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Reducing Psychosocial Stress: A Novel Mechanism of Improving Survival from Exercise Training

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ABSTRACT

BACKGROUND: Exercise training reduces mortality in patients with coronary artery disease. Behavioral characteristics, including depression, hostility, and overall psychosocial stress, have been shown to be independent risk factors for recurrent myocardial infarction and death in these patients. Exercise training can reduce these high-risk behaviors, but it remains uncertain as to what extent the health benefits of exercise training can be attributed to improving these behaviors.

METHODS: We evaluated the impact of exercise training during cardiac rehabilitation on mortality in 53 patients with coronary artery disease with high levels of psychosocial stress and in 469 patients with coronary artery disease with low levels of psychosocial stress and compared them with 27 control patients with high psychosocial stress who did not undergo formal cardiac rehabilitation and exercise training.

RESULTS: Mortality was approximately 4-fold greater in patients with high psychosocial stress than in those with low psychosocial stress (22% vs 5%; $P = .003$). Exercise training decreased the prevalence of psychosocial stress from 10% to 4% ($P < .0001$) and similarly improved peak oxygen uptake in patients with high and low psychosocial stress. Mortality in patients who improved exercise capacity by $\geq 10\%$ (high exercise change) was 60% lower than in patients who had $< 10\%$ improvement in exercise capacity (low exercise change) ($P = .009$). Mortality was lower in patients with high psychosocial stress with high exercise change compared with patients with high psychosocial stress with low exercise change (0% vs 19%; $P = .009$). In contrast, there was no significant improvement in mortality in patients with high versus low exercise change with low psychosocial stress (4% vs 8%; $P = .14$).

CONCLUSION: Psychosocial stress is an independent risk factor for mortality in patients with coronary artery disease, and exercise training can effectively reduce its prevalence. Exercise training reduces mortality in patients with coronary artery disease, and this effect seems to be mediated in part because of the salutary effects of exercise on psychosocial stress.

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KEYWORDS: Exercise; Heart disease; Mortality; Stress

Exercise capacity, quantified by assessment of peak oxygen uptake, has been shown to predict survival in the general population and in patients with coronary artery disease.[1-5] Peak oxygen uptake can be improved via exercise training, and its enhancement correlates to improved survival in patients with coronary artery disease.[6,7] Vanhees et al[8] demonstrated that peak oxygen uptake evaluated after physical training and its change in response to physical training are independent predictors of cardiovascular mortality, such that every 1% increase in peak oxygen uptake results in a 2% decrease in cardiovascular death. To date, numerous mechanisms for these exercise-related benefits have been proposed, but there has been no recognition for the potential role that exercise has in mollifying "high-risk" psychosocial behaviors.[9]

Several behavioral profiles, including depression, hostility, anxiety, and overall psychosocial stress, are prevalent in

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patients with coronary artery disease and have been shown to independently confer a high risk for subsequent myocardial infarction and death.[10-13] We, and others have demonstrated that exercise training during cardiac rehabilitation can markedly reduce these high-risk behaviors.[14-17] Moreover, we have recently reported significant improvements in overall survival after reduction in depression using cardiac rehabilitation and exercise training.[18]

To what extent the mortality benefits related to exercise training are due to improvement in these behaviors remains unanswered. The purpose of this investigation therefore was to further elucidate the mechanism by which exercise reduces mortality by evaluating the effects of exercise training on survival in patients with coronary artery disease with and without psychosocial stress.

CLINICAL SIGNIFICANCE

- High levels of psychosocial stress are prevalent in patients with coronary artery disease and independently increase mortality.
- Exercise training can reduce mortality in patients with coronary disease, as well as reduce levels of psychosocial stress.
- The principal survival benefit of exercise training in patients with coronary disease is in reducing high levels of psychosocial stress.

