A Randomized Controlled Trial of the Safety and Promise of Cognitive-Behavioral Therapy Using Imaginal Exposure in Patients With Posttraumatic Stress Disorder Resulting From Cardiovascular Illness

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Objective: We investigated the physical safety of cognitive-behavioral therapy (CBT) utilizing imaginal exposure in patients who suffered from posttraumatic stress disorder (PTSD) following a life-threatening cardiovascular event.

Method: In this phase I, prospective, single-blind trial conducted from April 2006 through April 2008, we randomly assigned 60 patients to receive either 3 to 5 sessions of imaginal exposure therapy (experimental group) or 1 to 3 educational sessions only (control group). Criteria for PTSD and other mental health disorders were evaluated according to *DSM-IV* using the full Structured Clinical Interview for *DSM-IV* (SCID). Safety assessments included patients' blood pressure and pulse before and after each study session and the occurrence of deaths, hospitalizations, repeat myocardial infarctions, or invasive procedures. We also investigated the effects of the treatment on PTSD symptoms (Impact of Event Scale and Posttraumatic Stress Disorder Scale), depression (Beck Depression Inventory-II), and the Clinical Global Impressions-Severity of Illness (CGI-S) scale.

Results: There were no significant differences between the experimental and control groups and between exposure and nonexposure sessions in any of the safety measures. In addition, confidence intervals were such that the nonsignificant effects of exposure therapy were not of clinical concern. For example, the mean difference in systolic pressure between control and exposure sessions was 0.5 mm Hg (95% CI, −6.1 to 7.1 mm Hg). Nonsignificant improvements were found on all psychiatric measures in the experimental group, with a significant improvement in CGI-S in the entire cohort (mean score difference, −0.6; 95% CI, −1.1 to −0.1; $P = .02$) and a significant improvement in PTSD symptoms in a subgroup of patients with acute unscheduled cardiovascular events and high baseline PTSD symptoms (mean score difference, −1.2; 95% CI, −2.0 to −0.3; $P = .01$).

Conclusions: Cognitive-behavioral therapy that includes imaginal exposure is safe and promising for the treatment of posttraumatic stress in patients with cardiovascular illnesses who are traumatized by their illness.

Trial Registration: clinicaltrials.gov Identifier: NCT00364910

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The treatment of psychiatric disorders in patients with cardiovascular illnesses has become the focus of recent research.[1] There have been several studies and reviews that have looked at the safety of psychiatric medications in this patient group.[2–5]

An alternative treatment modality is cognitive-behavioral therapy (CBT) or supportive therapy.[6–8] Psychotherapy is associated with significant biologic changes,[9–11] and it therefore can lead to harmful biologic sequelae. In patients with cardiovascular illnesses, the Enhancing Recovery in Coronary Heart Disease (ENRICHD) trial[6] reported a nonsignificant trend toward increased morbidity and mortality in women in the active CBT arm. Another study[8] found that women in the active treatment arm had increased physical morbidity. Yet, the physical safety of psychotherapy has never been investigated as a primary endpoint in these patients and is almost never investigated in any population.

The safety concern directly applies to protocols using imaginal exposure, in which patients reexperience the stressful event through the use of imagination.[12] This distressing reexperiencing can increase sympathetic activity,[13] and, thus, it may theoretically lead to cardiovascular compromise. However, CBT using imaginal exposure remains the best-studied[12] approach for survivors of an emotionally traumatic event, and it would be regrettable if therapists were to forgo this treatment modality because of a theoretical, but unproven, concern that it might be harmful.

We conducted a safety phase I, prospective, single-blind, randomized controlled trial of CBT utilizing imaginal exposure for the treatment of posttraumatic stress disorder (PTSD) in patients who survived a life-threatening cardiovascular event. Peripheral indices of sympathetic activity (pulse and blood pressure) were the a priori concerns associated with the treatment. Psychiatric treatment outcomes are also presented, but this small study was not powered to detect significant psychiatric treatment effects.

METHOD

Participants

Participants were recruited for the study, which was conducted from April 2006 through April 2008, from an outpatient cardiology clinic at Elmhurst Hospital

Medical Center in Queens, New York. Criteria for PTSD and other mental health disorders were evaluated according to *DSM-IV* using the full Structured Clinical Interview for *DSM-IV* (SCID).[14] The presence of a diagnosis of PTSD due to a cardiovascular event was essential for inclusion in the study. Comorbid substance use disorders, psychotic disorders (including mood disorders with a psychotic component), and current suicidality were exclusionary. Comorbid mood and anxiety disorders were not exclusionary. Enrolled participants were randomly assigned using a predetermined random order of sealed envelopes. Study procedures were approved by the Institutional Review Board of Mount Sinai Medical Center and the Research Review Committee of Elmhurst Medical Center and involved written informed consent (clinicaltrials.gov Identifier: NCT00364910).

