Positive Affect and Survival in Patients With Stable Coronary Heart Disease: Findings From the Heart and Soul Study

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ABSTRACT

Objective: Positive affect can improve survival, but the mechanisms responsible for this association are unknown. We sought to evaluate the association between positive affect and mortality in patients with stable coronary heart disease and to determine biological and behavioral factors that might explain this association.

Method: The Heart and Soul Study is a prospective cohort study of 1,018 outpatients with stable coronary heart disease. Participants were recruited between September 11, 2000, and December 20, 2002, and were followed up to June 2011. Baseline positive affect was assessed by using the 10-item positive affect subscale of the Positive and Negative Affect Schedule. Cox proportional hazards regression was used to estimate the risk of mortality (primary outcome measure) and cardiovascular events (heart failure, myocardial infarction, stroke, transient ischemic attack) associated with positive affect, adjusting for baseline cardiac disease severity and depression. We also evaluated the extent to which these associations were explained by potential biological and behavioral mediators.

Results: A total of 369 patients (36%) died during a mean ± SD follow-up period of 7.1 ± 2.5 years. Positive affect was not significantly associated with cardiovascular events (hazard ratio [HR]: 0.89; 95% CI, 0.79–1.00; $P = .06$). However, each standard deviation (8.8-point) increase in positive affect score was associated with a 16% decreased risk of all-cause mortality (HR: 0.84; 95% CI, 0.76–0.92; $P = .001$). After adjustment for cardiac disease severity and depressive symptoms, positive affect remained significantly associated with improved survival (HR: 0.87; 95% CI, 0.78–0.97; $P = .01$). The association was no longer significant after adjustment for behavioral factors, and particularly physical activity (HR: 0.92; 95% CI, 0.82–1.03; $P = .16$). Further adjustment for C-reactive protein and omega-3 fatty acids did not result in any meaningful changes (HR: 0.94; 95% CI, 0.84–1.06; $P = .31$).

Conclusions: In this sample of outpatients with coronary heart disease, positive affect was associated with improved survival. This association was largely explained by physical activity.

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Cardiovascular disease is the leading cause of death in the world. Psychological factors have been associated with increased morbidity and mortality in patients with coronary heart disease, but most research has focused on negative emotions, such as anxiety[1] and depression.[2] There is now growing recognition that positive emotions, such as joy and cheerfulness, may also provide important protective effects.[3] Accumulating evidence suggests that positive psychological factors may actually improve longevity[3,4] and decrease morbidity and mortality from cardiovascular disease.[5–7]

The idea that improving positive attitude might help people live longer has considerable appeal. However, several unresolved questions remain. First, it is important to examine whether positive and negative affect have independent prognostic effects. In 1 study,[8] adjustment for depressed mood attenuated the observed relationship between positive affect and long-term survival in cardiac catheterization patients. Second, the association between positive affect and cardiac prognosis may be confounded by worse severity of heart disease, with greater disease burden causing impairment in positive affect. Third, it is unclear what mechanisms could explain the association of positive affect with improved health outcomes.

We have previously found that depressive symptoms predicted adverse outcomes in patients with coronary heart disease, independent of baseline cardiac disease severity, and that this association was largely explained by poor health behaviors, especially medication nonadherence and physical inactivity.[9] These findings led us to wonder whether the improved survival associated with positive affect might also be explained by health behaviors. Therefore, the aims of this study were to examine whether positive affect is associated with improved survival and decreased cardiovascular morbidity, independent of cardiac disease severity and depression, and to explore biological and behavioral factors that could explain this association.

METHOD

Participants

The Heart and Soul Study is a prospective cohort study that focused on psychosocial factors and health outcomes in patients with coronary heart disease. Details regarding the study design have been described previously.[10] Between September 11, 2000, and December 20, 2002, 1,024 participants were recruited from 12 outpatient clinics in San Francisco. Patients had to meet the following inclusion criteria: history of myocardial infarction or coronary revascularization, angiographic evidence of at least 50% stenosis in at least 1 coronary vessel, or a diagnosis of coronary heart disease documented by an internist or cardiologist. Exclusion criteria were patients who had a history of myocardial infarction in the past 6 months, were unable to walk 1 block, or were planning to move from the local area within 3 years. All participants completed a comprehensive baseline

