HEMODYNAMIC AND LEFT VENTRICULAR VOLUMIC ALTERATION  
IN RESPONSE TO ISOMETRIC HANDGRIP EXERCISE

SHOZO ISHISE, M.D.

There is general agreement that the hemodynamic response to isometric exercise is characterized by an abrupt and progressive pressor response and increased cardiac output, due to increased heart rate. The instantaneous onset of this circulatory event suggests the involvement of an autonomic effector mechanism, but this exact mechanism has been remained unclear. There is also little information concerning the response of plasma renin activity (PRA) to isometric exercise, despite that the release of PRA is known to be mediated by the autonomic nervous system.

Although Hoel, B. L., et al. reported that hemodynamic responses to isometric exercise were similar between normotensives and hypertensives, there is no available information with respect to the cardiac performance, especially left ventricular volumic changes.

The present study was therefore designed to explore the possible role of sympathetic nervous system, especially β-adrenergic drive in cardiovascular responses to isometric handgrip exercise and secondly examine whether the cardiovascular response, especially left ventricular volumic change, to isometric exercise is different between hypertensives and normotensives, by echocardiography.

MATERIALS AND METHODS

This study included 12 patients with essential hypertension, 4 females and 8 males, aged 25 to 50 years (average 41.0 ± 4.0 years) and 12 normotensive volunteers, one female and 11 males, aged 23 to 63 years (average 41.4 ± 3.0 years). All hypertensive patients showed recumbent blood pressure of 150/90 mmHg or more on repeated determination in the ward. None had any sign of heart failure, ocular fundi more than Keith-Wagener II, cardiothoracic ratio exceeding 50% or ischemic finding on ECG.

In advance, maximum voluntary contraction (MVC) was determined by averaging three trials with the use of spring-loaded handgrip dynamometer. After four hours of bed rest, blood pressure of a non-contracting left arm was measured by sphygmomanometry. Electrocardiogram and echocardiogram were recorded on an Aloka echocardiograph equipped with a 2.25 MHz focused transducer. The 35 mm photographs of time-motion echo display were directly taken from the oscilloscope. All subjects were conducted in the left semilateral position and the transducer was placed in the fourth or fifth intercostal space close to the sternum. When the ultrasound beam was directed laterally and slightly inferior to the left, the echos were obtained from the interventricular septal endocardium and the left ventricular posterior wall endocardium, which is immediately inferior to the posterior mitral leaflet. The internal dimension of the left ventricle was taken as the distance between left sided interventricular septal endocardium and

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<table>
<thead>
<tr>
<th></th>
<th>No Medication</th>
<th>Administration of Propranolol</th>
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<tr>
<td></td>
<td>R</td>
<td>E</td>
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<tr>
<td><strong>Systolic BP (mmHg)</strong></td>
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</tr>
<tr>
<td>NT</td>
<td>110±2</td>
<td>137±4***</td>
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<td>HT</td>
<td>150±2</td>
<td>171±5***</td>
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<td><strong>Diastolic BP (mmHg)</strong></td>
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<tr>
<td>NT</td>
<td>72±2</td>
<td>89±2***</td>
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<tr>
<td>HT</td>
<td>94±3</td>
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<td><strong>Mean BP (mmHg)</strong></td>
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<tr>
<td>NT</td>
<td>86±1</td>
<td>105±4***</td>
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<tr>
<td>HT</td>
<td>113±3</td>
<td>132±4***</td>
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<td><strong>HR (beat/min)</strong></td>
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<tr>
<td>NT</td>
<td>60±2</td>
<td>67±3**</td>
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<td>HT</td>
<td>64±3</td>
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<td><strong>SV (ml/beat)</strong></td>
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<tr>
<td>NT</td>
<td>84±5</td>
<td>86±5</td>
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<tr>
<td>HT</td>
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<td><strong>CO (L/min)</strong></td>
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<tr>
<td>NT</td>
<td>5.04±0.57</td>
<td>5.80±0.73*</td>
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<tr>
<td>HT</td>
<td>5.56±0.52</td>
<td>6.45±0.63**</td>
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<td><strong>TPR (dyne·sec·cm⁻⁵)</strong></td>
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<td>155±184</td>
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<td>HT</td>
<td>1802±192</td>
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<td><strong>Dd (mm)</strong></td>
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<tr>
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<td>45.9±1.5</td>
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<td>HT</td>
<td>46.8±1.0</td>
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<td><strong>Ds (mm)</strong></td>
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<tr>
<td>NT</td>
<td>26.6±1.2</td>
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<td>HT</td>
<td>27.6±1.1</td>
<td>30.8±1.3**</td>
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<td><strong>EDV (ml)</strong></td>
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</tr>
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<td>105±18</td>
<td>113±10</td>
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<td>HT</td>
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<tr>
<td><strong>ESV (ml)</strong></td>
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<td>27±4</td>
</tr>
<tr>
<td>HT</td>
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<td>32±4*</td>
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<td><strong>EF (%)</strong></td>
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</tr>
<tr>
<td>NT</td>
<td>79.3±2.3</td>
<td>76.2±2.1</td>
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<tr>
<td>HT</td>
<td>78.8±2.1</td>
<td>73.6±2.3*</td>
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Each value represents the mean ±1 SEM. Abbreviations: R=resting state, E=during exercise, BP=blood pressure, NT=normotensive group, HT=hypertensive group, HR=heart rate, SV=stroke volume, CO=cardiac output, TPR=total peripheral resistance, Dd=left ventricular dimension during the maximum systole, Ds=left ventricular dimension during the maximum diastole, EDV=left ventricular end-diastolic volume, ESV=left ventricular end-systolic volume, EF=ejection fraction, *P<0.05, **P<0.01, ***P<0.001 (R vs E), +++P<0.05, ++++P<0.001, (R (no medication) vs R (propranolol)).
posterior wall endocardium. Left ventricular end-diastolic dimension (Dd) was measured on the R wave of the ECG, while the smallest distance between left interventricular septum and left ventricular posterior wall was considered as the left ventricular end-systolic dimension (Ds). Left ventricular volumic and hemodynamic variables were calculated from the following formula\textsuperscript{13}

