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Depressive Symptoms and Health-Related Quality of Life: The Heart and Soul Study

Bernice Ruo, MD, **John S. Rumsfeld, MD, PhD**, **Mark A. Hlatky, MD**, **Haiying Liu, MD, MPH**, **Warren S. Browner, MD, MPH**, and **Mary A. Whooley, MD**
Section of General Internal Medicine, Veterans Affairs Medical Center, San Francisco (Drs Ruo, Liu, and Whooley); Department of Medicine, University of California, San Francisco (Drs Ruo, Browner, and Whooley); Cardiology and Health Services Research, Denver Veterans Affairs Medical Center, Denver, Colo (Dr Rumsfeld); Health Research and Policy, Stanford University School of Medicine, Stanford, Calif (Dr Hlatky); Research Institute, California Pacific Medical Center, San Francisco (Dr Browner); Department of Epidemiology and Biostatistics, University of California, San Francisco (Drs Browner and Whooley)

Abstract

Context—Little is known regarding the extent to which patient-reported health status, including symptom burden, physical limitation, and quality of life, is determined by psychosocial vs physiological factors among patients with chronic disease.

Objective—To compare the contributions of depressive symptoms and measures of cardiac function to the health status of patients with coronary artery disease.

Design, Setting, and Participants—Cross-sectional study of 1024 adults with stable coronary artery disease recruited from outpatient clinics in the San Francisco Bay Area between September 2000 and December 2002.

Main Measures—Measurement of depressive symptoms using the Patient Health Questionnaire (PHQ); assessment of cardiac function by measuring left ventricular ejection fraction on echocardiography, exercise capacity on treadmill testing, and ischemia on stress echocardiography; and measurement of a range of health status outcomes, including symptom burden, physical limitation, and quality of life, using the Seattle Angina Questionnaire. Participants were also asked to rate their overall health as excellent, very good, good, fair, or poor.

Results—Of the 1024 participants, 201 (20%) had depressive symptoms (PHQ score ≥10). Participants with depressive symptoms were more likely than those without depressive symptoms to report at least mild symptom burden (60% vs 33%; $P<.001$), mild physical limitation (73% vs 40%; $P<.001$), mildly diminished quality of life (67% vs 31%; $P<.001$), and fair or poor overall health (66% vs 30%; $P<.001$). In multivariate analyses adjusting for measures of cardiac function and other patient characteristics, depressive symptoms were strongly associated with greater symptom burden

Corresponding Author and Reprints: Mary A. Whooley, MD, Veterans Affairs Medical Center (111A1), 4150 Clement St, San Francisco, CA 94121 (whooley@itsa.ucsf.edu).

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Acquisition of data: Whooley.
Analysis and interpretation of data: Ruo, Rumsfeld, Hlatky, Liu, Browner, Whooley.
Drafting of the manuscript: Ruo, Rumsfeld, Liu, Whooley.
Critical revision of the manuscript for important intellectual content: Rumsfeld, Hlatky, Browner, Whooley.
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Study supervision: Whooley.

(odds ratio [OR], 1.8; 95% confidence interval [CI], 1.3-2.7; *P*=.002), greater physical limitation (OR, 3.1; 95% CI, 2.1-4.6; *P*<.001), worse quality of life (OR, 3.1; 95% CI, 2.2-4.6; *P*<.001), and worse overall health (OR, 2.0; 95% CI, 1.3-2.9; *P*<.001). Although decreased exercise capacity was associated with worse health status, left ventricular ejection fraction and ischemia were not.

Conclusions—Among patients with coronary disease, depressive symptoms are strongly associated with patient-reported health status, including symptom burden, physical limitation, quality of life, and overall health. Conversely, 2 traditional measures of cardiac function—ejection fraction and ischemia—are not. Efforts to improve health status should include assessment and treatment of depressive symptoms.

A primary goal of therapy for patients with chronic disease is to improve their health status, including symptoms, functional status, and quality of life. In patients with coronary disease, cardiovascular interventions are known to improve health status,[1-4] but the extent to which such benefits result from changes in cardiac vs noncardiac factors is unclear. Most studies have found only limited associations between cardiac function and health status measures,[5-9] suggesting that other factors may be as important as cardiac function in determining the health status of patients with heart disease.

Depressive symptoms are known to be associated with worse health status among patients with coronary artery disease,[10-12] but their relative contributions compared with physiologic measures of disease severity are unknown.[13] To examine the relative influence of depressive symptoms and cardiac function on health status, we measured depressive symptoms, cardiac function (including left ventricular ejection fraction, exercise capacity, and ischemia), and a range of health status outcomes among 1024 patients with coronary artery disease. We hypothesized that depressive symptoms would be more strongly associated with health status than measures of cardiac function.

Methods

Participants

The Heart and Soul Study is a prospective cohort study of psychosocial factors and health outcomes in patients with coronary disease. We used administrative databases to identify outpatients with documented coronary artery disease at 2 Department of Veterans Affairs Medical Centers (San Francisco Veterans Affairs Medical Center and the Veterans Affairs Palo Alto Health Care System, California), 1 university medical center (University of California, San Francisco), and 9 public health clinics in the Community Health Network of San Francisco. Patients were eligible to participate if they had at least 1 of the following: a history of myocardial infarction, angiographic evidence of at least 50% stenosis in 1 or more coronary vessels, prior evidence of exercise-induced ischemia by treadmill or nuclear testing, a history of coronary revascularization, or a diagnosis of coronary artery disease by an internist or cardiologist.

A total of 15438 eligible patients were mailed an invitation to participate, and 2495 responded that they would be interested. Of the 2495 patients whom we attempted to contact by telephone to schedule a study appointment, 505 could not be reached and 596 declined to participate. An additional 370 patients were excluded because they had a history of myocardial infarction in the prior 6 months, deemed themselves unable to walk 1 block, or were planning to move out of the local area within 3 years.