Clinical Points

- Although the impact of negative emotions on cardiovascular prognosis has been studied extensively, research on positive affect has been relatively sparse.
- In a sample of 1,018 patients with stable coronary heart disease, we found that greater positive affect was associated with improved survival.
- The association between positive affect and mortality becomes nonsignificant after adjustment for physical activity.
- These findings seem to suggest that the improved survival associated with positive affect could potentially be enhanced with behavioral interventions that include exercise training.

examination. Of the 1,024 participants who completed the baseline examination, 1,022 completed a positive affect scale, and 4 participants were lost to follow-up, leaving 1,018 participants for this analysis. Participants were followed up to June 2011. The study protocol was approved by the appropriate institutional review boards, and all participants signed an informed consent.

Baseline Characteristics

Age, gender, ethnicity, educational achievement, and medical history were determined by self-reported questionnaire. Body mass index (BMI [kg/m^2]) was calculated based on weight and height. Participants were instructed to bring their medication bottles to their appointment; all current medications were recorded. Medications were categorized by using Epocrates Rx (San Mateo, California).

Positive Affect

Positive affect was measured by using the Positive and Negative Affect Schedule (PANAS),[11] which includes 10 items on positive affect: alert, inspired, active, interested, excited, strong, enthusiastic, determined, proud, and attentive. Patients rated the extent to which they had felt each of these items during the past week on a 5-point scale (ranging from 1 [not at all] to 5 [extremely]). Good concurrent validity and construct validity have been established for the PANAS, and the reliability has been reported to range from 0.86 to 0.90 for positive affect.[11,12] In the current study, estimates of internal consistency (Cronbach $\alpha = .93$) and mean inter-item correlations ($r = 0.57$) indicated the reliability of the PANAS measure of positive affect in our cohort of outpatients with stable coronary heart disease.

Cardiac Disease Severity

We assessed left ventricular ejection fraction by using resting echocardiography. Participants were categorized as having diastolic dysfunction if their mitral inflow ratio of peak early-to-late diastolic filling velocity was more than 0.75 and if the velocity time integral in their pulmonary vein was greater during diastole than during systole.[13] Fasting venous blood samples were drawn to determine low- and high-density lipoprotein cholesterol levels.

Depression

The presence of major depressive disorder (past month) was ascertained by using the Computerized Diagnostic Interview Schedule for the *DSM-IV* (CDIS-IV).[14] The validity and reliability of computerized versions of the CDIS-IV have previously been demonstrated to be acceptable.[15] We assessed depressive symptoms using the Patient Health Questionnaire (PHQ), a self-report instrument that measures the frequency of experiencing each symptom corresponding to the 9 *DSM-IV* criteria for depression. When a standard cut point of ≥ 10 was used, the PHQ has demonstrated excellent validity compared with a structured diagnostic interview for depression.[16,17]

Potential Biological Mediators

Heart rate variability was assessed by using 3-channel, 24-hour ambulatory Holter electrocardiography.[18] Measures of heart rate variability included the SD of 5-minute average NN intervals and the natural log of very low frequency power. Cortisol and norepinephrine excretion were measured in 24-hour urine samples.[19,20] High-pressure liquid chromatography with electrochemical detection to assay whole blood serotonin levels was used. High-sensitivity C-reactive protein (CRP) levels were measured by using Roche Integra assay or Beckman Extended Range assay.[21] We measured blood levels of 2 omega-3 fatty acids, docosahexaenoic acid and eicosapentaenoic acid, by capillary gas chromatography as the percentage composition of total fatty acid methyl esters in the red blood cell membranes.[22]

Potential Behavioral Mediators

Smoking and alcohol use were determined by self-report questionnaire. Smoking was defined as current smoking (yes/no). Regular alcohol use was defined as a score of 4 or greater on the Alcohol Use Disorders Identification Test Consumption.[23] Medication adherence was assessed by asking the following question: "In the past month, how often did you take your medications as the doctor prescribed?" Five possible responses ranged from "all of the time" (100%) to "less than half the time" (50%). Medication nonadherence was defined as taking prescribed medications 75% of the time or less.[24] Physical activity was assessed with self-report. Participants chose from the following categories: not at all active, a little active (1–2 times/mo), fairly active (3–4 times/mo), quite active (1–2 times/wk), very active (3–4 times/wk), extremely active (≥ 5 times/wk). Self-report has been shown to be a reliable, valid, and accurate method of assessing physical activity.[25,26]