Description of Study Conditions

Experimental group. The CBT manual was prepared through an iterative process that involved feedback from CBT treatment experts, cardiologists, and nurses. It was pilot tested in our previous study.[15]

The protocol was delivered over the course of 3 to 5 sessions and followed accepted procedures for brief imaginal exposure treatments.[12] There were several departures from other commonly used trauma-focused CBT protocols. First, this study did not use homework or in vivo exposure because of medical safety concerns (we wanted to make sure that prolonged imaginal exposure occurred only in a setting where a cardiac event, if it happened, could be addressed). Second, the number of sessions was less than is commonly used because previous results in similar populations suggest that patients with cardiovascular illnesses do not attend full CBT treatment if it includes many sessions.[6,15] Patients in the cardiology clinic do not necessarily perceive themselves as psychiatric patients and, therefore, are less motivated for treatment. Third, treatment sessions were delivered exclusively on the premises of the cardiology clinic to ensure that therapists and patients could easily access knowledgeable staff and appropriate equipment if a safety concern arose during treatment. Sessions were taped and randomly sampled for a fidelity review.

Control group. The control group patients received at least 1 and at most 3 educational sessions, which discussed adherence to their medical regimen. The control sessions were also taped and reviewed.

Credentials and Training of Therapists

The therapists, the first (E.S.) and second (R.A.A.) authors of this article, are a licensed psychiatrist and psychologist, respectively. They were trained in trauma-focused CBT during the "Train the Trainers" workshops delivered post–9/11 in New York and by the "Surviving Cancer Competently Intervention Program," a National Institutes of Health–funded intervention study targeting medical trauma.

In addition, the therapists, the monitor, the coordinators, and other study personnel participated in a dedicated 2-day workshop at the Duke Clinical Research Institute (DCRI) prior to the start of the study, in which study procedures including the full treatment manual were reviewed and tapes from actual treatment cases, from our previous pilot study,[15] were presented and discussed.

Monitoring of Treatment Fidelity

The monitor, a doctoral-level study coordinator from DCRI, was trained in the study manual and procedures during the 2-day workshop at DCRI. A checklist was used by the monitor to determine treatment fidelity in a randomly sampled selection of treatment tapes. The a priori intent was to have 90% fidelity to CBT elements.

Language

A large proportion of patients in this study were bilingual, with Spanish being the main language spoken other than English. While all of the patients spoke at least some English, to accommodate those patients who might be more comfortable answering questions in their native tongue, all measures were translated into Spanish, the study coordinator was Spanish-speaking, and therapists had the option to call upon an interpreter as needed.

Measures

Blood pressure and pulse. At the beginning of each control or experimental session, the patient's blood pressure and pulse (after 10 minutes of rest) were measured by a clinic nurse or the study psychiatrist using an automatic sphygmomanometer. At the end of each meeting, they were measured again. If a patient's blood pressure was beyond 170 (systolic) or 100 (diastolic), or if the pulse was above 100, per protocol a cardiologist was called to evaluate the patient. Cardiologists were also consulted for signs and symptoms of chest pain or excessive fatigue or for any other reason that the mental health clinician determined necessitated an immediate assessment.

Mean arterial pressure (MAP). Systolic and diastolic blood pressure values were used to calculate MAP (MAP = [systolic + (2 × diastolic)]/3).

Other safety parameters. We also examined death by any cause, a myocardial infarction during or immediately subsequent to treatment, the performance of a cardiovascular invasive procedure (eg, arterioplasty, catheterization for diagnostic or therapeutic reasons) during the study period, the need for a cardiology consult during a session, the need for an emergency room evaluation (for any reason), and the need for a hospital admission (for any reason).

