

Neurohumoral Features of Myocardial Stunning Due to Sudden Emotional Stress

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ABSTRACT

BACKGROUND

Reversible left ventricular dysfunction precipitated by emotional stress has been reported, but the mechanism remains unknown.

METHODS

We evaluated 19 patients who presented with left ventricular dysfunction after sudden emotional stress. All patients underwent coronary angiography and serial echocardiography; five underwent endomyocardial biopsy. Plasma catecholamine levels in 13 patients with stress-related myocardial dysfunction were compared with those in 7 patients with Killip class III myocardial infarction.

RESULTS

The median age of patients with stress-induced cardiomyopathy was 63 years, and 95 percent were women. Clinical presentations included chest pain, pulmonary edema, and cardiogenic shock. Diffuse T-wave inversion and a prolonged QT interval occurred in most patients. Seventeen patients had mildly elevated serum troponin I levels, but only 1 of 19 had angiographic evidence of clinically significant coronary disease. Severe left ventricular dysfunction was present on admission (median ejection fraction, 0.20; interquartile range, 0.15 to 0.30) and rapidly resolved in all patients (ejection fraction at two to four weeks, 0.60; interquartile range, 0.55 to 0.65; $P < 0.001$). Endomyocardial biopsy showed mononuclear infiltrates and contraction-band necrosis. Plasma catecholamine levels at presentation were markedly higher among patients with stress-induced cardiomyopathy than among those with Killip class III myocardial infarction (median epinephrine level, 1264 pg per milliliter [interquartile range, 916 to 1374] vs. 376 pg per milliliter [interquartile range, 275 to 476]; norepinephrine level, 2284 pg per milliliter [interquartile range, 1709 to 2910] vs. 1100 pg per milliliter [interquartile range, 914 to 1320]; and dopamine level, 111 pg per milliliter [interquartile range, 106 to 146] vs. 61 pg per milliliter [interquartile range, 46 to 77]; $P < 0.005$ for all comparisons).

CONCLUSIONS

Emotional stress can precipitate severe, reversible left ventricular dysfunction in patients without coronary disease. Exaggerated sympathetic stimulation is probably central to the cause of this syndrome.

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THE POTENTIALLY LETHAL CONSEQUENCES of emotional stress are deeply rooted in folk wisdom, as reflected by phrases such as “scared to death” and “a broken heart.” In the past decade, cardiac contractile abnormalities and heart failure have been reported after acute emotional stress,¹⁻⁶ but the mechanism remains unknown. We evaluated 19 patients with “stress cardiomyopathy,” a syndrome of profound myocardial stunning precipitated by acute emotional stress, in an effort to identify the clinical features that distinguish this syndrome from acute myocardial infarction and the cause of transient stress-induced myocardial dysfunction.

METHODS

STUDY PATIENTS

Nineteen previously healthy patients were admitted to the coronary care unit at Johns Hopkins Hospital or Johns Hopkins Bayview Medical Center in Baltimore with chest pain or symptomatic heart failure precipitated by acute emotional stress. Patients were evaluated by means of serial electrocardiography and serial measurement of cardiac isoenzymes, including creatine kinase, creatine kinase MB fraction, and troponin I. All 19 patients underwent coronary angiography; 16 also underwent concomitant left ventriculography. Five patients underwent right-heart catheterization and endomyocardial biopsy, and five underwent contrast-enhanced cardiac magnetic resonance imaging (MRI) to identify myocardial necrosis. All patients underwent two-dimensional transthoracic echocardiography within 24 hours after the onset of symptoms and again on hospital day 3, 4, 5, 6, or 7 (median, day 4); 17 patients underwent outpatient echocardiography a median of 21 days after presentation. Wall-motion abnormalities on echocardiography were assessed by means of a standard 16-segment model,⁷ with numerical scoring of contractile function (a score of 1 indicates normal contraction, a score of 2 mild hypokinesis, a score of 3 severe hypokinesis, a score of 4 akinesis, and a score of 5 dyskinesis).

