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Relation Between Depressive Symptoms and Treadmill Exercise Capacity in the Heart and Soul Study

Bernice Ruo, MD, John S. Rumsfeld, MD, PhD, Sharon Pipkin, MPH, and Mary A. Whooley, MD

From the Section of General Internal Medicine, VA Medical Center, and the Departments of Medicine and Epidemiology and Biostatistics, University of California, San Francisco, California; Cardiology and Health Services Research, Denver Veterans Affairs Medical Center, Denver, Colorado; and Department of Medicine, Northwestern University, Chicago, Illinois.

Abstract

To examine the association between depressive symptoms and exercise capacity, we performed a cross-sectional study of 944 outpatients with stable coronary artery disease and found that the presence of depressive symptoms was independently associated with poor exercise capacity (<5 MET tasks achieved; adjusted odds ratio 1.8, 95% confidence interval 1.1 to 2.7, $p = 0.01$). Depressive symptoms should be considered in the differential diagnosis of poor exercise capacity.

Our goal in this study was to examine the relation between depressive symptoms and treadmill exercise capacity in 944 patients with stable coronary artery disease (CAD). We hypothesized that depressive symptoms would be associated with poor exercise capacity independent of other clinical factors and measures of cardiac disease severity.

The Heart and Soul Study is a prospective cohort study of psychosocial factors and health outcomes in patients with CAD. Methods have been described previously.¹ In brief, we used administrative databases to identify outpatients with stable CAD at 2 Department of Veterans Affairs Medical Centers, 1 university medical center, and 9 public health clinics in San Francisco. Between September 2000 and December 2002, 1,024 participants completed a baseline study appointment that included a medical history interview, a physical examination, and a comprehensive health status questionnaire. Of these, 80 were not able to perform the exercise treadmill test, leaving 944 participants for analysis. This protocol was approved by the appropriate institutional review boards, and all participants provided written, informed consent.

Each participant underwent a symptom-limited, graded exercise treadmill test according to a standard Bruce protocol. To achieve maximum heart rate, participants who were unable to continue the standard Bruce protocol (for orthopedic or other reasons) were switched to slower settings on the treadmill and encouraged to exercise for as long as possible. Maximum exercise capacity was calculated as the total number of METs achieved. Beforehand, we categorized participants into those with poor (<5 METs) and normal (≥ 5 METs) exercise capacity.² To calculate percent maximum heart rate achieved, the maximum heart rate achieved was divided by $(220 - \text{age})$.

Our primary predictor variable was depressive symptoms as measured by the 9-item Patient Health Questionnaire (PHQ). The PHQ is a self-administered validated questionnaire with a sensitivity of 88% and a specificity of 88% for major depressive disorders using a cutpoint of ≥ 10 .³ For the primary analysis, we categorized participants as depressed if they scored ≥ 10 on the PHQ, representing the minimum number of symptoms required for a diagnosis of major depression.⁴ To examine the association between a range of depressive symptoms and exercise capacity, we further divided participants into categories representing no to minimal depressive symptoms (score 0 to 3), mild to moderate depressive symptoms (score 4 to 9), and symptoms consistent with major depression (≥ 10).

We assessed cardiac function using 3 measures: a self-report measure of angina frequency, an echocardiogram at rest for assessment of left ventricular ejection fraction, and a stress echocardiogram for evaluation of ischemia. To assess angina frequency, we asked participants: "Over the past 4 weeks, on average, how many times have you had chest pain, chest tightness, or angina?" Participants chose from the following responses: none, < 1 time/week, 1 to 2 times/week, ≥ 3 times/week but not every day, 1 to 3 times/day, or ≥ 4 times/day.⁵ We classified participants as having no angina (none) versus any angina (all other responses).

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

To account for fixed and exercise-induced wall motion defects, we calculated the wall motion score index at peak exercise as our measure of ischemia. 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,⁶ with a normally contracting left ventricle receiving a wall motion score index of 1 ($16/16 = 1$) and higher scores indicating worse contractility.

Age, ethnicity, education, income, marital status, medical history, smoking history, 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. Body mass index was calculated as weight in kilograms divided by the square of height in meters.

