RATE PRESSURE PRODUCT – A DIAGNOSTIC TOOL IN DETERMINING THE CARDIOVASCULAR RISK IN POSTMENOPAUSAL WOMEN

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ABSTRACT

Objective: Rate pressure product (RPP) is an indirect measure of Myocardial oxygen consumption (MVO₂). It increases progressively with exercise and the RPP at peak of exercise is Peak rate pressure product (PRPP). The low value of PRPP suggests significant compromise of coronary perfusion. In the present study effect of exercise on RPP of Pre menopausal women and Postmenopausal women were compared.

Research Design and Methods: The study was conducted on a total of 50 healthy volunteer women. They were subjected to treadmill exercise test and baseline and maximum RPP was calculated.

Results: The RPP in premenopausal women increased significantly from 10.83 ± 2.11 to 28.98 ± 2.93 mm of Hg beats / min x 10⁻³ during exercise and in postmenopausal from 12.52 ± 2.69 to 28.03 ± 4.14. The percentage increase in RPP was significantly more in Premenopausal women (63%) compared to postmenopausal women (55%).

Conclusions: It can be concluded that Rate pressure product reaches the critical value before the symptoms appear and the percentage increase in Rate pressure product was less in postmenopausal women. The results also suggest that the measurement of Peak rate pressure product in response to exercise can detect Coronary Artery Disease (CAD) even before the appearance of clinical signs and symptoms in postmenopausal women and thus can be used as a diagnostic tool.

INTRODUCTION

Menopause is a period used to express the permanent cessation of the prime function of the human ovaries, the ripening and release of ova and the release of hormones that cause both the creation of the uterine lining and the subsequent shedding of the uterine lining. Menopause signals the end of the fertile phase of a woman's life. Menopause has a wide starting range, but can usually be expected in the age range of 42–58(1). Menopause is associated with increased risk of Coronary Artery Disease (CAD) due to loss of cardio protective effect of estrogen. Estrogen deficient state affects myocardial efficiency by enhancing cardiovascular response to mental stress, by changing lipid profile, decreasing vascular reactivity (2) and by increasing homocysteine levels (3). Moreover there is
accelerated cell death in the aging myocardium leading to depletion of functional myocytes that decreases the contractile performance (4). Myocardial oxygen consumption (MVO$_2$) is a good indicator of the response of the coronary circulation to increased oxygen demand. Coronary blood flow (CBF) increases in direct proportion to the myocardial oxygen requirements. Thus the determinants of MVO$_2$ are also the determinants of CBF (5). Direct measurement of MVO$_2$ is difficult in routine clinical practice but it can be easily measured indirect methods like stroke work, Fick’s principle, the tension time index and rate pressure product (RPP) (6). RPP is the product of heart rate and systolic blood pressure. It reflects the work of the heart and correlates well with MVO$_2$. It is calculated as $\text{RPP} = \text{Heart rate (HR)} \times \text{Systolic blood pressure (SBP)} / 1000$. The value is divided by 1000 to make the number more manageable. (7). It increases with the increase of stress or workload on the heart. It is a simple non invasive easily measurable index, which defines the response of coronary circulation to myocardial metabolic demand. It is a good index of MVO$_2$ in patients with ischemic heart disease (8). It has been shown that in any particular patient with CAD, the onset of angina appears at a constant RPP. Most patients would complaint of some pain at a constant RPP of 20,000. (9) Rate pressure product is also called as Robinson index (10). The internal myocardial work performed is represented by RPP and external myocardial work performed is generally expressed as stages of exercise.

Many comparative studies have been done to know the influence of hormones on hemodynamic parameters in postmenopausal women but there are few reports on the effect of exercise on RPP in postmenopausal women. Hence this study was designed to evaluate the effect of exercise on RPP in postmenopausal women and determine the importance of RPP in the diagnosis and the prevention of CAD in postmenopausal women.

MATERIAL AND METHODS
The present study was done to access the cardiovascular performance in postmenopausal women by measuring various hemodynamic parameters like Heart rate, Systolic blood pressure and Rate pressure product. The study was conducted in 50 volunteer women. They were divided into two groups. The Group A consisted of 25 healthy postmenopausal women with no systemic disorder and Group B consisted of 25 postmenopausal women with and no systemic disorder. The study protocol was approved by the Institutional ethics committee. Written informed consent was taken from all the volunteers before enrollment.