Mortality and Cardiovascular Events

After the baseline examination, annual telephone interviews with participants or proxies were conducted in which they were asked about emergency room visits, hospitalizations, or death. For any reported cardiovascular event, medical records, death certificates, and coroner's reports were reviewed by 2 independent blinded adjudicators. In the event of disagreement, a third blinded adjudicator determined the

outcome variable. The primary study end point was mortality. We also evaluated cardiovascular events. To be diagnosed with heart failure, patients had to be hospitalized for an acute change in at least 2 of the following: paroxysmal nocturnal dyspnea, orthopnea, elevated jugular venous pressure, pulmonary rales, third heart sound, cardiomegaly, or pulmonary edema on chest radiography. Standard criteria were used for defining myocardial infarction.[27] Stroke was defined as new neurologic deficit that must not have been the result of brain trauma, tumor, infection, or other cause. Transient ischemic attack was defined as a focal neurologic deficit lasting between 30 seconds and 24 hours, with rapid evolution of the symptoms to the maximal level of deficit in less than 5 minutes and with subsequent complete resolution.

Statistical Analysis

For descriptive purposes, participants were grouped on the basis of the median split (ie, PANAS score ≥ 32) for categorizing low and high levels of positive affect, and were compared on clinical and demographic variables by using *t* tests and χ^2 tests. C-reactive protein was log-transformed because it did not have a normal distribution. We used Cox proportional hazards regression to estimate the risk of all-cause mortality associated with positive affect both as a continuous variable (ie, per SD increase) and as a dichotomous variable (ie, based on median split). As a secondary analysis, we also evaluated the association between positive affect and cardiovascular events (myocardial infarction, heart failure, stroke/transient ischemic attack).

To examine whether a covariate changed the strength of association between positive affect and all-cause mortality, the percent change in the effect size (age-adjusted log hazard ratio [HR] or β coefficient) was calculated for positive affect (entered as a dichotomous variable) after adjustment for the potential confounder or explanatory factor. Participants missing the covariate of interest were excluded from nested models to avoid artifacts due to different sample sizes. We sequentially considered demographic characteristics, comorbid conditions, cardiac disease severity, medication, and measures of depression as potential confounders. We then evaluated behavioral and biological mechanisms as potential explanatory factors. All variables that resulted in a more than 5% change in the effect size (log HR) for positive affect were considered potential confounders or explanatory variables and included in the final multivariable model.[28] To determine whether any effect of positive affect differed by age, sex, race, or depressive symptoms, we checked for interactions with these variables.

The log-linearity assumption for continuous variables was verified by checking for improvement in fit after addition of quadratic and cubic terms. The proportional hazards assumption of these models was verified by using log-minus-log survival plots and by checking for secular patterns in Schoenfeld residuals. A forest plot was constructed for visual interpretation of the results. The models were checked for multicollinearity, but we found no evidence for multicollinearity. Analyses were performed by using SPSS version 18.0.

Table 1. Baseline Characteristics of 1,018 Participants With Stable Coronary Heart Disease, by Positive Affect