Between September 2000 and December 2002, a total of 1024 participants enrolled, including 549 (54%) with a history of myocardial infarction, 237 (23%) with a history of revascularization but not myocardial infarction, and 238 (23%) with a diagnosis of coronary disease that was documented by their physician (based on a positive angiogram or treadmill

test in >98% of cases). Participants completed a daylong baseline study appointment that included a medical history interview, a physical examination, an exercise treadmill test with a stress echocardiogram, and a comprehensive health status questionnaire.

This protocol was approved by the following institutional review boards: the Committee on Human Research at the University of California, San Francisco; the Research and Development Committee at the San Francisco Veterans Affairs Medical Center; the Medical Human Subjects Committee at Stanford University; the Human Subjects Committee at the Veterans Affairs Palo Alto Health Care System; and the Data Governance Board of the Community Health Network of San Francisco. All participants provided written informed consent.

Outcome Variable: Health Status

Based on the model initially described by Wilson and Cleary,[13] and later modified for patients with coronary disease,[14,15] we used the Seattle Angina Questionnaire to assess 3 components of health status: symptom burden (2-item angina frequency scale), functional status (9-item physical limitation scale), and disease-specific quality of life (3-item disease perception scale).[16,17] As a measure of generic health status, we also asked participants, "Compared with other people your age, how would you rate your overall health?"[18,19] Participants chose from responses of "poor," "fair," "good," "very good," or "excellent."

For each subscale of the Seattle Angina Questionnaire, responses were scored from 0 to 100, with higher scores indicating better health status (ie, less symptom burden, less physical limitation, and better quality of life). Although Seattle Angina Questionnaire scale scores are continuous, they can be grouped for clinical interpretability. A priori, we divided the symptom burden scores into categories reflecting daily (0-30), weekly (31-60), monthly (61-90), or absent (91-100) angina; the physical limitation scores into severe (0-24), moderate (25-49), mild (50-74), or minimal (75-100) physical limitation; and the quality-of-life scores into severely diminished (0-24), moderately diminished (25-49), mildly diminished (50-74), or good to excellent (75-100) quality of life.[14]

Predictor Variables

Depressive Symptoms—Our primary predictor variable was depressive symptoms as measured by the 9-item Patient Health Questionnaire (PHQ).[20] For the primary analysis, we categorized participants as depressed if they scored 10 or greater on the PHQ, representing the minimum number of symptoms required for a diagnosis of major depression.[21] To examine the association between a range of depressive symptoms and health status, we further divided participants into categories representing no to minimal depressive symptoms (score 0-3), mild to moderate depressive symptoms (score 4-9), and symptoms consistent with major depression (score ≥10). Participants who were found to have high levels of depressive symptoms were informed that they may be depressed, instructed to discuss these symptoms with their primary care physician, and provided a list of local resources available for further evaluation and treatment.

Cardiac Function—We assessed cardiac function using a resting echocardiogram for measurement of left ventricular ejection fraction, an exercise treadmill test for measurement of exercise capacity, and a stress echocardiogram for assessment of ischemia. We performed a symptom-limited, graded exercise treadmill test according to a standard Bruce protocol. Peak exercise capacity was defined as total number of metabolic equivalent tasks (METs) achieved, including 3 categories defined a priori as low (<5 METs), medium (5-7 METs), and high (>7 METs) exercise capacity. Continuous, 12-lead electrocardiographic monitoring was performed throughout exercise.

Imaging and pulse wave Doppler echocardiography were performed using an Acuson Sequoia Ultrasound System (Mountain View, Calif) with a 3.5-MHz transducer. A complete resting 2-dimensional echocardiogram was performed just before exercise. Standard 2-dimensional parasternal short-axis and apical 2-chamber and 4-chamber views obtained during held inspiration were planimetered to determine left ventricular ejection fraction. At peak exercise, apical 2-chamber, 4-chamber, and precordial long-axis and short-axis views were obtained to detect the development of right or left ventricular dilatation or wall motion abnormalities during exercise.

To account for both fixed and exercise-induced wall motion defects, we calculated the wall motion score index at peak exercise as our measure of ischemia.[22] Each of 16 wall segments in the left ventricle was scored based on the contractility visualized at peak exercise (1=normal, 2=hypokinetic, 3=akinetic, 4=dyskinetic, 5=aneurysm). The wall motion score index was defined as the sum of wall motion scores divided by the number of segments visualized,[22] with a normally contracting left ventricle receiving a wall motion score index of 1 (16/16=1) and higher wall motion scores indicating worse contractility. We also measured inducible ischemia as a dichotomous variable, defined as the presence of exercise-induced electrocardiographic changes or new echocardiographic wall motion abnormalities at peak exercise.

Potential Confounding Variables—Age, ethnicity, education, income, marital status, medical history, smoking, and alcohol use were determined by questionnaire. Participants were instructed to bring their medication bottles to the study appointment, and study personnel recorded all current medications, including use of β-blockers, 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors (statins), renin-angiotensin system inhibitors, and antidepressant medications (selective serotinin reuptake inhibitors, tricyclics, or other antidepressants).

We measured stress using the 4-item Perceived Stress Scale[23] and considered participants to have stress if they scored 9 or greater on the 16-point scale, corresponding to experiencing at least 1 stressful symptom “fairly often.” We assessed social support by asking participants, “Do you have as much contact as you would like with someone you feel close to, someone in whom you can trust and confide (yes/no)?”[24] Body mass index was calculated as weight in kilograms divided by the square of height in meters.

Statistical Analysis

The goal of this study was to examine the contributions of depressive symptoms and cardiac function to patient-reported health status. Differences in characteristics between participants with and without depressive symptoms (PHQ score ≥10) were compared using *t* tests (or nonparametric equivalent) for continuous variables and χ^2 tests (or Fisher exact test if <5 expected observations in any cell) for dichotomous variables. We also compared the unadjusted frequency of health status outcomes among participants with and without depressive symptoms using a χ^2 test for trend.

