Abnormal left ventricular ejection fraction response to mental stress and exercise in cardiomyopathy

Dean E. Wolz, MD, Angel R. Flores, MD, Donald J. Grandis, MD, Judith E. Orie, MD, and Douglas S. Schulman, MD

Background. **A decline in left ventricular (LV) ejection fraction in response to mental stress and exercise is regarded as an indicator of myocardial ischemia. In patients with LV dysfunction, the ejection fraction is sensitive to afterload, which increases during stress. Thus, the effects of mental stress and exercise on LV systolic function in patients with cardiomyopathy were examined.**

Methods. **The ambulatory nuclear VEST (Capintec, Inc., Ramsey, N.J.) was used to monitor LV ejection fraction in patients with cardiomyopathy (10 idiopathic and 9 ischemic). Patients underwent a series of mental stress tests (serial 7s, Stroop color, and Paced auditory addition) and treadmill exercise. Heart rate, systolic blood pressure, and LV ejection fraction were measured.**

Results. **Mental stress and exercise increased heart rate and systolic blood pressure. For idiopathic cardiomyopathy, LV ejection fraction decreased during serial 7s, Stroop color, Paced auditory addition and exercise by $-8\% \pm 6\%$, $-7\% \pm 5\%$, $-7\% \pm 3\%$, $-9\% \pm 10\%$, respectively. For ischemic cardiomyopathy, LV ejection fraction declined by $-4\% \pm 3\%$, $-7\% \pm 5\%$, $-6\% \pm 3\%$, $-2\% \pm 6\%$ during the same stress tests. There was no difference between the idiopathic and ischemic groups. Each patient showed a 5% or greater decline in LV ejection fraction during one mental stress test. There was an inverse relation between changes in LV ejection fraction and systolic blood pressure during all mental stress tests and exercise ($r = -0.47, p < 0.0001$).**

Conclusions. **In patients with depressed baseline systolic function, the decline in systolic function during mental stress and exercise could be related in part to increases in LV afterload.**
(J NUCL CARDIOL 1995;2:144-50.)

Key words: VEST · cardiomyopathy left ventricular function · mental stress

Mental stress has been used to evaluate patients with systemic hypertension[1-3] and coronary artery disease.[4-6] Various mental stressors can affect cardiovascular parameters, such as heart rate, systolic blood pressure, and myocardial oxygen consumption, in a manner similar to exercise.[5,6] In addition, mental stress can cause a deterioration in hemodynamics independent of changes in heart rate and blood pressure in patients with recent myocardial infarction.[7]

From Division of Cardiology, Department of Internal Medicine, Medical College of Pennsylvania, Allegheny General Hospital, Pittsburgh, Pa.
Submitted for publication Sept. 29, 1994; revision accepted Dec. 12, 1994.
Reprint requests: Douglas S. Schulman, MD, Allegheny General Hospital, 320 E. North Ave., Pittsburgh, PA 15212.

1071-3581/95/$3.00 + 0 **43/1/62697**

By increasing myocardial oxygen demand, mental stress can precipitate myocardial ischemia in patients with coronary artery disease.[5,6,8-12] A decline in left ventricular (LV) ejection fraction with mental stress, as with exercise, is considered an indicator of myocardial ischemia.[6] The decrease in ejection fraction with mental stress has been demonstrated in patients with ischemic heart disease who have mild to moderate LV dysfunction.[6,13] However, LV ejection fraction is sensitive to afterload, especially when LV function is abnormal.[7] As afterload is a primary determinant of LV function,[14] decreases in LV ejection fraction during mental stress testing could be secondary to the effect of increased afterload rather than because of ischemia. It is well appreciated that LV ejection fraction can decline during exercise in patients with cardiomyopathy.[15] We postulated that patients with cardiomyopathy would have declines in LV ejection fraction during mental stress and exercise

that were due to changes in LV afterload as estimated by systolic blood pressure, and that these changes would be independent of ischemia. The effects of mental stress in patients with dilated cardiomyopathy have been described for diastolic function,[16] but have not been studied for systolic function.

