Screening for Depression in Patients With Coronary Heart Disease (Data from the Heart and Soul Study)

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Major depression is associated with adverse outcomes in patients who have coronary heart disease. How best to identify depression in busy cardiology practices is unknown. We compared the test characteristics of 4 depression screening instruments with an interview diagnosis of depression (Diagnostic Interview Schedule) in 1,024 outpatients who had coronary heart disease. Screening instruments were the 10-item Center for Epidemiologic Studies Depression Scale-10, the Patient Health Questionnaire-9, the Patient Health Questionnaire-2, and a simple 2-item instrument that asks (1) "During the past month, have you often been bothered by feeling down, depressed, or hopeless?" and (2) "During the past month, have you often been bothered by little interest or pleasure in doing things?" Of the 1,024 participants, 224 (22%) had major depression based on the Diagnostic Interview Schedule. Areas under the receiver-operating characteristic curves were similar for all instruments (range 0.84 to 0.87). In conclusion, a positive response to 1 of the 2 items was 90% sensitive and 69% specific for depression, with a negative likelihood ratio of 0.14. Thus, negative responses to the 2 items effectively ruled out depression. A score ≥10 on the Patient Health Questionnaire-9 was 54% sensitive and 90% specific, with a positive likelihood ratio of 5.4. Thus, a cutpoint ≥10 was virtually diagnostic for depression. **(Am J Cardiol 2005;96:1076–1081)**

Major depression is a common condition in patients who have coronary heart disease (CHD), with a prevalence of 20% to 30%.[1,2] Depression is associated with poor health-related quality of life and adverse cardiovascular outcomes in patients who have CHD.[3,4] However, it is not known how best to detect depression in busy cardiology practices. We evaluated the test characteristics of 4 depression screening instruments compared with a diagnostic interview for depression in a sample of 1,024 adults who had stable CHD and were enrolled in the Heart and Soul Study.

Methods

Study participants: The Heart and Soul Study is a prospective cohort study of psychosocial factors and health outcomes in patients who have CHD. Methods have been previously described.[3] In brief, administrative databases were used to identify outpatients who had documented coronary artery disease at 2 Department of Veterans Affairs medical centers (Veterans Affairs Medical Center, San Francisco and the Veterans Affairs Palo Alto Health Care System, Palo Alto, California), 1 university medical center (University of California, San Francisco), and 9 public health clinics in San Francisco. Patients were eligible to participate in the study if they had ≥1 of the following characteristics: history of myocardial infarction, angiographic evidence of ≥50% stenosis in ≥1 coronary vessel, previous evidence of exercise-induced ischemia by treadmill or nuclear testing, history of coronary revascularization, or a diagnosis of coronary artery disease by an internist or cardiologist.

A total of 15,438 eligible patients was mailed an invitation to participate, and 2,495 responded that they would be interested. Of the 2,495 patients, 505 could not be reached and 596 declined participation. An additional 370 patients were excluded because they had a history of myocardial infarction in the previous 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, 1,024 participants enrolled. Participants completed a daylong study appointment that included a medical interview, physical examination, an exercise treadmill test with a stress echocardiogram, and a comprehensive questionnaire that included 4 depression screening instruments. The study was approved by the appropriate institutional review boards, and all participants provided written informed consent.

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Depression screening instruments: We evaluated the test characteristics of 4 screening instruments for depression. We administered a 10-item short form of the Center for Epidemiologic Studies Depression Scale (CES-D), a self-report instrument that assesses the number and duration of depressive symptoms. Use of this 10-item version of the CES-D has been well validated.[5,6] Although the 20-item version of the CES-D uses a standard cutpoint of ≥16 for mild to moderate depression or ≥27 for severe depression, the standard cutpoint for the 10-item CES-D is ≥10 (range 0 to 30).[6]

We also administered the Patient Health Questionnaire-9 (PHQ-9), a 9-item tool that was designed for primary care providers to aid in the diagnosis of depression.[7] The PHQ-9 has been validated as a depression screening tool.[8] Each item asks about 1 of the 9 symptoms of depression according to the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*, and patients choose 1 of 4 responses to indicate how often they experience each symptom during the previous 2 weeks (not at all, several days, more than half the days, or nearly everyday). We used the standard cutpoint of ≥10 to identify depression (range 0 to 27).[8]