\[
\begin{align*}
    \text{End-diastolic volume (EDV)} &= \frac{\pi}{3} \times Dd^3 \text{ (ml)} \\
    \text{End-systolic volume (ESV)} &= \frac{\pi}{3} \times Ds^3 \text{ (ml)} \\
    \text{Stroke volume (SV)} &= \text{EDV} - \text{ESV} \text{ (ml/best)} \\
    \text{Ejection Fraction (EF)} &= \frac{\text{SV}}{\text{EDV}} \% \\
    \text{Cardiac Output (CO)} &= \text{SV} \times \text{Heart Rate} \times \frac{1}{1000} \text{ (L/min)} \\
    \text{Total Peripheral Resistance (TPR)} &= \frac{1.332 \times 60 \times \text{Mean Blood Pressure (MBP)/CO}}{\text{dyne·sec·cm}^{-5}}
\end{align*}
\]

The blood pressure, electrocardiogram and left ventricular echocardiogram were recorded during the short pause of expired phase and in the left semi-lateral position.

Blood sample for the plasma renin activity (PRA) was drawn through a indwelling plastic catheter inserted in the left antecubital vein. Plasma renin activity was determined by the modified Skinner’s bioassay method\textsuperscript{14}

**PROTOCOL**

Following the control measurement of hemodynamics and blood sampling for PRA assay, an isometric exercise was carried out at 30% of MVC for 4 minutes. During the exercise, the subjects were carefully watched to assure a normal breathing and exclude Valsalva maneuver. Just prior to release of hand squeezing, hemodynamic measurements and blood were again obtained.

After the first exercise test the subjects rested for at least 15 minutes or until the heart rate and blood pressure had returned to the control levels. Thereafter, propranolol (0.2 mg/kg body weight) was injected intravenously over 4 minutes and the subjects were allowed to elapse more 6 minutes. Then the completely same hemo-

dynamic studies and blood sampling as the first exercise were performed before and after the isometric exercise.

**RESULTS**

**First Exercise**

Blood pressures and heart rate increased significantly in the normotensive and hypertensive groups (Table I). Cardiac output increased significantly from 5.04 to 5.80 (P < 0.05) and from 5.56 to 6.45 L/min (P < 0.01) in normotensive and hypertensive group, respectively. These increases in cardiac output consisted of the increased heart rate rather than stroke volume, because stroke volume was not increased in either group. Total peripheral resistance tended to increase in normotensives, but not in hypertensives. There were no significant changes in left ventricular variables in normotensives, whereas there were significant increases in Dd (P < 0.05), Ds (P < 0.01) and ESV (P < 0.05) in hypertensives. EF decreased from 79.3 to 76.2% and from 78.8 to 73.6% in normotensives and hypertensives, respectively, but significant in the latter group (P < 0.05). However, there was no significant difference in these responses between normotensive and hypertensive groups.

