Hemodynamic Response to Different Types of Mental Stress in Patients with Recent Myocardial Infarction

Giorgio Mazzuero, M.D., Anna Maria Zotti, Ph.D.,* Giorgio Bertolotti, Ph.D.,* and Luigi Tavazzi, M.D.

SUMMARY

The purpose of this study was to analyze the cardiovascular effects induced by mental stress evoked by different stressors in patients with recent uncomplicated myocardial infarction. Twenty four males, aged 52±10 years, were studied 45±22 days after uncomplicated myocardial infarction in the absence of specific cardiovascular drugs. During electrocardiographic and hemodynamic monitoring with a Swan-Ganz catheter the patients underwent 4 different stressors: mental arithmetic, Sacks test, Raven progressive matrices, white noise. All hemodynamic parameters were significantly (p<0.001) modified by 3 of the 4 stressors, while noise significantly affected (p<0.005) only blood pressure. Mental arithmetic was more powerful in inducing hemodynamic effects than either the Sacks test or the Raven matrices. Thus, experimentally induced mental stress challenges the recently infarcted patient’s cardiovascular system to a quantifiable extent, causing important increments in left ventricular filling pressure. Hemodynamic response is different depending on the stressor employed.

Additional Indexing Words:
Mental stress Myocardial infarction Hemodynamics
dynamic response to four standardized stressors in patients with ischemic heart disease.

METHODS

Subjects:

Subjects selected for the study were post recent myocardial infarction patients hospitalized for functional evaluation and rehabilitation and with the following characteristics: a) recent Q infarction; b) able to discontinue medications; c) NYHA functional class I or II, without spontaneous angina or significant arrhythmias; d) not receiving digitalis or amiodarone; e) absence of psychopathologic traits on routine psychologic testing; f) informed written consent of the patient.

Twenty six males referred consecutively to the hemodynamic laboratory for ergometric evaluation entered the study, with 24 completing it and 2 being eliminated because of failure to complete the second evaluation in the psychophysiology laboratory, due to a technical error in 1 case and to the onset of acute pulmonary edema in the hemodynamic laboratory in the other. Mean age of the 24 patients was 52±10 years (range 26–73).

The interval following acute myocardial infarction was 45±22 days (range 24–126). Infarction site was anterior in 8 patients, inferior in 14 and anterior+inferior in 2 patients. Daily medication was continued with sulfynpirazone in 5 patients, with acetylsalycilic acid in 4 and with ticlopidine in 1. All other drugs were discontinued with a minimum washout of 24 hours for nitrates, 48 hours for calcium channel blockers and 72 hours for beta blockers.

Psychologic investigation:

Every patient was routinely evaluated in the Psychology Unit by an interview and a standardized battery of tests; all subjects completed this evaluation by the Wechsler Bellevue form (IQ) and the Italian versions of the Life Experience Survey, Coronary Prone Behavior Questionnaire, Rathus Assertiveness Schedule and the State Trait Anxiety Inventory (STAI). The latter was compiled immediately before and after cardiac catheterization.

Stressors:

A 4 stressor battery was administered to each patient: a) mental arithmetic performed aloud with three levels of difficulty: serial subtraction of the number 17 beginning from 1013 for subjects with an IQ>110, of 7 beginning from 251 for subjects with an IQ of 90 to 110, of 3 beginning from 101 for subjects with an IQ<90. Such differentiation allowed all subjects to achieve
a good performance. Two seconds timed by a metronome were allowed for each answer, after which the patient was told whether it was right or wrong immediately; b) Sacks and Levy sentence completion test, composed of 30 incomplete sentences regarding areas of sociality, individuality, affectivity and sexuality which the patient was requested to complete aloud, in the shortest time possible; c) Raven Progressive Matrices 1947 (PM 47), a stressor consisting of problem puzzles illustrated on slides; d) white noise with continuous and random impulsive components administered using head phones. Stressor sequence was different for each patient according to a 4! randomized design in order to characterize hemodynamic response to each stressor independently of stressor order in the sequence. Each stressor lasted 3', and was preceded and followed by a 5' rest period. The 4 stressor battery lasted 37'.