NEUROHUMORAL ASSESSMENT

Plasma levels of catecholamines, metabolites, and neuropeptides were measured on hospital day 1 or 2; day 3, 4, or 5; and day 7, 8, or 9 in 13 patients with stress cardiomyopathy and a convenience sample of 7 female patients hospitalized with Killip

class III myocardial infarction. The latter patients were chosen for comparison because they had similar clinical presentations and were expected to have high sympathetic tone. Patients remained supine for at least 60 minutes before undergoing phlebotomy. Blood samples were placed on ice and immediately centrifuged, and the plasma was flash-frozen. Plasma levels of catecholamines and their metabolites were measured by high-performance liquid chromatography⁸; brain natriuretic peptide and neuropeptide Y were measured by enzyme immunoassay or radioimmunoassay.^{9,10}

STATISTICAL ANALYSIS

Continuous variables are presented as medians and interquartile ranges; ordinal variables are presented as means \pm SD. The Mann-Whitney test (SAS software, version 8.0; SAS Institute) was used to compare plasma catecholamine levels in patients with stress cardiomyopathy with those in patients with Killip class III myocardial infarction. For plasma catecholamine levels, P values of less than 0.005 remained significant after Bonferroni correction for multiple comparisons. The Wilcoxon signed-rank test was used to compare ejection fractions and echocardiographic scores at various times in the group of patients with stress cardiomyopathy. A two-tailed P value of less than 0.05 was considered to indicate statistical significance.

The study was conducted between November 1999 and September 2003. All authors participated in data collection. Oral informed consent was obtained from all patients, and the protocol was approved by the institutional review board of Johns Hopkins University School of Medicine.

RESULTS

CLINICAL CHARACTERISTICS

The median age of patients with stress cardiomyopathy was 63 years (interquartile range, 52 to 71). Eighteen patients (95 percent) were women, of whom all but two were postmenopausal (Table 1). News of an unexpected death precipitated cardiac dysfunction in about half the patients. The remainder experienced a variety of causes of emotional stress (Table 1). All patients had severe chest pain, dyspnea, or both during emotional stress and presented to the emergency department a median of two hours (interquartile range, one to five) after the onset of symptoms. Three patients required intraaortic balloon counterpulsation for hemody-

Table 1. Clinical Characteristics of 19 Patients with Stress Cardiomyopathy on Admission.*

Patient No.	Age yr	Sex	Race or Ethnic Origin	Coronary Risk Factors	Emotional Stressor	Time after Symptom Onset† hr	Clinical Presentation		
							Heart Rate beats/min	MAP mm Hg	Symptoms
1	62	F	B	HTN, smoking	Mother's death	12	71	96	Chest pain
2	63	F	AA	HTN, Chol	Car accident	1	86	52	Heart failure; hypotension
3	48	F	W	HTN, Chol, smoking	Surprise reunion	4	85	88	Chest pain
4	60	F	W	HTN	Surprise party	2	109	53	Chest pain; hypotension (IABP)
5	66	F	W	HTN, FH	Father's death	5	65	91	Chest pain
6	77	F	W	HTN, FH	Husband's death	6	106	98	Chest pain
7	52	F	W	Smoking	Friend's death	2	92	50	Chest pain; hypotension (IABP)
8	52	F	W	HTN	Father's death	5	88	93	Chest pain
9	32	F	W	Chol, FH	Mother's death	1	74	90	Chest pain
10	61	F	W	Chol	Fear of procedure	1	108	45	Chest pain; shock (IABP)
11	66	F	W	Smoking	Fierce argument	2	66	109	Chest pain
12	87	F	W	HTN, Chol, DM	Friend's death	1	99	75	Chest pain
13	69	M	W	HTN, Chol	Court appearance	2	81	73	Chest pain
14	50	F	W	None	Fear of choking	2	84	100	Chest pain; heart failure
15	71	F	W	None	Public speaking	1	67	108	Chest pain
16	76	F	W	HTN, DM, smoking	Husband's death	2	109	101	Chest pain
17	65	F	W	HTN, Chol, smoking	Armed robbery	2	95	91	Chest pain
18	71	F	W	HTN	Son's death	6	70	66	Chest pain; VF
19	27	F	A	None	Tragic news	3	64	52	Chest pain; hypotension

* MAP denotes mean arterial pressure, B Bermudan, HTN hypertension, AA African American, Chol hypercholesterolemia, W white, IABP intraaortic balloon pump, FH family history, DM diabetes mellitus, VF ventricular fibrillation, and A African. † Values are times from the onset of symptoms to presentation at the emergency department.

dynamic support, and one patient had ventricular fibrillation.