Psychiatric outcomes. We investigated pretreatment and posttreatment scores on the Impact of Event Scale (IES),[16] the Posttraumatic Stress Diagnostic Scale (PDS),[17] the Beck Depression Inventory-II (BDI-II),[18] and the Clinical Global Impressions-Severity of Illness (CGI-S) scale.[19]

The IES[16] measures distressing responses to traumatic events and has been used extensively in medically ill populations, including patients with cardiovascular illnesses.[15] We did not use the newer version of this measure[20] because

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it overlaps highly with general anxiety in patients with cardiovascular illnesses.[21]

The PDS is a more specific PTSD scale that has been used in several treatment studies and also in patients with cardiovascular illnesses.[22]

The BDI-II is a depression scale that has been used extensively in patients with cardiovascular illnesses.[23]

The CGI-S scale asks the clinician to rate the degree of severity of mental illness of a patient on a 7-point scale, in which 1 = normal and 7 = the most extremely ill patients. The CGI-S has been shown to correlate well with standard, well-known research scales[24,25] and was used in our pilot study.[15]

Subgroup analyses. We sought to determine which subgroup of patients might benefit more from the proposed treatment. Predetermined subgroups included patients with an initial PDS score of 20 or above and patients with scheduled surgical trauma (ie, elective cardiovascular surgery or catheterization) as opposed to unexpected trauma (eg, a myocardial infarction)—the designation of "scheduled surgical" versus "unexpected" events was determined by a cardiologist who was blinded to the rest of the data.

Table 1. Patient and Treatment Characteristics by Study Group

Characteristic	Experimental Group, N = 30	Control Group, N = 30
Age, mean (SD), y	56.50 (10.65)	57.77 (11.46)
Male sex, n (%)	20 (67)	20 (67)
English-speaking, n (%)	15 (50)	20 (67)
Trauma, n (%)		
Myocardial infarction	13 (43)	12 (40)
Catheterization	6 (20)	3 (10)
Coronary artery bypass graft/surgery	3 (10)	3 (10)
Angioplasty	2 (7)	3 (10)
Stent placement	2 (7)	3 (10)
Pacemaker placement	1 (3)	2 (7)
Valve replacement	1 (3)	1 (3)
Stroke	0 (0)	2 (7)
Other	2 (7)	1 (3)
Baseline vital signs, mean (SD)		
Systolic blood pressure, mm Hg	134.59 (11.99)	127.95 (17.29)
Diastolic blood pressure, mm Hg	77.56 (11.30)	74.59 (11.30)
Mean arterial pressure, mm Hg	136.15 (14.94)	130.48 (18.02)
Pulse, beats per minute	79.48 (10.77)	75.41 (12.93)
Number of sessions, n (%)		
0	3 (10)	1 (3)
1	4 (13)	5 (17)
2	3 (10)	20 (67)
3	9 (30)	4 (13)
4	10 (33)	0 (0)
5	1 (3)	0 (0)

Statistical Analyses

It was hypothesized that any adverse effect on vital signs would be most pronounced at the first exposure therapy session (most often session 2). We also hypothesized that groups might differ in autonomic response at the first session, during which the group allocation was described (session 1), because—so we hypothesized—patients who are told that they will have to recount their trauma in the next session (experimental group) will be more distressed than the rest (controls). Therefore, experimental and control groups were compared with respect to vital signs at both sessions 1 and 2. Because the number of sessions varied between treatment groups, groups were also compared with respect to the last session for each patient.

Statistical significance is perhaps not as relevant in evaluating safety as it is in evaluating efficacy because a "safe" therapy will demonstrate no statistically significant difference with the control. The lack of statistical significance could be due to either lack of adverse effect or lack of statistical power to detect a meaningful difference. The question we set out to answer in the safety analyses is whether a meaningful difference in vital sign changes could be ruled out with a reasonable level of confidence (95%).

Values taken before session 1 were "baseline" values, and baseline-adjusted mean differences between groups with associated 95% confidence intervals were estimated from analysis of covariance (ANCOVA) models for both the changes from baseline to postsession and the changes from presession to postsession. Mean presession and postsession vital signs were estimated using least-squares means from similar models. Baseline-adjusted overall treatment group differences adjusted for session were estimated from repeated-measures ANCOVA models. In addition, exposure sessions were compared with other sessions in subjects randomly assigned to the experimental group; repeated-measures ANCOVA, adjusted for session, was used for these analyses. Analyses were conducted using SAS, release 9.1 (SAS Institute, Inc; Cary, North Carolina). Statistical analyses were supervised by B.D.W., from Momentum Research (an enterprise based in Durham, North Carolina, devoted to supporting innovative research to improve medical outcomes).