To further evaluate the association between independent variables (depressive symptoms and cardiac function) and outcome variables (symptom burden, physical limitation, disease-specific quality of life, and overall health), we used multivariate ordinal logistic regression, a method that allows the outcome variable to have more than 2 categories. Ordinal logistic regression calculates a single odds ratio (OR) for the association between a predictor variable (eg, presence of depressive symptoms) and each combination of higher risk vs lower risk outcome categories (eg, severe physical limitation vs other categories; severe or moderate physical limitation vs other categories; severe, moderate, or mild physical limitation vs no physical limitation).

For the multivariate analyses, we entered all variables from Table 1 into forward stepwise ordinal logistic regression models ($P<.20$ for inclusion in the models) with each of the 4 health status measures as outcomes. Depressive symptoms and the 3 measures of cardiac function (left ventricular ejection fraction, exercise capacity, and wall motion score index) were forced into these models as predictor variables. Continuous variables were entered per SD change. We also examined the association of depressed left ventricular ejection fraction and inducible ischemia (entered as dichotomous variables) with health status outcomes. In all regression models, we tested for interactions between sex and exercise capacity, depressive symptoms and category of inclusion criteria, and depressive symptoms and measures of cardiac function. The proportional odds assumption was verified for all models. Results are reported as ORs with 95% confidence intervals (CIs). Analyses were performed using SAS version 8 (SAS Institute, Inc, Cary, NC).

Results

Patient Characteristics

Of the 1024 participants, 201 (20%) had depressive symptoms (PHQ score ≥10). Compared with participants who did not have depressive symptoms, those with depressive symptoms were younger, had lower income, and were less likely to be male or married (Table 1). They were more likely to have a history of myocardial infarction or diabetes mellitus, to smoke, and to report greater stress and worse social support. Participants with depressive symptoms had higher body mass index and lower exercise capacity.

Depressive Symptoms and Health Status

We observed a dose-response relationship between depression score and all 4 measures of health status (Figure 1, Figure 2). Participants with depressive symptoms (PHQ score ≥10) were more likely than those without depressive symptoms to report at least mild symptom burden (60% vs 33%; $P<.001$), mild physical limitation (73% vs 40%; $P<.001$), and mildly diminished quality of life (67% vs 31%; $P<.001$). They were also more likely to report fair or poor overall health (66% vs 30%; $P<.001$) (Table 2).

In analyses adjusted for measures of cardiac function and other patient characteristics, depressive symptoms were independently associated with all 4 measures of health status (Table 3). Even after further adjustment for the presence of angina symptoms, depressive symptoms remained strongly associated with worse physical limitation (OR, 2.9; 95% CI, 2.0-4.3; $P<.001$), worse quality of life (OR, 2.8; 95% CI, 1.9-4.1; $P<.001$), and worse overall health (OR, 1.7; 95% CI, 1.2-2.6; $P=.006$).

When entered as a continuous variable in the multivariate models, each SD (5.5-point) increase in depression score was associated with greater symptom burden (OR, 1.5; 95% CI, 1.3-1.7; $P<.001$), worse physical limitation (OR, 2.1; 95% CI, 1.8-2.4; $P<.001$), worse quality of life (OR, 1.9; 95% CI, 1.6-2.2; $P<.001$), and worse overall health (OR, 1.6; 95% CI, 1.4-1.9; $P<.001$).

We did not observe any interaction between depressive symptoms and category of inclusion criteria (all P values for interaction >.20). Depressive symptoms were strongly associated with worse health status in all 3 diagnostic subgroups (history of myocardial infarction, history of revascularization but not myocardial infarction, and diagnosis of coronary disease documented by a physician). Likewise, there were no interactions between depressive symptoms and measures of cardiac function in any of the 4 health status models (all P values for interaction >.20). In particular, we observed similar associations between depression score and worse health status in all 3 strata of exercise capacity (Figure 2).

Cardiac Function and Health Status

We observed no interaction between sex and exercise capacity in any of the health status models (all *P* values for interaction >.70). In adjusted models, decreased exercise capacity by treadmill testing was associated with greater symptom burden, greater physical limitation, worse quality of life, and worse overall health (Table 3). However, resting left ventricular ejection fraction and wall motion score index were not associated with any of the 4 health status measures.

Overall, 12% of participants had a depressed left ventricular ejection fraction (≤50%), and 33% of participants had inducible ischemia (defined as the presence of exercise-induced electrocardiographic changes or new echocardiographic wall motion abnormalities at peak exercise). When entered as a dichotomous variable, depressed left ventricular ejection fraction was not associated with symptom burden (OR, 1.1; 95% CI, 0.7-1.7; *P*=.67), physical limitation (OR, 1.1; 95% CI, 0.7-1.7; *P*=.66), diminished quality of life (OR, 1.2; 95% CI, 0.8-1.9; *P*=.34), or worse overall health (OR, 1.3; 95% CI, 0.9-2.0; *P*=.16). Likewise, the presence of inducible ischemia was not associated with symptom burden (OR, 1.1; 95% CI, 0.8-1.5; *P*=.57), physical limitation (OR, 1.0; 95% CI, 0.8-1.4; *P*=.82), diminished quality of life (OR, 0.9; 95% CI, 0.7-1.2; *P*=.48), or worse overall health (OR, 1.1; 95% CI, 0.9-1.5; *P*=.32).

Comment

Among patients with coronary disease, we found that depressive symptoms were strongly associated with health status outcomes, including symptom burden, physical limitation, quality of life, and overall health. In contrast, 2 physiological measures of disease severity—left ventricular ejection fraction and ischemia—were not. Exercise capacity by treadmill testing was also predictive of health status outcomes, but depressive symptoms remained associated with health status in all strata of exercise capacity. Although the causal pathways between depressive symptoms and health status outcomes cannot be determined by this cross-sectional study and are almost certainly bidirectional, our results suggest that depressive symptoms are an important factor in the perceived health status of patients with coronary disease.