ELECTROCARDIOGRAPHY

The initial electrocardiogram showed sinus rhythm in all patients with stress cardiomyopathy, with a median heart rate of 85 beats per minute. Five patients (26 percent) had a prolonged PR interval, and five (26 percent) had a prolonged QT interval

corrected for heart rate (QTc). Two patients (11 percent) had ST-segment elevation of at least 1 mm, and three patients (16 percent) had diffuse T-wave inversion. Pathologic Q waves were seen in leads V₁, V₂, and V₃ in seven patients (37 percent) and in lead aVL in five (26 percent). Within 48 hours after the onset of symptoms, all 19 patients had marked prolongation of the QT interval (median QTc, 542 msec; interquartile range, 490 to 592) and all but

1 had deep, symmetric, T-wave inversion (Fig. 1). In most patients, the QTc normalized within one or two days, whereas the T-wave inversion resolved more slowly and often only partially. Pathologic precordial Q waves typically resolved before hospital discharge, with restoration of normal R-wave progression.

CARDIAC ENZYMES

Peak troponin I levels were only mildly elevated, with a median value of 0.18 ng per milliliter (interquartile range, 0.08 to 0.69; normal value, <0.06). Troponin I was undetectable in two patients. The peak creatine kinase level was 133 IU per liter (interquartile range, 114 to 273; normal value, <170), and the peak creatine kinase MB level was 10 ng per milliliter (interquartile range, 5 to 14; normal value, <7).

ECHOCARDIOGRAPHY

The median left ventricular ejection fraction on the initial echocardiogram (hospital day 1) was 0.20 (interquartile range, 0.15 to 0.30) (Fig. 2). All patients had a similar contractile pattern, with preserved basal function, moderate-to-severe dysfunction in the midventricle, and apical akinesis or dyskinesis (mean echocardiographic scores, 1.2±0.2, 3.2±0.5, and 3.7±0.5, respectively). By hospital day 3, 4, 5, 6, or 7 (a median of four days

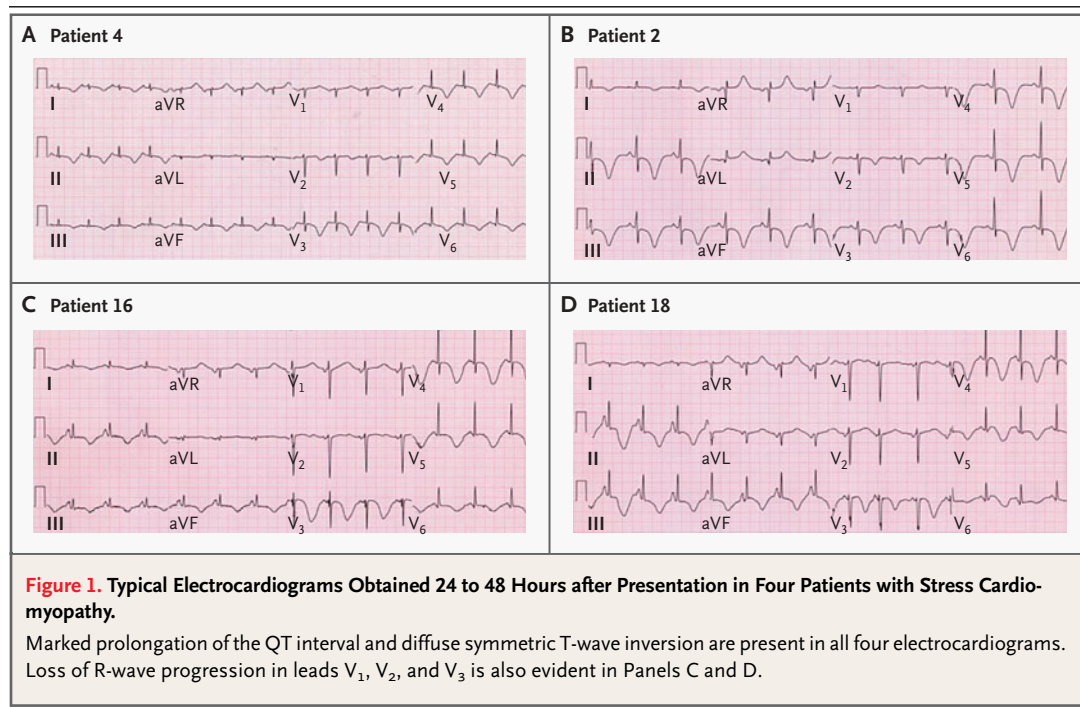
after presentation), the left ventricular ejection fraction had improved to 0.45 and the midventricular and apical segments were only mildly hypokinetic, with echocardiographic scores of 1.0±0.0 at the base, 1.9±0.7 at the midventricle, and 2.3±1.2 at the apex. At outpatient follow-up (a median of 21 days after presentation), the left ventricular ejection fraction was 0.60 (interquartile range, 0.55 to 0.65; P<0.001 for the comparison with values at presentation and during inpatient follow-up), and all segments had normal contractility.