METHODS

Patient Population. Patients were recruited for the study from an outpatient heart failure clinic. All patients had LV dysfunction but were clinically stable and able to perform treadmill exercise. Patients were in the New York Heart Association class 3 by subjective assessment and by measurement of maximal oxygen consumption during exercise. We excluded patients with a recent myocardial infarction (6 months), exertional angina, recent hospitalization (3 months) for an exacerbation of congestive heart failure, or cardiac rhythm other than sinus rhythm or sinus tachycardia. We also excluded patients who did not have prior coronary angiography to define the cause of the LV dysfunction or could not exercise. Finally, we eliminated patients who did not have exercise ^{201}Tl scintigraphy performed within 3 months of the study or who had evidence of myocardial ischemia on the study. We divided the patients into two groups based on the presence or absence of coronary artery disease. There were 10 patients who had ischemic cardiomyopathy with prior myocardial infarction and angiographically demonstrated coronary artery disease and 11 patients who had normal coronary arteries and idiopathic cardiomyopathy. One patient in each group had a technically inadequate VEST study and they were excluded from further analysis. The clinical severity of the LV dysfunction in the 19 patients included in this analysis is notable by their poor prognosis. In the 18 months since recruitment was completed, seven patients had heart transplantations, five died, and seven remained with class 3-4 congestive heart failure.

As noted, all patients had maximal exercise testing with ^{201}Tl scintigraphy within 3 months before entering the protocol. Patients exercised on a modified Naughton protocol until developing dyspnea or fatigue. No patient had angina during exercise. At peak exercise patients were injected with 3 mCi ^{201}Tl intravenously and then exercised for an additional minute. Patients had planar imaging in left anterior, 45-degree and 70-degree, and left lateral positions using standard techniques. After a 3- to 4-hour delay, patients returned for repeat imaging in the same views. Images were interpreted qualitatively by nuclear cardiologists blinded to the clinical data. No patient had ^{201}Tl redistribution suggesting ischemia.

Radionuclide Angiography. The patient's red blood cells were labeled with 25 mCi ^{99m}Tc pertechnetate by the in vivo technique. A standard gamma camera (GE Starcam, Milwaukee, Wis.) was positioned over the patient in the best left anterior oblique view. Radionuclide data were acquired of 4000 counts/pixel in the field of view. Regions of interest were drawn around the end-diastolic and end-systolic frames, and LV ejection fraction was calculated from the background corrected images in a standard manner.

VEST. The VEST (Capintec, Inc, Ramsey, N.J.) consists of one sodium iodide and one cadmium telluride radiation detector (the former positioned over the LV blood pool, the latter over the lung to measure background) attached to a semirigid plastic garment, a microprocessor, an electrocardiographic (ECG) gating device, a battery power supply, and a modified Holter tape recorder. Count data were acquired in a gated format starting with the R wave of the ECG. A background factor was determined to equate the VEST baseline ejection fraction to that obtained by the gamma camera. Because the background activity monitored over the lung did not change during the stress tests, this constant factor was applied in the calculation of subsequent ejection fractions. The VEST continuously records the ECG waveform and the radioactivity counts from the LV blood pool. Data analyses were performed off-line with a dedicated minicomputer. Heart rate, LV ejection fraction, end-diastolic and end-systolic counts, and the ST segment level were calculated for each 30-second interval. Relative counts were expressed as 100% at the beginning of the study so that changes in cardiac volume could be determined during the various stress tests. The optimal position of the VEST detector over the left ventricle was determined in the best LAO view with the gamma camera and a positioning target in place of the detector. The VEST was positioned initially with the patient in the supine position. Then the patient was placed in the semirecumbent position, and small adjustments of the detector were made. The position of the detector over the left ventricle was confirmed in the standing position. This procedure was repeated at the end of the protocol to ensure that no significant movement of the detector had occurred.

Stress Testing. During a 10-minute rest period, heart rate, blood pressure, and data from the VEST were recorded. Blood pressure was measured every 60 seconds with an automated blood pressure cuff (Dinamap, Critikon, Tampa, Fla.). The patient performed a series of three mental stress tests. The tests were administered with the patient in a semirecumbent position. Each test required between 1.5 to 5 minutes to complete. After each test, heart rate and blood pressure were allowed to return to rest levels. This required at least 5 minutes. The patient was asked to perform serial 7s, subtracting 7 from a fixed number in a serial fashion as quickly and accurately as possible. The patient then performed the Stroop color word test in which conflicting visual data was presented at rapid delivery rates. The third test was the Paced auditory serial addition task. The patient was instructed to add two sequential numbers as he hears a list of numbers from a tape recording. The numbers are presented on the tape at increasing speed. After at least a 10-minute rest period, the patient underwent symptom-limited treadmill exercise testing, which used the modified Naughton protocol. The test was performed while the patient was wearing the VEST. Heart rate was recorded continuously. Blood pressure readings were obtained by cuff sphyganomometry at 3-minute intervals.