We found that depressive symptoms were associated with overall and disease-specific health status, independent of cardiac function. Indeed, depressive symptoms were as strongly associated with disease-specific health status as was exercise capacity, one of the primary variables used to validate the Seattle Angina Questionnaire.[17] Previous studies have demonstrated an association between depressive symptoms and health status outcomes in patients with coronary disease,[10,25-28] but these studies did not measure severity of cardiac disease simultaneously. Other studies have found that symptoms of anxiety and depression lead to poor health status, independent of the degree of angiographic stenosis, but these studies did not assess cardiac function by measuring exercise capacity, ejection fraction, or ischemia.[11,28,29]

Our results suggest that efforts to improve the health status of cardiac patients should include assessment and treatment of depressive symptoms. Treatment of depression leads to improvements in health status,[30,31] and improved health status is associated with better health outcomes.[14,32-36] Some antidepressant therapies, such as selective serotonin reuptake inhibitors, may even improve cardiovascular outcomes among patients with coronary disease.[37,38] Health care professionals can easily identify depression by administering 2 simple screening questions (“During the past month, have you often been bothered by feeling down, depressed, or hopeless?” and “During the past month, have you often been bothered by having little interest or pleasure in doing things?”) and a brief follow-up interview if one of the questions is answered affirmatively.[39,40] For maximal benefit, detection and treatment of depression should be combined with patient-support programs, such as frequent nursing follow-up and close monitoring of adherence to therapy.[41,42]

Our findings demonstrate that depressive symptoms are at least as important as cardiac function in the health-related quality of life of patients with coronary disease. Indeed, “low-tech” measures of health, including depressive symptoms and exercise capacity, were more strongly associated with health status outcomes than “high-tech” measures of cardiac disease severity, including ejection fraction and ischemia. These results are consistent with a large body of literature demonstrating poor correlation between “high-tech” physiological measures and health-related quality of life in patients with other chronic diseases such as asthma,[43] chronic obstructive pulmonary disease,[44,45] peptic ulcer disease,[46] diabetes,[47] prostate hypertrophy,[48] and musculoskeletal disorders.[49,50]

Health status measures are increasingly used to assess the benefits of the rapies in clinical trials.[51] Since many cardiac interventions can alter both physiology and mood,[2,52] it is plausible that some quality-of-life improvements found in these trials may be due to noncardiac factors. Our results suggest that studies measuring quality-of-life outcomes should attempt to determine whether changes are due to cardiac or to noncardiac factors.

If improvements in depressive symptoms are responsible for changes in quality of life, then future efforts to enhance the health status of cardiac patients could focus on modifying depressive symptoms.[30] Such efforts would have substantial implications for care in patients with coronary disease, where the traditional focus has been on cardiac physiology and psychosocial factors such as depression are often overlooked.[53,54]

Several limitations must be considered in interpreting our results. First, we chose to focus on depressive symptoms and coronary disease because they are the most common chronic mental and physical disorders and the 2 leading causes of disability in the world.[55] However, only 7% of eligible patients actually enrolled in the study, and the majority of participants were men, so our results may not generalize to other groups of patients. Second, our study population was recruited based on the presence of coronary disease and did not require a diagnosis of heart failure. Thus, the prevalence of systolic dysfunction was low (12%). However, the prevalence of other cardiac conditions was relatively high in our sample, including a history of myocardial infarction in over half of the participants, a history of revascularization in over half of the participants, inducible ischemia in a third of the participants, and a wide range of exercise capacity. Thus, we believe our sample represents an appropriate population in which to examine the contributions of depressive symptoms and cardiac function to health status.

Third, since the PHQ does not assess duration or recurrence of depressive symptoms, we were not able to explore potential differences in the association between depressive symptoms and health status by duration of depression or number of recurrences. Finally, our cross-sectional design precludes determination of the direction of causality between depressive symptoms and health status. However, since health status is by definition a subjective internal experience, a cross-sectional measurement of its association with psychological and cardiac function provides insight that would not be achieved by assessing health status at a subsequent time point when the patient's physiologic or psychological state could have changed.

Conclusion

In summary, we found that depressive symptoms, a modifiable risk factor, are strongly associated with symptom burden, physical function, disease-specific quality of life, and perceived overall health among patients with coronary disease. In contrast, 2 traditional measures of disease severity—ejection fraction and ischemia—were not associated with health status outcomes. Future efforts to improve the health status of patients with coronary artery disease should include a focus on depressive symptoms.

