Aortic Elastic Properties in Patients With Hypertensive Response to Exercise

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**Background** The aim of this study was to evaluate whether there is a relationship between aortic elastic properties in patients with a suggestive response to treadmill exercise testing.

**Methods and Results** The study group comprised 32 patients suggesting hypertensive response to exercise and 20 patients suggesting normal blood pressure response to treadmill exercise testing. Baseline demographic characteristics were similar in both groups. However, the mean aortic stiffness index of patients suggesting hypertensive response to treadmill exercise testing was significantly higher (4.8±1.26 vs 2.36±1.09; p=0.001) whereas aortic distensibility was significantly lower (12.82±5.84 vs 22.64±14.54; p=0.001) than the control group. The aortic strain of patients with hypertensive response to exercise was lower than the control group (12±3% vs 19.2±5%; p<0.001). The left ventricular mass (LVM) of these patients was also higher than control group (206.5±46.3 vs 134.2±19.97; p=0.01). A negative correlation between LVM and distensibility was found (r=-0.64; p=0.001) well as a positive correlation between LVM and aortic stiffness index (r=0.51; p=0.004) in patients suggesting hypertensive response to exercise. Pressure–rate product was also found to be correlated with LVM (r=0.47; p=0.006).

**Conclusion** Elastic properties of the aorta may be impaired in subjects showing exaggerated blood pressure response to exercise long before clinically manifest hypertension, particularly if the LVM is increased. (Circ J 2007; 71: 727–730)

**Key Words:** Aortic stiffness; Exercise testing; Hypertensive response; Left ventricular mass; Treadmill

Treadmill exercise testing is generally accepted as an important diagnostic tool for coronary artery disease. It can also provide accurate estimates of blood pressure (BP) reactivity to physical exertion. It has been shown that latent hypertension can be exacerbated by exercise. It has also been shown that physiopathological changes indicating hypertension and its complications have occurred in those suggesting hypertensive response to exercise even in clinically normotensive states.

Recently, the identification of a close relationship between aortic stiffness and cardiovascular mortality has aroused the interest of investigators to carry out studies related to aortic stiffness. In many diseases, aortic stiffness has been studied to show whether the great vessels are involved and to obtain information about the pathophysiology of the great arteries. Accordingly, it has been shown that aortic stiffness is increased in patients with hypertension, diabetes and in postmenopausal women. Although it is well known that hypertension causes stiff arteries, there is insufficient data regarding aortic elastic properties in patients suggesting hypertensive response to treadmill exercise testing before hypertension has manifested clinically. Therefore, the aim of this study was to evaluate aortic elastic properties in patients suggesting hypertensive response to treadmill exercise testing.

**Methods**

**Patients**

A total of 52 patients who underwent treadmill exercise testing with the suspicion of coronary artery disease but showing no ischemic changes during exercise were included in the study. They were divided into 2 groups according to their test results: those suggesting hypertensive responses to exercise (group-1) and those suggesting normal BP responses to exercise (group-2).

All subjects underwent treadmill exercise testing using the modified Bruce protocol. Prior to testing, all subjects were instructed to not eat, drink any beverages, or smoke for 3h before the testing. Heart rate (HR), ECG, and BP were recorded at the onset and at the end of each stage. BP was measured automatically by sphygmomanometry (Tango Stress BP, Morisville NC, USA). Also, pressure–rate product (PRP) at peak exercise of treadmill test was calculated as follows: PRP=systolic arterial pressure×HR (beats/min)×10-2.

All subjects also underwent echocardiographic evaluation in order to exclude left ventricular wall motion abnormality, systolic dysfunction and valvular disorders. Hypertensive response to treadmill exercise testing was defined as ≥210/105 mmHg and ≥190/105 mmHg at peak exercise in males and females, respectively. Exclusion criteria were resting BP ≥140/90 mmHg, those taking antihypertensive medications, those with moderate to severe valvular regurgitation or stenosis, diabetes mellitus, congenital heart disease,
atrial fibrillation, left ventricular systolic dysfunction, renal disease, the presence of familial hypercholesterolemia, obesity, smoking habit, the use of oral contraceptives or estrogen replacement therapy, the presence of aortic disease such as aneurysm, Marfan’s syndrome, coarctation or previous aortic surgery and insufficient echocardiographic evaluation due to poor echocardiographic windows. Informed consent was given by all participants and the local ethics committee approved the study protocol.