Table 1. Demographics

	Idiopathic	Ischemic
Age (yr)	58 ± 9	56 ± 7
Sex (M/F)	9/1	8/1
Systolic blood pressure (mm Hg)	128 ± 13	118 ± 15
Heart rate (BPM)	70 ± 9	77 ± 12
Left ventricular ejection fraction (%)	33 ± 9	27 ± 9
Medications:		
Digoxin	10	8
ACEI	8	7
Diuretics	10	9
Enoximone	3	3
Anticoagulants	10	9
Antiarrythmics	3	3
Nitrates	1	7*
Diltiazem	0	4†
Propranolol	1	1

*p = 0.02; †p = 0.07 ischemic vs idiopathic; ACEI = angiotensin converting enzyme inhibitor.

Table 2. Hemodynamic and ejection fraction response to stress

Stress	Change HR (b/min)	Change SPB (mmHg)	Change LVEF (%)	Decline LVEF ≥5% (no. of patients)
Idiopathic cardiomyopathy				
Serial 7s	+13 ± 13*	+10 ± 7*	−8 ± 6*	7/10
Stroop	+10 ± 8*	+13 ± 4*	−7 ± 5*	7/10
Addition	+10 ± 8*	+12 ± 6*	−7 ± 3*	8/10
Exercise	+68 ± 27*	+18 ± 16*	−9 ± 10*	9/10
Ischemic cardiomyopathy				
Serial 7s	+5 ± 4	+8 ± 4*	−4 ± 3*	6/9
Stroop	+7 ± 3*	+13 ± 4*	−7 ± 3*	8/9
Addition	+5 ± 3	+9 ± 4*	−6 ± 3*	7/9
Exercise	+50 ± 25*	+15 ± 13*	−4 ± 6	6/9

Data are expressed as mean ± SD or number of patients.
*p < 0.05 baseline vs stress.
HR = Heart rate; *LVEF* = left ventricular ejection fraction; *SBP* = systolic blood pressure.

Analysis. Data are presented as mean ± SD. The change in each variable from the preceding baseline was calculated. VEST radionuclide data for two successive 30-second intervals were averaged. Thus the new baseline consisted of the two readings just preceding the next stress test. The two successive lowest ejection fractions during each mental stress were recorded. During the exercise testing, the ejection fractions 30 seconds before and at peak exercise were recorded. The relative end-diastolic and end-systolic volumes during those two 30-second readings were noted. The ST segment depression was considered significant if it were 1 mm or more and persisted for 60 seconds or longer.

Within each group, the effects of the four stresses on the various cardiovascular parameters were compared by repeated measures analysis of variance (ANOVA). If a significant difference was detected by the ANOVA, a Neuman-Keuls test was performed to ascertain where the differences were. Demographic differences between the two groups were analyzed by Student t test. Linear regression analysis was used to correlate the changes in systolic blood pressure and LV ejection fraction during mental stress and exercise.

RESULTS

Patient Characteristics. (Table 1). There were 10 patients with idiopathic and 9 with ischemic cardiomyopathy. The two groups were similar with respect to age, sex, resting heart rate, blood pressure, and LV ejection fraction. Most patients were taking digoxin, diuretics, anticoagulants, and angiotensin converting enzyme inhibitors. More patients in the ischemic group were treated with nitrates and calcium