Demographic Characteristic	Low Positive Affect[a] (n = 514)	High Positive Affect[b] (n = 504)	*P* Value
Age, mean (SD), y	66.2 (11.1)	67.6 (10.6)	.04
Male sex, n (%)	419 (81.5)	416 (82.5)	.67
White, n (%)	309 (60.1)	303 (60.1)	.99
High school graduate, n (%)	434 (84.4)	452 (90.0)	.01
BMI (kg/m^2), mean (SD)	28.8 (5.7)	28.0 (4.9)	.02
Comorbid condition, n (%)			
Hypertension	370 (72.4)	349 (69.2)	.27
Myocardial infarction	268 (52.5)	277 (55.3)	.38
Stroke	69 (13.5)	78 (15.5)	.38
Revascularization	289 (56.6)	311 (61.7)	.09
Congestive heart failure	91 (17.8)	87 (17.4)	.85
Diabetes mellitus	140 (27.3)	124 (24.7)	.33
Medication use, n (%)			
Aspirin	395 (76.8)	394 (78.2)	.61
β-Blocker	294 (57.0)	298 (59.1)	.49
Angiotensin system inhibitor	259 (50.4)	264 (52.4)	.52
Statin	316 (61.5)	337 (66.9)	.07
Cardiac disease severity			
LVEF, mean (SD), y	61.7 (9.6)	61.7 (9.7)	.97
Diastolic dysfunction, n (%)	56 (12.2)	60 (13.4)	.60
LDL cholesterol, mean (SD), mg/dL	104.0 (33.5)	104.4 (33.9)	.85
HDL cholesterol, mean (SD), mg/dL	44.9 (13.7)	46.7 (14.4)	.04
Depression, n (%)			
Major depressive disorder	165 (32.2)	83 (16.5)	< .001
Depressive symptoms	163 (31.7)	36 (7.1)	< .001
Tricyclic antidepressant use	21 (4.1)	23 (4.6)	.71
SSRI use	69 (13.4)	28 (5.6)	< .001
Other antidepressant use	51 (9.9)	27 (5.4)	.006
Biological factors, mean (SD)			
HRV (SDANN), ms	108.6 (34.4)	109.2 (37.8)	.80
HRV (lnVLF), ms^2	6.3 (0.81)	6.4 (0.94)	.45
Serotonin (non-SSRI users), ng/mL	118.2 (68.7)	123.7 (86.8)	.30
Cortisol, μg/d	34.1 (22.0)	35.7 (20.4)	.28
Norepinephrine, μg/d	51.1 (26.8)	52.4 (26.3)	.46
Log hsCRP, mg/L	0.82 (1.31)	0.60 (1.31)	.009
Fatty acids, DHA + EPA, %	4.1 (2.0)	4.3 (2.10)	.09
Behavioral factors, n (%)			
Regular alcohol use	139 (27.3)	153 (30.5)	.26
Smoking	130 (25.4)	69 (13.7)	< .001
Medication nonadherence	59 (11.6)	24 (10.4)	< .001
Physical activity			
Not at all active	136 (26.6)	52 (10.4)	< .001
A little active	108 (21.1)	74 (14.7)	
Fairly active	83 (16.2)	73 (14.5)	
Quite active	70 (13.7)	84 (16.7)	
Very active	81 (15.8)	136 (27.1)	
Extremely active	34 (6.6)	83 (16.5)	

[a]Positive and Negative Affect Schedule score < 32.
[b]Positive and Negative Affect Schedule score ≥ 32.
Abbreviations: BMI = body mass index, CRP = C-reactive protein, DHA = docosahexaenoic acid, EPA = eicosapentaenoic acid, HDL = high-density lipoprotein, HRV = heart rate variability, hsCRP = high-sensitivity C-reactive protein, lnLVF = natural log of very low frequency, LDL = low-density lipoprotein, LVEF = left ventricular ejection fraction, SDANN = SD of 5-minute average NN intervals, SSRI = selective serotonin reuptake inhibitor.

RESULTS

The baseline characteristics of the study population categorized by low or high positive affect are presented in Table 1. Compared with participants who had low positive

Table 2. Association Between Positive Affect Cardiovascular Events and Mortality per Standard Deviation (8.8-point) Increase in Positive Affect Score

Event	No. of Events	Age-Adjusted HR (95% CI) per SD Increase	*P* Value
Heart failure	171	0.87 (0.74–1.01)	.07
Myocardial infarction	123	0.93 (0.78–1.11)	.44
Stroke or transient ischemic attack	46	1.03 (0.76–1.38)	.87
Composite outcome[a]	261	0.89 (0.79–1.00)	.06
All-cause mortality	369	0.84 (0.76–0.92)	.001

[a]Composite outcome of heart failure, myocardial infarction, or cerebrovascular disease.
Abbreviation: HR = hazard ratio.

affect, those with high positive affect were older, were more educated, had lower BMI, had higher levels of HDL, and were less likely to be depressed or to use antidepressants. High positive affect was also associated with lower CRP, less smoking, more medication adherence, and more physical activity.

A total of 369 patients (36%) died during a mean ± SD follow-up period of 7.1 ± 2.5 years.

Each standard deviation (8.8-point) increase in PANAS positive affect score was associated with a 16% decreased risk of death (age-adjusted HR: 0.84; 95% CI, 0.76–0.92; *P* = .001). Positive affect was not significantly associated with subsequent heart failure, myocardial infarction, stroke, or transient ischemic attack (Table 2).