MAGNETIC RESONANCE IMAGING

In the five patients who underwent cardiac MRI, cine studies confirmed the pattern and degree of left ventricular dysfunction seen on echocardiography. None of the patients had evidence of myocardial necrosis on contrast-enhanced imaging (Fig. 3C).

CARDIAC CATHETERIZATION

Thirteen patients underwent emergency angiography on admission, and six underwent angiography on hospital day 3, 4, 5, or 6. Eighteen patients (95 percent) had normal coronary arteries or mild luminal irregularities; one patient had a luminal narrowing of 70 percent in the proximal left anterior descending coronary artery. No patient had an-



giographic evidence of epicardial spasm. Patients undergoing catheterization on hospital day 1 had a median left ventricular end-diastolic pressure of 30 mm Hg (interquartile range, 25 to 31). Contrast-enhanced left ventriculography revealed apical and midventricular akinesis or dyskinesis with normal contractility of the base (Fig. 3A and 3B) and an ejection fraction of 0.25 (interquartile range, 0.15 to 0.30). Patients undergoing ventriculography on day 3, 4, 5, or 6 had a significant improvement in the left ventricular end-diastolic pressure (median, 16 mm Hg; interquartile range, 15 to 24; $P=0.005$) and the ejection fraction (0.43; interquartile range, 0.40 to 0.50; $P=0.007$), as compared with values on day 1.

ENDOMYOCARDIAL BIOPSY

Of the five patients who underwent endomyocardial biopsy, four had interstitial infiltrates consisting primarily of mononuclear lymphocytes and macrophages and contraction bands without myocyte necrosis. The other patient had an extensive

inflammatory lymphocytic infiltrate and multiple foci of contraction-band myocyte necrosis.

PLASMA CATECHOLAMINES AND NEUROPEPTIDES

All subgroups had similar demographic characteristics. The median age was 66 years among the 13 patients who underwent neurohumoral assessment, 63 years among the 6 patients who did not undergo neurohumoral assessment, and 60 years among the 7 control patients with myocardial infarction. On hospital day 1 or 2, plasma levels of catecholamines (i.e., epinephrine, norepinephrine, and dopamine) among patients with stress cardiomyopathy were 2 to 3 times the values among patients with Killip class III myocardial infarction and 7 to 34 times published normal values¹¹ (Table 2). Initial levels of plasma dihydroxyphenylalanine, dihydroxyphenylglycol, and dihydroxyphenylacetic acid among patients with stress cardiomyopathy were approximately two times the values among patients with myocardial infarction and two to three times normal values, consistent with the presence of enhanced catecholamine synthesis, neuronal reuptake, and neuronal metabolism, respectively.

Plasma levels of metanephrine and normetanephrine, which are extraneuronal catecholamine metabolites, were also proportionately increased among patients with stress cardiomyopathy. Plasma levels of neuropeptide Y, which is stored with catecholamines in postganglionic sympathetic nerves and adrenal chromaffin cells and released during stress, were markedly increased among patients with stress cardiomyopathy, as were plasma levels of brain natriuretic peptide and serotonin.

By hospital day 7, 8, or 9, plasma levels of most catecholamines, neuronal metabolites, and neuropeptides in patients with stress cardiomyopathy were one third to one half of the peak values but remained substantially higher than those in patients with myocardial infarction. In contrast, plasma brain natriuretic peptide levels declined rapidly in the patients with stress cardiomyopathy (correlating with rapidly improving left ventricular systolic function) and by day 7, 8, or 9 were lower than those in patients with myocardial infarction.