The goal of this study was to examine the association between depressive symptoms and treadmill exercise capacity, an objective measure of functional status. Differences in characteristics between participants with poor exercise capacity (METs < 5) and those with normal exercise capacity (METs ≥ 5) were compared using *t* tests (or nonparametric equivalent) for continuous variables and chi-square tests for dichotomous variables. We compared the unadjusted association between categories of depressive symptoms and poor exercise capacity by using a chi-square test for trend. We used analysis of covariance to compare mean exercise capacity in participants with and without depressive symptoms and adjusted for potential confounding variables.

To further evaluate the association between depressive symptoms and exercise capacity, we used multivariable logistic regression. For the multivariable analyses, we entered all variables listed in Table 1 into a backward elimination logistic regression model (with $p < 0.10$ for retention in the model). We tested for interactions of depressive symptoms with angina, ejection

fraction, and ischemia. Results are reported as odds ratios with 95% confidence intervals. Analyses were performed with SAS 8 (SAS Institute, Inc., Cary, North Carolina).

Characteristics of participants are presented in Table 1. Of the 944 participants, 172 (18%) had depressive symptoms (PHQ score ≥ 10), and 229 (24%) had poor exercise capacity (METs < 5). Participants with depressive symptoms were more likely than those without depressive symptoms to have poor exercise treadmill capacity. The proportion of participants with poor exercise capacity ranged from 21% in those with no or minimal depressive symptoms (PHQ score 0 to 3) to 34% in those with a depression score ≥ 10 (Figure 1). In analyses adjusted for measures of cardiac function and other patient characteristics, the presence of depressive symptoms remained independently associated with worse exercise capacity (Table 2). Each SD (5.4 points) increase in depression score was associated with a 20% increased odds of poor exercise capacity (adjusted odds ratio 1.2, 95% confidence interval 1.0 to 1.5, $p = 0.02$).

When examining exercise capacity as a continuous variable, participants with depressive symptoms had significantly lower mean exercise capacity than did those who were not depressed (6.5 ± 3.2 METs vs 7.5 ± 3.3 METs; $p < 0.001$). This difference persisted after adjustment for ejection fraction, age, ethnicity, income, body mass index, stroke, diabetes, β -blocker use, statin use, and current smoking (6.6 vs 7.5 METs; $p < 0.001$).

In adjusted models, decreased left ventricular ejection fraction was associated with worse exercise capacity, but angina and ischemia were not associated with exercise capacity. Even when ischemia was entered as dichotomous variable (presence or absence of inducible wall motion abnormalities), it was not associated with poor exercise capacity (adjusted odds ratio 0.8, 95% confidence interval 0.6 to 1.2, $p = 0.24$).

Depressed participants achieved lower mean percent maximum heart rate than did participants without depressive symptoms (78 ± 16 vs 86 ± 15 ; $p < 0.0001$), and adjusting for percent maximum heart rate achieved appeared to eliminate the association between depressive symptoms and poor exercise capacity (odds ratio 1.3, 95% confidence interval 0.8 to 2.1, $p = 0.25$). We did not observe any significant interactions between depressive symptoms and ejection fraction, ischemia, percent maximum heart rate achieved, or angina (all p values for interaction > 0.20).

The goal of this study was to evaluate the relation between depressive symptoms and exercise capacity among outpatients with CAD. We found that depressive symptoms were present in 18% of participants and were associated with reduced treadmill exercise capacity. This finding persisted even after adjustment for patient characteristics and measures of CAD severity, including angina frequency, left ventricular ejection fraction, and myocardial ischemia by stress echocardiography. Further adjustment for percent maximum heart rate achieved appeared to eliminate this association, suggesting that the association between depressive symptoms and poor exercise capacity may be due in part to motivational factors.

The results of this study suggest that depression should be considered in the differential diagnosis of reduced exercise capacity in patients with CAD. Reduced exercise capacity is associated with worse cardiac outcomes and increased mortality,² and the identification of poor exercise capacity has implications for further cardiac testing and therapeutic interventions. In addition to other conditions related to exercise tolerance, such as age, cardiac function, comorbid medical conditions, and physical fitness,⁷ it is important to consider depressive symptoms as a modifiable factor associated with poor exercise capacity in patients with CAD.

