Gender Differences in Circulatory Response Measured by the Double Product Break-Point Method

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Abstract. The purposes of this study were to evaluate the gender difference in exercise tolerance. We analyzed the relationship between the double product (DP) at the double product break-point (DPBP) and the systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressure (MAP), pulse pressure (PP), heart rate (HR) at DPBP. The subjects were 18 healthy men and 15 healthy women. Exercise tests were performed on a cycle ergometer. The DP at DPBP increased more in women than in men (p<0.05). There were no significant differences in DBP, MAP, PP or HR at DPBP between the groups. At DPBP of men, DP was significantly correlated with SBP, MAP, PP and HR (p<0.05). In women, the only significant correlation was between HR and DP at DPBP (p<0.05). This suggests that the configuration factors of exercise tolerance differ between men and women, although men have a blood pressure dominant response at DPBP, women have a heart rate dominant response.

Key words: Double product break-point, Gender, Exercise tolerance

INTRODUCTION

Cardiac rehabilitation programs are based on electrocardiography, cardiac ultrasonography, angiography, and evaluation of exercise tolerance to measure the anaerobic threshold using oxygen uptake kinetics1–13). Tanaka et al.8) developed the DPBP method, a simple method for measuring the anaerobic threshold (AT) and lactate threshold (LT). The double product (DP) is calculated as the product of heart rate (HR) and systolic blood pressure (SBP). Recently, its safety and usefulness as a simple means of measurement have been reported in hospitals and other health facilities10, 13). When the independent variable is time or intensity of exercise during an incremental exercise test and the dependent variable is DP, the intersection of two linear regression lines may be identified as the DPBP, the point at which DP increases sharply during exercise. The intersection point has been reported to be largely consistent with AT and LT determined by expired gas analysis7, 8, 10, 13).

There have been numerous studies on the effects of gender and age using static evaluations1, 2, 11, 12). Most of these studies reported arrhythmias, and there have been numerous studies reporting oxygen uptake kinetics and heart rate threshold in relation to exercise tolerance, gender and age1–9). However, we have found no previous reports of DPBP in relation to gender and age. Carhart et al.15) investigated lifestyle, morbidity and mortality in relation to gender, in order to provide the information needed to develop gender-specific cardiac rehabilitation programs. Cardiac

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rehabilitation programs comprise mainly guidance on exercise (therapeutic exercise), diet and daily life activities. Exercise guidance occupies an important position in these programs15).

The purposes of this study were to evaluate the gender difference in exercise tolerance. We analyzed the relationship between the DP at DPBP and SBP, diastolic blood pressure (DBP), mean blood pressure (MAP), pulse pressure (PP) and HR at DPBP in healthy adult men and women.

MATERIALS AND METHODS

Subjects
Eighteen healthy men and fifteen healthy women gave their written informed consent to participate in this study, which was approved by the ethics committee of Kawasaki University.

The physical characteristics of the subjects are summarized in Table 1. None of the subjects consumed any form of medication or alcohol, and abstained from smoking.

Experimental design
Tests were performed on the subjects at least 3 hours after a meal and 12 hours after caffeine ingestion. After establishment of baseline measures, data were collected during a 5-min period of supine rest.

All subjects performed a graded ergometric test, that is generally used, in an upright body position using an electromagnetically braked cycle ergometer (Monark model 814E; Varberg, Sweden). Subjects sat on the saddle so that they were able to comfortably extend and flex the knees while pedaling.

The subjects remained in a state of rest on the ergometer for at least 5 min immediately after they entered the laboratory. The subjects were then instructed to try to keep the number of pedal revolutions at 60 rpm. After warm up at 0 W for 3 min, starting at 30 W, the workload was increased by 10 W every 2 min. The test was continued until the predicted maximal HR (220–age) was reached or the subject could no longer maintain the prescribed rate of wheel revolutions because of fatigue. The test was performed in a temperature-controlled room (24°C, relative humidity 50%).