MATERIALS AND METHODS

Patients

We evaluated 522 consecutive patients who were referred to, attended, and completed phase II cardiac rehabilitation and exercise training at the Ochsner Clinic Foundation in New Orleans, La, between January 2000 and July 2005. All patients entered the program between 2 and 6 weeks after a coronary event, including acute myocardial infarction (30%), coronary bypass surgery (35%), and percutaneous coronary intervention (44% of patients; some patients had >1 clinical event). We further followed a control group of 27 patients with high psychosocial stress scores who entered cardiac rehabilitation but dropped out within 2 weeks of entry (all patients received <5 sessions of cardiac rehabilitation) to evaluate the impact of psychosocial stress in patients not undergoing cardiac rehabilitation. All patients who received cardiac rehabilitation completed validated questionnaires before and after the program. None of these patients were being treated with antidepressive or anxiolytic medications, and dosages of all other medications were stable for at least 2 weeks before study entry and were not altered during the course of the program. Survival status was obtained January 1, 2006, after a mean follow-up of 1296 ± 551 days (range 109-2188 days) from the National Death Index in the entire cohort. The protocol was approved by the Institutional Review Committee at Ochsner Clinic Foundation.

Behavioral Testing

The Kellner Symptom Questionnaire was used to assess behavioral characteristics, including symptoms of depression, anxiety, somatization, and hostility, with a lower score being more favorable for each behavioral symptom.[19] The instrument has been validated for its ability to discriminate between patients with psychiatric illness and normal patients, and for its test–retest and half-split reliabilities.[20-22] Depression and hostility symptoms were scored from 1 to 22, and anxiety symptoms were scored from 1 to 23 points. Psychosocial stress was considered significant when the total of these 3 scores exceeded 25.[15] The Medical Outcomes Short Form 36 survey was used to assess quality of life, with a high score indicating a more favorable quality of life trait.[23]

Protocol

Protocol, data collection, and statistical analysis were performed as previously described.[24] Patients were referred to and participated in outpatient phase II cardiac rehabilitation and exercise training consisting of 12 weeks of 36 educational and exercise sessions. Program duration, however, was altered occasionally according to a patient's ability to improve coronary risk factors and independently perform and monitor the prescribed exercise portion of the program. Each session consisted of approximately 10 minutes of warm-up exercises, including stretching and calisthenics, followed by 30 to 40 minutes of continuous upright aerobic and dynamic exercise (eg, various combinations of walking, bicycling, jogging, rowing), light isometric exercise (ie, hand weights), and approximately 10 minutes of cool-down stretching and calisthenics. Exercise intensity was prescribed individually so that the patient's heart rate was approximately 70% to 85% of the maximum heart rate, or 10 to 15 beats/min below the level of any exercise-induced symptomatic or silent myocardial ischemia. In addition to the supervised exercise sessions, all patients were encouraged to exercise approximately 1 to 3 times per week outside of the formal program. Each patient's exercise prescription was periodically adjusted to encourage a gradual increase in overall exercise performance.

At baseline, we instructed all patients on the American Heart Association Step II diet with a Mediterranean modification, and dieticians, exercise physiologists, nurses, and physicians frequently encouraged patients to comply with both the exercise and dietary portions of the cardiac rehabilitation program. Daily lectures and group sessions, usually directed by a clinical nurse trained in cardiac rehabilitation and occasionally directed by either a licensed exercise physiologists or a registered dietician, were given for patients and their spouses or significant others. In these sessions, patients learned about coronary risk factors, general information about coronary artery disease (eg, symptoms,

Table 1 Baseline Differences in Patients with Coronary Disease with High and Low Levels of Psychosocial Stress on Entry into Cardiac Rehabilitation and Exercise Training