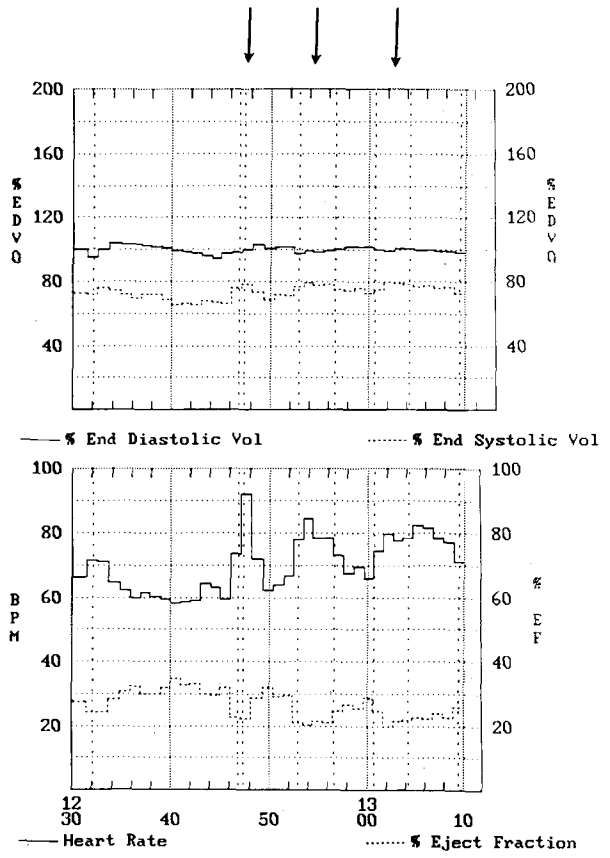

Figure 1. Example of continuous recording from patient no. 12 (idiopathic cardiomyopathy) during three mental stress tests: serial 7s, Stroop color, and Paced auditory serial addition task. Vertical lines denote onset and termination of each mental stress test. *Arrow* during each stress is added for clarity. On top, relative LV volumes, end-diastolic *(solid line)* and end-systolic *(broken line)*. On bottom, heart rate in beats/min (BPM) *(solid line)* and LV ejection fraction *(EF)* in percent *(%) (broken line)*.

channel blockers. One patient in each group was treated with propranolol at low doses.

Response to Mental Stress and Exercise. (Table 2). Mental stress was associated with an increase in heart rate and systolic blood pressure. Patients with idiopathic cardiomyopathy tended to have a greater increment in heart rate and blood pressure, and a larger decline in LV ejection fraction than patients with ischemic cardiomyopathy. As expected, heart rate increased to a greater degree during exercise in comparison with mental stress. The increase in systolic blood pressure during exercise was comparable to the change during mental stress. Both groups showed a similar decline in LV ejection fraction during mental stress and exercise. A patient example is illustrated in Figure 1. Similar to the example, the decline in LV ejection fraction during the mental stress tests in both groups was abrupt.

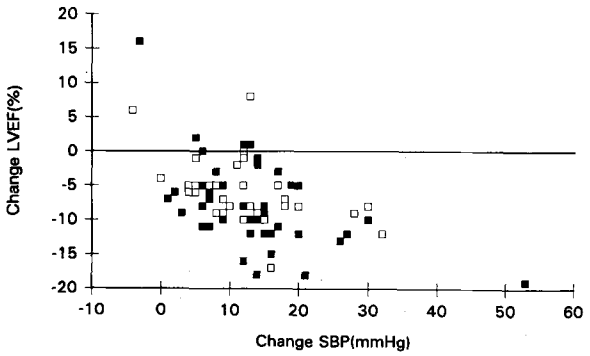

Figure 2. Plot of change in left ventricular ejection fraction (LVEF) and systolic blood pressure (SBP) during mental stress and exercise (4 data points/patient). *Closed squares* = idiopathic, *open squares* = ischemic.

During the exercise, however, changes in ejection fraction were continuous, tending to reach a maximum toward peak exercise. Each patient showed a 5% or greater decline in LV ejection fraction during one mental stress test.