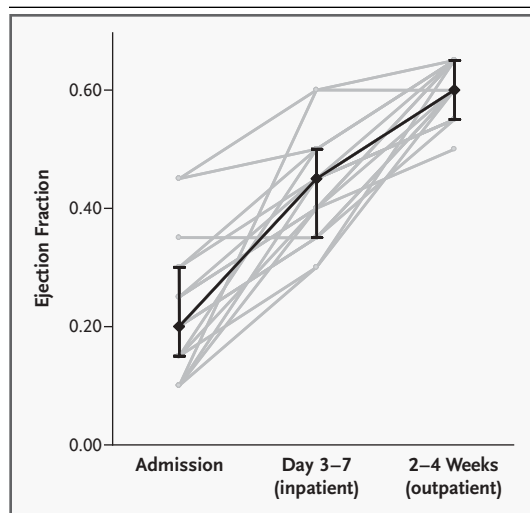
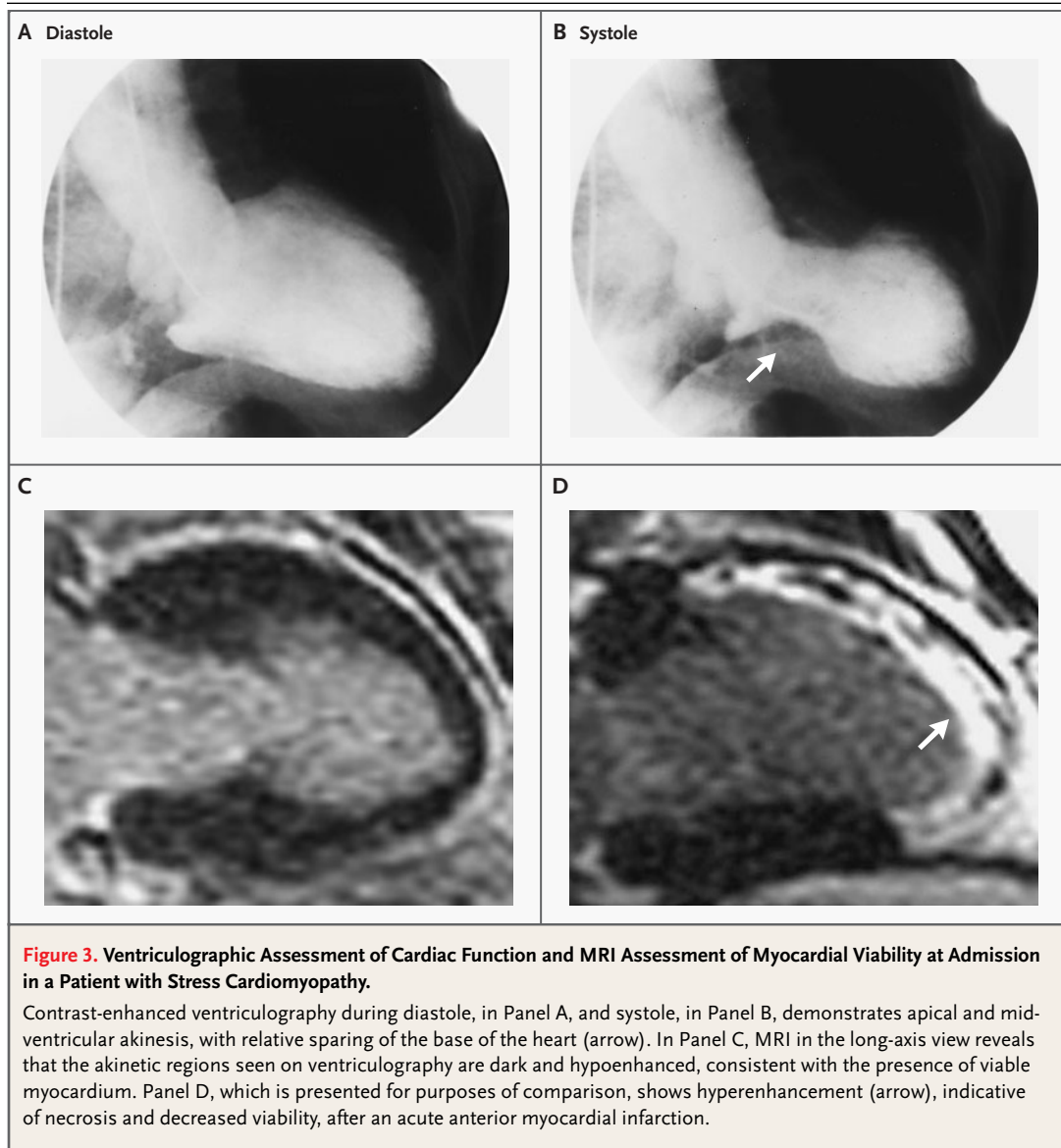