	High Psychosocial Stress (n = 53)	Low Psychosocial Stress (n = 469)	*P*
Age (y)	60 ± 12	65 ± 10	.005
% Male	74%	73%	NS
BMI (kg/m^2)	28.3 ± 5.6	28.5 ± 5.0	NS
Active smokers (%)	2%	1%	NS
Hypertensives (%)	31%	32%	NS
Diabetes (%)	14%	22%	NS
Married (%)	73%	73%	NS
Peak oxygen uptake (mL/kg/min)	16.5 ± 5.2	16.7 ± 5.2	NS
Total cholesterol (mg/dL)	171 ± 33	166 ± 38	NS
HDL, cholesterol (mg/dL)	41 ± 13	41 ± 13	NS
LDL, cholesterol (mg/dL)	99 ± 29	97 ± 37	NS
Triglycerides (mg/dL)	159 ± 78	148 ± 86	NS
hs-CRP (mg/dL)	6.3 ± 10.6	5.5 ± 9.1	NS
Ejection fraction (%)	54 ± 13	54 ± 12	NS
Depression	12.3 ± 3.6	2.3 ± 2.6	<.0001
Anxiety	13.5 ± 3.8	3.0 ± 3.3	<.0001
Hostility	9.8 ± 4.5	1.7 ± 2.2	<.0001
Somatization	10.8 ± 4.0	6.1 ± 3.6	<.0001
Quality of life	81.1 ± 15.2	105.3 ± 16.3	<.0001

BMI = body mass index; HDL = high-density lipoprotein; LDL = low-density lipoprotein; hs-CRP = high-sensitivity C-reactive protein; NS = not significant.

signs, testing strategies, therapeutic modalities), and psychosocial adaptations to this disease. Although patients and other participants who were taught about behavioral factors, stress, and sexual function could ask general and specific questions, we did not routinely provide individual attention to these areas, including individual counseling directed at "high-risk" patients.

Height, weight, body mass index (BMI), age, gender, fasting blood lipids, and high-sensitivity C-reactive protein were assessed at baseline (~2-6 weeks after myocardial infarction; average 4 weeks) and again 1 week after completing cardiac rehabilitation. Peak oxygen uptake was measured by cardiopulmonary stress testing at baseline and on completion of the program as previously reported.[25] Change in peak oxygen uptake (exercise change) was calculated as the difference between post-program and baseline peak oxygen uptake.

Statistical Analysis

Statview software 5.0.1 (SAS Institute, Cary, NC) was used for statistical analysis. Results are mean ± standard deviation or frequencies expressed as percentages. Differences in continuous variables between 2 groups were assessed by paired Student *t* test or nonparametric tests as appropriate. Univariate relations between variables were assessed as partial correlations. A 2-tailed *P* value ≤ .05 was considered statistically significant. Logistic regression analysis was performed to determine independent predictors of mortality. Actuarial survival analysis was used to compute cumulative hazard over time.

RESULTS

Baseline Characteristics

The mean age of the 522 patients completing cardiac rehabilitation was 64 ± 10 years, and 73% of the subjects were male. The mean ejection fraction was 54% ± 12%, and the mean peak oxygen uptake was 16.6 ± 5.2 mL/kg/min. Elevated psychosocial stress was identified in 53 patients (10%) on entry into cardiac rehabilitation. Table 1 highlights the baseline differences between subjects with low and high psychosocial stress scores. Patients with high psychosocial stress were younger and had worse scores for depression, anxiety, hostility, somatization, and quality of life (all *P* < .0001) than patients with low psychosocial stress scores.

Effect of Exercise Training on Psychosocial Stress and Other Risk Factors

Tables 2 and 3 demonstrate the benefits of cardiac rehabilitation and exercise training in patients with high and low psychosocial stress, respectively. Patients with high psychosocial stress demonstrated improvements in exercise capacity (+10%; *P* = .0005), high-density lipoprotein cholesterol (+7%; *P* = .03), and all behavioral parameters, including psychosocial stress (−57%; *P* < .0001). Patients with low psychosocial stress revealed improvements in BMI (−1%; *P* < .0001), exercise capacity (+14%; *P* < .0001), high-

Table 2 Benefits of Cardiac Rehabilitation and Exercise Training in Patients with Coronary Disease with High Psychosocial Stress (n = 53)