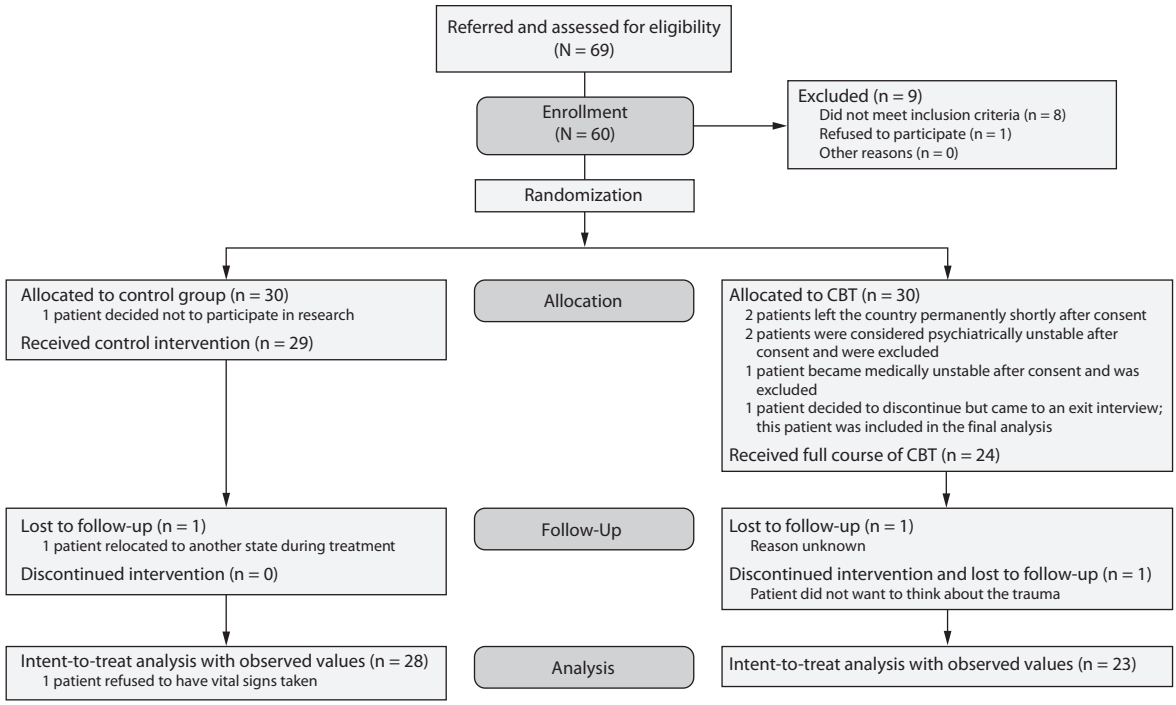
Psychiatric outcomes were compared pretreatment versus posttreatment; 95% CIs and *P* values of significance are presented.

RESULTS

Patients' Baseline and Treatment Characteristics

The mean age of the 60 enrolled patients was 57.13 years (SD = 10.99 years), and 67% (n = 40) were male. Fifty-eight percent of the sample (n = 35) spoke primarily English, while the remaining 42% (n = 25) were native Spanish speakers although they also spoke English. Safety data are available for 59 patients because 1 patient (in the control condition) refused to have his vital signs taken. Thirty patients were randomly assigned each to the experimental condition and the control group. Cardiovascular events resulting in study inclusion were as follows: myocardial infarction (25 patients), cardiac catheterization (9 patients), coronary artery bypass graft/open heart surgery (6 patients), angioplasty (5 patients), cardiac stenting (5 patients), pacemaker insertion (3 patients), stroke (2 patients), valve replacement (2 patients), or other (3 patients). Group characteristics were fairly similar (Table 1). Most patients in the experimental condition were treated for 3 to 4 sessions with a median of 3 sessions, while most patients in the control condition

Figure 1. CONSORT Flowchart of Study Recruitment and Follow-Up



Abbreviations: CBT = cognitive-behavioral therapy, CONSORT = Consolidated Standards of Reporting Trials.

were treated for 1 to 2 sessions with a median of 2 sessions. Figure 1 is a Consolidated Standards of Reporting Trials (CONSORT)-style diagram of recruitment and follow-up.