Circulatory responses
SBP, DBP and HR were measured continuously for the 5 min of rest and during the exercise. An arm blood pressure cuff (15 cm) was fitted at the right brachial artery site, using an automatic indirect manometer (model BP-203i; Colin Med Tech). DP, SBP, DBP and HR were measured continuously, MAP and PP were calculated at 1-min intervals. They were calculated with the following equations:

\[
\text{MAP} = \frac{(\text{SBP} - \text{DBP})}{3} + \text{DBP}; \quad \text{PP} = \text{SBP} - \text{DBP}; \quad \text{DP} = \text{SBP} \times \text{HR}.\]

The DPBP was determined using a computer algorithm as follows. After excluding the first-stage data obtained at 30 W, the linear regression lines of DP as a function of W were calculated for all possible divisions of the data into two adjustment groups, and the break-point was determined by the intersection of the two lines, which represented the minimum residual sum of the squares.

The estimated maximal oxygen uptake was calculated from the regression line of load and HR, and was calculated according to the formula

\[
12.47 \times \text{maximal physical activity ÷ body weight (kg)}.\]

The men were divided into two groups by BMI, above and below the median, and we analyzed the relationship of SBP, DBP, MAP, PP and HR with DP at DPBP in the two groups.

Statistical analysis
All analyses were performed using SSPS in Windows 2006. Data were expressed as mean ± SD. Differences between men and women were analyzed using the paired t-test. Pearson product-moment correlations were calculated to show the relationship between DP at DPBP and SBP, DBP, MAP, PP, and HR at DPBP in men and women. An alpha level of 0.05 was used as the criterion of statistical significance.

RESULTS

Characteristics of the two subject groups
Table 1 shows selected characteristics of the two subject groups. Height, weight, and BMI were lower in the women than in the men.

Comparison of resting circulatory response in the groups
The baseline resting circulatory response was similar in men and women (Table 2). There were significant correlations between resting HR, MAP, and resting DP in men. On the other hand, a
significant correlation was found only between resting HR and resting DP in women (Table 3).

**Typical responses of circulatory response and work rate (W) in one subject during incremental exercise**

Representative changes in SBP, DBP, PP and MAP with respect to work rate (one subject) are shown in Fig. 1. SBP and PP were characterized by two inflection points at lower and higher blood pressures and could be expressed as third-order regression equations. While DBP in exercise showed a decreasing trend, MAP showed a slight increase. Representative changes in HR with respect to work rate. The change in HR could be expressed by a second-order regression equation without two inflection points at higher and lower blood pressures. HR did not change substantially within workload 30–50 W, but increased steeply at approximately 80 W. The steep increase slowed at approximately 100 W. DP showed an increasing

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**Table 1.** Characteristics of the two subject groups

<table>
<thead>
<tr>
<th></th>
<th>Men (n=18)</th>
<th>Women (n=15)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>25.2 ± 2.1</td>
<td>23.4 ± 4.0</td>
<td>n.s</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>169.6 ± 6.9</td>
<td>154.8 ± 4.1</td>
<td>**</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>67.3 ± 13.6</td>
<td>49.3 ± 4.7</td>
<td>**</td>
</tr>
<tr>
<td>BMI (kg·m⁻²)</td>
<td>23.1 ± 3.8</td>
<td>20.6 ± 2.6</td>
<td>*</td>
</tr>
<tr>
<td>BSA (m²)</td>
<td>1.8 ± 0.2</td>
<td>1.5 ± 0.1</td>
<td>n.s</td>
</tr>
</tbody>
</table>

Mean ± SD.
BMI: Body Mass Index. BSA: Body Surface Area
n.s: not significant. *p<0.05. **p<0.01.