Several markers of disease severity and depression were considered as potential confounding factors of the link between positive affect and mortality. Adjustments for history of myocardial infarction, left ventricular ejection fraction, depressive symptoms, and use of SSRIs each changed the strength of association between positive affect and mortality by ≥ 5% and thus met the criterion for potential confounding (Table 3). Adjustment for several biological (CRP, omega-3 fatty acids) and behavioral (smoking, medication nonadherence, physical activity) factors also diminished the strength of association between positive affect and mortality. Accounting for physical activity resulted in the largest (30%) reduction in the strength of the positive affect–mortality relationship.

After adjustment for potential confounding factors, positive affect remained significantly associated with decreased mortality (HR: 0.87; 95% CI, 0.78–0.97; *P* = .01). The association between positive affect and mortality was no longer significant after further adjustment for smoking, medication adherence, and physical activity (HR: 0.92; 95% CI, 0.82–1.03; *P* = .16). Further adjustment for potential biological mediators (CRP and omega-3 fatty acids) did not result in any meaningful changes (HR: 0.94; 95% CI, 0.84–1.06; *P* = .31) (Table 4). We found no evidence that the association between positive affect and mortality varied by age, sex, race, and depressive symptoms (all *P* values for interaction ≥ .10).

When positive affect was assessed as a dichotomous variable, 33% (167/504) of patients with high positive affect and 39% (202/514) of patients with low positive affect died. High positive affect was associated with a 27% decreased risk of death (HR: 0.73; 95% CI, 0.59–0.89; *P* = .002) (Table 4; Figure 1). This association remained essentially unchanged when we adjusted for potential confounding factors (HR: 0.74; 95% CI, 0.60–0.93; *P* = .01), but there was no significant association between positive affect and mortality after adjustment for smoking, medication adherence, and physical activity (HR: 0.85; 95% CI, 0.68–1.06; *P* = .15). The association was only modestly attenuated after further adjustment for potential biological mediators (HR: 0.87; 95% CI 0.69–1.10; *P* = .25).

Table 3. Change in the Strength of Association Between Positive Affect and Mortality (expressed as the percent change in the β coefficient for positive affect) After Adjustment for Potential Confounders and Mediators

Variable	No. of Participants	Change in Effect Size After Adjustment, %[a]
Demographic characteristic		
Male sex	1,022	1.5
White	1,022	1.0
High school graduate	1,020	−1.5
BMI	1,022	3.1
Comorbid conditions		
Hypertension	1,019	−0.6
Myocardial infarction	1,015	**8.1**
Stroke	1,018	1.7
Revascularization	1,019	−0.9
Congestive heart failure	1,016	−0.9
Diabetes mellitus	1,019	−2.8
Cardiac disease severity		
LVEF	1,020	**5.5**
Diastolic dysfunction	909	4.7
LDL cholesterol	992	−0.5
HDL cholesterol	1,020	−2.5
Medication use		
Aspirin	1,022	−1.1
β-Blocker	1,022	−0.1
Angiotensin system inhibitor	1,022	0.8
Statin	1,022	−0.2
Depression		
Major depressive disorder	1,021	−3.2
Depressive symptoms	1,022	**−19.9**
Tricyclic antidepressant use	1,022	2.4
SSRI use	1,022	**−7.9**
Other antidepressant use	1,022	−4.7
Potential biological mediators		
HRV (SDANN)	873	2.1
HRV (lnVLF)	477	−2.0
Serotonin in non-SSRI users	977	−1.5
Cortisol	886	−2.6
Norepinephrine	960	−0.1
C-reactive protein	983	**−10.3**
Omega-3 fatty acids	987	**−7.5**
Potential behavioral mediators		
Regular alcohol use	1,014	−1.1
Smoking	1,019	**−19.1**
Medication nonadherence	1,013	**−5.4**
Self-reported physical activity	1,018	**−30.2**

[a]Changes > 5% in the effect size for positive effect are presented in boldface.
Abbreviations: BMI = body mass index, HDL = high-density lipoprotein, HRV = heart rate variability, lnVLF = natural log of very low frequency, LDL = low-density lipoprotein, LVEF = left ventricular ejection fraction, SDANN = SD of 5-minute average NN intervals, SSRI = selective serotonin reuptake inhibitor.