Safety Outcomes

Comparison of experimental and control conditions. Mean differences between groups with respect to mean changes from baseline to postsession are given in Table 2. None of those differences were statistically significant. Blood pressure increased slightly more in the experimental than in the control condition from baseline to the end of sessions 1 and 2 and the last session. At the end of session 2 (the first imaginal exposure session in the experimental group), the upper 95% CI bound for the increase in systolic blood pressure was 11.3 mm Hg, for diastolic blood pressure it was 9.8 mm Hg, and for pulse it was 4.0 bpm. Averaged over all sessions, the mean differences between treatment groups with respect to changes from baseline to postsession were 1.6 mm Hg (95% CI, −3.8 to 6.9 mm Hg) for systolic blood pressure, 2.6 mm Hg (95% CI, −1.3 to 6.5 mm Hg) for diastolic blood pressure, and 0.2 bpm (95% CI, −3.3 to 3.7 bpm) for pulse.

Baseline-adjusted changes in vital signs from before to after sessions were very similar in the experimental and control conditions (Table 3). Averaged over all sessions, the baseline-adjusted mean differences from presession to postsession between treatment groups were 0.8 mm Hg (95% CI, −3.8 to 5.3 mm Hg) for systolic blood pressure, 2.8 mm Hg (95% CI, −0.4 to 6.0 mm Hg) for diastolic blood pressure, and −0.8 bpm (95% CI, −3.3 to 1.7 bpm) for pulse.

Exposure sessions versus nonexposure sessions in the experimental condition. For patients who were randomly assigned to the experimental condition, sessions either included imaginal exposure (no. = 38) or were introductory or focused on the processing of the memory rather than a controlled re-experiencing of the event (no. = 34). We wanted to assess for the sessions in which imaginal exposure was employed whether blood pressure and pulse indicators were more likely to change than in other sessions in the same subjects. Table 4 illustrates these comparisons. None of the differences were statistically significant. Systolic blood pressure increased more from presession to postsession during exposure sessions than during nonexposure sessions, but the pattern was reversed for diastolic pressure. Pulse decreased on average for both session types. Mean differences between session types (exposure vs nonexposure) were 2.9 mm Hg (95% CI, −6.1 to 11.9 mm Hg) for systolic blood pressure, −1.1 mm Hg (95% CI, −6.4 to 4.3 mm Hg) for diastolic blood pressure, and −3.4 bpm (95% CI, −8.3 to 1.5 bpm) for pulse.

Need for a cardiology consult. A cardiologist was called to consult on 3 different episodes in 3 different patients. Two of the cases were in control patients. In all cases, the cardiologist was called before the session had begun. The reasons for the cardiology consults were a high presession reading of blood pressure (2 cases) and patient's "not looking good" (weakness) in 1 case. None of these cases resulted in admission or emergency referrals or procedures. However, all 3 instances triggered a change in the patient's medical management (ie, increase in the dose of an antihypertensive).

Table 2. Baseline-Adjusted Mean Differences Between Experimental and Control Conditions From Baseline to Postsession for Select Sessions[a]

Vital Sign	Session 1, Mean Difference (95% CI)	Session 2,[b] Mean Difference (95% CI)	Last Session, Mean Difference (95% CI)	Overall Mean Difference Adjusted for Session (95% CI)
Systolic blood pressure, mm Hg	0.3 (−7.1 to 7.6)	4.3 (−2.6 to 11.3)	2.2 (−5.6 to 10.0)	1.6 (−3.8 to 6.9)
Diastolic blood pressure, mm Hg	4.3 (−1.2 to 9.8)	3.7 (−2.5 to 9.8)	1.2 (−5.1 to 7.5)	2.6 (−1.3 to 6.5)
Mean arterial pressure, mm Hg	1.6 (−4.9 to 8.0)	4.1 (−2.1 to 10.3)	1.9 (−4.7 to 8.5)	2.0 (−2.5 to 6.5)
Pulse, beats per minute	1.6 (−1.7 to 4.9)	−1.6 (−7.2 to 4.0)	−1.1 (−7.1 to 5.0)	0.2 (−3.3 to 3.7)

[a]None of the differences are statistically significant.
[b]Session 2 was the first imaginal exposure session in the experimental group; however, for 1 patient, the first exposure session was session 3.