Figure 2. Serial Echocardiographic Assessment of the Ejection Fraction in 19 Patients with Stress Cardiomyopathy.

Echocardiography was performed on admission; on hospital day 3, 4, 5, 6, or 7 (median, day 4); and at outpatient follow-up (a median of 21 days after the onset of symptoms). Gray lines illustrate values for individual patients. The black bar represents the median ejection fraction at each time; error bars show the interquartile range. $P<0.001$ for the comparison between admission and inpatient values, and $P<0.001$ for the comparisons between admission and outpatient values and between inpatient and outpatient values.

DISCUSSION

There have been several reports of patients with profound, reversible left ventricular dysfunction after sudden emotional stress.¹⁻⁶ Some reports are from Japan, where the pattern of left ventricular



dysfunction has been referred to as “takotsubo cardiomyopathy,”⁶ named for the fishing pot with a narrow neck and wide base that is used to trap octopus. More recently, the term “transient left ventricular apical ballooning” has been used to describe similar cardiac contractile abnormalities in patients after emotional or physical stress.^{5,14} Despite the increasing awareness of acute stress-induced myocardial dysfunction, the mechanism remains unknown.

Our patients with stress cardiomyopathy had supraphysiologic levels of plasma catecholamines and stress-related neuropeptides. Initial plasma lev-

els were several times those of patients with myocardial infarction and remained markedly elevated even a week after the onset of symptoms. Our data suggest the activation of the adrenomedullary hormonal system, with marked elevation in plasma epinephrine and metanephrine levels. Enhanced sympathetic activity is also suggested by the increased plasma levels of dihydroxyphenylalanine, dihydroxyphenylglycol, norepinephrine, and normetanephrine, reflecting increased synthesis of norepinephrine, neuronal reuptake and metabolism, spillover, and extraneuronal metabolism, respectively.

Table 2. Plasma Catecholamine and Neuropeptide Levels.*

Variable	Patients with Stress Cardiomyopathy (N=13) <i>median (interquartile range)</i>			Patients with Killip Class III Myocardial Infarction (N=7)			Normal Value
	Day 1 or 2	Day 3, 4, or 5	Day 7, 8, or 9	Day 1 or 2	Day 3, 4, or 5	Day 7, 8, or 9	
Catecholamine precursor (pg/ml)							
Dihydroxyphenylalanine	2859 (2721–2997)†	2495 (2386–2761)†	1656 (1065–2011)	1282 (1124–1656)	1203 (1193–1873)	907 (749–937)	1755‡
Catecholamines (pg/ml)							
Epinephrine	1264 (916–1374)†	1044 (733–1118)†	348 (180–550)	376 (275–476)	330 (220–385)	275 (220–311)	37‡
Norepinephrine	2284 (1709–2910)†	1573 (1235–2589)†	1142 (525–1252)	1100 (914–1320)	829 (727–914)	541 (516–660)	169‡
Dopamine	111 (106–146)†	77 (63–110)	56 (47–77)	61 (46–77)	61 (61–77)	38 (30–61)	15‡
Neuronal metabolites (pg/ml)							
Dihydroxyphenylglycol	2706 (2382–3131)†	2689 (2246–2842)†	2161 (2093–2416)§	1625 (1412–1702)	1583 (1497–1668)	1259 (1191–1446)	800‡
Dihydroxyphenylacetic acid	2758 (2573–3077)	2598 (2354–2892)†	1345 (1194–1682)	1513 (1211–1648)	1228 (1026–1362)	1009 (908–1059)	1497‡
Extraneuronal metabolites (pg/ml)							
Metanephrine	178 (140–187)	509 (385–789)	659 (590–738)§	106 (89–124)	203 (177–213)	205 (189–243)	59‡
Normetanephrine	216 (130–319)	456 (229–569)	661 (551–696)§	160 (145–170)	196 (181–209)	271 (225–288)	55‡
Peptides (pg/ml)							
Neuropeptide Y	186 (162–236)§	185 (158–214)†	136 (90–182)§	77 (60–90)	69 (61–71)	60 (40–65)	51¶
Brain natriuretic peptide	1033 (805–1783)§	450 (205–684)	142 (72–236)	264 (192–483)	268 (249–574)	297 (142–419)	10–93
Serotonin and metabolite (pg/ml)							
5-Hydroxytryptamine	2585 (2165–2816)†	2379 (2290–2900)†	1602 (864–1989)	1308 (1074–1721)	1214 (1114–1643)	1065 (1003–1251)	1004***
5-Hydroxyindoleacetic acid	5596 (4531–7380)	7839 (5698–9644)	6471 (3308–7074)	3977 (3604–6074)	4607 (4128–6003)	4282 (3887–4416)	6730***