**Table 2.** Comparison of resting circulatory response of the groups

<table>
<thead>
<tr>
<th></th>
<th>Men (n=18)</th>
<th>Women (n=15)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP (mmHg)</td>
<td>114.6 ± 5.7</td>
<td>114.4 ± 7.5</td>
<td>n.s</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>63.2 ± 2.6</td>
<td>62.1 ± 4.0</td>
<td>n.s</td>
</tr>
<tr>
<td>PP (mmHg)</td>
<td>51.5 ± 5.3</td>
<td>52.2 ± 8.9</td>
<td>n.s</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>81.1 ± 4.1</td>
<td>79.5 ± 3.5</td>
<td>n.s</td>
</tr>
<tr>
<td>DP (mmHg·beats·min⁻¹)</td>
<td>7,988.7 ± 1,008.4</td>
<td>7,384.0 ± 725.5</td>
<td>n.s</td>
</tr>
<tr>
<td>HR (beats·min⁻¹)</td>
<td>69.7 ± 7.8</td>
<td>64.5 ± 4.2</td>
<td>n.s</td>
</tr>
</tbody>
</table>

Mean ± SD.
SBP: systolic blood pressure. DBP: diastolic blood pressure. PP: pulse pressure.
MAP: mean arterial blood pressure. DP: double product. HR: heart rate. n.s: not significant.
*p<0.05. **p<0.01.

**Table 3.** Relationship between circulatory response and resting DP of the groups

<table>
<thead>
<tr>
<th></th>
<th>Men (n=18)</th>
<th>Women (n=15)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP (mmHg)</td>
<td>0.33</td>
<td>0.43</td>
<td></td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>0.37</td>
<td>−0.11</td>
<td></td>
</tr>
<tr>
<td>PP (mmHg)</td>
<td>0.04</td>
<td>0.43</td>
<td></td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>0.53*</td>
<td>0.28</td>
<td></td>
</tr>
<tr>
<td>HR (beats·min⁻¹)</td>
<td>0.51*</td>
<td>0.71**</td>
<td></td>
</tr>
</tbody>
</table>

SBP: systolic blood pressure. DBP: diastolic blood pressure. PP: pulse pressure.
MAP: mean arterial blood pressure. HR: heart rate. n.s: not significant. *p<0.05. **p<0.01.
pattern similar to that of SBP. The DPBP was obtained from the intersection as shown in Fig. 2. The workload at which subjects stopped exercise ranged from 70 to 80 W.

Comparison of circulatory responses and DP at DPBP in the groups

DP and SBP at DPBP were comparatively lower in the women than in the men. MAP, DBP and PP at DPBP, and HR at DPBP were not different for the two genders (Table 4), and predicted that maximal oxygen consumption was lower in the women than in the men (40.2 ± 9.5 versus 34.2 ± 3.8 ml min⁻¹ kg⁻¹). The work load at DPBP tended to be lower in the women than in the men (61.1 ± 9.7 versus 54.6 ± 10.4 W). The work rate at DPBP was not different in the two genders. At DPBP of men, DP was significantly correlated with SBP, HR, MAP and PP. On the other hand, there was a significant correlation only between HR at DPBP and DP at DPBP in women (Table 5).

Correlation between BMI and circulatory responses at DPBP

Men were divided into two groups according to the median BMI, 23.3. At DPBP, DP was significantly correlated with SBP, HR and MAP in both groups; PP was also significantly correlated with DP in the group with BMI <23.3 (Table 6).

DISCUSSION

Because of its strong correlation with myocardial oxygen consumption and exponential increase with increasing exercise intensity, DP is used as an indirect index of myocardial workload during exercise7, 8, 16). Tanaka et al.8) found that the rate of increase in DP changed at a point close to LT, and developed the DPBP method. With respect to its mechanism, they noted that myocardial oxygen consumption represented the relationship between blood lactate levels and sympathetic nerve activity. Riley et al.7) reported that the correlation coefficient between DPBP and LT or AT was 0.86, and Tanaka et al. reported that it was 0.90, indicating no substantial difference. DPBP was recently reported to be useful as a simple index of optimal exercise intensity in healthy adults, older individuals, and patients with heart disease.

In this study, all subjects had normal blood pressures (SBP <120 mmHg, DBP <80 mmHg) according to the Japanese Society of Hypertension17), and BMIs in the twenties. It is considered that diet and physical characteristics do not have a great influence on exercise blood pressure (Tables 1 and 2).