Table 3. Baseline-Adjusted Mean Differences Between Experimental and Control Conditions From Presession to Postsession for Select Sessions[a]

Vital Sign	Session 1, Mean Difference (95% CI)	Session 2,[b] Mean Difference (95% CI)	Last Session, Mean Difference (95% CI)	Overall Mean Difference Adjusted for Session (95% CI)
Systolic blood pressure, mm Hg	0.3 (−7.1 to 7.6)	0.5 (−6.1 to 7.1)	0.3 (−6.4 to 7.0)	0.8 (−3.8 to 5.3)
Diastolic blood pressure, mm Hg	4.3 (−1.2 to 9.8)	2.0 (−3.0 to 6.9)	1.4 (−3.8 to 6.6)	2.8 (−0.4 to 6.0)
Mean arterial pressure, mm Hg	1.6 (−4.9 to 8.0)	0.9 (−4.5 to 6.3)	0.6 (−5.0 to 6.2)	1.5 (−2.3 to 5.3)
Pulse, beats per minute	1.6 (−1.7 to 4.9)	−2.0 (−6.3 to 2.4)	−1.9 (−5.2 to 1.3)	−0.8 (−3.3 to 1.7)

[a]None of the differences are statistically significant.
[b]Session 2 was the first imaginal exposure session in the experimental group; however, for 1 patient, the first exposure session was session 3.

Table 4. Session-Adjusted Mean Changes From Presession to Postsession in the Experimental Group by Session Type[a]

Vital Sign	Exposure Session, Mean (95% CI)	Nonexposure Session, Mean (95% CI)	Exposure-Nonexposure Difference, Mean (95% CI)
Systolic blood pressure, mm Hg	2.2 (−5.6 to 9.9)	−0.7 (−7.3 to 5.9)	2.9 (−6.1 to 11.9)
Diastolic blood pressure, mm Hg	0.9 (−3.7 to 5.5)	1.9 (−2.0 to 5.8)	−1.1 (−6.4 to 4.3)
Mean arterial pressure, mm Hg	1.7 (−4.4 to 7.8)	0.2 (−5.0 to 5.3)	1.6 (−5.5 to 8.7)
Pulse, beats per minute	−4.0 (−8.2 to 0.2)	−0.6 (−4.2 to 2.9)	−3.4 (−8.3 to 1.5)

[a]None of the differences are statistically significant.

Other safety considerations. During the study, there were no deaths or rehospitalizations, and no patients had an invasive procedure or a recurrent myocardial infarction. One patient in the experimental condition had an emergency room visit for chest pain 2 weeks after his treatment session. This visit did not meet clinical criteria for a myocardial infarction and did not result in hospitalization.

Psychiatric Outcomes

Integrity of treatment was above 90% of the checklist items for both therapists. Psychiatric outcomes are presented in Table 5. While all measures improved more in the experimental as opposed to the control situation, only the improvement in CGI-S was significant. The subgroup of patients with an elevated baseline PDS score (20 or above) who experienced an unscheduled trauma (acute myocardial infarction) benefited most from the intervention.

DISCUSSION

Imaginal exposure–based therapies are safe in patients with cardiovascular compromise. Overall, patients' blood pressure and pulse readings were not significantly altered by the protocol. The 95% CI margins showed differences that were not larger than 10.3 mm Hg. These differences can be encountered in the course of any person's normal daily activities.[26] Furthermore, these differences are substantially smaller than the differences observed during a standard Bruce protocol treadmill exercise test,[27] which is considered safe in patients with cardiovascular illnesses.[28,29] Therefore, we conclude that none of the differences within the 95% CIs that we calculated should be cause for worry.

While exposure sessions might have led to a very slightly higher degree of increase in systolic (but not diastolic) blood pressure than nonexposure sessions in patients in the treatment condition, these differences are too modest to be significant clinically.

We did not have continuous blood pressure monitoring throughout the session, and, thus, we cannot rule out transient changes in blood pressure during the specific moments in which imaginal exposure was conducted. But even if there was such a change, it certainly did not lead to any immediate posttreatment effects or to any sustained medical effects. This study was not large enough to detect differences in rare outcomes. While it is reassuring that we found no differences in death, rehospitalization, and reinfarction, only a far larger study could confidently rule out differences in rare events.

The fact that the few cardiology consultations that therapists asked for led to a change in medical management can, in our opinion, serve as a reminder that the best model of care is integrated. Placing a therapist on the premises of a cardiology clinic can improve the detection of medical and psychiatric morbidity.