Procedure:

Testing was carried out in the hemodynamic laboratory in the morning after a light breakfast with the patient in a supine position. A conventional 12 lead electrocardiogram (ECG) was recorded every minute during the entire test using a 6 channel Siemens-Elema Mingograph 62; 2 leads were monitored continuously. Blood pressure (BP) was measured every minute during the entire test using a mercury sphygmomanometer. A 7F Swan-Ganz catheter for thermodilution was introduced percutaneously into the right femoral or right basilic vein and positioned in the pulmonary artery under fluoroscopic monitoring. Right atrial (RAP) and pulmonary arterial pressures (PAP) were monitored continuously by Hewlett-Packard Quartz 1290 A-transducers and recorded on a tape by a four track Tandberg IRS 115 recorder; each minute during the entire test they were also recorded on graph paper together with the respective mean pressures (automatic integration).

At the end of the test after another 5–10' rest period, the patients, still supine, performed the ergometric test. The day after (12 subjects) or before (12 subjects) at the same time each patient repeated the stress test following the same protocol but with noninvasive recording of cardiovascular parameters (ECG and BP) together with other psychophysiological parameters: skin conductance level, peripheral skin temperature and frontal electromyogram.

Statistical analysis:

For each parameter the data are expressed as means and standard deviations. Baseline (mean of the 3' preceding each stimulation), maximum values (peaks) reached during stimulation, mean of the 3' stimulation and mean increases (calculated as the difference between mean level during stimulation and baseline and expressed as percent of the baseline) are considered for each hemodynamic parameter. The means were compared using analysis of vari-
ance for repeated measures according to Ullrich-Pitz's and Newman-Keuls' post-hoc tests. Correlations between the various parameters were evaluated by linear and stepwise multiple regression analysis.

**RESULTS**

Both heart rate and blood pressure baselines recorded during the hemodynamic test, and the respective increments during the 4 periods of stimulation, were superimposable on those recorded in the psychophysiology laboratory during the noninvasive test. Moreover, the baseline values were not different from those observed at the bedside on the days prior to testing. Baseline levels before each stressor did not differ for any of the parameters measured, so that comparison of the hemodynamic responses following the 4 stressors was possible. The subjects had normal mean values of heart rate and blood pressure at rest, with left and right ventricular filling pressures higher than normal, a usual finding in post-infarct NYHA class I–II patients on no medication. Administration of the 4 stressors produced different degrees of hemodynamic activation. Table I reports the peak variations of each parameter during the 4 periods of stress ("stress" values are the peak values reached); Table II shows the mean variations ("stress" values are the mean values of the 3' of each stress period). Figure 1 shows the mean increments of each parameter in response to each stressor expressed as percent of the baseline value.

All hemodynamic parameters were significantly (p<0.001) altered after administration of the mental arithmetic, Sacks test and Raven matrices, whereas noise administration induced a significant change only in blood pressure (p<0.005), with a mean increase of 8±7/4±5 mmHg.

The increases observed in systolic and diastolic pulmonary artery pressures (p<0.05 and p<0.01, respectively) and left ventricular filling pressure (p<0.01) were greater after mental arithmetic than after either the Sacks test or the Raven matrices.

The increment in right ventricular filling pressure was greatest during mental arithmetic, and significantly higher (p<0.01) than during the Sacks test, but not significantly different, although somewhat lower, with the Raven matrices. On the other hand, the increments in heart rate (p<0.01) and systolic (p<0.01) and diastolic (p<0.05) blood pressures were significantly greater during mental arithmetic than during the Raven matrices, whereas the mean differences in the increments of the same parameters during mental arithmetic and the Sacks test were not statistically significant. The only difference in the response to the Sacks test and Raven matrices was in diastolic
### Table I. Hemodynamic Response to 4 Different Stressors: Peak Levels (means±SD)

<table>
<thead>
<tr>
<th></th>
<th>Mental arithmetic</th>
<th>Sacks test</th>
<th>Raven progressive matrices</th>
<th>Noise</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Peak</td>
<td>Baseline</td>
<td>Peak</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>76±14***</td>
<td>91±17</td>
<td>74±13***</td>
<td>84±13</td>
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<tr>
<td>sAP (mmHg)</td>
<td>130±21***</td>
<td>151±29</td>
<td>131±23***</td>
<td>149±28</td>
</tr>
<tr>
<td>dAP (mmHg)</td>
<td>89±12***</td>
<td>101±16</td>
<td>90±13***</td>
<td>98±14</td>
</tr>
<tr>
<td>RAP (mmHg)</td>
<td>7.4±2.2***</td>
<td>10.4±2.3</td>
<td>7.3±2.2***</td>
<td>9.1±2.4</td>
</tr>
<tr>
<td>sPAP (mmHg)</td>
<td>33±8***</td>
<td>40±10</td>
<td>32±9***</td>
<td>38±10</td>
</tr>
<tr>
<td>dPAP (mmHg)</td>
<td>15±4***</td>
<td>20±5</td>
<td>15±5***</td>
<td>18±5</td>
</tr>
<tr>
<td>PWP (mmHg)</td>
<td>15±6***</td>
<td>22±7</td>
<td>16±6***</td>
<td>20±7</td>
</tr>
</tbody>
</table>

