Reducing Emotional Distress Improves Prognosis in Coronary Heart Disease

9-Year Mortality in a Clinical Trial of Rehabilitation

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Background—The impact of treating emotional distress on prognosis in coronary heart disease (CHD) has not been documented convincingly. We tested the hypothesis that treatment-related changes in emotional distress may explain the beneficial effect of rehabilitation on prognosis.

Methods and Results—In this nonrandomized clinical trial, 150 men with CHD participated in rehabilitation (n=78) or received standard medical care (n=72). There were no differences between rehabilitation and control patients with regard to left ventricular ejection fraction (LVEF) or standard care. End points were reduction in distress after 3 months and mortality after 9 years. At the end of the 3-month trial, 64 patients (43%) reported improvement and 22 (15%) reported deterioration in negative affect. Rehabilitation patients improved more (P=0.004) and deteriorated less (P=0.001) than control patients; rehabilitation was effective in reducing distress. After 9 years of follow-up, 15 patients had died (13 cardiac and 2 cancer deaths). Mortality was associated with LVEF ≤50% (P=0.038) and deterioration in negative affect (P=0.007). Rate of death was 17% (12/72) for control patients versus 4% (3/78) for rehabilitation patients (P=0.009); rehabilitation was effective in reducing mortality. LVEF ≤50% (OR 3.2; 95% CI 1.1 to 9.8; P=0.041) and rehabilitation (OR 0.2; 95% CI 0.1 to 0.7; P=0.016) were independent predictors of mortality.

Rehabilitation warded off the deleterious effect of deterioration in negative affect on prognosis.

Conclusions—Deterioration in negative affect is associated with a high long-term mortality risk. Warding off deterioration in negative affect is a mechanism that may explain the beneficial effect of comprehensive rehabilitation on prognosis in patients with CHD. (Circulation. 2001;104:2018-2023.)

Key Words: myocardial infarction ■ mortality ■ stress ■ depression ■ trials

Emotional distress in patients with coronary heart disease (CHD) has been associated with a poor prognosis. Hence, physicians need to incorporate assessment of mood and to refer CHD patients with emotional distress for additional treatment. Psychosocial interventions may improve risk factor profile in coronary patients. The impact of these interventions on emotional distress and cardiac events has not been documented convincingly, however.

Cardiac rehabilitation aims at promoting optimal physical and psychological function, but more research is needed to examine its psychological effect. Although some studies indicate that rehabilitation after myocardial infarction (MI) may reduce mortality by 20% to 25%, a recent study failed to confirm these findings. Cardiac rehabilitation, however, is characterized by a lack of sensitive outcome measures and a wide variability in treatment strategies.

The present study is based on the notion that the short-term psychological effect of cardiac rehabilitation may affect long-term prognosis; ie, rehabilitation programs that are successful in reducing emotional distress may be more successful in reducing mortality than programs without psychological effects. Cognitive models of behavior hold that enhancing the patient’s sense of control decreases negative affect, which, in turn, promotes maintenance of changes in lifestyle that may enhance prognosis. In addition, reduction in distress might modify pathophysiological mechanisms that have been associated with stress-related cardiac events.

To study the effect of reduction in distress on prognosis, the intervention should be effective in reducing distress and tailored to the needs of each patient. Therefore, the present study used a sensitive distress measure to evaluate a comprehensive rehabilitation program. The goal of the study was to test the hypotheses that (1) cardiac rehabilitation reduces emotional distress in the short term and mortality in the long term and (2) reducing emotional distress is one mechanism that may explain this beneficial effect of rehabilitation on prognosis.
Methods

Subjects
Patients were 150 men (age 57.6±8.1 years) who experienced an MI (76%) and/or underwent coronary artery bypass graft surgery (CABG, 42%) between July 1989 and December 1990. They were drawn from a sample of 170 CHD patients who participated in a rehabilitation trial;20 20 patients did not have an assessment of left ventricular ejection fraction (LVEF) and were excluded. Evidence shows that women report more emotional distress after MI than men28; this sex effect was controlled by including only male patients in the present study.