Regarding mental health outcomes of the intervention: this pilot phase I study was not powered to detect treatment effects. The intentional modifications in our approach (short duration, lack of homework assignments, placing the

Table 5. Efficacy of the Study Intervention Overall and by Subgroup According to the Clinical Global Impressions-Severity of Illness (CGI-S) Scale, the Impact of Event Scale (IES), the Posttraumatic Stress Diagnostic Scale (PDS), and the Beck Depression Inventory-II (BDI-II)

		CGI-S			IES			PDS			BDI-II		
Group	N	Condition Difference[a]	95% CI	*P* Value	Condition Difference[a]	95% CI	*P* Value	Condition Difference[a]	95% CI	*P* Value	Condition Difference[a]	95% CI	*P* Value
Overall[b]	51	−0.6	−1.1 to −0.1	.02	−4.4	−12.5 to 3.7	.28	−2.8	−8.0 to 2.4	.29	−3.5	−7.7 to 0.7	.10
Patients with a PDS score ≥ 20 and unexpected trauma	23	−1.2	−2.0 to −0.3	.01	−9.5	−21.9 to 2.9	.12	−9.2	−17.2 to −1.1	.03	−9.6	−17.6 to −1.6	.02

[a]The computed difference is between baseline (before first session) and 2 months postenrollment for all subjects (control and experimental conditions).
[b]The N of 51 represents the total intent-to-treat population.

treatment on the premises of a cardiology clinic where the environment is less auspicious for a long discussion in a quiet room) may have led to a dilution of treatment effects. Our chosen control situation—an educational control—is an improvement over wait-list controls, which are prevalent in CBT studies, but it is not ideal. In a full efficacy trial, an attention control would have been desirable. Nevertheless, treatment seemed to be at least promising. Treatment seemed to be most effective in the subgroup of patients who had relatively high pretreatment PTSD symptom scores and who experienced a frightening, unexpected event (eg, a myocardial infarction) rather than an expected one (eg, scheduled catheterization). In the entire cohort, nonsignificant improvements were observed on all psychiatric measures, with significant improvement in the CGI-S. We therefore believe that our results are encouraging.

More patients dropped out of the experimental group as compared with the control condition. The experimental condition required attendance at more sessions and, therefore, more patient commitment to the procedures. We believe that this differential attrition may, at least in part, be related to the increased burden on the patients who were randomly assigned to the experimental condition.

Limitations include a small sample size, the targeted but limited definition of *safety*, and the fact that we recruited only relatively stable patients. However, as is the case with phase I medication studies, the fact that no clear safety concern was raised at this stage is sufficiently reassuring enough to proceed with larger studies. Our results provide an anchor for future studies that would conclusively examine the efficacy of exposure-based treatments in medically ill patients and also perhaps try to examine the effects of comorbidity (eg, comorbid depression) on treatment outcomes.

Exposure-based approaches are safe even in the very vulnerable population that we studied. Cardiovascular patients should not be deprived of exposure-based approaches because of safety concerns.

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REFERENCES

1. Frasure-Smith N, Lespérance F. Depression: a cardiac risk factor in search of a treatment. *JAMA*. 2003;289(23):3171–3173.
2. Parissis J, Fountoulaki K, Paraskevaidis I, et al. Sertraline for the treatment of depression in coronary artery disease and heart failure. *Expert Opin Pharmacother*. 2007;8(10):1529–1537.
3. Rasmussen SL, Overø KF, Tanghøj P. Cardiac safety of citalopram: prospective trials and retrospective analyses. *J Clin Psychopharmacol*. 1999;19(5):407–415.
4. Glassman AH, O'Connor CM, Califf RM, et al. Sertraline Antidepressant Heart Attack Randomized Trial (SADHEART) Group. Sertraline treatment of major depression in patients with acute MI or unstable angina. *JAMA*. 2002;288(6):701–709.
5. Roose SP, Spatz E. Treating depression in patients with ischaemic heart disease: which agents are best to use and to avoid? *Drug Saf*. 1999;20(5):459–465.
6. Berkman LF, Blumenthal J, Burg M, et al. Enhancing Recovery in Coronary Heart Disease Patients Investigators (ENRICHD). Effects of treating depression and low perceived social support on clinical events after myocardial infarction: the Enhancing Recovery in Coronary Heart Disease Patients (ENRICHD) Randomized Trial. *JAMA*. 2003;289(23):3106–3116.
7. Wiggers LC, Oort FJ, Dijkstra A, et al. Cognitive changes in cardiovascular patients following a tailored behavioral smoking cessation intervention. *Prev Med*. 2005;40(6):812–821.
8. Frasure-Smith N, Lespérance F, Gravel G, et al. Long-term survival differences among low-anxious, high-anxious and repressive copers enrolled in the Montreal Heart Attack Readjustment Trial. *Psychosom Med*. 2002;64(4):571–579.
9. Lehto SM, Tolmunen T, Joensuu M, et al. Changes in midbrain serotonin transporter availability in atypically depressed subjects after one year of psychotherapy. *Prog Neuropsychopharmacol Biol Psychiatry*. 2008;32(1):229–237.
10. Linden DE. How psychotherapy changes the brain: the contribution of functional neuroimaging. *Mol Psychiatry*. 2006;11(6):528–538.
11. Martin SD, Martin E, Rai SS, et al. Brain blood flow changes in depressed patients treated with interpersonal psychotherapy or venlafaxine hydrochloride: preliminary findings. *Arch Gen Psychiatry*. 2001;58(7):641–648.
12. Foa EB. Psychosocial therapy for posttraumatic stress disorder. *J Clin Psychiatry*. 2006;67(suppl 2):40–45.
13. Foa EB, Rothbaum BO. *Cognitive Behavioral Therapy for PTSD*. New York, NY: Guilford Press; 1998:147.
14. Spitzer RL, Williams JB, Gibbon M, et al. *Structured Clinical Interview for DSM-IV, Patient Version (SCID-P), Version 2.0*. Washington, DC: American Psychiatric Press; 1995.
15. Shemesh E, Koren-Michowitz M, Yehuda R, et al. Symptoms of