Echocardiographic Measurements

Transthoracic echocardiography was performed by an experienced echocardiographer, using a System-Five Performance instrument (General Electric, Vingmed, Norway) with a 2.5 MHz phased-array transducer. The right brachial artery was used to calculate systolic and diastolic pressures during echocardiographic evaluation. At least 3 consecutive measurements were obtained and the results were averaged. Recordings were taken with patients positioned in the left lateral decubitus position. The M-mode traces were recorded at a speed of 50 mm/s and the Doppler signals were also recorded at a speed of 100 mm/s.

Simultaneous electrocardiographic recordings were also taken. The average of 3 consecutive cycles were calculated for each parameter. Measurement of the left ventricle (LV) diameters and the left atrial systolic diameter was performed on M-mode traces recorded in the parasternal long axis view according to established standards. Diameter of the ascending aorta was measured from the same view on the ascending aorta was measured from the same view on the M-mode tracing at 3 cm above the aortic valve. The aortic systolic diameter was measured at the maximal anterior motion of the aorta, whereas the diastolic diameter was measured at the peak of the QRS complex on the simultaneously recorded electrocardiogram.

Calculation of the Elastic Parameters of the Aorta

The aortic strain, $\varepsilon$ index and aortic distensibility were used as aortic elasticity parameters. The formulae used in the calculation of these parameters were as follows: aortic strain ($\%$) = [(aortic systolic diameter – diastolic diameter)×100]/diastolic diameter; aortic stiffness index = ln(systolic pressure/diastolic pressure)/aortic strain; distensibility (cm²/dyn)= (2×aortic strain)/(systolic pressure-diastolic pressure). In addition, the left ventricular mass (LVM) was calculated by using the Devereux formula: LVM = $0.8 \times 1.04$ [interventricular septum thickness in diastole + LV internal diameter in diastole + posterior wall thickness in diastole] – LV internal diameter in diastole$^3$. 17–21

Biochemical Analysis

Venous blood samples were obtained from all subjects after an overnight fast and serum glucose, total cholesterol, triglyceride, high-density lipoprotein (HDL) and low-density lipoprotein (LDL) levels were immediately measured by an autoanalyzer (Olympus AU 5200, Japan).

Statistical Analysis

Statistical analysis was performed with SPSS for Windows version 10.0 (SPSS Inc Chicago, IL, USA). Data are presented as mean±SD. For continuous variables the Mann-Whitney U test and for categorical changes the chi-square test was used.

Relationships between various variables were examined with Pearson correlation coefficients. A p-value <0.05 was considered to indicate statistical significance.

Results

Baseline demographic properties were similar in both groups (Table 1). There was no significant difference between the 2 groups with regard to serum total cholesterol, HDL-cholesterol (C), LDL-C, triglyceride and serum glucose levels (Table 1). Comparison of transthoracic echocardiographic parameters is shown in Table 2. The mean aortic stiffness index of patients suggesting hypertensive response to treadmill exercise testing was significantly higher (4.8±1.26 vs 2.36±1.09; p=0.001) whereas aortic distensibility was significantly lower (12.82±5.84 vs 22.64±14.54; p=0.001) than the control group. The aortic strain of patients with hypertensive response to exercise was lower than the control group (12±3% vs 19.2±5%, p<0.001). The LVM of these patients was also higher than control group (206.5±46.3 g/m² vs 134.2±19.97 g/m²; p=0.01). We also found a negative correlation between LVM and distensibility (r=−0.64; p=0.001) as well as a positive correlation between LVM and aortic stiffness index (r=0.51; p=0.004) in patients suggesting hypertensive response to exercise.