	Before	After	*P*
BMI (kg/m^2)	28.3 ± 5.6	28.2 ± 5.4	NS
Peak oxygen uptake (mL/kg/min)	16.5 ± 5.2	18.1 ± 6.2	.0005
Total cholesterol (mg/dL)	171 ± 33	167 ± 34	NS
HDL, cholesterol (mg/dL)	41 ± 13	44 ± 12	.03
LDL, cholesterol (mg/dL)	99 ± 29	101 ± 50	NS
Triglycerides (mg/dL)	159 ± 78	142 ± 78	NS
hs-CRP (mg/dL)	6.3 ± 10.6	4.4 ± 6.4	.13
Depression score	12.3 ± 3.6	5.0 ± 4.7	<.0001
Anxiety score	13.5 ± 3.8	5.9 ± 4.8	<.0001
Hostility score	9.8 ± 4.5	4.4 ± 4.7	<.0001
Somatization score	10.8 ± 4.0	6.8 ± 4.6	<.0001
Quality of life score	81.1 ± 15.2	103.9 ± 19.5	<.0001
Psychosocial stress	35.5 ± 8.7	15.3 ± 12.2	<.0001

BMI = body mass index; HDL = high-density lipoprotein; LDL = low-density lipoprotein; hs-CRP = high-sensitivity C-reactive protein; NS = not significant.

Table 3 Benefits of Cardiac Rehabilitation and Exercise Training in Patients with Coronary Disease with Low Psychosocial Stress (n = 469)

	Before	After	*P*
BMI (kg/m²)	28.5 ± 5.0	28.3 ± 4.8	<.0001
Peak oxygen uptake (mL/kg/min)	16.7 ± 5.2	19.1 ± 6.2	<.0001
Total cholesterol (mg/dL)	166 ± 38	166 ± 34	NS
HDL, cholesterol (mg/dL)	41 ± 13	44 ± 13	<.0001
LDL, cholesterol (mg/dL)	97 ± 37	95 ± 28	.1
Triglycerides (mg/dL)	148 ± 86	132 ± 70	<.0001
hs-CRP (mg/dL)	5.5 ± 9.1	4.0 ± 6.2	<.0001
Depression score	2.3 ± 2.6	1.4 ± 2.1	<.0001
Anxiety score	3.0 ± 3.3	1.8 ± 2.7	<.0001
Hostility score	1.7 ± 2.2	1.3 ± 2.2	.0004
Somatization score	6.1 ± 3.6	4.5 ± 3.4	<.0001
Quality of life score	105.3 ± 16.3	118.5 ± 14.2	<.0001
Psychosocial stress	7.1 ± 6.4	4.6 ± 5.9	<.0001

BMI = body mass index; HDL = high-density lipoprotein; LDL = low-density lipoprotein; hs-CRP = high-sensitivity C-reactive protein; NS = not significant.

density lipoprotein cholesterol (+7%; $P < .0001$), triglycerides (−11%; $P < .0001$), high-sensitivity C-reactive protein (−27%; $P < .0001$), and all behavioral parameters, including psychosocial stress (−35%; $P < .0001$). After cardiac rehabilitation, the prevalence of psychosocial stress was reduced from 10% to 4% ($P < .0001$).

Effect of Psychosocial Stress on Mortality

To demonstrate the impact of psychosocial stress on subsequent mortality, psychosocial stress was assessed on completion of cardiac rehabilitation and mortality was determined (Figure 1). Patients with high psychosocial stress had a 4-fold higher mortality than patients with low psychosocial stress (22% vs 5%; $P = .003$). In addition, control patients with high psychosocial stress control who did not undergo formal cardiac rehabilitation had a subsequent mortality of 19%, demonstrating the strength of psychosocial stress as a risk factor for subsequent mortality.

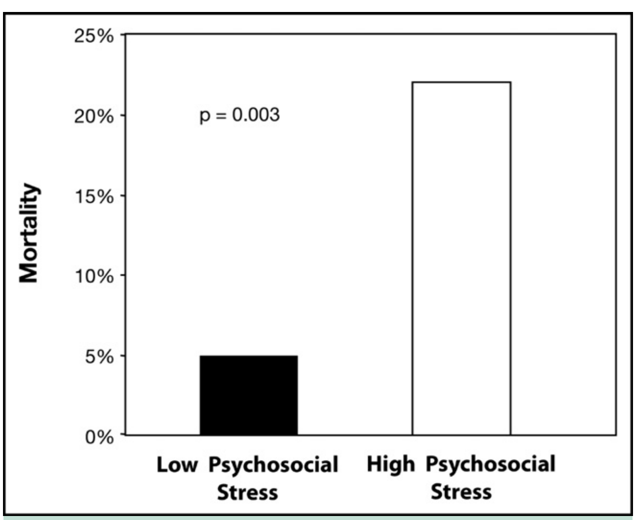

Figure 1 Impact of psychosocial stress on subsequent mortality in patients with coronary disease completing cardiac rehabilitation and exercise training (n = 522).