The study included recording of anthropometric parameters like age, height and weight. All the subjects were first thoroughly examined and those having systemic disease were excluded. The baseline heart rate, systolic blood pressure and ECG were recorded. SBP was recorded by auscultatory method. Baseline RPP was calculated. RPP, which is the product of systolic blood pressure and heart rate, was computed as (7): $\text{RPP} = \text{SBP in mm Hg} \times \text{HR beats/ min} \times 10^{-3}$.

Exercise stress test was performed on Treadmill, which is the most commonly used dynamic exercise device for this test. The subject was subjected to graded exercise. The treadmill is started at a relatively slow speed. The treadmill speed (km/hr) and its grade of slope (%) or inclination are increased every three minutes according to a preprogrammed protocol. Bruce protocol is the commonest protocol used. The protocol dictates the precise speed and slope of treadmill. According to this, each three minute interval is called as a stage. The treadmill is set with the stage I, speed (2.74 km/hr) and grade of slope (10%) and subject commences the test. At the appropriate times during the test, the speed and slope of treadmill are adjusted. So after 3 minutes, the speed is adjusted to 4.02 km/hr and slope to 12%. After 6 minutes, the speed is adjusted to...
5.47 km/hr and slope to 14%. The subject was made to run on a treadmill till exhaustion. Treadmill exercise variables of HR, SBP and ECG were determined. The ECG was constantly displayed on the monitor. It was also recorded on paper at one minute interval. The patient’s blood pressure was recorded during second minute of each stage. The maximum RPP was calculated.

The maximum RPP at maximum exercise is called as Peak RPP (PRPP). The exercise test is said to be maximal when the subject appears to give true maximal effort i.e. Effort done to the point of body exhaustion or when other clinical end points are reached. The exercise stress test was terminated in the subjects if the target heart rate was achieved or they complained of fatigue. Exercise was also discontinued if there were abnormal changes like decrease in SBP of 10 mm Hg along with evidence of ischemia, abnormal ECG pattern like ST segment displacement, appearance of arrhythmias, bundle branch block or if subject complains of chest pain.

**Statistical analysis**

Data was represented as mean and standard deviation (SD). Analysis was done using Student’s paired t-test and Wilcoxon Signed Ranks Test. P-value<0.05 was considered as statistically significant.

### OBSERVATIONS AND RESULTS

The subjects of group A and Group B were comparable for demographic characteristics (Table I). The mean age of Group A was 40 years and Group B was also 57 years.

**Table I showing Demographic profile of subjects at baseline in both groups**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>39.6 ± 6.0</td>
<td>56.5 ± 6.1</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>73.7 ± 20.9</td>
<td>67.4 ± 10.7</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>157.0 ± 6.2</td>
<td>156.3 ± 4.8</td>
</tr>
</tbody>
</table>

Group A₁ = 25, Group B = 25
All values are mean ±SD

**Table II shows changes in hemodynamic parameters (SBP, HR and RPP) in both the groups**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Baseline</th>
<th>Maximum</th>
<th>Percentage change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group A</td>
<td>84.32±11.18</td>
<td>168.96 ± 11.40#</td>
<td>59</td>
</tr>
<tr>
<td>Group B</td>
<td>88.92±18.06</td>
<td>157.6 ±21.14* #</td>
<td>43*</td>
</tr>
<tr>
<td>SBP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group A</td>
<td>128 ± 14.71</td>
<td>172.08 ± 18.96#</td>
<td>25</td>
</tr>
<tr>
<td>Group B</td>
<td>141.12 ± 12.01*</td>
<td>178.08± 13.74**</td>
<td>21</td>
</tr>
<tr>
<td>RPP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group A</td>
<td>10.83± 2.11</td>
<td>28.98 ± 2.93#</td>
<td>63</td>
</tr>
<tr>
<td>Group B</td>
<td>12.52 ± 2.69*</td>
<td>28.03± 4.14#</td>
<td>55*</td>
</tr>
</tbody>
</table>

All values are mean ±SD
* P < 0.05 as compared to group A
# P < 0.05 as compared to baseline value

All the baseline hemodynamic parameters were significantly more in healthy postmenopausal women as compared to healthy Premenopausal women. There was significant increase in SBP, HR and RPP during exercise in both the groups. The RPP in Group A increased significantly from 10.83 ± 2.11 to 28.98 ± 2.93 mm of Hg beats / min x 10⁻³ during exercise. Group B also showed a significant increase in RPP from 12.52 ± 2.69 to 28.03 ± 4.14. The percentage increase in RPP was significantly more in Premenopausal women (63%) as compared to postmenopausal women (55%). Maximum HR was significantly less in group B as compared to group A. The percentage increase in HR was significantly more in Premenopausal
women (59%) as compared to Premenopausal women (43%).
There was no statistically significant difference in percentage change in SBP between the groups.