The declines in LV ejection fraction during mental stress were associated with no change from baseline in relative end-diastolic volume ($+0.4\% \pm 3.2\%$ and $-0.6\% \pm 3.1\%$, p = ns), but an increase in relative end-systolic volume ($+6\% \pm 3\%$ and $+5\% \pm 2\%$, $p < 0.05$ for both) in idiopathic and ischemic cardiomyopathy, respectively. Because the increase in heart rate was accompanied by a decline in stroke volume, there was no significant change in relative cardiac output in either group during each mental stress test. Exercise intensity was similar in both groups, 4.6 ± 1.5 and 3.8 ± 1.7 METS in idiopathic and ischemic cardiomyopathy, respectively. During exercise, relative end-diastolic and end-systolic volumes increased in both groups. For the patients with idiopathic cardiomyopathy, end-diastolic and end-systolic volumes increased by $+3\% \pm 4\%$ and $+7\% \pm 5\%$, $p < 0.05$ versus baseline. For the ischemic group the corresponding changes in LV volumes were $+4\% \pm 5\%$ and $+5\% \pm 5\%$, $p < 0.05$ versus baseline. Relative cardiac output increased significantly during exercise in both groups. There was an inverse relation between changes in LV ejection fraction and systolic blood pressure during all mental stress tests and exercise for all patients ($r = -0.47$, $p < 0.0001$, SEE = 5.1) (Figure 2). There was a less significant relation between the change in heart rate and LV ejection fraction during stress ($r = -0.28$, $p = 0.01$, SEE = 5.53). In patients without left bundle branch block ($n = 12$), no patient demonstrated 1 mm or greater ST segment depression for 60 seconds or longer during mental stress or exercise.

DISCUSSION

In this study, we examined the effects of mental stress and treadmill exercise on LV systolic function in patients with cardiomyopathy. The data suggest that part of the decline in LV ejection fraction during mental stress and exercise in these patients is related to an increase in systolic blood pressure.

LV ejection fraction usually remains unchanged or increases modestly during mental stress in normal subjects.[17-19] In contrast, patients with coronary disease have a decline in LV ejection fraction during mental stress, thought to be secondary to provocable myocardial ischemia.[6,17,20] In the study of Rozanski and colleagues,[6] 59% of their coronary patients had wall-motion abnormalities and 36% had a fall in LV ejection fraction of 5% or greater during mental stress. Their patients had significant elevations in blood pressure and heart rate during mental stress, major determinants of myocardial oxygen consumption. Declines in LV ejection fraction were considered to be ischemic in origin since they were highly associated with regional wall-motion abnormalities.[6] In several studies in which nonimaging radionuclide detectors have been used a decline in LV ejection fraction during mental stress,[17,20] exercise,[17] or routine activity[21,22] has been relied on as a sign of ischemia. With the use of coronary angiography, Yeung and associates[23] demonstrated that mental stress caused paradoxical vasoconstriction of coronary segments that correlated to the abnormalities produced by the intracoronary injection of acetylcholine. These data imply that mental stress prompts an abnormal vasomotor response in coronary segments with atherosclerotic changes and endothelial dysfunction.[23] Therefore both increases in myocardial oxygen demand and decreases in coronary blood flow could precipitate ischemia during mental stress in patients with coronary artery disease.

Decreases in LV ejection fraction in response to mental stress and exercise could be in part secondary to the effects of increased afterload. Afterload is a major determinant of ejection performance.[14] LV ejection fraction is more sensitive to changes in afterload in the setting of reduced LV function.[24,25] Since mental stress results in substantial increases in blood pressure, a major component of wall stress, it is likely that this form of stress increases LV afterload. The effects of mental stress on ventricular performance in cardiomyopathy and the association with LV afterload have not been described previously. Our data correspond with the information on mental stress and exercise obtained by Breisblatt et al.[26] in hypertensive patients. In their hypertensive patients with evidence of LV hypertrophy, mental stress and exercise caused significant elevations in blood pressure and declines in LV ejection fraction measured by the VEST. The authors noted that the decline in LV ejection fraction during stress was preceded by substantial elevations in blood pressure. Furthermore, stresses causing the greatest increase in blood pressure were associated with the largest declines in ejection fraction.[26] The modest inverse relation between changes in systolic blood pressure and LV ejection fraction in the current study, suggests a role for LV afterload in mediating the decline in ejection fraction in patients with severe systolic dysfunction.

A decline in LV ejection fraction has been described previously in patients with cardiomyopathy during exercise.[15] In the study of Schoolmeester and colleagues,[15] the patients with ischemic cardiomyopathy demonstrated a decline in LV ejection fraction during exercise, whereas those with idiopathic cardiomyopathy showed an increase. However, in the studies of Hecht et al.[27] and Port et al.,[28] a wide variation in exercise ejection fraction was noted. In Port's study, an increase in LV ejection fraction was noted in many patients with ischemic cardiomyopathy.[28] Differences between studies likely reflect the position of exercise (supine vs upright), sex differences, the degree of LV dysfunction at rest, exercise intensity, and the amount of inducible ischemia.