Nonrandomization Design
Seventy-eight patients from the Antwerp University Hospital participated in rehabilitation. A control group of 72 patients from 2 community hospitals received standard care. At the time the study was initiated, no rehabilitation program was available for these patients. Of all patients available for trial recruitment, only 5% (rehabilitation) and 3% (control) refused to participate. Patients with heart failure, stroke, malignancy, or renal disease were excluded. Frequency matching was used to ensure that the rehabilitation and control groups had a similar makeup in terms of MI, cardiac procedures, and emotional distress.25 Control patients were all treated by a cardiologist, and cardiac procedures in these patients were all performed in teaching hospitals (OLV Hospital Aalst, University Hospitals of Ghent and Antwerp). We also controlled for the use of such evidence-based therapies as thrombolytic therapy and β-blockers.

Rehabilitation Program
This program was based on an accelerated (ie, immediately after hospitalization) approach and comprised all core components of multifaceted rehabilitation.17 The duration was 3 months, including both group and individual interventions. The exercise component comprised 36 sessions that were performed in groups of 8 patients. The first 24 sessions (3 times per week) included ECG-monitored aerobic exercise. The intensity of exercise was prescribed as a target heart rate; ie, 65% to 85% and 50% to 75% of peak oxygen consumption for low- and high-risk patients, respectively. The last 12 sessions (2 times per week) were performed without ECG monitoring. The psychosocial group intervention comprised 6 sessions (2 hours, 1 time per week) that were held in a group of 8 to 20 patients and spouses to promote a healthy lifestyle. Two sessions focused on how to monitor signs of stress, how to deal with stressful events, and how to enhance assertiveness.

To tailor the program to the needs of each patient, it also included individualized intervention. When they entered the program, all patients were screened psychologically during a 1-hour semistructured interview. Individual psychological therapy was provided to individualized intervention. When they entered the program, all patients and spouses to promote a healthy lifestyle. Two sessions focused on how to monitor signs of stress, how to deal with stressful events, and how to enhance assertiveness.

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Short-Term Changes in Emotional Distress
Traditional distress scales are less sensitive in capturing the psychological effect of cardiac rehabilitation.9 The Global Mood Scale (GMS),14 however, is a sensitive outcome measure.9 It is composed of 10 negative (eg, listless, wearied) and 10 positive (eg, cheerful, lively) mood terms; patients rate on a 5-point scale the extent to which they have experienced each of these mood states lately. The mean scores were 9.1 (SD 7.7, range 0 to 32) for negative affect and 18.0 (SD 7.7, range 0 to 39) for positive affect.

Patients filled out the GMS twice; 3 to 6 weeks after MI/CABG and 3 months later (which corresponds to the end of the program in the rehabilitation group). Change in average scores may be statistically significant without necessarily being clinically meaningful and may mask the fact that some patients might actually deteriorate. Therefore, effect sizes (ES) were calculated by taking the difference between the baseline and 3-month follow-up scores and dividing it by the SD at baseline.15 An ES ≥0.5 was considered to indicate clinically meaningful improvement, whereas ES ≤−0.5 indicated deterioration. These cutoff points are arbitrary, however.

Long-Term Prognosis
The follow-up interval, as determined by the timing of the initial assessment, varied between 9 and 10 years (mean 9.3 years). Patients and their families were contacted by telephone and mail to determine health status. This study was designed to link any short-term changes in emotional distress with long-term prognosis. Hence, the main end point in the study was death from all causes. Mortality data were derived from hospital records, and the patient’s attending physician was always involved in the classification of cause of death.

Prognostic Factors
Treatment effects measured in randomized and nonrandomized studies achieve best approximation when prognostic factors are controlled for in a nonrandomization design.18 A decrease in LV function was defined as LVEF ≤50%;25 it is the most powerful biomedical predictor of cardiac events in patients attending the Antwerp rehabilitation program.25 Other prognostic factors included diagnosis of MI, thrombolysis, revascularization, and treatment with β-blockers or ACE inhibitors at the end of the trial. A significant number of patients received thrombolysis (41%), CABG (42%), or β-blockers (57%); these interventions are known to improve prognosis.22 Age (≥55/≥56 years) was included as a demographic factor.