Table 4 Baseline Differences in Patients with High and Low Exercise Change during Cardiac Rehabilitation and Exercise Training

	High Exercise Change (n = 282)	Low Exercise Change (n = 240)	*P*
Age (y)	63 ± 11	65 ± 10	.04
% Male	74%	73%	NS
BMI (kg/m²)	28.8 ± 5.2	28.2 ± 5.1	NS
Active smokers (%)	1%	2%	NS
Hypertensives (%)	28%	42%	.002
Diabetes (%)	22%	20%	NS
Married (%)	70%	75%	NS
Peak oxygen uptake (mL/kg/min)	16.0 ± 5.1	17.5 ± 5.2	.0007
Total cholesterol (mg/dL)	167 ± 38	168 ± 38	NS
HDL, cholesterol (mg/dL)	40 ± 13	42 ± 13	.08
LDL, cholesterol (mg/dL)	99 ± 30	97 ± 41	NS
Triglycerides (mg/dL)	141 ± 72	158 ± 95	.03
hs-CRP (mg/dL)	5.5 ± 8.0	5.8 ± 10.8	NS
Ejection fraction (%)	53 ± 12	55 ± 11	NS
Depression	3.3 ± 3.6	3.5 ± 4.6	NS
Anxiety	4.2 ± 4.5	4.1 ± 4.7	NS
Hostility	2.5 ± 3.4	2.7 ± 3.7	NS
Somatization	6.5 ± 3.9	6.7 ± 4.0	NS
Quality of life	102.5 ± 17.4	102.7 ± 18.2	NS
Psychosocial stress	9.9 ± 10.3	10.3 ± 11.9	NS

BMI = body mass index; HDL = high-density lipoprotein; LDL = low-density lipoprotein; hs-CRP = high-sensitivity C-reactive protein; NS = not significant.

Effect of Exercise Training on Mortality

Patients were divided into 2 groups on the basis of the degree of change in exercise capacity incurred during cardiac rehabilitation and exercise training. Patients exhibiting a significant training effect, demonstrated by a peak oxygen uptake increase ≥ 10%, were labeled "high exercise change" and compared with those with minimal or no improvement in exercise capacity (change in peak oxygen uptake < 10%, or "low exercise change"). Baseline differences between these 2 groups are described in Table 4. Patients with high exercise change were younger, were less likely hypertensive, and had lower peak oxygen uptake and triglycerides than patients with low exercise change.

At follow-up (Figure 2), patients with high exercise change (n = 282) had a 60% lower mortality than patients with low exercise change (4% vs 10%; $P = .009$). By multivariate analysis in a model incorporating age, presence of

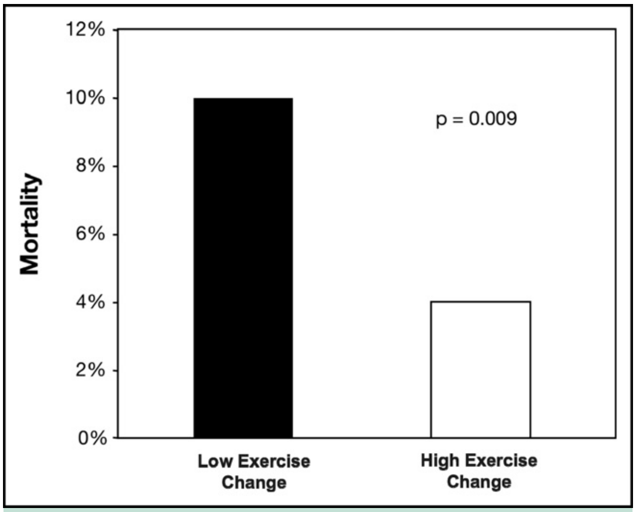

Figure 2 Effects of exercise change on mortality in patients with coronary disease completing cardiac rehabilitation and exercise training (n = 522).