DISCUSSION

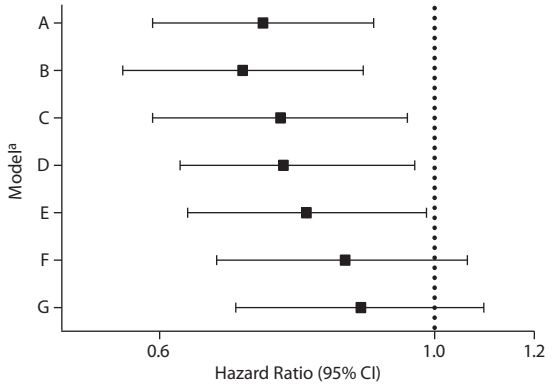
In this prospective cohort study of more than 1,000 outpatients with stable coronary heart disease, we found

Table 4. Association Between Positive Affect and Mortality, With Sequential Adjustment for Potential Confounders and Mediators

	Positive Affect (median split)		Positive Affect (per 8.8-point increase)	
Variable[a]	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
Potential confounders				
Model A	0.73 (0.59–0.89)	.002	0.84 (0.76–0.92)	.001
Model B	0.70 (0.57–0.86)	.001	0.84 (0.76–0.93)	.001
Model C	0.74 (0.60–0.93)	.01	0.87 (0.78–0.97)	.01
Potential mediators				
Model D	0.78 (0.62–0.96)	.02	0.88 (0.79–0.98)	.02
Model E	0.79 (0.63–0.98)	.03	0.89 (0.79–0.99)	.03
Model F	0.85 (0.68–1.06)	.15	0.92 (0.82–1.03)	.16
Model G	0.87 (0.69–1.10)	.25	0.94 (0.84–1.06)	.31

[a]Adjustment variables: model A = age, model B = model A + history of myocardial infarction and left ventricular ejection fraction, model C = model B + depressive symptoms and selective serotonin reuptake inhibitor use, model D = model C + smoking, model E = model D + medication adherence, model F = model E + physical activity, model G = model F + C-reactive protein and omega-3 fatty acids.
Abbreviation: HR = hazard ratio.

Figure 1. Association Between Positive Affect (entered as a dichotomous variable) and All-Cause Mortality, With Sequential Adjustment for Potential Confounders and Mediators



[a]Adjustment variables: model A = age, model B = model A + history of myocardial infarction and left ventricular ejection fraction, model C = model B + depressive symptoms and selective serotonin reuptake inhibitor use, model D = model C + smoking, model E = model D + medication adherence, model F = model E + physical activity, model G = model F + C-reactive protein and omega-3 fatty acids.

that positive affect was associated with a 27% reduction in mortality during a mean follow-up of 7 years. After adjustment for cardiac disease severity and depressive symptoms, positive affect remained associated with improved survival. The association between positive affect and survival was no longer significant after adjustment for behavioral factors, particularly physical activity. Potential biological mediators did not seem to have an additional effect on this association. These findings suggest that patients with a positive attitude may live longer because they are more successful at adopting a healthier lifestyle and, particularly, at getting more exercise than patients without a positive attitude.

Increasing evidence indicates that high levels of positive affect are associated with increased survival,[3,4] although mixed findings have been reported.[8,29] Our study extends this literature in several important ways. First, we carefully measured and adjusted for both major depressive disorder and depressive symptoms to verify that the association between positive affect and mortality was independent of depression. Second, we performed a detailed assessment of baseline cardiovascular disease severity and risk factors to rule out the possibility that greater underlying cardiac disease severity was responsible for this association. Third, we simultaneously examined numerous potential behavioral and biological mediators and evaluated the extent to which each of these potential mechanisms might explain the association between positive affect and mortality.

There is an ongoing debate in the literature as to whether positive affect and negative affect are independent of each other or rather bipolar extremes of the same mood dimension.[3,8] In a study[8] of cardiac catheterization patients, adjustment for depressive emotion attenuated the observed relationship between positive affect and long-term survival, whereas positive affect was independently associated with cardiac outcomes in coronary patients after adjustment for depressive symptoms.[5] In our sample, adjusting for depressive symptoms reduced the effect size for positive affect by 20%. However, even after controlling for depressive symptoms, we found that positive affect remained significantly associated with improved survival. The robustness of this association after accounting for depressive symptoms suggests important and separate relationships between positive emotions and survival. These findings are consistent with the understanding that optimal functioning transcends the simple absence of negative affect.[30]