The results of this study also suggest that efforts to improve exercise capacity among patients with CAD should include assessment and treatment of depressive symptoms. Increasing

functional status is an important goal for long-term management of CAD,^{8,9} and, in patients with CAD, improvement in depression score is a strong predictor of improvements in functional status.^{10,11} Increased functional status can diminish indirect costs related to lost productivity, which far exceed direct medical costs in patients with CAD.¹² In addition, treatment of depression improves quality of life,^{13,14} and improved quality of life is associated with better health outcomes.^{15–17} Some antidepressant therapies, such as selective serotonin reuptake inhibitors, may even improve cardiovascular outcomes of patients with CAD.^{18–20}

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References

1. Ruo B, Rumsfeld JS, Hlatky MA, Liu H, Browner WS, Whooley MA. Depressive symptoms and health-related quality of life: the Heart and Soul Study. *JAMA* 2003;290:215–221. [PubMed: 12851276]
2. Myers J, Prakash M, Froelicher V, Do D, Partington S, Atwood JE. Exercise capacity and mortality among men referred for exercise testing. *N Engl J Med* 2002;346:793–801. [PubMed: 11893790]
3. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med* 2001;16:606–613. [PubMed: 11556941]
4. Diagnostic and Statistical Manual of Mental Disorders. Vol. 4th. Washington, DC: American Psychiatric Association; 1994.
5. Spertus JA, Winder JA, Dewhurst TA, Deyo RA, Prodzinski J, McDonnell M, Fihn SD. Development and evaluation of the Seattle Angina Questionnaire: a functional status measure for coronary artery disease. *J Am Coll Cardiol* 1995;25:333–341. [PubMed: 7829785]
6. Schiller NB, Shah PM, Crawford M, DeMaria A, Devereux R, Feigenbaum H, Gutgesell H, Reichek N, Sahn D, Schnittger I. 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]
7. Gibbons RJ, Balady GJ, Bricker JT, Chaitman BR, Fletcher GF, Froelicher VF, Mark DB, McCallister BD, Mooss AN, O'Reilly MG, et al. ACC/AHA 2002 guideline update for exercise testing: summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1997 Exercise Testing Guidelines). *Circulation* 2002;106:1883–1892. [PubMed: 12356646]
8. Inouye SK, Peduzzi PN, Robison JT, Hughes JS, Horwitz RJ, Concato J. Importance of functional measures in predicting mortality among older hospitalized patients. *JAMA* 1998;279:1187–1193. [PubMed: 9555758]
9. Gardner SC, Grunwald GK, Rumsfeld JS, Mackenzie T, Gao D, Perlin JB, McDonald G, Shroyer ALG. Risk factors for intermediate-term survival after coronary artery bypass grafting. *Ann Thorac Surg* 2001;72:2033–2037. [PubMed: 11789789]
10. Ades PA, Maloney A, Savage P, Carhart RL Jr. Determinants of physical functioning in coronary patients: response to cardiac rehabilitation. *Arch Intern Med* 1999;159:2357–2360. [PubMed: 10547176]
11. Kempen GI, Sullivan M, van Sonderen E, Ormel J. Performance-based and self-reported physical functioning in low-functioning older persons: congruence of change and the impact of depressive symptoms. *J Gerontol B Psychol Sci Soc Sci* 1999;54:380–386.

12. Haelan WR, Parsons PE, Thomas JW, Murt HA, Lepkowski JM, Guire KE. Health care utilization and costs of adult cardiovascular conditions. *Natl Med Care Util Expend Surv C* 1987;7:1–69.
13. Miller MD, Schulz R, Paradis C, Houck PR, Mazumdar S, Frank E, Dew MA, Reynolds CF III. Changes in perceived health status of depressed elderly patients treated until remission. *Am J Psychiatry* 1996;153:1350–1352. [PubMed: 8831449]
14. 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]
15. Rumsfeld JS, MaWhinney S, McCarthy M Jr, Shroyer AL, VillaNueva CB, O'Brien M, Moritz TE, Henderson WG, Grover FL, Sethi GK, Hammermeister KE. Health-related quality of life as a predictor of mortality following coronary artery bypass graft surgery. Participants of the Department of Veterans Affairs Cooperative Study Group on Processes, Structures, and Outcomes of Care in Cardiac Surgery. *JAMA* 1999;281:1298–1303. [PubMed: 10208145]
16. 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]
17. 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]
18. Sauer WH, Berlin JA, Kimmel SE. Selective serotonin reuptake inhibitors and myocardial infarction. *Circulation* 2001;104:1894–1898. [PubMed: 11602490]
19. Serebruany VL, Glassman AH, Malinin AI, Nemeroff CB, Musselman DL, van Zyl LT, Finkel MS, Krishnan KR, Gaffney M, Harrison W, et al. Sertraline AntiDepressant Heart Attack Randomized Trial Study Group. Platelet/endothelial biomarkers in depressed patients treated with the selective serotonin reuptake inhibitor sertraline after acute coronary events: the Sertraline AntiDepressant Heart Attack Randomized Trial (SADHART) Platelet Substudy. *Circulation* 2003;108:939–944. [PubMed: 12912814]
20. Glassman AH, O'Connor CM, Califf RM, Swedberg K, Schwartz P, Bigger JT Jr, Krishnan KR, van Zyl LT, Swenson JR, Finkel MS, et al. Sertraline Antidepressant Heart Attack Randomized Trial (SADHART) Group. Sertraline treatment of major depression in patients with acute MI or unstable angina. *JAMA* 2002;288:701–709. [PubMed: 12169073]

