Effect of Mental Stress on Hemodynamics and Left Ventricular Diastolic Function in Patients With Ischemic Heart Disease

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Mental stress is an important factor affecting cardiac function. We evaluated the effect of a mental calculation stress (MS) test on hemodynamics and left ventricular (LV) diastolic function in patients with ischemic heart disease, and compared the hemodynamic responses with a treadmill exercise test. Fifteen patients were studied. Seven had old myocardial infarction with significant coronary artery stenosis (group I) and 8 had chest pain syndrome with non-significant coronary artery stenosis (group II). The MS test was performed as follows: after memorizing 6 random numeral digits, patients repeated these numbers in reverse order for 5 min followed by serial subtraction of 1000 minus 17 for 5 min. Blood pressure (BP) and heart rate (HR) were measured every 1-5 min. Doppler mitral flow velocity (MFV) was recorded every 2-5 min. During the MS test, BP, HR, and rate pressure product increased by 38.3%, 17.3%, and 62.1% on average, respectively. Early diastolic MFV decreased by 10.0% in group I and 3.3% in group II. First third filling rate of MFV decreased by 32.3% in group I and 22.8% in group II. A/E ratio increased by 39.3% in group I and 25.8% in group II. These data indicate that the MS test led to a deterioration in LV diastolic function. The MS test induced LV diastolic dysfunction to a greater extent in patients with significant coronary artery stenosis than in those without significant coronary stenosis. Myocardial ischemia may be induced by increased left ventricular afterload and/or vasoconstrictive reflex of coronary microcirculation. (Jpn Circ J 1998; 62: 173-177)

Key Words: Mental stress; Exercise stress; Hemodynamics; Left ventricular diastolic function; Ischemic heart disease

Mental stress is an important factor affecting cardiac systolic and diastolic function in daily life, especially stressful modern daily life. It has been reported that mental stress increases blood pressure, heart rate, and rate pressure product. We evaluated the effect of a mental calculation stress test on hemodynamics in patients with ischemic heart disease. We also compared the effect of a mental stress test on hemodynamics, including heart rate, blood pressure, and rate pressure product with a treadmill exercise test.

It has been reported that left ventricular diastolic function deteriorates in the early phase of ischemic events. However, few data are available on left ventricular diastolic function during mental stress in patients with ischemic heart disease. We also evaluated the effect of a mental calculation stress test on the left ventricular diastolic function using Doppler mitral flow velocity recordings.

Subjects

Fifteen patients with angina pectoris or chest pain syndrome were entered into our study. There were 10 men and 5 women (age range 43-75 years). Coronary arteriography was performed in all patients. Subjects were divided into 2 groups: group I contained 7 patients with old myocardial infarction and significant coronary artery stenosis (1 patient had dyskinesia at the apex, 3 patients had akinesis, and 3 patients had hypokinesis of left ventricular wall motion); group II contained 8 patients with chest pain syndrome and non-significant coronary artery stenosis. Table 1 summarizes the clinical characteristics of the patients.

Methods

Mental Calculation Stress Test

The mental stress test was performed in the chronic stable phase in all patients. Patients rested for 30 min, underwent a mental stress test for 10 min, and rested for 10 min. The mental calculation stress test was performed as follows: after memorizing 6 random numeral digits, patients repeated these numbers in reverse order for 5 min (for example 384962-269483) followed by serial subtraction of 1000 minus 17 for 5 min (for example 1000-17=983, 983-17=966, ...).

Recordings During Mental Stress Test

Blood pressure was measured by cuff sphygmomanometer every 1-5 min. Electrocardiogram was recorded for 10 sec every 1-5 min. Doppler mitral flow velocity was recorded every 2-5 min from apex using a Toshiba SSH 160A ultrasound machine with a 3.5 MHz transducer.
Sampling volume was set at mitral orifice on apical 2-chamber view image.

**Treadmill Exercise Test**

A treadmill exercise test was also performed according to symptom-limited modified Bruce protocol in all patients. Table I summarizes the endpoint and stage in all patients. Blood pressure was measured by cuff sphygmomanometer every 2-5 min. The exercise test was performed within a few days of the mental stress test.

**Coronary Angiographic Study**

Coronary angiography was performed in all patients. Significant coronary stenosis was defined as stenosis greater than 75%.