* p<0.05,  *** p<0.001.

Abbreviations: HR=heart rate; s=systolic; d=diastolic; AP=arterial pressure; RAP=mean right arterial pressure; PAP=pulmonary arterial pressure; PWP=mean pulmonary wedge pressure.

### Table II. Hemodynamic Response to 4 Different Stressors: Mean Levels (means±SD)

<table>
<thead>
<tr>
<th></th>
<th>Mental arithmetic</th>
<th>Sacks test</th>
<th>Raven progressive matrices</th>
<th>Noise</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Stress</td>
<td>Baseline</td>
<td>Stress</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>76±14***</td>
<td>87±16</td>
<td>74±13***</td>
<td>82±13</td>
</tr>
<tr>
<td>sAP (mmHg)</td>
<td>130±21***</td>
<td>147±28</td>
<td>131±23***</td>
<td>146±28</td>
</tr>
<tr>
<td>dAP (mmHg)</td>
<td>89±12***</td>
<td>99±15</td>
<td>89±12***</td>
<td>98±14</td>
</tr>
<tr>
<td>RAP (mmHg)</td>
<td>7.4±2.2***</td>
<td>9.9±2.2</td>
<td>7.3±2.2***</td>
<td>8.7±2.4</td>
</tr>
<tr>
<td>sPAP (mmHg)</td>
<td>33±8***</td>
<td>39±10</td>
<td>32±9***</td>
<td>36±10</td>
</tr>
<tr>
<td>dPAP (mmHg)</td>
<td>15±4***</td>
<td>19±5</td>
<td>15±5***</td>
<td>17±5</td>
</tr>
<tr>
<td>PWP (mmHg)</td>
<td>15±6***</td>
<td>21±7</td>
<td>16±6***</td>
<td>19±7</td>
</tr>
</tbody>
</table>

** p<0.05,  *** p<0.001.
blood pressure (p<0.05).

No patient had symptoms during the four tests. The oldest patient, 73 years old, studied 51 days after an anterior myocardial infarction, showed premature atrial and polymorphic ventricular beats during mental arithmetic, which had also been recorded during a 24 hour ambulatory ECG (Lown's class III) but absent during exercise testing. The same patient and another 56 years old, the latter studied 33 days after an anterior myocardial infarction, during mental arithmetic and Raven matrices showed ST-segment elevation in the precordial leads with pathologic Q waves and a rate-pressure-product threshold equal to that following exercise testing. In no case was ST-segment depression recorded.

Complications:

No patient became symptomatic during administration of the 4 stressors. One patient, as already mentioned (Subjects), presented acute pulmonary edema after testing and was immediately given appropriate treatment; he did not repeat testing in the Psychophysiology Laboratory and was taken off the protocol. Another patient, 52 years old, studied 31 days after an anterior myocardial infarction, also developed acute pulmonary edema in a similar fashion; he had completed the noninvasive test in the Psychophysiology
Laboratory without problems the previous day, with superimposable changes in the only parameters measured both days (ECG and BP).

The 2 cases of acute pulmonary edema are discussed in detail in another report.\textsuperscript{61}

Other observations:

The study population was subdivided into 3 different age groups: group A, <50 years (mean = 42, range 26–48, n = 9); group B, 50 to 60 years (mean = 55, range 52–57, n = 11); group C, > 60 years (mean = 66, range 62–73, n = 4), no significant differences in the hemodynamic behavior of the 3 groups were observed.

In the overall population no correlation between the hemodynamic stress profile and psychologic characteristics was evident.

The hemodynamic stress profile was independent of the baseline hemodynamic situation.

Pulmonary wedge pressure increases during stress were not correlated with increases in either heart rate or blood pressure.