In general, it has been reported that PP tends to increase in individuals under 30 years and those above 60 years18). Since the subjects in this study were in their 20s and blood pressure after resting was within the range of optimal values, pathological
factors of the vessel itself, including arteriosclerosis, were excluded. In youngsters, it is considered that an increase in PP increases stroke volume, and in people aged 60 years and above, it is involved in decrease of vascular compliance\(^{19}\).

Recently, PP and heart rate have been recognized as cardiovascular risk factors independent of blood pressure, and mean blood pressure has been recognized as a cerebral blood vessel risk factor\(^{18, 19}\). Factors leading to increased SBP on exercise include an increase in venous return with decreased intrapleural pressure during inspiration, on the basis of muscle pumping and hyperventilation and an increase in cardiac output with hypersympathicotonus. Because absolute muscle force is proportional to the physiological cross-section of muscles, women usually have less muscle force than men. Muscle force in women is considered to be approximately 55–65% of that in men\(^{20}\).

### Table 4. Comparison of circulatory responses and DP at DPBP of the groups

<table>
<thead>
<tr>
<th></th>
<th>Men (n=18)</th>
<th>Women (n=15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP (mmHg)</td>
<td>153.8 ± 12.5</td>
<td>135.6 ± 8.5**</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>65.2 ± 9.6</td>
<td>63.0 ± 0.6 n.s</td>
</tr>
<tr>
<td>PP (mmHg)</td>
<td>86.7 ± 20.3</td>
<td>72.6 ± 9.2 n.s</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>91.3 ± 13.6</td>
<td>87.2 ± 3.9 n.s</td>
</tr>
<tr>
<td>DP (mmHg·beats·min(^{-1}))</td>
<td>19,139.3 ± 2,523.6</td>
<td>15,959.0 ± 1,285.8**</td>
</tr>
<tr>
<td>HR (beat·min(^{-1}))</td>
<td>124.2 ± 10.6</td>
<td>117.8 ± 8.5 n.s</td>
</tr>
</tbody>
</table>

Mean ± SD.
SBP: systolic blood pressure. DBP: diastolic blood pressure. PP: pulse pressure. MAP: mean arterial blood pressure. HR: heart rate. DP: double product.

n.s: not significant. *p<0.05. **p<0.01.

### Table 5. Relationship between circulatory response and DP at DPBP

<table>
<thead>
<tr>
<th></th>
<th>Men (n=18) Correlation coefficient</th>
<th>Women (n=15) Correlation coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP (mmHg)</td>
<td>0.78**</td>
<td>0.48</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>0.14</td>
<td>-0.08</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>0.66*</td>
<td>0.29</td>
</tr>
<tr>
<td>PP (mmHg)</td>
<td>0.49*</td>
<td>0.48</td>
</tr>
<tr>
<td>HR (beat·min(^{-1}))</td>
<td>0.78**</td>
<td>0.66**</td>
</tr>
</tbody>
</table>

SBP: systolic blood pressure. DBP: diastolic blood pressure. PP: pulse pressure. MAP: mean arterial blood pressure. HR: heart rate. n.s: not significant. *p<0.05. **p<0.01.

### Table 6. Relationship between circulatory response at DPBP in males with different BMI

<table>
<thead>
<tr>
<th></th>
<th>Men (n=9 BMI&gt;23.3) Correlation coefficient</th>
<th>Men (n=9 BMI&lt;23.3) Correlation coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP (mmHg)</td>
<td>0.84**</td>
<td>0.82**</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>0.12</td>
<td>0.22</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>0.63*</td>
<td>0.75*</td>
</tr>
<tr>
<td>PP (mmHg)</td>
<td>0.43</td>
<td>0.66*</td>
</tr>
<tr>
<td>HR (beat·min(^{-1}))</td>
<td>0.90*</td>
<td>0.73*</td>
</tr>
</tbody>
</table>