**Measurement and Calculation of the Data**

Percent change in blood pressure (BP) was calculated as (max BP during stress test - min BP at rest)/(min BP at rest) x 100%. Percent change in heart rate (HR) was calculated as (max HR during stress test - min HR at rest)/(min HR at rest) x 100%. Rate pressure product was calculated as (systolic blood pressure) x (HR).

On the pulsed Doppler mitral flow velocity recordings, early diastolic mitral flow velocity (E-velocity) and late diastolic mitral flow velocity (A-velocity) were measured. The A/E ratio was calculated as (A-velocity)/(E-velocity). The A/E ratio is a parameter of left ventricular diastolic function. The first third filling ratio (F 1/3) of mitral flow was calculated as (mitral flow time velocity integral in first 1/3 interval)/(mitral flow time velocity integral in full diastole) x 100%. E-velocity and F 1/3 are parameters of left ventricular early diastolic function.

**Data Analysis**

All data were expressed as means ± standard deviation. Student’s t-test was used for statistical analysis. Significant difference was assumed as a p-value less than 0.05.

**Results**

**Example of Change in Blood Pressure and Heart Rate in the Mental Stress Test**

Fig. 1 shows an example of the change in blood pressure and heart rate in the mental stress test. Systolic and diastolic blood pressure increased abruptly at the start, were maintained during stress, and decreased abruptly at the end of the mental stress test. Heart rate also increased abruptly at the start, was maintained during stress, and decreased abruptly at the end of the mental stress test. This pattern was observed in all patients.

**Change in Blood Pressure in the Mental Stress and Exercise Tests**

Fig. 2 shows the percent change in systolic blood pressure in groups I and II. Systolic blood pressure increased by 33.9-42.1% in the mental stress test and by 21.7-31.7% in the treadmill exercise test. Percent increase in systolic blood pressure was greater in the mental stress test than in the treadmill exercise test, but not significantly so. Percent increase in diastolic blood pressure was also greater in the mental stress test than in

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**Table 1 Summary of Clinical Characteristics and Treadmill Exercise Test**

<table>
<thead>
<tr>
<th>Group</th>
<th>Age</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Treadmill Exercise Test</th>
<th>End point</th>
<th>Stage</th>
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</thead>
<tbody>
<tr>
<td>Group I</td>
<td>1</td>
<td>49</td>
<td>M</td>
<td>OMI (anti-ep)</td>
<td>LF</td>
<td>4-3</td>
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<tr>
<td>2</td>
<td>51</td>
<td>M</td>
<td>OMI (inf) with AP</td>
<td>THR</td>
<td>4-2</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>61</td>
<td>M</td>
<td>OMI (inf) with AP</td>
<td>COF</td>
<td>5-3</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>64</td>
<td>M</td>
<td>OMI (anti-ep) with AP</td>
<td>DYS</td>
<td>4-2</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>70</td>
<td>F</td>
<td>OMI (inf-post-fat) with AP</td>
<td>LF</td>
<td>4-1</td>
<td></td>
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<tr>
<td>6</td>
<td>73</td>
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<td>OMI (anti-ep) with AP</td>
<td>LF</td>
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<td></td>
</tr>
<tr>
<td>7</td>
<td>75</td>
<td>M</td>
<td>OMI (anti-ep) with AP</td>
<td>COF</td>
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<td></td>
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<tr>
<td>Group II</td>
<td>8</td>
<td>43</td>
<td>M</td>
<td>Chest pain syndrome</td>
<td>THR</td>
<td>4-2</td>
</tr>
<tr>
<td>9</td>
<td>53</td>
<td>F</td>
<td>Chest pain syndrome</td>
<td>THR</td>
<td>5-1</td>
<td></td>
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<tr>
<td>10</td>
<td>60</td>
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<td>Chest pain syndrome</td>
<td>CDIS</td>
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<tr>
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<tr>
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<tr>
<td>15</td>
<td>71</td>
<td>F</td>
<td>Chest pain syndrome</td>
<td>LF</td>
<td>3-2</td>
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</tr>
</tbody>
</table>

AP, angina pectoris; CDIS, chest discomfort; COF, chest oppressive feeling; DYS, dyspnea; LF, leg fatigue; OMI, old myocardial infarction; SOB, shortness of breath; THR, target heart rate.
Effect of Mental Stress on Hemodynamics and LV Function

Fig 2. Percent changes in systolic blood pressure in the mental stress test and exercise test. Shaded bars indicate the percent change in blood pressure in the mental stress test. Open bars indicate the percent change in blood pressure in the treadmill exercise test. Blood pressure increased by 20–40% in both the mental and treadmill exercise stress tests.