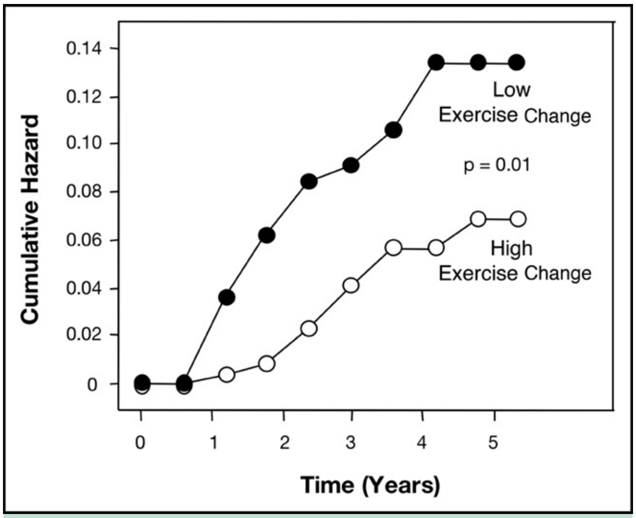

Figure 3 Actuarial cumulative hazard plot for survival time based on changes in exercise capacity after exercise training during cardiac rehabilitation (n = 522).

hypertension, gender, ejection fraction, BMI, and peak exercise change category, a low exercise change status remained an independent predictor of mortality ($\chi^2 = 5.1$; $P = .02$), thereby demonstrating the benefits of exercise training in reducing subsequent mortality (Table 5A). Time-dependent actuarial cumulative hazard plot for survival was assessed in patients with high and low exercise change (Figure 3). Patients with low exercise change reveal an early incremental increased mortality compared with patients with high exercise change ($P = .01$).

Table 5 Multivariate Analysis of Independent Predictors of Mortality in Patients Who Completed Cardiac Rehabilitation and Exercise Training (n = 522)

(A) Incorporating Age, Gender, Triglycerides, Presence of Hypertension, Ejection Fraction, Exercise Change Category, and BMI

Variable	χ^2	*P* value
Lower ejection fraction	13.6	.0002
Low exercise change	5.1	.02
Lower BMI	4.3	.04
Higher age	3.8	.05

(B) Incorporating Age, Gender, Triglycerides, Presence of Hypertension, Ejection Fraction, Exercise Change Category, BMI, and Final Psychosocial Stress Score

Variable	χ^2	*P* value
Lower ejection fraction	11.2	.0008
Higher age	9.5	.002
Higher psychosocial stress	4.3	.04
Lower BMI	3.1	.08
Low exercise change	2.9	.09

BMI = body mass index.

Effect of Exercise Training on Mortality Based on Psychosocial Stress Status

The impact of psychosocial stress was evaluated as a function of change in exercise capacity by evaluating patients in the 2 exercise change strata separated by psychosocial stress status (Table 6). Patients with low psychosocial stress who had a high exercise change had only a trend toward a lower mortality than did patients with low psychosocial stress with low exercise change (4% vs 8%; $P = .14$), suggesting no statistical benefit of exercise training on mortality in patients with low psychosocial stress. In contrast, patients with high psychosocial stress and high exercise change had a marked reduction in mortality compared with patients with high psychosocial stress with low exercise change (0% vs 19%; $P = .03$), suggesting a pronounced effect of exercise training in patients with high psychosocial stress. Moreover, patients with high psychosocial stress with low exercise change had mortality similar to control patients with psychosocial stress, suggesting the mortality changes observed during this study were a result of cardiac rehabilitation and

Table 6 Mortality in Patients with Coronary Disease with High and Low Psychosocial Stress Based on Degree of Change in Peak Oxygen Consumption after Exercise Training (n = 522)

	Low Exercise Change (n = 240)	High Exercise Change (n = 282)	*P*
Low psychosocial stress (n = 469)	8%	4%	.14
High psychosocial stress (n = 53)	19%	0%	.03
P	.04	NS	

NS = not significant.