In comparison with graded exercise, mental stress has a sudden onset and is associated with a precipitous increase in systolic blood pressure. In addition, the pattern of catecholamine secretion during mental stress is one of epinephrine predominance compared with the predominant norepinephrine secretion during exercise.[29] Despite these differences, our patients had similar hemodynamic and functional responses to the different stressors. The down regulation of myocardial beta-adrenoreceptors in patients with cardiomyopathy may account for the failure of the increase in circulating catecholamines to prevent the fall in LV ejection fraction during mental stress.[30] This mechanism may also help to explain the declines in LV ejection fraction found in all our patients during stress compared with the more typical response in patients with coronary artery disease and preserved LV function. Approximately 50% to 60% of the latter group demonstrate a decline in ejection fraction during mental stress and exercise.[6,13,17,20] Furthermore, patients with chronic congestive failure and severe limitations to their lifestyle may have developed aggressive personality traits, which have been correlated with stress-induced LV dysfunction in patients wtih coronary artery disease and preserved LV function.[31] Diastolic function also deteriorates during mental stress in patients with cardiomyopathy,

which could contribute to the systolic dysfunction found in the current study.[16] In a group of cardiac transplant patients, we have demonstrated that those patients with abnormal peak filling rates have a decline in ejection fraction when challenged with methoxamine compared with patients with normal diastolic function.[32] In the study by Breisblatt et al.,[26] 12 of 15 patients with hypertension, LV hypertrophy, and diastolic dysfunction demonstrated a decline in LV ejection fraction during mental stress. Changes in valvular regurgitation and the effects of pericardial constraint may also influence the functional response to increased afterload in the current study. Finally, since previous studies examined patients with relatively intact systolic function, the role of LV afterload in those patients was likely to be less than in our cohort of patients with myopathic ventricles.

In our patients with either idiopathic or ischemic cardiomyopathy, the depression in LV ejection fraction during mental stress and exercise occurred without evidence of demonstrable ischemia. The degree to which ischemia contributed to this response is difficult to discern without further study. The patients with idiopathic cardiomyopathy had normal coronary arteries. However, patients with this disease may have abnormal endothelium-dependent coronary vasodilator function and decreased coronary flow reserve.[33] In the setting of abnormal flow reserve, significant elevation in myocardial oxygen demand and possible coronary artery vasoconstriction could precipitate ischemia during stress. The patients with ischemic cardiomyopathy had severe coronary disease and prior myocardial infarctions. Although they had fixed perfusion abnormalities on stress ^{201}Tl scintigraphy, subendocardial ischemia would not have been easily detected. Also, we did not perform ^{201}Tl reinjection that may have detected ischemia in a proportion of these patients with fixed defects on stress-redistribution imaging.[34] While no patient had significant ST segment depression during mental stress, this finding is not sensitive for ischemia during these maneuvers.[6,17,19-22] Finding no change in regional wall motion may have increased the specificity of our conclusion that ischemia was not a predominant role in the stress-induced LV dysfunction. However, it is also likely that the reliability of detecting wall-motion abnormalities in these patients with diffusely abnormal wall motion would be low. Future studies that use metabolic imaging or coronary sinus lactate sampling during stress in these populations may help clarify the role of myocardial ischemia.

Limitations. We used systolic blood pressure as an estimation of LV afterload. Blood pressure is one element of afterload. Measurements of wall stress, arterial elastance, or impedance may give better correlations with the changes in ejection fraction in this population. We did not measure a load independent measure of contractility. It is likely that variable increases in contractility during stress contributed to the finding that changes in systolic blood pressure and LV ejection fraction were only modestly correlated. In patients with coronary disease and varying degrees of LV dysfunction, Marmor and associates[35] demonstrated that cardiac peak power, an index of contractility, increased significantly during supine exercise, whereas LV ejection fraction was unchanged. These data illustrate the afterload dependence of LV ejection fraction in these circumstances.[35] Our data also suggest a role for increased afterload in the change in LV ejection fraction during mental stress in this setting. We did not withhold medications before stress testing. Thus ischemia may have been averted in the ischemic group. Furthermore, rises in blood pressure may have been blunted by vasodilator therapy. Nonetheless, our results in this cohort of patients on medical therapy can be translated better into activities of daily life.