Fig 3. Percent changes in heart rate in the mental stress test and exercise test. Shaded bars indicate the percent change in heart rate in the mental stress test. Open bars indicate the percent change in heart rate in the treadmill exercise test. Heart rate increased by 20% in the mental stress test and by 70% in the treadmill exercise test. Percent change in heart rate was significantly greater in the treadmill exercise test than in the mental stress test (p<0.01).

Fig 4. Percent changes in rate pressure product (RPP) in the mental stress and exercise test. Shaded bars indicate the percent change in RPP in the mental stress test. Open bars indicate the percent change in RPP in the treadmill exercise test. Rate pressure products increased by 50–60% in the mental stress test and by 110–120% in the treadmill exercise test. Percent change in RPP was significantly greater in the treadmill exercise test than in the mental stress test (p<0.01 and 0.05).

Example (Mitral Flow Velocity Before and After Mental Stress)

Before

E-Velocity = 50 cm/sec
A-Velocity = 38 cm/sec
A/E = 0.76

After

E-Velocity = 37 cm/sec
A-Velocity = 43 cm/sec
A/E = 1.16

Fig 5. Example of change in mitral flow velocity pattern before (top) and after (bottom) the mental stress test. This patient was a 70-year-old woman in group I. After the mental stress test, early diastolic filling velocity (E-velocity) decreased from 50 to 37 cm/sec and late diastolic filling velocity (A-velocity) increased from 38 to 43 cm/sec. The A/E ratio increased from 0.76 to 1.16.

Change in Heart Rate in the Mental Stress and Exercise Tests

Fig 3 shows the percent change in heart rate in groups I and II. Heart rate increased by 16.6–18.1% in the mental stress test and by 64.6–76.8% in the treadmill exercise test. Percent increase in heart rate was significantly greater in the treadmill exercise test than in the mental stress test (p<0.01).
Table 2 Changes of Mitral Flow Velocity Parameters During Mental Stress Test

<table>
<thead>
<tr>
<th></th>
<th>E-Velocity</th>
<th>A-Velocity</th>
<th>A/E Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>-10.0±13.2%+24.4±15.9%+39.3±7.9%</td>
<td></td>
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</tr>
<tr>
<td>Group II</td>
<td>-3.3±15.4%+20.7±17.3%+25.8±8.9%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

E-velocity, early diastolic filling velocity of mitral flow; A-velocity, late diastolic (atrial) filling velocity of mitral flow; A/E ratio, ratio of A-velocity and E-velocity.

Fig 6. Percent change in the A/E ratio of mitral flow velocity in the mental stress test. The A/E ratio increased by 39.3±7.9% in group I and by 25.8±8.9% in group II. Percent change in the A/E ratio was significantly greater in group I than group II (p<0.05).

Example of Change in the Mitral Flow Velocity Pattern in the Mental Stress Test

Fig 5 shows an example of mitral flow velocity pattern before and after the mental stress test. During the mental stress test, E-velocity decreased and A-velocity increased. The A/E ratio increased from 0.76 to 1.16, by 52.6%. These data indicate that left ventricular diastolic function deteriorated after the mental stress test in this patient.

Changes in Mitral Flow Velocity Parameters in the Mental Stress Test

Table 2 indicates the change in E-velocity, A-velocity, and the A/E ratio during the mental stress test in groups I and II. E-velocity decreased by 10.0±13.2% in group I and by 3.3±15.4% in group II. A-velocity increased by 24.4±15.0% in group I and by 20.7±17.3% in group II. The A/E ratio increased by 39.3±7.9% in group I and 25.8±8.9% in group II.

Fig 6 shows the percent change in the A/E ratio during the mental stress test in groups I and II. The A/E ratio increased during the mental stress test. This indicated that the mental stress test caused left ventricular diastolic function to deteriorate. Increase in the A/E ratio was significantly greater in group I than in group II.

Fig 7 shows the percent change in the first third filling rate (F1/3) of mitral flow velocity. This indicated that the mental stress caused deterioration in left ventricular early diastolic function. The decrease in F1/3 was greater in group I than group II.