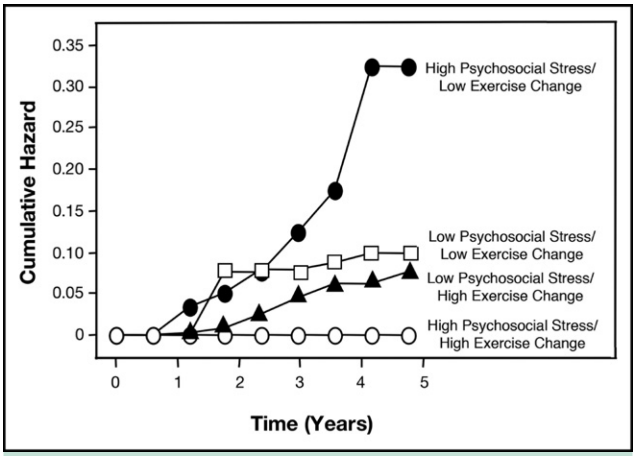

Figure 4 Actuarial cumulative hazard plot for survival time based on changes in exercise capacity (high exercise change vs low exercise change) after exercise training split by baseline psychosocial stress (high psychosocial stress vs low psychosocial stress) (n = 522).

exercise training. In a new multivariate model (Table 5B) that now incorporates the final psychosocial stress score with the previous model, psychosocial stress was found to be a significant independent predictor of mortality ($\chi^2 = 4.3$, $P = .04$), whereas exercise change status was not ($\chi^2 = 2.9$, $P = .09$).

Time-dependent actuarial cumulative hazard plot for survival was assessed in patients with high and low exercise change divided by psychosocial stress status (Figure 4). Patients with high psychosocial stress/low exercise change reveal an early incremental increased mortality compared with all other groups ($P = .001$). Although low psychosocial stress/high exercise change appeared to initially have a survival advantage over low psychosocial stress/low exercise change, there was no statistical difference between these groups at 5 years.

DISCUSSION

There are several important implications from this study. First, elevated psychosocial stress is a potent risk factor for future mortality in patients with coronary artery disease, leading to a 4-fold increase in subsequent mortality. Second, cardiac rehabilitation and exercise training is an effective modality in improving exercise capacity, conventional cardiovascular risk factors, quality of life, and psychosocial stress. Third, patients with coronary disease who significantly increase exercise capacity realize a survival benefit over those patients with minimal or no change in exercise capacity, thus confirming the value of improving peak aerobic capacity in patients with coronary artery disease. Finally, the primary beneficiaries of mortality reduction secondary to improvement in exercise capacity are those patients exhibiting high psychosocial stress.

Physical inactivity is considered to be one of the most significant public health concerns,[9] and levels of physical fitness are known to be potent predictors of major cardiovascular disease, cardiovascular mortality, and all-cause mortality.[1-3] Low levels of cardiovascular fitness have been shown to be as strong a predictor of mortality as more conventional coronary artery disease risk factors, such as smoking, hypertension, and hyperlipidemia.[4,5,26,27] The importance of physical fitness and exercise capacity as an indicator of prognosis has been demonstrated in epidemiologic and population-based studies, as well as from cohorts with known or suspected coronary artery disease.[1,4,6,27-30] Because exercise capacity in most cohorts is modifiable, much attention has been directed toward improving cardiovascular fitness and its attendant changes in overall prognosis. Vanhees et al[8] demonstrated that improving peak oxygen uptake after physical training is an important independent predictor of cardiovascular mortality, such that every 1% increase in peak oxygen uptake results in a 2% decrease in cardiovascular death. This reduction in mortality has been attributed to the numerous physiologic benefits resulting from exercise, including improvements in lipids, autonomic function, inflammation, blood rheology, vasomotor function, blood pressure, insulin resistance and glucose intolerance, and obesity.[9,24,31-34]