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References

1. Coronary Artery Surgery Study (CASS): a randomized trial of coronary artery bypass surgery: quality of life in patients randomly assigned to treatment groups. Circulation 1983;68:951–960. [PubMed: 6137293]
2. Croog SH, Levine S, Testa MA, et al. The effects of antihypertensive therapy on the quality of life. N Engl J Med 1986;314:1657–1664. [PubMed: 3520318]
3. Hlatky MA, Rogers WJ, Johnstone I, et al. Medical care costs and quality of life after randomization to coronary angioplasty or coronary bypass surgery: Bypass Angioplasty Revascularization Investigation (BARI) Investigators. N Engl J Med 1997;336:92–99. [PubMed: 8988886]
4. Pilote L, Lauzon C, Huynh T, et al. Quality of life after acute myocardial infarction among patients treated at sites with and without on-site availability of angiography. Arch Intern Med 2002;162:553–559. [PubMed: 11871923]
5. Sjoland H, Wiklund I, Caidahl K, Albertsson P, Herlitz J. Relationship between quality of life and exercise test findings after coronary artery bypass surgery. Int J Cardiol 1995;51:221–232. [PubMed: 8586471]
6. Wiklund I, Comerford MB, Dimenas E. The relationship between exercise tolerance and quality of life in angina pectoris. Clin Cardiol 1991;14:204–208. [PubMed: 1672842]
7. Nelson CL, Herndon JE, Mark DB, Pryor DB, Califf RM, Hlatky MA. Relation of clinical and angiographic factors to functional capacity as measured by the Duke Activity Status Index. Am J Cardiol 1991;68:973–975. [PubMed: 1927964]
8. Gorkin L, Follick MJ, Geltman E, et al. Quality of life among patients post-myocardial infarction at baseline in the Survival and Ventricular Enlargement (SAVE) trial. Qual Life Res 1994;3:111–119. [PubMed: 8044157]
9. Mattera JA, De Leon CM, Wackers FJ, Williams CS, Wang Y, Krumholz HM. Association of patients' perception of health status and exercise electrocardiogram, myocardial perfusion imaging, and ventricular function measures. Am Heart J 2000;140:409–418. [PubMed: 10966538]
10. Spertus JA, McDonell M, Woodman CL, Fihn SD. Association between depression and worse disease-specific functional status in outpatients with coronary artery disease. Am Heart J 2000;140:105–110. [PubMed: 10874270]
11. Sullivan MD, LaCroix AZ, Spertus JA, Hecht J. Five-year prospective study of the effects of anxiety and depression in patients with coronary artery disease. Am J Cardiol 2000;86:1135–1138. A1136–A1139. [PubMed: 11074214]
12. Spitzer RL, Kroenke K, Linzer M, et al. Health-related quality of life in primary care patients with mental disorders: results from the PRIME-MD 1000 Study. JAMA 1995;274:1511–1517. [PubMed: 7474219]
13. Wilson IB, Cleary PD. Linking clinical variables with health-related quality of life: a conceptual model of patient outcomes. JAMA 1995;273:59–65. [PubMed: 7996652]
14. Spertus JA, Jones P, McDonell M, Fan V, Fihn SD. Health status predicts long-term outcome in outpatients with coronary disease. Circulation 2002;106:43–49. [PubMed: 12093768]
15. Rumsfeld JS. Health status and clinical practice: when will they meet? Circulation 2002;106:5–7. [PubMed: 12093759]
16. Spertus JA, Winder JA, Dewhurst TA, Deyo RA, Fihn SD. Monitoring the quality of life in patients with coronary artery disease. Am J Cardiol 1994;74:1240–1244. [PubMed: 7977097]

17. Spertus JA, Winder JA, Dewhurst TA, et al. Development and evaluation of the Seattle Angina Questionnaire: a new functional status measure for coronary artery disease. J Am Coll Cardiol 1995;25:333–341. [PubMed: 7829785]
18. Cunny KA, Perri MD. Single-item vs multiple-item measures of health-related quality of life. Psychol Rep 1991;69:127–130. [PubMed: 1961779]
19. Guyatt G, Feeny D, Patrick D. Issues in quality-of-life measurement in clinical trials. Control Clin Trials 1991;12:81S–90S. [PubMed: 1663862]
20. Spitzer RL, Kroenke K, Williams JBW, Patient Health Questionnaire Primary Care Study Group. Validation and utility of a self-report version of PRIME-MD: the PHQ Primary Care Study. JAMA 1999;282:1737–1744. [PubMed: 10568646]
21. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. Washington, DC: American Psychiatric Association; 1994.
22. Schiller NB, Shah PM, Crawford M, et al. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. American Society of Echocardiography Committee on Standards, Subcommittee on Quantitation of Two-Dimensional Echocardiograms. J Am Soc Echocardiogr 1989;2:358–367. [PubMed: 2698218]
23. Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. J Health Soc Behav 1983;24:385–396. [PubMed: 6668417]
24. Williams RB, Barefoot JC, Califf RM, et al. Prognostic importance of social and economic resources among medically treated patients with angiographically documented coronary artery disease. JAMA 1992;267:520–524. [PubMed: 1729574]published erratum appears inJAMA 1992;268:2652.
25. Watson D, Pennebaker JW. Health complaints, stress, and distress: exploring the central role of negative affectivity. Psychol Rev 1989;96:234–254. [PubMed: 2710874]
26. Rumsfeld JS, Magid DJ, Plomondon ME, et al. Predictors of quality of life following acute coronary syndromes. Am J Cardiol 2001;88:781–784. [PubMed: 11589849]
27. Rumsfeld JS. History of depression, angina, and quality of life following acute coronary syndromes. Am Heart J 2003;145:493–499. [PubMed: 12660673]
28. Sullivan MD, LaCroix AZ, Russo JE, Walker EA. Depression and self-reported physical health in patients with coronary disease: mediating and moderating factors. Psychosom Med 2001;63:248–256. [PubMed: 11292272]
29. Sullivan MD, LaCroix AZ, Baum C, Grothaus LC, Katon WJ. Functional status in coronary artery disease: a one-year prospective study of the role of anxiety and depression. Am J Med 1997;103:348–356. [PubMed: 9375701]
30. Miller MD, Schulz R, Paradis C, et al. Changes in perceived health status of depressed elderly patients treated until remission. Am J Psychiatry 1996;153:1350–1352. [PubMed: 8831449]
31. Cossette S, Frasure-Smith N, Lesperance F. Clinical implications of a reduction in psychological distress on cardiac prognosis in patients participating in a psychosocial intervention program. Psychosom Med 2001;63:257–266. [PubMed: 11292273]
32. Mossey JM, Shapiro E. Self-rated health: a predictor of mortality among the elderly. Am J Public Health 1982;72:800–808. [PubMed: 7091475]
33. Kaplan GA, Camacho T. Perceived health and mortality: a nine-year follow-up of the human population laboratory cohort. Am J Epidemiol 1983;117:292–304. [PubMed: 6829557]
34. Idler EL, Kasl SV, Lemke JH. Self-evaluated health and mortality among the elderly in New Haven, Connecticut, and Iowa and Washington counties, Iowa, 1982-1986. Am J Epidemiol 1990;131:91–103. [PubMed: 2293757]
35. Idler EL, Angel RJ. Self-rated health and mortality in the NHANES-I Epidemiologic Follow-up Study. Am J Public Health 1990;80:446–452. [PubMed: 2316767]
36. Rumsfeld JS, MaWhinney S, McCarthy M Jr, et al. Health-related quality of life as a predictor of mortality following coronary artery bypass graft surgery. JAMA 1999;281:1298–1303. [PubMed: 10208145]
37. Sauer WH, Berlin JA, Kimmel SE. Selective serotonin reuptake inhibitors and myocardial infarction. Circulation 2001;104:1894–1898. [PubMed: 11602490]
38. Glassman AH, O'Connor CM, Califf RM, et al. Sertraline treatment of major depression in patients with acute MI or unstable angina. JAMA 2002;288:701–709. [PubMed: 12169073]