Figure 1. Proportion of participants with poor exercise capacity (METs < 5) stratified by depression score (p for trend < 0.001)

Table 1

Characteristics of 944 Participants With Coronary Artery Disease Grouped by Exercise Capacity

Variables	Poor Exercise Capacity (METs <5) (n = 229)	Normal Exercise Capacity (METs ≥5) (n = 715)	p Value
Demographic			
Age (yrs)	71 ± 11	65 ± 10	<0.001
Men	183 (80%)	602 (84%)	0.17
White	150 (66%)	424 (59%)	0.10
High school graduate	189 (83%)	637 (89%)	<0.01
Annual income <\$20,000	149 (65%)	295 (41%)	<0.001
Married	75 (33%)	330 (46%)	<0.001
Medical history			
Hypertension	178 (78%)	483 (68%)	<0.01
Myocardial infarction	121 (54%)	380 (53%)	0.90
Coronary revascularization	119 (52%)	447 (63%)	0.005
Stroke	48 (21%)	80 (11%)	<0.001
Diabetes mellitus	76 (33%)	160 (22%)	<0.01
Chronic pulmonary disease	47 (21%)	100 (14%)	0.02
Medication use			
β Blocker	139 (61%)	411 (57%)	0.39
Statin	127 (55%)	488 (68%)	<0.001
Renin-angiotensin inhibitor	135 (59%)	349 (49%)	<0.01
Aspirin	169 (74%)	572 (80%)	0.05
Antidepressant	48 (21%)	127 (18%)	0.28
Other characteristics			
Regular alcohol use	59 (26%)	218 (31%)	0.15
Current smoking	52 (23%)	132 (19%)	0.16
Depressive symptoms score	5.9 ± 6.7	4.7 ± 5.0	<0.01
Body mass index (kg/m ²)	29 ± 6	28 ± 5	<0.01
Cardiac function			
Current angina (any vs none)	88 (38%)	248 (35%)	0.30
Ejection fraction (%)	60 ± 10	62 ± 9	0.02
Wall motion score index	1.2 ± 0.3	1.2 ± 0.3	0.07

Mean ± SD or number of subjects (%).

Table 2

Factors Associated With Poor Exercise Capacity in Participants With Coronary Artery Disease

Variable	Adjusted OR (95% CI) [†] (n = 931)	p Value
Depressive symptoms*	1.8 (1.1–2.7)	0.01
Ejection fraction (/10% decrease)	1.3 (1.1–1.5)	0.01
Age (/10-yr increase)	2.7 (2.2–3.3)	<0.0001
White	1.5 (1.0–2.1)	0.04
Income <\$20,000	3.4 (2.4–4.9)	<0.0001
Body mass index (/5-kg/m ² increase)	1.5 (1.3–1.8)	<0.0001
History of stroke	1.9 (1.2–2.9)	<0.01
Diabetes mellitus	2.1 (1.4–3.0)	<0.001
β-Blocker use	1.4 (1.0–2.0)	0.08
Statin use	0.4 (0.3–0.6)	<0.0001
Current smoker	2.4 (1.5–3.9)	<0.001

* PHQ score ≥10.

[†] All variables from Table 1 were entered into a backward elimination model. Those variables associated with poor exercise capacity (METs <5 at p <0.1) were retained in the final model.

CI = confidence interval; OR = odds ratio.