 to 24.9 Kg/m^2 (n = 25) (male = 13 & female = 12) students were considered to form the study groups.

Normal weight students with BMI < 22.9 $Kg.m^2$ (n = 30) were selected randomly using random number table to form the control group. This sample size was estimated to be enough to detect a clinically relevant difference of 10% in the parameters under study at 5% level of significance with 80% power. The study was approved by the Ethical committee of JSS Medical College, Mysore. Subjects were informed about the purpose of the study, the study protocol and the informed consent was obtained.

Waist circumference (WC) and hip circumference (HC) were measured and the ratio of WC to HC (WHR) was calculated to know the central fat distribution. Waist Stature Ratio (WSR) was calculated as the ratio of WC to height.

Study was carried out in the human experiment laboratory in Department of Physiology JSSMC, Mysore, India under controlled conditions by a single observer. Subjects were briefed about the experiment protocol and familiarized with the set up. After relaxation for 10 minutes resting blood pressure (BP) was measured in the sitting position using a mercury sphygmomanometer by auscultatory method and Pulse rate was measured by examining radial pulse.

Then Steady dynamic exercise test was done on Motorized Treadmill, Model: MT 600. Male subjects were made to exercise for 5 minutes with a steady speed of 6 km / hr at grade 0 whereas Female subjects were made to exercise for 5 minutes at a steady speed of 4.5 km/hr at grade 0. This exercise load is equivalent to stage II of Bruce protocol and calculated equivalent METs is approximately 4 according to ACSM guidelines (Haskell et al., 2007). BP was recorded using the Sphygmomanometer by auscultatory method during 3rd minute of exercise when the heart rate was maximum and stabilized on the monitor of treadmill, immediately after cessation of exercise and after 5 minutes of recovery. Pulse rate was measured by examining radial pulse immediately after cessation of exercise and after 5 minutes of recovery. Pulse rate during exercise was noted down from the monitor on the treadmill. RPP was calculated as product of heart rate (bpm) and systolic blood pressure (mmHg) at rest, during exercise, immediately after cessation of exercise and after 5 minutes of recovery.

Statistical analysis:
Data were presented as Mean and standard deviation. Test of differences between the groups were carried out using One way Analysis of Variance (ANOVA) and post-hoc test. Pearson's correlation coefficients were estimated to quantify the linear relationship between the indices of obesity and RPP. Simple linear regressions were fit to know the role of individual parameters followed by multiple regressions to find the role of significant parameters collectively in prediction of RPP. All statistics were performed using the SPSS 17.

RESULTS

The characteristics of the three study groups were as shown in table I. There were significant differences ($p<0.05$) in the mean of weight, BMI, WC and HC of the obese and over-weight when compared with the normal weight group. However, there was no significant difference in the mean of age, height and WHR among the groups. Resting mean level of systolic blood pressure and diastolic blood pressure among overweight and obese young adults was significantly higher ($p<0.05$) as compared to the

Table 1. Physical characteristics among normal, overweight and obese subjects

Variables	Normal	Overweight	Obese
Age (Yr)	18.43 ± 0.85	18.32 ± 0.99	18.40 ± 0.89
Weight (Kg)	57.13 ± 8.16* #	66.92 ± 8.61	80.07 ± 9.85
Height (m)	1.40 ± 0.17	1.39 ± 0.17	1.44 ± 0.14
WC (cm)	77.45 ± 6.60#	83.36 ± 7.94#	89.75 ±12.55
HC (cm)	92.37 ± 5.75* #	100.12 ± 5.51	104.75 ±13.65
WHR	0.84 ± 0.06	0.83 ± 0.007	0.86 ± 0.06
BMI(Kg/m^2)	20.39 ± 1.46* #	24.04 ± 0.59#	27.78 ±1.86

BMI= Body Mass Index, WC= Waist circumference, HC= Hip Circumference, WHR= ratio of WC to HC, *: Significantly different from overweight group. #: Significantly different from obese group

normal weight group. No significant difference in resting mean level of systolic blood pressure and diastolic blood pressure was found between overweight and obese young adults. There was no change in the resting pulse rate between the groups.