39. Whooley MA, Avins AL, Miranda J, Browner WS. Case-finding instruments for depression: two questions are as good as many. J Gen Intern Med 1997;12:439–445. [PubMed: 9229283]
40. Whooley MA, Simon GE. Managing depression in medical outpatients. N Engl J Med 2000;343:1942–1950. [PubMed: 11136266]
41. Wells KB, Sherbourne CD, Schoenbaum M, et al. Impact of disseminating quality improvement programs for depression in managed primary care: a randomized controlled trial. JAMA 2000;283:212–220. [PubMed: 10634337]
42. Pignone MP, Gaynes BN, Rushton JL, et al. Screening for depression in adults: a summary of the evidence for the US Preventive Services Task Force. Ann Intern Med 2002;136:765–776. [PubMed: 12020146]
43. Burdon JG, Juniper EF, Killian KJ, Hargreave FE, Campbell EJ. The perception of breathlessness in asthma. Am Rev Respir Dis 1982;126:825–828. [PubMed: 7149447]
44. Alonso J, Permanyer-Miralda G, Cascant P, Brotons C, Prieto L, Soler-Soler J. Measuring functional status of chronic coronary patients: reliability, validity and responsiveness to clinical change of the reduced version of the Duke Activity Status Index (DASI). Eur Heart J 1997;18:414–419. [PubMed: 9076377]
45. Mahler DA, Weinberg DH, Wells CK, Feinstein AR. The measurement of dyspnea: contents, interobserver agreement, and physiologic correlates of two new clinical indexes. Chest 1984;85:751–758. [PubMed: 6723384]
46. Peterson WL, Sturdevant RA, Frankl HD, et al. Healing of duodenal ulcer with an antacid regimen. N Engl J Med 1977;297:341–345. [PubMed: 876324]
47. Nerenz DR, Repasky DP, Whitehouse FW, Kahkonen DM. Ongoing assessment of health status in patients with diabetes mellitus. Med Care 1992;30(5 suppl):MS112–MS124. [PubMed: 1583926]
48. Frimodt-Moller PC, Jensen KM, Iversen P, Madsen PO, Bruskewitz RC. Analysis of presenting symptoms in prostatism. J Urol 1984;132:272–276. [PubMed: 6204066]
49. Dwosh IL, Giles AR, Ford PM, Pater JL, Anastassiades TP. Plasmapheresis therapy in rheumatoid arthritis: a controlled, double-blind, crossover trial. N Engl J Med 1983;308:1124–1129. [PubMed: 6339939]
50. Wiesel SW, Tsourmas N, Feffer HL, Citrin CM, Patronas N. A study of computer-assisted tomography, I: the incidence of positive CAT scans in an asymptomatic group of patients. Spine 1984;9:549–551. [PubMed: 6495024]
51. Wenger NK, Mattson ME, Furberg CD, Elinson J. Assessment of quality of life in clinical trials of cardiovascular therapies. Am J Cardiol 1984;54:908–913. [PubMed: 6333175]
52. Newman MF, Kirchner JL, Phillips-Bute B, et al. Longitudinal assessment of neurocognitive function after coronary-artery bypass surgery. N Engl J Med 2001;344:395–402. [PubMed: 11172175]
53. Rozanski A, Blumenthal JA, Kaplan J. Impact of psychological factors on the pathogenesis of cardiovascular disease and implications for therapy. Circulation 1999;99:2192–2217. [PubMed: 10217662]
54. Ziegelstein RC. Depression in patients recovering from a myocardial infarction. JAMA 2001;286:1621–1627. [PubMed: 11585486]
55. Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990-2020: Global Burden of Disease Study. Lancet 1997;349:1498–1504. [PubMed: 9167458]