Since depression of LV systolic and diastolic function occurs during mental stress and exercise in patients with both ischemic and idiopathic cardiomyopathy, these findings may have clinical relevance. One can speculate that frequent, repeated episodes of LV dysfunction in this setting may contribute to exacerbations of clinical heart failure. Furthermore, if these episodes of increased myocardial oxygen demand during stress are associated with insufficient increases in coronary blood flow, the potential exists for repeated episodes of myocardial ischemia that cause LV dysfunction (stunning). With the use of positron emission tomography, Vanovershielde and associates[36] demonstrated the role for recurrent episodes of myocardial ischemia in producing chronic LV dysfunction in patients with coronary artery disease. Further studies in patients with cardiomyopathy are indicated in this regard.

We appreciate the assistance of Sandra J. Mertz, RN, Kathleen A. Deloplaine, RN, and Lon Wilson, Jr., who helped recruit patients and process data.

References

1. Brod G, Fencl V, Hejl Z, Jirka J. Circulatory changes underlying blood pressure elevation during acute emotional stress (mental arithmetic) in normotensive and hypertensive subjects. Clin Sci 1959;19:269-79.
2. Nestel PJ. Blood pressure and catecholamine excretion after mental stress in labile hypertension. Lancet 1969;1:692-4.
3. Nyberg G. Blood pressure and heart rate response to isometric