posttraumatic stress disorder in patients who have had a myocardial infarction. *Psychosomatics*. 2006;47(3):231–239.
16. Horowitz M, Wilner N, Alvarez W. Impact of Event Scale: a measure of subjective stress. *Psychosom Med*. 1979;41(3):209–218.
17. Foa EB. Posttraumatic Stress Diagnostic Scale (PDS). Pearson Assessments web site. http://www.pearsonassessments.com/pds.aspx. Verified February 2, 2010.
18. Beck AT, Steer RA, Brown GK. Beck Depression Inventory-II (BDI-II). Pearson Assessments web site. http://pearsonassess.com/haiweb/cultures/en-us/productdetail.htm?pid=015-8018-370. Verified February 2, 2010.
19. Guy W, ed. *ECDEU Assessment Manual for Psychopharmacology*. Rockville, MD: US Department of Health, Education, and Welfare; 1976:218–222.
20. Weiss D, Marmar C. The Impact of Event Scale-Revised. In: Wilson J, Keane T, eds. *Assessing Psychological Trauma and PTSD*. New York, NY: Guilford Press; 1997.
21. Baumert J, Simon H, Gündel H, et al. The Impact of Event Scale-Revised: evaluation of the subscales and correlations to psychophysiological startle response patterns in survivors of a life-threatening cardiac event: an analysis of 129 patients with an implanted cardioverter defibrillator. *J Affect Disord*. 2004;82(1):29–41.
22. Chung MC, Berger Z, Jones R, et al. Posttraumatic stress and co-morbidity following myocardial infarction among older patients: the role of coping. *Aging Ment Health*. 2008;12(1):124–133.
23. Frasure-Smith N, Lespérance F. Depression and anxiety as predictors of 2-year cardiac events in patients with stable coronary artery disease. *Arch Gen Psychiatry*. 2008;65(1):62–71.
24. Leucht S, Kane JM, Kissling W, et al. Clinical implications of Brief Psychiatric Rating Scale scores. *Br J Psychiatry*. 2005;187(4):366–371.
25. Leucht S, Engel RR. The relative sensitivity of the Clinical Global Impressions Scale and the Brief Psychiatric Rating Scale in antipsychotic drug trials. *Neuropsychopharmacology*. 2006;31(2):406–412.
26. Melamed S, Kristal-Boneh E, Harari G, et al. Variation in the ambulatory blood pressure response to daily work load: the moderating role of job control. *Scand J Work Environ Health*. 1998;24(3):190–196.
27. Criqui MH, Haskell WL, Heiss G, et al. Predictors of systolic blood pressure response to treadmill exercise: the Lipid Research Clinics Program Prevalence Study. *Circulation*. 1983;68(2):225–233.
28. Senaratne MP, Smith G, Gulamhusein SS. Feasibility and safety of early exercise testing using the Bruce protocol after acute myocardial infarction. *J Am Coll Cardiol*. 2000;35(5):1212–1220.
29. Best PJ, Tajik AJ, Gibbons RJ, et al. The safety of treadmill exercise stress testing in patients with abdominal aortic aneurysms. *Ann Intern Med*. 1998;129(8):628–631.