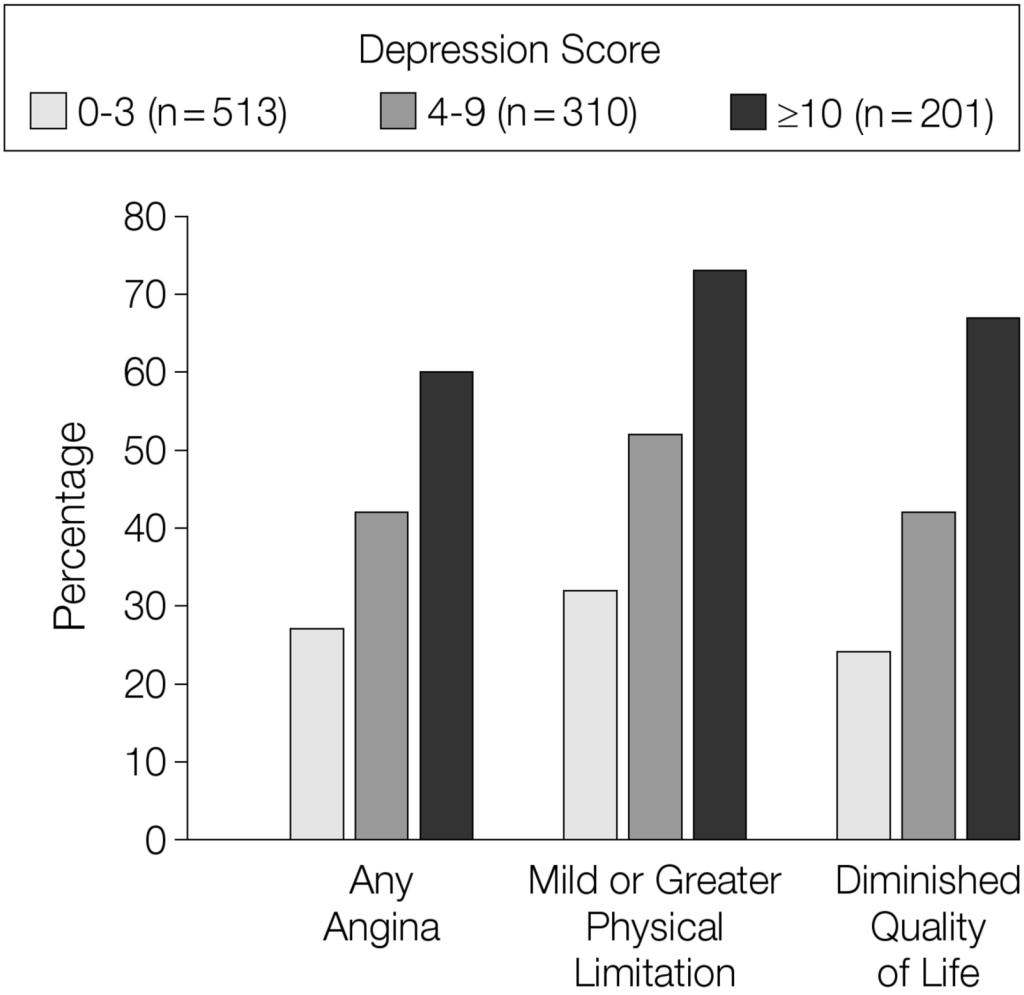

Figure 1.
Proportion of Participants With Poor Health Status, Stratified by Depression Score
Of the 513 patients with a depression score between 0 and 3,27% have angina. All *P* values for trend <.001.

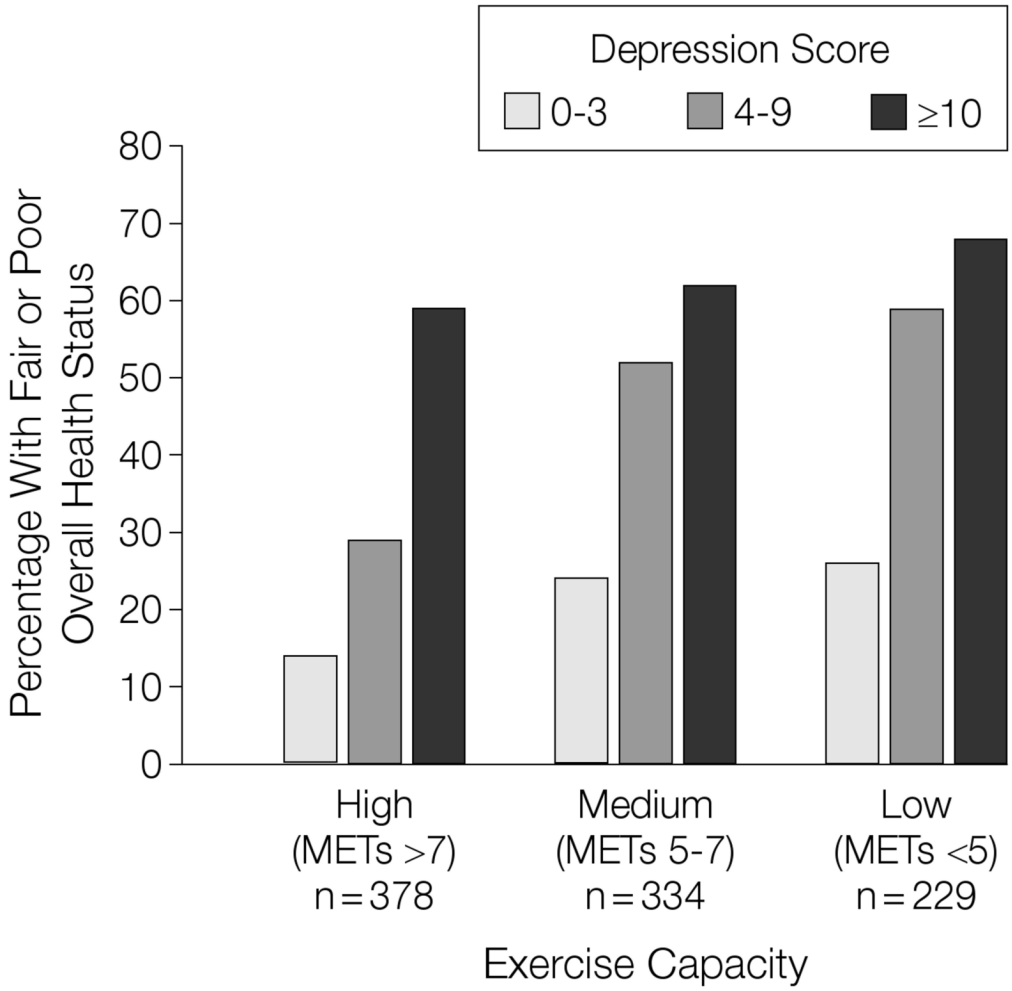

Figure 2.
Proportion of Participants With Fair or Poor Overall Health, Stratified by Exercise Capacity and Depression Score
All *P* values for trend <.001. METs indicates metabolic equivalent tasks. About 70 patients could not complete the treadmill test, so values do not sum to 1024.