Relationship Between Hemodynamic Response to Treadmill Test and Cardiac Mass

We formed 2 groups (Group-1: BP >210/105 mmHg, males and >190/105 mmHg in females) and compared the

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**Table 1** Demographic and Biochemical Variables

<table>
<thead>
<tr>
<th></th>
<th>Group I (32)</th>
<th>Group II (20)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>48.7±5</td>
<td>47.8±5</td>
<td>NS</td>
</tr>
<tr>
<td>Sex</td>
<td>15 F 17 M</td>
<td>9 F 11 M</td>
<td>NS</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24±5</td>
<td>25±4</td>
<td>NS</td>
</tr>
<tr>
<td>TC (mg/dl)</td>
<td>198±34</td>
<td>185±34</td>
<td>NS</td>
</tr>
<tr>
<td>LDL-C (mg/dl)</td>
<td>122±12</td>
<td>115±10</td>
<td>NS</td>
</tr>
<tr>
<td>HDL-C (mg/dl)</td>
<td>45±11</td>
<td>46±11</td>
<td>NS</td>
</tr>
<tr>
<td>TG (mg/dl)</td>
<td>140±60</td>
<td>133±59</td>
<td>NS</td>
</tr>
<tr>
<td>Plasma glucose (mg/dl)</td>
<td>100±11</td>
<td>99±19</td>
<td></td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>0.95±0.12</td>
<td>0.90±0.14</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS, not significant; BMI, body mass index; TC, total cholesterol; LDL-C, low-density lipoprotein-cholesterol; HDL-C, high-density lipoprotein-cholesterol; TG, triglycerides.

**Table 2** Comparison of the Echocardiography of Both Groups Values

<table>
<thead>
<tr>
<th></th>
<th>Group I (32)</th>
<th>Group II (20)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LA (cm)</td>
<td>3.4±0.2</td>
<td>3.2±0.3</td>
<td>NS</td>
</tr>
<tr>
<td>EF (%)</td>
<td>68±17</td>
<td>65±6</td>
<td>NS</td>
</tr>
<tr>
<td>FS (%)</td>
<td>39±5</td>
<td>44±6</td>
<td>NS</td>
</tr>
<tr>
<td>AO (cm)</td>
<td>3.06±0.3</td>
<td>3.1±0.3</td>
<td>NS</td>
</tr>
<tr>
<td>RA (cm)</td>
<td>3.2±1.8</td>
<td>2.9±1.9</td>
<td>NS</td>
</tr>
<tr>
<td>LV systolic diameter (cm)</td>
<td>3.15±0.3</td>
<td>2.9±0.4</td>
<td>NS</td>
</tr>
<tr>
<td>LV diastolic diameter (cm)</td>
<td>5.15±0.4</td>
<td>4.9±0.5</td>
<td>NS</td>
</tr>
<tr>
<td>Aortic systolic diameter (cm)</td>
<td>3.15±0.4</td>
<td>3.0±0.5</td>
<td>NS</td>
</tr>
<tr>
<td>Aortic diastolic diameter (cm)</td>
<td>2.9±0.3</td>
<td>2.6±0.3</td>
<td>0.001</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>118±9.4</td>
<td>118±33</td>
<td>NS</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>77±15</td>
<td>75±4</td>
<td>NS</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>73±9</td>
<td>70±4</td>
<td>NS</td>
</tr>
</tbody>
</table>

LA, left atrial diameter; EF, ejection fraction; FS, fractional shortening; AO, aortic root diameter; RA, right atrial diameter; LV, left ventricular; SBP, systolic blood pressure; DBP, diastolic blood pressure. Other abbreviation see in Table 1.
parameters; however, the degree of hemodynamic response to treadmill test and amounts of cardiac mass might be continuously and widely distributed. Therefore, the relationship between PRP (which was calculated at the peak of the treadmill test) and cardiac mass (which was evaluated by the echocardiographic study) was evaluated in all of the patients in Group I and Group II. PRP was found to correlate with LVM (r=0.47; p=0.006) (Fig 1). Among LVM, aortic stiffness and distensibility, LVM was best correlated with exercise-induced BP increase (r=0.51; p=0.004). However, we found no correlation between pulse pressure and exercise-induced BP increase.