The mean resting RPP was significantly higher in overweight and obese groups as compared to the normal weight group. No statistically significant difference was found between overweight and obese groups. There was significant increase in RPP during exercise in all three groups [mean increase in normal weight group was 8270.93 (99.61%), in overweight group was 10593.12 (118.39%) and in obese group was 10897.33(118.10%)]. The percentage increase during exercise and immediately after was significantly higher in overweight and obese groups when compared normal weight group. The RPP after 5 min of recovery from exercise remained higher in these groups when compared to baseline which was statistically significant.

Pearson's correlation coefficient (Table 3) showed that RPP was significantly correlated positively with all the obesity indices. Table 4 shows results of simple linear regression analysis for RPP which was significantly correlated with obesity indices, the percentage variation explained by different obesity indices individually varied from 6.8% to 18.2%. BMI was the most important individual parameter in

Table 3. Pearson's correlation coefficient between RPP and obesity indices

Obesity indices	Correlation coefficient
BMI	0.422*
WC	0.369*
HC	0.316*
WHR	0.242*
WSR	0.300*

BMI= Body Mass Index, WC= Waist circumference, HC= Hip Circumference, WHR= ratio of WC to HC, WSR=Waist Stature Ratio * p< 0.0001

Table 4. Regression coefficient (β), Variation explained (R^2) and p- value for significance of β between Relative Pressure Product and predictors of adiposity.

Dependent variable	**Predictor**	**B**	**R^2 (%)**	**P-value**
RPP	BMI	136.80	18.2	3.906E-12
	WC	48.19	17.9	4.976E-12
	HC	56.79	15.3	2.200E-10
	WHR	4690.26	6.8	3.560E-05
	WSR	7466.61	12.9	7.525E-09

RPP= Relative Pressure Product, BMI= Body Mass Index, WC= Waist circumference, HC= Hip Circumference, WHR= ratio of WC to HC, WSR=Waist Stature Ratio

Table 2. Mean±SD of the Heart Rate, Systolic Blood Pressure and Relative Pressure Product in normal, overweight and obese subjects

	Variables	**Normal**	**Overweight**	**Obese**
Before exercise				
	HR	79.37 ± 7.70	79.48 ± 6.35	79.83 ± 7.22
	SBP	105.07 ± 9.21* #	112.40 ± 9.88	115.33 ± 10.18
	RPP	8302.8 ± 770.26* #	8946.80 ± 1153.82	9227.33 ± 1331.41
During Exercise				
	HR	122.3 ± 15.59	131.72 ± 19.05	129.1 ± 20.88
	SBP	134.07 ± 9.09* #	147.12 ± 13.88	151.67 ± 14.93
	RPP	16573.73 ± 2717.75* #	19539.92 ± 4223.55	20124.67 ± 4089.27
Immediately after cessation of Exercise				
	HR	122.2 ± 17.48	135.40 ± 21.45	136.03 ± 20.66
	SBP	126.87 ± 15.74* #	138.32 ± 12.84	139 ± 9.18
	RPP	15604.47 ± 3613.16* #	18795.76 ± 3638.05	18972.93 ± 3555.10
After 5min of recovery				
	HR	85.3 ± 13.13	92.20 ± 12.90	90.07 ± 12.21
	SBP	104.93 ± 8.63* #	113 ± 2.0	112 ± 5.64
	RPP	8940.40 ± 1496.36* #	10460 ± 1823.52	10132.47 ± 1369.72

HR=Heart Rate, SBP=Systolic Blood Pressure, RPP=Relative Pressure Product, *: Significantly different from overweight group. #: Significantly different from obese group

prediction of RPP followed by WC. On multiple regression analysis it was found that the significant obesity indices taken together were responsible for 22 percent of variation in which BMI and WSR were the significant contributors. Multiple regression equation is as follows:

RPP= 5396.90+100.59*BMI[#]+52.52*WC+1.12*HC –199.12*WHR – 6216.96*WSR[#].