Statistical Analyses
Unpaired t test and χ² statistic were used to examine differences in LVEF and cardiac treatment between the rehabilitation and control groups. Baseline measures of LVEF, cardiac treatment, and changes in distress were dichotomized, and the OR for fatal events for each pair of groups was assessed by logistic regression analysis and the χ² statistic. ORs for changes in emotional distress (3-month follow-up) and death (9-year follow-up) were assessed to examine any effects of the rehabilitation program. Multiple logistic regression analysis was used to determine the independent predictors of long-term prognosis. Criteria for entry and removal were based on the likelihood ratio test, with limits set at P≤0.05 and P>0.05.

Results

Comparability of the 2 Groups
There were no significant differences between the rehabilitation and control groups in severity of cardiac disorder, diagnosis of MI, thrombolytic therapy, or medical/surgical treatment during the trial (Table 1). Decreased LV function is a major predictor of mortality,19–21 whereas CABG, thrombolysis, and β-blockade improve prognosis.22 This absence of significant differences in major prognostic factors warrants further comparison of rehabilitation and control patients regarding their prognosis.18

Long-Term Prognosis
No patients were lost to follow-up. After 9 to 10 years of follow-up, 15 of 150 patients (10%) had died; there were 13 cardiac deaths and 2 cancer deaths. Total mortality was significantly associated with LVEF ≤50%, and MI patients also tended to have a greater mortality risk (Table 2). Prognosis was not related to differences in treatment strategies, suggesting an accurate level of cardiac care in both rehabilitation and control patients. Hence, cardiac treatment—
related variables could not explain any differences in 9-year mortality. Sixty-four patients (43%) reported improvement in negative affect (ES $0.5$) at the end of the 3-month trial, whereas 22 patients (15%) reported deterioration in negative affect (ES $-0.5$). These initial changes in negative affect were associated with mortality 9 years later (Table 2, bottom). Survivors reported less deterioration ($P<0.007$) and tended to report more improvement ($P=0.074$) in negative affect than nonsurvivors. Changes in positive affect were not associated with mortality. These findings suggest that changes in negative affect are associated with prognosis.

### Effect of Comprehensive Rehabilitation

As reported previously, a decrease of the negative affect score was a consistent result of the program. Rehabilitation patients reported a mean decrease of 5.2 ($P<0.0001$), whereas control patients reported a decrease of only 0.6 ($P=0.42$). A greater percentage of rehabilitation patients improved (Figure 1, top) and a smaller percentage deteriorated (Figure 1, middle) in negative affect compared with control patients. Rehabilitation was also associated with a significant decrease in 9-year mortality (Figure 1, bottom).

Rate of death was 17% (12/72) for control patients versus 4% (3/78) for rehabilitation patients; ie, rehabilitation was inversely related to mortality (OR 0.20; 95% CI, 0.05 to 0.74; $P=0.016$). Hence, rehabilitation was effective in decreasing distress (short-term) and mortality (long-term).

### Independent Predictors of Mortality

A regression model estimating the relative risk of death included LVEF $\leq 50\%$ (OR 3.2) and cardiac rehabilitation (OR 0.2) (Table 3). In other words, rehabilitation (1) was still a predictor of enhanced prognosis after adjustment for the severity of cardiac disorder and (2) accounted for the relation between changes in negative affect and prognosis. Given the small numbers of patients and end points, this analysis may have lacked statistical power to evaluate the independent contributions of affect; eg, deterioration in negative affect was marginally significant in the model (Table 3).

### Rehabilitation in MI Patients

Fourteen of 15 deaths occurred in the subgroup of 114 MI patients. Of note, MI patients in the rehabilitation group had a significantly lower rate of death than MI patients in the control group (Figure 2). MI patients with an LVEF $\leq 50\%$ or