Discussion

The principle findings of this study are (1) aortic stiffness is higher and distensibility is lower in patients suggesting hypertensive response to treadmill exercise testing when compared to those with normal BP response to exercise; (2) the patients suggesting hypertensive response to treadmill exercise testing have higher LVM when compared to those with normal BP response to exercise; and (3) LVM is inversely correlated with aortic distensibility, but is positively correlated with aortic stiffness in patients suggesting hypertensive response to exercise.

Several different techniques to evaluate arterial compliance have been described. Segers et al used ultrasound and magnetic resonance imaging to measure central pressure and flow waveforms in 26 patients with Marfan’s syndrome and 26 age- and gender-matched controls. Aortic systolic and diastolic cross-sectional areas were measured at the ascending aorta, diaphragm, and lower abdominal aorta. From these measurements, local characteristic impedance and local reflection coefficients were calculated. Calculated global wave reflection indexes were defined as augmentation index and the ratio of backward to forward pressure wave. They concluded that the major determinants of augmentation index were pulse wave velocity and the effective length of the arterial system. Lind et al compared 3 different methods to determine arterial compliance in a population-based study. Assessment of arterial distensibility by ultrasound in the carotid artery, by pulse wave analysis (augmentation index) and the stroke volume to pulse pressure ratio by echocardiography were inter-related and only carotid artery distensibility and the stroke volume to pulse pressure ratio were independently related to coronary risk. Also, Tanriverdi et al using M-mode echocardiography measured elastic properties of aorta in 40 patients with obstructive sleep apnea and respiratory disturbance index showed a positive correlation with aortic stiffness and a negative correlation with distensibility. In our study we used the same technique to measure aortic elastic properties.

Previous studies have shown that aortic compliance decreases in hypertensive subjects. A long follow-up study showed that the increase in stiffness over a period of 6 years is more marked in treated hypertensives than in normotensives, indicating accelerated arterial aging among treated hypertensives. Three factors were identified as being responsible for accelerated progression of arterial stiffness in treated hypertensive patients, as follows: uncontrolled BP values, increased HR, and increased serum creatinine. Tomiyama et al assessed the clinical significance of the LV geometry and physical fitness in 192 patients with borderline and mild hypertension. They found that patients with concentric hypertrophy exhibited slightly impaired levels of physical fitness and cardiac work efficiency, and the progression of concentric hypertrophy demonstrated further impairments of these conditions. The authors concluded that not only lowering BP, but also improving LV hypertrophy (LHV), cardiovascular hemodynamics, and physical fitness might be required in patients with concentric hypertrophy. Even in the absence of hypertension, exaggerated BP responses during exercise testing suggest a probability of LHV, finding associated with the cardiac “end-organ” manifestations of hypertension. Change in BP due to exercise may act as a mechanical stimulus to the myocytes, activating protein synthesis and hypertrophy. Cardiac sympathetic nervous activity may also affect myocyte development.

Study Limitations

In a small number of patients, we did not measure the relationship between the indices of target organ damage such as renal, vascular and cardiac changes and elastic properties of aorta, although none of the patients had apparent renal, cardiac or other systemic disease. On the other hand, prospective studies have demonstrated that target organ damage in essential hypertension is more closely associated with ambulatory BP than it is with clinical BP and the incidence of cardiovascular events is correlated with BP on a long-term course of BP.
Conclusions
In the present study we have found a relationship between arterial stiffness and LVM in patients with hypertensive response to exercise. These findings may indicate that elastic properties of the aorta may be impaired in subjects showing exaggerated BP response to exercise long before clinically manifest hypertension, particularly if the LVM is increased. However, these results need to be validated with further large-scale studies and long-term follow-up.

References