* All P values are for comparison of levels in patients with Killip class III myocardial infarction measured at similar times.

† P<0.005.

‡ Data are from Goldstein et al.¹¹

§ P<0.01

¶ Data are from Onuoha et al.¹⁰|| Data are from Redfield et al.¹²*** Data are from Spreux-Varoquaux et al.¹³

The mechanism underlying the association between sympathetic stimulation and myocardial stunning is unknown. One possibility is ischemia resulting from epicardial coronary arterial spasm. Increased sympathetic tone from mental stress can cause vasoconstriction in patients without coronary disease.¹⁵ In an angiographic study of patients with takotsubo cardiomyopathy, 70 percent had coronary spasm in response to provocative maneuvers, and electrocardiographic evidence of ST-segment elevation was common at presentation.⁶ Our patients, however, had no angiographic evidence of epicardial spasm, and ST-segment elevation was rarely seen. The patients did initially have contractile abnormalities in multiple vascular territories, but multivessel epicardial spasm as an explanation for this finding seems unlikely, given the relative absence of ST-segment elevation and minimal enzymatic evidence of myocardial necrosis.

An alternative mechanism is microvascular spasm. Abnormal coronary flow in the absence of obstructive disease has recently been reported in patients with stress-related myocardial dysfunction.¹⁶ Others have demonstrated reduced coronary-flow reserve and regional defects on cardiac [¹²³I]metaiodobenzyl-guanidine-enhanced imaging in such patients,¹⁷ suggesting the presence of sympathetically mediated microcirculatory dysfunction.

A third possible mechanism of catecholamine-mediated myocardial stunning is direct myocyte injury. Elevated catecholamine levels decrease the viability of myocytes through cyclic AMP-mediated calcium overload.¹⁸ Catecholamines are also a potential source of oxygen-derived free radicals and, in animal models, cause myocyte injury that is attenuated by antioxidants.¹⁹ Free radicals can interfere with sodium and calcium transporters, possibly resulting in myocyte dysfunction through increased transsarcolemmal calcium influx and cellular calcium overload.²⁰ Histologically, catecholamines have been associated with contraction-band necrosis, a unique form of myocyte injury characterized by hypercontracted sarcomeres, dense eosinophilic transverse bands, and an interstitial mononuclear inflammatory response that is distinct from the polymorphonuclear inflammation seen with infarction. Contraction-band necrosis has been described in clinical states of catecholamine excess such as pheochromocytoma²¹ and subarachnoid hemorrhage.²² It has also been observed post mortem in people who died under terrifying circum-

stances such as fatal asthma²³ and violent assault,²⁴ suggesting that catecholamines may be an important link between emotional stress and cardiac injury. The biopsy findings in our patients are consistent with the presence of an elevated catecholamine state: four of five patients had mononuclear inflammatory infiltrates, while the fifth had extensive contraction-band necrosis.