ST-T Change on ECG and Left Ventricular Systolic Function

No significant ST-T changes were recorded on ECG during the mental stress test in all patients. Significant ST depression was recorded on ECG in 9 of 15 patients (4/7 in group I and 5/8 in group II) during the treadmill exercise test. No significant decrease in left ventricular systolic function (left ventricular ejection fraction) was detected using echocardiography in all patients. No newly developed left ventricular wall motion abnormalities were detected using 2-dimensional echocardiography in all patients.

Discussion

Effect of Mental Stress on Hemodynamics

Our study indicated that the mental calculation stress test increased blood pressure, heart rate, and rate pressure product. The percent change in systolic blood pressure was greater in the mental stress test than in the treadmill exercise test. Diastolic blood pressure also increased in the mental stress test, and the percent change was greater in the mental stress test than the treadmill exercise stress test. This may be due to a difference in peripheral arterial vasoconstrictive reflex.

However, the percent change in heart rate was smaller in the mental stress than in the treadmill exercise test. Rozanski et al.11 reported that mental stress caused low heart rate elevations and significant blood pressure increases compared with exercise stress. They reported that the differences between mental- and exercise-induced myocardial ischemia have provided a means of studying
the complex pathophysiology of myocardial ischemia.

**Mental Stress and Myocardial Ischemia**

Mental stress is an important trigger for myocardial infarction. It is reported that mental stress reduces coronary blood flow and induces myocardial ischemia. Myocardial ischemia is induced by the increase in left ventricular afterload during mental stress. Coronary blood flow is also reduced by vasoconstriction at microcirculation level. Platelet activation by emotional stress reduces coronary blood flow in patients with coronary heart disease. These mechanisms may reduce coronary blood flow and induce myocardial ischemia during mental stress in clinical cases.

**Effect of Mental Stress on Left Ventricular Systolic Function in Patients With Ischemic Heart Disease**

Ishibashi et al. reported that mental stress increased left ventricular ejection fraction by 6% in normal subjects. However, Mazzuero et al. reported that mental stress caused a deterioration in ventricular pump function in patients with post-myocardial infarction. In our study, no significant decrease in left ventricular systolic function was detected. Mental arithmetic calculation stress may be weaker than other mental stress test methods.

**Left Ventricular Diastolic Function in Patients With Ischemic Heart Disease**

Left ventricular diastolic function is reduced in patients with ischemic heart disease. Polak et al. indicated that diastolic dysfunction was detected, with no evidence of systolic dysfunction, using radionuclide angiography in patients with ischemic heart disease. Furukawa et al. reported that left ventricular diastolic dysfunction was detected using pulsed Doppler transmural flow recordings during transient myocardial ischemia. Yoshio et al. in a study using pulsed Doppler echocardiography, also reported that left ventricular diastolic dysfunction was detected during an exercise test in patients with ischemic heart disease. Yoshida et al. reported that left ventricular filling pressure was increased by supine leg exercise in patients with silent myocardial ischemia.

Our study demonstrates that the mental calculation stress test reduced left ventricular diastolic function. The reduction was greater in patients with old myocardial infarction with significant coronary artery stenosis (group I) than in patients with non-significant coronary artery stenosis (group II). The mental stress test induced diastolic dysfunction in patients with significant coronary artery stenosis without ST-T change on ECG and/or left ventricular systolic dysfunction. The mental stress test may induce myocardial ischemia through increased left ventricular afterload and/or neurohumoral vasoconstrictive reflex of coronary microcirculation. We speculated that the grade of myocardial ischemia was more severe in group I than group II; therefore, deterioration in left ventricular diastolic function was greater in group I than group II. Wall motion abnormalities caused by old myocardial infarction might affect left ventricular diastolic function as well as myocardial ischemia in group I.

**Conclusions**

The mental calculation stress test increased blood pressure by 30–40%, heart rate by 20%, and rate pressure product by 50–60% in patients with ischemic heart disease. However, the increase in rate pressure product was smaller than in the treadmill exercise test. The mental stress test induced left ventricular diastolic dysfunction, especially early diastolic dysfunction, without ST-T change and/or left ventricular systolic dysfunction in patients with ischemic heart disease and significant coronary artery stenosis. Left ventricular diastolic dysfunction during the mental stress test indicates the early phase of myocardial ischemia. Mental stress may induce myocardial ischemia through increased left ventricular afterload and/or neurohumoral vasoconstrictive reflex of coronary microcirculation.

**References**