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**TABLE 1. Comparability of Rehabilitation and Control Groups (N=150)**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Rehabilitation (n=78)</th>
<th>Control (n=72)</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic characteristic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, y*</td>
<td>57.9 (7.5)</td>
<td>57.2 (8.8)</td>
<td>0.56</td>
</tr>
<tr>
<td>Severity of cardiac disorder</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVEF*</td>
<td>58.8 (13.7)</td>
<td>58.1 (16.0)</td>
<td>0.80</td>
</tr>
<tr>
<td>Decreased LV function, n (%)†</td>
<td>22 (28)</td>
<td>22 (30)</td>
<td>0.75</td>
</tr>
<tr>
<td>MI, n (%)</td>
<td>58 (74)</td>
<td>56 (78)</td>
<td>0.62</td>
</tr>
<tr>
<td>Medical/surgical treatment, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombolysis after MI</td>
<td>20 (35)</td>
<td>27 (48)</td>
<td>0.14</td>
</tr>
<tr>
<td>Bypass surgery</td>
<td>33 (42)</td>
<td>30 (42)</td>
<td>0.94</td>
</tr>
<tr>
<td>β-Blocker therapy</td>
<td>45 (58)</td>
<td>41 (57)</td>
<td>0.93</td>
</tr>
<tr>
<td>ACE-inhibitor therapy</td>
<td>6 (8)</td>
<td>4 (6)</td>
<td>0.60</td>
</tr>
</tbody>
</table>

*Mean and SD.†Patients with an LVEF $\leq 50\%$.

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**TABLE 2. Biomedical Characteristics and Changes in Negative Affect According to 9-Year Vital Status (N=150)**

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>Alive (n=135)</th>
<th>Dead (n=15)</th>
<th>OR [95% CI], $P^*$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severity of cardiac disorder, % (n)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVEF $\leq 50%$</td>
<td>27 (36)</td>
<td>53 (8)</td>
<td>3.1 [1.1 to 9.3], 0.038</td>
</tr>
<tr>
<td>MI</td>
<td>74 (100)</td>
<td>93 (14)</td>
<td>4.9 [0.6 to 38.6], 0.13</td>
</tr>
<tr>
<td>Medical/surgical treatment, % (n)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombolysis after MI</td>
<td>41 (41)</td>
<td>43 (6)</td>
<td>1.1 [0.3 to 3.3], NS</td>
</tr>
<tr>
<td>Bypass surgery</td>
<td>44 (59)</td>
<td>27 (4)</td>
<td>0.5 [0.1 to 1.5], NS</td>
</tr>
<tr>
<td>β-Blocker therapy</td>
<td>57 (77)</td>
<td>60 (9)</td>
<td>1.1 [0.4 to 3.4], NS</td>
</tr>
<tr>
<td>ACE-inhibitor therapy</td>
<td>6 (8)</td>
<td>13 (2)</td>
<td>2.4 [0.5 to 12.7], NS</td>
</tr>
<tr>
<td>Changes in negative affect, % (n)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Improvement</td>
<td>45 (61)</td>
<td>20 (3)</td>
<td>0.3 [0.1 to 1.1], 0.074</td>
</tr>
<tr>
<td>Deterioration</td>
<td>12 (16)</td>
<td>40 (6)</td>
<td>5.0 [1.6 to 15.8], 0.007</td>
</tr>
</tbody>
</table>

*Univariate analysis; NS indicates not significant ($P>0.20$).
a deterioration in negative affect (high risk) had a higher mortality rate than MI patients without deterioration in cardiac and emotional status (low risk); ie, 9 of 45, 20%, versus 5 of 69, 7%, \( P = 0.043 \). There was a significant rehabilitation-by-risk interaction effect, however (OR 0.25, 95% CI 0.08 to 0.84, \( P = 0.024 \)). Accordingly, high-risk and low-risk MI patients who participated in rehabilitation had similar mortality rates, whereas high-risk MI patients receiving standard care had a greater mortality rate than MI patients participating in rehabilitation (OR 2.3, 95% CI 1.3 to 4.0, \( P = 0.003 \)). In other words, cardiac rehabilitation was an effective way to ward off the potential deleterious effects of cardiac and emotional disorder in patients recovering from an MI.

### Table 3. Independent Predictors of 9-Year Prognosis

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>95% CI</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Logistic regression model*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVEF ( \leq 50% )</td>
<td>3.2</td>
<td>1.1 to 9.8</td>
<td>0.041</td>
</tr>
<tr>
<td>Cardiac rehabilitation</td>
<td>0.2</td>
<td>0.1 to 0.7</td>
<td>0.016</td>
</tr>
<tr>
<td>Changes in negative affect†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Improvement</td>
<td>1.8</td>
<td></td>
<td>0.18</td>
</tr>
<tr>
<td>Deterioration</td>
<td>3.2</td>
<td></td>
<td>0.074</td>
</tr>
</tbody>
</table>

*Independent predictors of mortality.
†Variables that were not retained in the final model (\( P > 0.05 \)).