In earlier reports^{5,6,14} and in our series, stress-related myocardial stunning was characterized by contractile abnormalities of the apex and midportion of the left ventricle with relative sparing of the basal segments (Fig. 3A and 3B). The reason for this distinctive contractile pattern is unknown. Local release of catecholamines from cardiac sympathetic efferent neurons is an unlikely explanation, given the higher norepinephrine content²⁵ and greater density of sympathetic nerves²⁶ at the base of the heart than in the apex. There is evidence that apical myocardium has enhanced responsiveness to sympathetic stimulation,²⁷ potentially making the apex more vulnerable to sudden surges in circulating catecholamine levels. Alternatively, a base-to-apex perfusion gradient, similar to that described in patients with coronary risk factors,²⁸ could result in regional differences in myocardial blood flow in the setting of catecholamine-mediated epicardial or microvascular vasoconstriction.

Although the striking preponderance of women in our study and in other reports^{5,6,14,16} suggests a biologic susceptibility to stress-related myocardial dysfunction, the basis of this predisposition is unknown. Sex hormones exert important influences on the sympathetic neurohormonal axis²⁹ as well as on coronary vasoreactivity,³⁰ but sex-related differences in catecholamine metabolism and responsiveness are complex and remain poorly understood. Men have higher levels of basal sympathetic activity than women,²⁹ produce higher levels of plasma catecholamines in response to emotional stress,³¹ and are more sensitive to catecholamine-mediated vasoconstriction.³² However, women appear to be more vulnerable to sympathetically mediated myocardial stunning, as evidenced by increased catecholamine production³³ and transient left ventricular dysfunction³⁴ after subarachnoid hemorrhage.

Although the incidence of stress cardiomyopathy is unknown, it is likely to be more common than generally thought. Though we reported on only patients with emotional sources of stress, we have observed identical presentations in patients

after a wide variety of neurologic injuries (unpublished data); others have previously reported a similar pattern of transient myocardial dysfunction in patients after numerous types of nonemotional stress.^{5,6,14,35} The overlapping clinical features in all these presentations suggest that myocardial stunning resulting from emotional stress may share a common mechanism with “neurogenic stunned myocardium,” which has been described after subarachnoid hemorrhage³⁶ and stroke³⁷ and which is believed to be mediated by catecholamines.

Because patients with stress cardiomyopathy typically present with clinical features resembling those of acute myocardial infarction, coronary angiography is indicated in most cases. In the absence of critical coronary arterial disease, the diagnosis of stress cardiomyopathy should be considered when the history taking reveals that cardiac symptoms were precipitated by intense emotional stress, when there is a unique pattern of left ventricular dysfunction characterized by apical and midventricular contractile abnormalities with sparing of the basal segments, and when there is minimal elevation of cardiac enzymes despite the presence of large regions of focal akinesis in the myocardium. The clinical diagnosis is reinforced by the development of a markedly prolonged QT interval with deep precordial or global T-wave inversion on electrocardiography during the first 48 hours in the hospital, as well as rapidly improving cardiac contractility on serial echocardiography.

The treatment of stress cardiomyopathy, beyond standard supportive care for congestive heart failure with diuretics and vasodilators, remains largely empirical. Because our data implicate massive catecholamine release in stress-induced myocardial stunning, we avoid using pressors and beta-agonists whenever possible and instead rely on me-

chanical circulatory support in patients with severe hemodynamic compromise. When medical support is provided initially, patients with stress cardiomyopathy have rapid clinical and echocardiographic improvement and have an excellent prognosis. In the four years that we have followed these patients, none have died, had a recurrence, or had a decline in left ventricular function. This outcome accords with the favorable prognosis that has been previously reported.⁵

Our study has the inherent limitations of any small, observational case series. Although the age and sex of the seven control patients with Killip class III myocardial infarction were similar to those of our patients with stress cardiomyopathy, they were not selected by means of systematic random sampling, and thus, selection bias is possible, albeit unlikely. In addition, although our data show an intriguing association between sympathetic activation and stress cardiomyopathy, they do not prove a causal relationship. Elevated plasma catecholamine levels may be an epiphenomenon or a secondary response in patients with stress cardiomyopathy, rather than the root cause.

In conclusion, a unique pattern of transient myocardial dysfunction can occur after severe emotional stress. Patients with this syndrome have evidence of exaggerated sympathetic activation, with plasma catecholamine levels several times those in age- and sex-matched patients with Killip class III myocardial infarction. Although our data suggest that catecholamines may be central to the mechanism of stress-related myocardial stunning, a more complete understanding of the pathogenesis of this syndrome awaits further research.

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