**Effect of Propranolol on the Resting Variables**

When the control resting values were compared before and after the administration of propranolol, blood pressures tended to increase, but this increase was significant only in diastolic and mean blood pressures of normotensive group.

Following propranolol injection, cardiac output decreased significantly due to the decreased heart rate in the two groups. With respect to the volumic change, propranolol produced the increases in Dd, Ds and ESV, and decrease in EF in both groups. However, there were no significant differences between normotensive and hypertensive groups.

**Second Exercise after the Administration of Propranolol**

The hemodynamic and left ventricular volumic changes were essentially same with those obtained by the first exercise (Table I).

**Responses of Plasma Renin Activity**

Plasma renin activity was determined in five normotensives and six hypertensives. Following the first isometric handgrip exercise, PRA increased from 1.7 ± 0.5 to 2.3 ± 0.3 mg/ml/hr
(P < 0.05) in normotensives, but increased from 1.6 ± 0.4 to 3.2 ± 0.5 ng/ml/hr (P < 0.01) in the hypertensive group.

The resting PRA changed from 1.7 ± 0.5 to 1.8 ± 0.7 and from 1.6 ± 0.4 to 1.4 ± 0.3 ng/ml/hr in normotensive and hypertensive groups, respectively, but there were no significant differences between them in both groups.

After propranolol, PRA was not any more increased by the isometric exercise even in the hypertensive group.

**DISCUSSION**

The pressor response evoked by isometric exercise might be caused hemodynamically by the increased cardiac output and little change in total peripheral resistance in subjects without serious impairment of cardiac function and the increased resistance and little change in output in patients with impaired left ventricular performance regardless of blood pressure values.

In the first exercise, the author observed that the pressor response was due to the increased cardiac output in both normotensive and hypertensive groups, suggesting the hypertensive patients selected in the present studies might not have so serious cardiac dysfunction. Additionally, these results agreed with those by Hoel, B. L. et al. who postulated that the hemodynamic response to isometric exercise in hypertensives was similar to that in normotensives.

However, no information is available regarding the left ventricular performance and especially volumic alteration. During the first isometric exercise, Dd, Ds and ESV increased and EF decreased significantly only in hypertensive group, but not altered in normotensive group.

Although the effect of acute afterload by isometric exercise on the left ventricular performance is still controversial among the previous studies these differences might be due to the differences in the selected patients of each study, mainly due to whether they had impaired or normal left ventricular function.

Flessas, A. P. et al. recently showed the diminished left ventricular function during handgrip in patients with impaired cardiac function. LVEDP increased, EDV decreased and ESV increased, as EF declined. On the other hand, the subjects without abnormal cardiac function improved the left ventricular function during handgrip. LVEDP decreased or remained constant, EDV decreased and ESV decreased, as EF remained constant.

In addition, hypertensive people with normal cardiac function might show the increased cardiac performance during the handgrip and also, the hyperkinetic movement of the left ventricle was demonstrated in hypertensive patients in the present study.

From the viewpoint of autonomic nervous responses, the pressor responses and enhanced ventricular performance might be elicited by the augmentation of sympathetic activity or predominantly through a withdrawal of vagal tone. However, the author doesn’t know which mechanism was predominant in the isometric exercise. The results after propranolol injection suggest that β-adrenergic drive may not play a large part in the hemodynamic alteration by isometric exercise. However, the above finding does not necessarily ignore the β-adrenergic drive, because the cardiac output and heart rate responses were reduced in the present results and other's.

It is well known that the PRA increased during dynamic exercise and also this renin release was mediated by the sympathetic acceleration.

Static exercise has been reported to have no detectable effect on PRA in normal subjects. However, there is no available report about it in patients with essential hypertension. The author observed the increased PRA in response to handgrip exercise in either normotensive or hypertensive patient, but this increment was blocked on the second exercise after the administration of propranolol.

However, it is interesting that hemodynamic and left ventricular performance was performed on the second exercise almost same as the first exercise even in hypertensive group, despite β-adrenergic blocking state.

Increased heart rate and blood pressure could be mediated by the autonomic nervous mechanism in origin, because these responded abruptly and returned quickly to the basal control state after the release of squeezing. Moreover, if the adrenergic activity works dominantly, heart rate should be reduced by the baroreceptor reflex. If β-adrenergic drive initiates, the typical responses should be abolished on the second exercise. On the other hand, it was reported that plasma catecholamine increased significantly in eight normal subjects during the isometric exercise and this increase was greater than that induced by
Hemodynamic and Left Ventricular Volumetric Alteration in Response to Isometric Handgrip Exercise

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