SBP: systolic blood pressure. DBP: diastolic blood pressure. PP: pulse pressure. MAP: mean arterial blood pressure. HR: heart rate. n.s: not significant. *p<0.05. **p<0.01.
The significant increase in SBP and DP at DPBP in men was considered to be related to the greater muscle pumping ability in men than in women. PP in men tends to increase more than in women. Considering that the probability of detecting the DPBP is significantly greater for men than women and that the estimated maximal oxygen uptake is significantly lower for women, it is considered that the same mechanism is applicable here also. DPBP and AT were observed to be strongly correlated, and increases in the secretory rate of plasma catecholamine and blood lactate level have been observed in the physiological response during DPBP detection. Balady et al. studied the effect of age and gender on the physiological response during exercise and showed that AT was higher in men than in women, and HR at AT was higher in women than in men. In the present study, although DPBP was significantly greater in men than in females, no significant difference was observed between the HR of men and women.

We consider the DPBP in women can be detected early, and the load at DPBP is smaller in women than in men. However, the mechanism of this is unknown and further investigation is needed. On the other hand, SBP showed a decreasing trend, but the difference was not significant. In addition, mean blood pressure showed a slight increase. Usually, MAP shows a gradual increase with increasing exercise intensity and it is generally considered that SBP increases markedly, and DBP increases slightly, with increasing exercise intensity. This study also produced similar results. Tanaka et al. estimated DPBP of 141 healthy adults (126 men and 15 women) using bicycle ergometers and found a value of 14,700 ± 2,500 mmHg × bpm. Riley et al. measured DPBP in 10 healthy adults (9 men and 1 woman) and reported a value of 13,970 ± 4,910 mmHg × bpm. However, when Kyu et al. estimated DPBP in 11 healthy men, they observed that some subjects showed a break-point near 20,000 mmHg × bpm. 14,700 and 20,000 values are intermediate between those of previous studies.

SBP, PP, MAP and HR at DPBP were significantly correlated with DP at DPBP. On the other hand, for women, only the HR at DPBP showed a significant correlation with DP (Table 5). The chemoreceptor reflex and baroreceptor reflex (cardiopulmonary pressure receptor and arterial pressure receptor) respond rapidly to blood pressure changes, and there is a strong regulatory response to fluctuations in blood pressure induced by exercise and postural change. Dementra et al. studied sex differences in the variation in arterial baroreflex (29 men, 28 ± 1 years; 22 women, 27 ± 1 years), and concluded that the effects of SBP, acting through the arterial baroreflex, are significantly smaller in women than in men. They also suggested that this might be attributable to the activity of sympathetic nerve adrenaline receptors in women, which are less inhibitory than those in men. Bruce et al.22) and Van et al. studied the relationship between DP and arterial baroreflex, and reported that stabilization of HR, a component of DP, is necessary to stabilize the arterial baroreflex. Therefore, women are considered to continue exercising while attempting to stabilize HR. In addition, hormone secretions differ between the genders. In males, the kidneys secrete more erythropoietin than in females by the anabolic action of androgens, and men have a higher red blood cell count. The more hemoglobin in the blood, the more oxygen it can carry. A lower hemoglobin content may lead to anemia and a subsequent decline in the oxygen-transporting capacity of the blood. This in turn results in decreased aerobic exercising ability. Women are considered to possess a dominant cardiac activity.

In the present study, the male group was divided into two at the median BMI, 23.3, and the relationship between the blood pressure response and HR on the break-point in DP was analyzed (Table 6). For men, SBP, MAP and HR at DPBP were significantly correlated with the DP at DPBP in the groups with BMI above and below the median. This suggests that the size of the body affects HR and the blood pressure response at DPBP, and the configuration factors of exercise tolerance differ between men and women. In brief, we consider that although men have a blood pressure dominant response at DPBP, women have a heart rate dominant response.

The results of this study suggest that although men and women have similar blood pressure responses during rest, the HR and blood pressure response during exercise may differ between the genders. We used healthy adults in this study. To enable future clinical application, repeated studies with older subjects and disease characteristics are needed.
ACKNOWLEDGMENTS

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REFERENCE