exercise and mental arithmetic in normotensive and hypertensive subjects. Clin Sci Mol Med 1976;51:681-5.
4. Bassan MM, Marcus HS, Ganz W. The effect of mild-to-moderate mental stress on coronary hemodynamics in patients with coronary artery disease. Circulation 1980;62:933-5.
5. Speccia G, De Servi S, Facone C, et al. Mental arithmetic stress testing in patients with coronary artery disease. Am Heart J 1984;108:56-63.
6. Rozanski A, Bairey CN, Krantz DS, et al. Mental stress and the induction of silent myocardial ischemia in patients with coronary artery disease. N Engl J Med 1988;318:1005-12.
7. Mazzuero G, Temporelli PL, Tavazzi L. Influence of mental stress on ventricular pump function in postinfarction patients. Circulation 1991;83:II-145-II-154.
8. Deanfield JE, Shea M, Kensett M, et al. Silent myocardial ischemia due to mental stress. Lancet 1984;2:1001-5.
9. Campbell S, Barry J, Rebecca GS, et al. Active transient myocardial ischemia during daily life in asymptomatic patients with positive exercise tests and coronary disease. Am J Cardiol 1986;57:1010-6.
10. Tzivoni D, Gavish A, Benhorin J, Keren A, Stern S. Myocardial ischemia during daily activities and stress. Am J Cardiol 1986;58:47B-50B.
11. Freeman LJ, Nixon PGF, Sallabank P, Reaveley D. Psychological stress and silent myocardial ischemia. Am Heart J 1987;114:477-82.
12. Giubbini R, Galli M, Campini R, Bosimini E, Bencivelli W, Tavazzi L. Effects of mental stress on myocardial perfusion in patients with ischemic heart disease. Circulation 1991;83:II-100-II-107.
13. Bairey CN, Krantz DS, Rozanski A. Mental stress as an acute trigger of ischemic left ventricular dysfunction and blood pressure elevation in coronary disease. Am J Cardiol 1990;66: 28G-31G.
14. Sonnenblick EH, Downing SE. Afterload as a primary determinant of ventricular performance. Am J Physiol 1963;204: 604-10.
15. Schoolmeester WL, Simpson AG, Sauerbrunn BJ, Fletcher RD. Radionuclide angiographic assessment of left ventricular function during exercise in patients with a severely reduced ejection fration. Am J Cardiol 1981;47:804-9.
16. Giannuzzi P, Shabetai R, Imparato A, et al. Effects of mental exercise in patients with dilated cardiomyopathy and congestive heart failure. Circulation 1991;83:II-155-II-165.
17. Breisblatt WM, Weiland FL, McLain JR, Tomlinson GC, Burns MJ, Spaccavento LJ. Usefulness of ambulatory radionuclide monitoring of left ventricular function early after acute myocardial infarction for predicting residual myocardial ischemia. Am J Cardiol 1988;62:1005-10.
18. Kiess MC, Dimsdale JE, Moore RH, et al. The effects of stress on left ventricular ejection fraction. Eur J Nucl Med 1988;14: 12-6.
19. Bairey CN, Yang LD, Berman DS, et al. Comparison of physiologic ejection fraction responses to differing stimuli: implications for clinical testing. J Am Coll Cardiol 1990;16: 847-54.
20. LaVeau PJ, Rozanski A, Drantz DS, et al. Transient left ventricular dysfunction during provocative mental stress in patients with coronary artery disease. Am Heart J 1989;118: 1-8.
21. Tamaki N, Yasuda T, Moore RH, et al. Continuous monitoring of left ventricular function by an ambulatory radionuclide detector in patients with coronary artery disease. J Am Coll Cardiol 1988;12:669-79.
22. Kayden DS, Wackers FJTh, Zaret BL. Silent left ventricular dysfunction during routine activity following thrombolytic therapy for acute myocardial infarction. J Am Coll Cardiol 1990;15:1500-7.
23. Yeung AC, Vekshtein VI, Krantz DS, et al. The effect of atherosclerosis on the vasomotor response of coronary arteries to mental stress. N Engl J Med 1991;325:1551-6.
24. Ross, Jr. J, Braunwald E. The study of left ventricular function in man by increasing resistance to ventricular ejection with angiotensin. Circulation 1964;29:739-49.
25. Kass DA, Maughan WL, Guo ZM, Kono A, Sunagawa K, Sagawa K. Comparative influence of load versus inotropic states on indexes of ventricular contractility: experimental and theoretical analysis based on pressure-volume relationships. Circulation 1987;76:1422-36.
26. Breisblatt WM, Wolf CJ, McElhinny B, Salerni R, Smith VE. Comparison of ambulatory left ventricular ejection fraction and blood pressure in systemic hypertension in patients with and without increased left ventricular mass. Am J Cardiol 1991;67:597-603.
27. Hecht HS, Karahalios SE, Ormiston JA, Schnugg SJ, Hopkins JM, Singh BN. Patterns of exercise response in patients with severe left ventricular dysfunction: radionuclide ejection fraction and hemodynamic cardiac performance evaluations. Am Heart J 1982;104:718-24.
28. Port S, McEwan P, Cobb FR, Jones RH. Influence of resting left ventricular function on the left ventricular response to exercise in patients with coronary artery disease. Circulation 1981;63:856-63.
29. Dimsdale JE, Moss J. Plasma catecholamines in stress and exercise. J Am Med Assoc 1980;243:340-2.
30. Bristow MR, Ginsburg R, Minobe W, et al. Decreased catecholamine sensitivity and beta-adrenergic-receptor density in failing human hearts. N Engl J Med 1982;307:205-11.
31. Burg MM, Jain D, Soufer R, Kerns RD, Zaret BL. Role of behavioral and psychological factors in mental stress-induced silent left ventricular dysfunction in coronary artery disease. J Am Coll Cardiol 1993;22:440-8.
32. Schulman DS, Herman BA, Edwards TD, Uretsky BF. Abnormal diastolic function in cardiac transplant recipients: an important factor in the response to increased afterload. Am Heart J 1993;123:435-42.
33. Treasure CB, Vita JA, Cox DA, et al. Endothelium-dependent dilation of the coronary microvasculature is impaired in dilated cardiomyopathy. Circulation 1990;81:772-9.
34. Dilsizian V, Rocco TP, Freedman NMT, Leon MB, Bonow RO. Enhanced detection of ischemic but viable myocardium by the reinjection of thallium after stress-redistribution imaging. N Engl J Med 1990;323:141-6.
35. Marmor A, Jain D, Cohen LS, Nevo E, Wackers FJTh, Zaret BL. Left ventricular peak power during exercise: a noninvasive approach for assessment of contractile reserve. J Nucl Med 1993;34:1877-85.
36. Vanoverschelde J-LJ, Wijns W, Depre C, et al. Mechanisms of chronic regional postischemic dysfunction in humans: new insights from the study of noninfarcted collateral-dependent myocardium. Circulation 1993;87:1513-23.