Order of presentation of the stressors did not influence hemodynamic response. There were no significant differences in the stress profiles of the four sequences of baseline-stress-recovery, which were different for the 24 patients, considering either mean or peak stress values.

DISCUSSION

The first consideration arising from these data is that in patients with recent myocardial infarction without clinically evident complications, pump function is affected by mental stress to a significant extent with objective evidence of hemodynamic distress.

The mean increase in pulmonary wedge pressure of 40\% observed during mental arithmetic, in patients with mean baseline values of 15–16 mmHg, is not at all negligible from a clinical point of view, in particular, considering that the stress induction was not individualized and was poor in emotional content. The mean increase in left ventricular filling pressure appears out of proportion to the modest increases observed both in heart rate and blood pressure.

The absence of subjective symptoms and the lack of correlation between “noninvasive” parameters (heart rate and blood pressure) and “invasive” parameters (pulmonary wedge pressure) do not allow identification of hemodynamic distress on the basis of the “usual” stress profile (i.e. analysis of heart rate and blood pressure).

The possibility of inducing hemodynamic stress or distress by mental
The "stressor power" of the four psychologic stimuli appeared remarkably different. Noise, the stressor characterized mainly by an "intake" component was least effective in stimulating hemodynamic arousal. On the contrary, mental arithmetic, the stressor with the most marked "rejection" characteristics, was the most activating stimulus. Balanced stressors, the Sacks test and Raven matrices, induced intermediate hemodynamic arousal. These findings seem to agree with Lacey's theory as well as with previous and recent observations on central and autonomic nervous activation induced by mental stress; mental arithmetic appears to be a pure adrenergic stressor with an effect prevalently on beta receptors, while intake-rejection stressors, used typically for measuring reaction time, could produce an initial vagal response followed by an orthosympathetic response.

In other words, mental arithmetic can be presumed to pose an immediate comprehension problem: a repetitive task requiring attentive elaboration and an active coping behavior leading to a typical "fight or flight" reaction. On the contrary, the Raven matrices pose a new problem after each answer, and consequently, alternating periods of attention-preparation (vagal activation?) and periods of elaboration-reply (sympathetic activation) with the addition of an important emotional component for the Sacks test. Thus for both the Sacks test and the Raven matrices, a mixture of coping (fight or flight) and defensive reaction with "playing dead" behavior can be hypothesized with a more complex autonomic response.

This type of model would justify the lack of hemodynamic response to noise, which can be considered as a lack of an orthosympathetic response, or more probably, as a parasympathetic activation of sufficient degree to counterbalance the adrenergic activation.

The hemodynamic impairment does not seem to be attributable to the "invasive" situation. Heart rate and blood pressure profiles were superimposable on the noninvasive values recorded at an interval of 24 hours in the Psychophysiology Laboratory.

Patients at risk were not identified by this approach; age, infarction site, basal hemodynamic situation and the psychological assessment did not allow differentiation of the hemodynamic response to stress.

A 4 stressor sequence does not seem to offer advantages, because the stress response depends on the stressor used and not on its order in the sequence. On the other hand, it is worthy to note that when submitted to 4 stressors lasting a total of 37 min, 2 of 26 patients developed acute pulmonary
edema immediately after stress testing. This complication was never observed in the more than 300 patients with recent myocardial infarction, who were all evaluated by 2 stressors, mental arithmetic and the Sacks test, lasting a maximum of 21'; 228 of these cases were published and 34 also underwent cardiac catheterization.

If test length influences induction of hemodynamic distress (although not revealed by the parameters studied) a stressor sustaining psychophysiological activation for a longer period would be useful; the common standardized stressors such as mental arithmetic do not maintain such activation for more than a few minutes.

The ECG did not show evidence of ischemic changes and did not explain the hemodynamic distress evident from the instrumentally derived data of this study and clinically evident in 2 patients. An ischemic origin of the hemodynamic distress does not, therefore, seem to be involved. However, it cannot be excluded on the basis of the conventional ECG alone. Using positron emission tomography (myocardial uptake of 82Rb) Deanfield et al documented defects in myocardial perfusion in 12 of 16 patients with stable angina pectoris (13 postinfarct patients) submitted to low difficulty mental arithmetic, but only 6 of them had electrocardiographic modifications (ST segment depression). Such a finding leads one to postulate that mental stress, insufficient to induce typical electrocardiographic modifications, may be sufficient to induce alterations in myocardial mechanics responsible for hemodynamic impairment.

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