Behavioral factors, including depression, hostility, anxiety, and overall psychosocial stress, have been demonstrated to be potent risk factors for the development of myocardial infarction and death, yet remain underappreciated as contemporary coronary risk factors.[11,35-38] The Interheart study evaluated cardiovascular risk factors in 29,972 people from 52 countries to investigate the risk of first myocardial infarction.[39] Nine independent risk factors including psychosocial factors accounted for 90% of the population attributable risk in men and 94% in women. These psychosocial factors, which included depression and psychosocial stress, increased the odds of first myocardial infarction by approximately 3-fold and accounted for 33% of the population attributable risk for the development of myocardial infarction, a magnitude similar to standard risk factors such as smoking, diabetes, and hypertension.[40] In patients with known coronary artery disease, particularly after a major coronary event, the risk of subsequent myocardial infarction and death related to psychosocial factors appears much higher.[41-43] Frasure-Smith et al[35] reported that depression was associated with a more than 4-fold increase risk of mortality during the first 6 months after an acute myocardial infarction after adjustment for other risk factors. In that study, the pathogenicity of depression as a risk factor for mortality postmyocardial infarction was similar to that of left ventricular dysfunction and previous myocardial infarction. Several epidemiologic studies suggest that hostility and unexpressed anger are risk factors for coronary artery disease.[44-48] Allison et al[49] demonstrated that among patients referred for cardiac rehabilitation, those with high psychologic stress had a 2.5-fold increased risk of rehospitalization, a 5-fold increased risk of major cardiac events, and a 4-fold increase in medical costs compared with patients with low levels of psychologic stress. Frasure-

Smith et al[50] demonstrated that high-stress men with non–Q-wave myocardial infarction exhibited a 5-year mortality of more than 50%, 3-fold greater than in patients with low stress.[50] Shibeshi et al[13] recently reported the effect of anxiety, measured using the Kellner Symptom Questionnaire used in this study, in 516 stable patients with coronary artery disease who were followed for an average of 3.4 years. They report anxiety scores were strong independent predictors of subsequent nonfatal myocardial infarction and total mortality.

We and others have demonstrated the salutary effects of exercise training on these high-risk behaviors in which indices of hostility, depression, and overall psychosocial stress can be reduced by 50% to 70%.[14-17,51-53] Data from a recent randomized trial demonstrated that exercise training can decrease depressive symptoms as effectively as antidepressant medication in patients with clinical depression.[51,54] Whether reduction in any of these high-risk behaviors can lead to a subsequent reduction in mortality was recently reported by us, where depressed patients with coronary disease completing exercise training demonstrated a 73% lower mortality than depressed controls.[18] To what extent the health benefits of exercise training are in part due to its effects on high-risk behaviors has thus far been unanswered.

This investigation again confirms the concept that psychosocial stress remains an important independent risk factor for subsequent mortality and that exercise training using cardiac rehabilitation is an effective tool in reducing this high-risk behavior. Moreover, it seems that improving exercise capacity in patients without psychosocial stress offers less mortality benefit over time than does its effect in patients with high psychosocial stress. This suggests that reduction of psychosocial stress is a contributory mechanism by which exercise training enhances survival in patients with coronary artery disease.

STUDY LIMITATIONS

There are several limitations of this study worthy of mention. First, this was an observational study, and patients were not prospectively randomized into an exercise program versus usual care based on psychosocial stress status; as a result, confounding factors unaccounted for may be playing a role in our findings.

Second, there might be selection bias because the study group did not represent all patients who have coronary events but rather those selected for referral and who attended and completed the formal cardiac rehabilitation program. Finally, our study assessed all-cause mortality, a powerful end point. Although our patients with psychosocial stress did not have interim events during cardiac rehabilitation, our data do not allow us to determine the impact of cardiac rehabilitation and psychosocial stress on other potentially important end points.

CONCLUSIONS

The physiologic benefits of exercise training are numerous, many of which contribute to improving health and reducing mortality in patients with coronary artery disease. This investigation suggests that reduction of high-risk psychosocial behaviors is an additional mechanism by which exercise training improves survival in patients with cardiovascular disease.

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