DISCUSSION

In the present study over weight and obese young adults showed significantly increased RPP values at rest, during submaximal exercise and subsequent recovery from exercise when compared with normal young adults. RPP indirectly determine the MVO_2 and thus cardiovascular risk of subjects. Thus we can state that at rest the hearts of overweight and obese subjects consume more oxygen than those of control subjects. The higher RPP in study subjects was mainly due to increase in SBP which indicates increase in myocardial activity and thus the MVO_2 at rest. Myocardial oxygen uptake is primarily determined by intramyocardial wall stress (ie, the product of left ventricular [LV] pressure and volume, divided by LV wall thickness), contractility, and heart rate. Other, less important factors include external work performed by the heart, the energy necessary for activation, and the basal metabolism of the myocardium. Thus the study shows that there is hemodynamic stress to the heart in study subjects (Fletcher et al., 2001). The results are similar to the other studies which have shown increased resting RPP in obese children and adults (Martin et al., 2005; Ikonomidis et al., 2007; Fei Ho et al., 1995; Lin et al., 2011). This MVO_2 increase could be due to the effect of obesity on cardiac remodeling and the fact that obesity increases sympathetic tone, hemodynamic load due to increase in blood volume and fatty acid metabolism in myocardium (Alpert 2001, Peterson et al., 2004, Ihlen et al ., 1984). Results from studies in animal models demonstrate that obesity increases myocardial fatty acid metabolism and oxygen consumption leading to increased oxidative stress, cardiac dysfunction, and apoptosis (Zhou et al., 2000; Listenberger et al., 2001; Aasum et al., 2003; Vincent et al., 2001). In humans also, obesity and insulin resistance are related to similar increases in myocardial oxygen consumption and fatty acid metabolism and oxidative stress markers (Peterson et al., 2004; Vincent et al., 2007). MVO_2 and myocardial fatty acid utilization has been showed to decrease after weight loss from gastric bypass surgery or diet in obese persons (Fei ho et al., 1995,).

During submaximal exercise and immediately after exercise, all three groups showed an increase in RPP. The percentage increase in RPP was significantly higher in the overweight and obese subjects than that of normal weight subjects which shows increased cardiac activity and thus MVO_2 in these subjects. During exercise the heart rate increased by 54% in normal weight group, 71% in over weight group and 70% in obese group whereas SBP increased by 28% in normal weight group, 31.2% in over weight group and 31.3% in obese group. Thus the increase in RPP was mainly due to increase in heart rate rather than SBP during exercise which could be due to increase in sympathetic activity in overweight and obese subjects**.** It is showed that cardiac stroke volume increases to over resting values at low levels of work, but there is no further increase once cardiac frequency has risen to 120 bpm (Jones. 1988). The increased RPP during exercise shows that individual not only has an increased risk of heart disease but also has a very large stress on the heart with regard to oxygen delivery needs. This could result in a faster onset of fatigue during moderate to severe exercise and an increased rate of perceived exertion during all submaximal activity. Previous studies have shown that obesity is associated with disproportionate increases in the RPP during physical exertion (Alexander, 1964). Obese patients have demonstrated a greater RPP and oxygen consumption ($\dot{V}O_2$) for a given submaximal workload, and relative chronotropic incompetence compared with control subjects (Salvadori et al., 1999).

This study also shows that the RPP remained higher in overweight and obese groups even after 5 mins of recovery when compared to baseline which was statistically significant. This higher RPP after recovery was due to reduced heart rate recovery in study groups which could be due to autonomic imbalance with reduced parasympathetic activity and increased sympathetic activity in overweight and obese groups which has been demonstrated by previous studies at rest and during exercise stress (Nageswari et al., 2007; Valensi et al., 1999). All the cardiac alterations in over weight and obesity are reversible on weight reduction. Hence early detection of cardiac abnormalities in these persons is essential.

The present study though not exhaustive shows that increased adiposity in young adults is associated with elevated resting RPP and much higher RPP response to exercise. This indicates that there is increased MVO_2 suggesting larger hemodynamic stress to the heart. Thus the subtle cardiovascular changes in over weight and obese young adults can lead to overt cardiovascular diseases in adulthood. RPP changes to exercise which is an indirect measure and good indicator of MVO_2 could be used for early detection of cardiac dysfunction.

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