Table 1

Characteristics of 1024 Participants With Coronary Artery Disease, Divided by the Presence of Depressive Symptoms*

Variables	With Depressive Symptoms (n = 201)†	Without Depressive Symptoms (n = 823)	*P* Value
Demographic			
Age, mean (SD), y	62 (12)	68 (10)	<.001
Male	154 (77)	686 (83)	.02
White	111 (55)	505 (61)	.12
High school graduate	168 (84)	724 (88)	.10
Annual income <$20 000	130 (65)	371 (45)	<.001
Married	66 (33)	370 (45)	.002
Medical history			
Hypertension	152 (76)	573 (70)	.07
Myocardial infarction	124 (62)	426 (52)	.008
Coronary revascularization	110 (55)	493 (60)	.23
Stroke	33 (16)	115 (14)	.35
Diabetes mellitus	68 (34)	198 (24)	.004
Medication use			
β-Blocker	120 (60)	475 (58)	.59
Statin	113 (56)	545 (66)	.009
Renin-angiotensin system inhibitor	104 (52)	421 (51)	.88
Aspirin	152 (76)	642 (78)	.52
Antidepressant	76 (38)	113 (14)	<.001
Other characteristics			
Regular alcohol use	57 (29)	238 (29)	.91
Current smoking	68 (34)	134 (16)	<.001
Perceived stress	86 (43)	64 (8)	<.001
Poor social support	113 (56)	218 (26)	<.001
Body mass index, mean (SD)‡	29.2 (5.6)	28.2 (5.2)	.02
Cardiac function			
Resting left ventricular ejection fraction, %, mean (SD)	61 (10)	62 (10)	.06
Wall motion score index at peak exercise, mean (SD)	1.21 (0.41)	1.16 (0.34)	.15
Exercise capacity, METs, mean (SD)	6.5 (3.2)	7.5 (3.3)	<.001

Abbreviation: METs, metabolic equivalent tasks.

*Data are expressed as number (percentage) unless otherwise indicated.

†Patient Health Questionnaire score of 10 or higher.

‡Body mass index calculated as weight in kilograms divided by the square of height in meters.

Table 2

Univariate Associations Between Depressive Symptoms and Measures of Health Status in 1024 Participants With Coronary Artery Disease

Health Status (N)	With Depressive Symptoms, No. (%) (n = 201)*	Without Depressive Symptoms, No. (%) (n = 823)	*P* Value
Symptom burden			
No angina (633)	80 (40)	553 (67)	
Monthly angina (278)	75 (37)	203 (25)	
Weekly angina (102)	41 (20)	61 (7)	
Daily angina (11)	5 (3)	6 (1)	
Physical function			<.001

Health Status (N)	With Depressive Symptoms, No. (%) (n = 201)*	Without Depressive Symptoms, No. (%) (n = 823)	*P* Value
Minimal or no limitation (517)	50 (27)	467 (60)	
Mild limitation (272)	55 (29)	217 (28)	
Moderate limitation (146)	65 (35)	81 (11)	
Severe limitation (25)	17 (9)	8 (1)	
Quality of life			<.001

Health Status (N)	With Depressive Symptoms, No. (%) (n = 201)*	Without Depressive Symptoms, No. (%) (n = 823)	*P* Value
Good to excellent (636)	66 (33)	570 (69)	
Mildly diminished (245)	58 (29)	187 (23)	
Moderately diminished (103)	46 (23)	57 (7)	
Severely diminished (38)	31 (15)	7 (1)	
Overall health			<.001

Health Status (N)	With Depressive Symptoms, No. (%) (n = 201)*	Without Depressive Symptoms, No. (%) (n = 823)	*P* Value
Excellent (75)	5 (3)	70 (8)	
Very good (218)	14 (7)	204 (25)	
Good (355)	49 (24)	306 (37)	
Fair or poor (376)	133 (66)	243 (30)	<.001

*Patient Health Questionnaire score of 10 or higher.

Table 3

Multivariate Associations of Depressive Symptoms, Cardiac Function, and Health Status in Participants With Coronary Artery Disease

	Greater Symptom Burden (n = 921)		Greater Physical Limitation (n = 867)		Worse Quality of Life (n = 926)		Worse Overall Health (n = 920)	
	OR (95% CI)*†	*P* Value	OR (95% CI)*‡	*P* Value	OR (95% CI)*§	*P* Value	OR (95% CI)*//	*P* Value
Exercise capacity (per 3.3-MET decrease)	1.3 (1.1-1.5)	.003	2.4 (2.0-2.9)	<.001	1.5 (1.3-1.8)	<.001	1.7 (1.5-2.0)	<.001
Depressive symptoms¶	1.8 (1.3-2.7)	.002	3.1 (2.1-4.6)	<.001	3.1 (2.2-4.6)	<.001	2.0 (1.3-2.9)	<.001
Left ventricular ejection fraction (per 10% decrease)	1.0 (0.8-1.2)	.86	1.0 (0.8-1.2)	.96	1.0 (0.9-1.2)	.79	1.0 (0.9-1.2)	>.99
Wall motion score index (per 0.35-point increase)	1.0 (0.8-1.2)	.80	1.1 (0.9-1.3)	.48	1.0 (0.9-1.2)	.74	1.1 (1.0-1.3)	.15

Abbreviations: CI, confidence interval; MET, metabolic equivalent task; OR, odds ratio.

*Odds ratio from ordinal logistic regression, representing the independent association between the predictor variable (eg, presence of depressive symptoms) and each combination of higher risk vs lower risk outcome categories (eg, severe symptom burden vs other categories; severe or moderate symptom burden vs other categories; severe, moderate, or mild symptom burden vs no symptom burden).

†The other variables associated with greater symptom burden at the $P<.05$ level were being married, current smoking, and poor social support.

‡The other variables associated with worse physical limitation at the $P<.05$ level were female sex, income less than $20 000, being married, higher body mass index, history of hypertension, myocardial infarction, stroke, current smoking, antidepressant use, and perceived stress.

§The other variables associated with worse quality of life at the $P<.05$ level were younger age, nonwhite race, being married, β-blocker use, statin nonuse, current smoking, perceived stress, and poor social support.

//The other variables associated with worse overall health at the $P<.05$ level were younger age, income less than $20 000, being married, history of hypertension, diabetes, statin use, nonuse of regular alcohol, current smoking, and perceived stress.

¶Patient Health Questionnaire score of 10 or higher.