### Discussion

The present findings supported the hypothesis that comprehensive rehabilitation reduces emotional distress (short-term) and mortality (long-term) in CHD patients. Apart from a decrease in LVEF, long-term mortality was also associated with deterioration in negative affect. Rehabilitation patients deteriorated less in negative affect than patients who received standard care alone. Hence, warding off emotional distress during the first few months after MI/CABG may be one mechanism to explain the beneficial effect of rehabilitation on prognosis. Rehabilitation was especially effective in post-MI patients with a high risk of cardiac events. Rate of death of high-risk MI patients receiving standard care was 2.3 times greater than that of MI patients in the rehabilitation group. Multivariate analysis yielded 2 independent predictors of 9-year mortality: LVEF \( \leq 50\% \) increased mortality risk, and rehabilitation decreased mortality risk.

Limitations of this study include the relatively small number of patients and the exclusion of female patients.
Another limitation concerns the nonrandomized design of the study. Rehabilitation and control patients did not differ in LVEF, cardiac procedures were all performed in teaching hospitals, and control patients were all treated by a cardiologist. Cardiac treatment–related variables were not associated with mortality, indicating an accurate level of standard care. This lack of differences in prognostic factors suggests that the effects of rehabilitation in this nonrandomized clinical trial approximate those of a randomized trial.18

Nevertheless, the quality of care in the university and community hospitals is an important issue; eg, factors such as the timing of intervention or dosing of medication were not controlled for. Hence, the finding that reducing emotional distress may enhance prognosis in CHD needs to be replicated in a randomized controlled trial. In addition, it is impossible to determine which components of the Antwerp rehabilitation program (exercise training, psychological intervention, etc) were responsible for the mood and survival effects. Exercise training, for example, has been shown to be effective in reducing distress among patients with major depressive disorder.23

Previously documented effects of cardiac rehabilitation include improved ventricular function24 and exercise capacity25 and prevention of arrhythmias.26 Our findings suggest an additional mechanism that may explain the beneficial effect of rehabilitation on survival.6,7 Evidence from this study supports the notion that reducing emotional distress may improve prognosis in CHD.3 Unfortunately, this study was not designed to uncover any changes in lifestyle that may have occurred during follow-up as a function of enhanced emotional well-being. The short-term psychological effect of rehabilitation may set the stage for an increased sense of control over the disease process11 and maintenance of changes in lifestyle,12 whereas depression may lead to noncompliance with medical treatment.27

Other explanations include decreased pathophysiological vulnerability1 or increased benefit findings, such as greater appreciation of life and enhanced interpersonal relationships.28 Finally, exercise training might have improved both mood and survival. A decrease in negative affect, however, was still marginally significant as an independent predictor of death after control for rehabilitation.

Studies of the effect of treating emotional distress on prognosis in CHD produced mixed findings,1 suggesting that moderating factors must be involved. The present findings are at variance with those of 2 large randomized trials of psychosocial rehabilitation that could not demonstrate an effect on prognosis.29,30 These trials, however, used ineffective interventions1; ie, no reduction in emotional distress was observed in either trial.29,30 In contrast, the intervention in the present study comprised all core components of cardiac rehabilitation,17 including “patient-specific” treatment,1 and was quite effective in reducing emotional distress.

In conclusion, we found that (1) comprehensive rehabilitation enhances emotional well-being and survival and (2) the short-term psychological effect of rehabilitation may be one mechanism to improve prognosis in patients with CHD. Well-designed observational studies18 and randomized, controlled trials may yield similar estimates of the treatment effects.31 The reduction in mortality observed in the present study was also consistent with the findings from a Scandinavian rehabilitation trial.32 Hence, we disagree that future trials of psychosocial rehabilitation will need to address outcomes other than survival.30 Rather, any intervention that promises reduction in emotional distress in patients with CHD is worthy of replication.

Acknowledgments
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