It is plausible that multiple biological and behavioral pathways may link positive emotional experience with health outcomes. In 1 experimental study,[31] positive affect was related to higher norepinephrine levels and lower cortisol response to awakening in a sample of 328 individuals. In the Whitehall II study,[32] positive affect was associated with reduced levels of the inflammatory marker CRP in healthy women but not in men. Another mechanism through which positive affect may protect against adverse outcome is the increase of heart rate variability.[33] Although little is known about the association of positive affect with omega-3 fatty acids, both CRP and omega-3 fatty acids accounted for a more than 5% change in the effect size of positive affect. However, adjusting for CRP and omega-3 fatty acids did not seem to have an additional effect on the association between positive affect and survival in the present study.

Happy individuals may also have more favorable health habits and make healthier behavioral choices than less happy people. Higher-state positive affect is related to lower prevalence of smoking,[34] reduced alcohol consumption,[35] and regular exercise.[36] Positive affect might also increase adherence to medical regimens among patients, resulting in less severe illness, faster recovery, and longer survival.[3] In this study, we found that the association between positive affect and survival was no longer present after adjustment for

physical activity. These findings raise the possibility that the increased survival rate associated with positive affect could be explained by physical activity and other positive health behaviors that travel with exercise.

Because we evaluated positive affect and physical activity at the same point in time, we cannot determine whether physical activity was the cause or result of positive affect. The association is almost certainly bidirectional, because high positive affect is associated with a greater likelihood of engaging in physical activity,[37] and engaging in physical activity induces positive affect.[38] Regardless of whether physical activity was the cause or a result of positive affect, it appeared to explain a large part of the association between positive affect and survival. These findings underscore the many reasons to encourage exercise in patients with coronary heart disease.

In contrast to all-cause mortality, we did not find a significant association between positive affect and cardiovascular events. These findings are consistent with results from the Whitehall II study,[39] which found no relationship between positive mood and cardiovascular morbidity. However, they are in contrast to the results of other studies demonstrating reduced cardiovascular morbidity with high positive mood.[5–7] We are not sure why there was no relationship between positive affect and cardiovascular outcomes. One possible explanation is that we did not have enough power to evaluate cardiovascular outcomes (369 participants died, but only 261 had cardiovascular events). Although the 95% CIs overlapped 1, the HRs for heart failure and myocardial infarction were in the expected direction, estimating a 13% reduction in heart failure hospitalization and a 7% reduction in myocardial infarction for each 8.8-point increase in positive affect score. However, even if power had been adequate, the point estimates for cardiovascular outcomes suggested a less protective effect than was observed for mortality. Another possibility is that patients with positive affect were healthier at baseline and that our multivariable adjustments did not capture this unmeasured confounding. However, we measured and adjusted for a comprehensive set of covariates. A third possible explanation, and the one that we endorse, is that positive affect may have a more beneficial effect on general health than it does on cardiovascular outcomes. The reasons why positive affect might be more protective for general health than for cardiovascular disease deserve further study.

If the findings of the current study are confirmed, positive affect may provide a new target for intervention trials. Up to now, trials have mainly focused on negative emotions. However, psychological interventions should not only target the reduction of negative emotions but also seek to enhance positive emotions. The findings of the present study suggest the possibility that the improved survival associated with positive affect could be enhanced by behavioral interventions that include exercise training.

This study has several strengths, including the prospective design with a mean follow-up duration of 7 years, the large cohort size, and the careful measurement of potential biological and behavioral explanatory factors. However, a number of limitations must be considered. First, we included only outpatients with stable coronary heart disease and thus cannot comment on the effects of positive affect in the general population. Nonetheless, cardiovascular disease remains the leading cause of death worldwide, and reducing mortality in patients with cardiovascular disease would have major public health importance. Second, the participants in this study were mainly older men, and the results may not be generalizable to other patient populations. However, we did not observe any interaction between positive affect and gender. Finally, although we carefully assessed cardiac disease severity, we cannot rule out the possibility of unmeasured or residual confounding.

In conclusion, the current study showed that, after a mean follow-up of 7 years, positive affect was associated with improved survival in patients with coronary heart disease. This association was not explained by biological markers but largely by physical activity. Enhancing a cardiac patient's ability to experience positive affect may open new avenues to improve survival in patients with coronary heart disease.

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