DISCUSSION
Abnormal hemodynamic response to exercise may indicate an increased risk of CAD, even if signs and symptoms of ischemia are absent. Both HR and SBP are important variables determining changes in myocardial oxygen consumption between rest and exercise (9). During exercise HR, SBP and RPP increases with increase work load on the heart to provide adequate blood supply to the active myocardium.

All the hemodynamic parameters increase significantly with exercise in both the groups. This is due to increase in sympathetic discharge during exercise (11,12). RPP increases progressively with exercise and attained the peak value of 28.98 ± 2.93 mm Hg x beats per minute x 10^{-3} in premenopausal women and 28.03 ± 4.14 in postmenopausal women. The percentage increase in RPP was significantly less in postmenopausal women (55%) as compared to premenopausal women (63%). The less percentage increase in postmenopausal women is due to age related depletion of functional myocytes, cardiac receptors and increased myocardial stiffness that decreases the ventricular pumping and cardiovascular response of the heart to exercise. (13)

Angina results from imbalance between oxygen supply and demand and is precipitated due to increase in work of myocardium to a critical level which is fixed in each patient. The work of the myocardium is measured by RPP. Most normal individuals develop a RPP of 20 to 35 mm Hg x beats / min x 10^{-3}. In many patients with significant Ischemic Heart Disease, RPP value exceeding 25 mm Hg x beats / min x 10^{-3} are unusual (14). Studies reported the rate pressure product exceeding 22,000 is commonly associated with myocardial ischemia and angina (9). In the present study the PRPP was 28.98 and 28.03 mm Hg x Beats / min x 10^{3} in pre menopausal women and post menopausal women respectively. The percentage increase in RPP was 63% in premenopausal women and 55% in postmenopausal women. The peak RPP is an accurate reflection of the myocardial oxygen demand and myocardial work load. The higher the RPP, the higher will be the MVO_2. The ability to reach high RPP is associated with more adequate coronary perfusion. Reaching the high RPP without symptoms or evidence of severe ischemia suggests adequate left ventricular functions and the low value of PRPP suggests significant limitation of coronary perfusion and decreased LV function leads to angina. Maximum RPP is reported to range from 10^{th} percentile value of 25,000 to a 90^{th} percentile of 40,000 (15). RPP exceeding 22 is commonly associated with myocardial ischemia and angina (8).

Both HR and SBP are also useful in the diagnosis of ischemic heart disease in postmenopausal women. In our study there was a significant increase in HR and SBP in both the groups during exercise. The percentage increase in SBP was comparable in both the groups. On the other hand the percentage increase in HR was significantly less in postmenopausal women as compared to premenopausal women. The less increase in HR is due to age related depletion of cardiac myocytes which has been proposed as a mechanism for decreased contractile performance and decrease hemodynamic responses (3).

The baseline HR, SBP and RPP were more in postmenopausal women than premenopausal women. It may be attributed due to marked sympathetic activation and decrease parasympathetic activity due to low estrogen. The increased sympathetic activation in postmenopausal women is due to endothelial dysfunction. Also with menopause, there is increased level of vasoconstriction and oxidative stress. All these factors contribute to hyperkinetic
circulation characterized by elevated HR and SBP. Menopause also increases aortic stiffness.

CONCLUSION
Results from this study indicate that HR x SBP, easily measurable hemodynamic parameters are valid predictors of MVO$_2$ during exercise in a population of postmenopausal women. It can be concluded that RPP reaches the critical value before the symptoms appear and the percentage increase in RPP was less in postmenopausal women. The results also suggest that the measurement of PRPP in response to exercise can detect CAD even before the appearance of clinical signs and symptoms in postmenopausal women and thus can be used as a diagnostic tool.

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