We also administered the PHQ-2, a 2-item subscale of the PHQ-9 that has been shown to have test characteristics similar to those of the PHQ-9 in general populations.[9] The PHQ-2 asks, "Over the last 2 weeks, how often have you been bothered by (1) little interest or pleasure in doing things" or (2) "feeling down depressed, or hopeless." For each of the 2 items, participants choose from among the 4 responses listed above. We used the standard PHQ-2 cutpoint of ≥3 to identify depression (range 0 to 6).[9]

We administered an even more simplified screen that asks 2 simple yes/no items: (1) "During the past month, have you often been bothered by feeling down, depressed, or hopeless?" and (2) "During the past month, have you often been bothered by little interest or pleasure in doing things?" A yes answer to 1 of these 2 items was considered a positive screening test result (range 0 to 2).[10,11]

Criterion standard: The National Institute of Mental Health Diagnostic Interview Schedule is a highly structured interview that is designed to be administered by lay interviewers to yield psychiatric diagnoses according to criteria of the *Diagnostic and Statistical Manual of Mental Disorders*.[12] We used the computerized version of the Diagnostic Interview Schedule as the criterion standard to assess the presence of major depression in the previous month. The Diagnostic Interview Schedule has been used extensively to study the epidemiology of depression,[13] and the use of the computerized version has been well validated.[14]

Other measurements: Self-reported age, gender, race, income, education, marital status, smoking status, social support, and New York Heart Association functional classification were determined by questionnaire. Participants were instructed to bring their medications to the study appointment. Exact medication names and dosing, including antidepressant medications, were recorded by study personnel. Alcohol use was measured by use of the Alcohol Use Disorders Identification Test of Alcohol Consumption questionnaire, and a score ≥4 was used to define regular alcohol use.[15] We assessed use of illicit drugs by asking participants: "Have you ever used illicit drugs?" Those who answered "Yes, during the last year" (vs "Yes, but not in the last year" or "No") were considered illicit drug users. Substance use was defined as regular alcohol use or illicit drug use in the previous year. A complete 2-dimensional echocardiogram at rest including all standard

Table 1
Characteristics of 1,024 participants with coronary heart disease

Characteristic	No. (%)
Age (yrs)*	67 ± 11
Men	839 (82%)
Race/ethnicity	
Non-Hispanic White	615 (60%)
Hispanic White	89 (9%)
African-American	169 (16%)
Asian	118 (12%)
Other	33 (3%)
High school education	891 (87%)
Annual income (dollars)	
<20,000	499 (49%)
20,000–29,999	138 (14%)
30,000–39,999	95 (9%)
40,000–50,000	98 (10%)
>50,000	188 (18%)
Marital status	
Married or permanent partnership	434 (43%)
Divorced	239 (23%)
Single (never married)	193 (19%)
Widowed	119 (12%)
Other	36 (4%)
Medical history	
Hypertension	723 (71%)
Myocardial infarction	548 (54%)
Coronary revascularization	604 (59%)
Congestive heart failure	180 (18%)
Stroke	147 (14%)
Diabetes mellitus	266 (26%)
Use of antidepressant medication	188 (18%)
Regular alcohol use	294 (29%)
Current smoking	202 (20%)
Illicit drug use	77 (8%)
NYHA classification	
I	376 (37%)
II	416 (41%)
III	183 (18%)
IV	48 (5%)
Left ventricular ejection fraction ≤50%	117 (11%)
Inducible ischemia	228 (24%)
Poor social support	330 (32%)
Current depression (CDIS)	224 (22%)

* Mean ± SD.

CDIS = computerized version of the Diagnostic Interview Schedule; NYHA = New York Heart Association.

Table 2
Test characteristics of four depression screening instruments in 1,024 participants with coronary heart disease

Screening Instrument	Cutpoint	% Sensitivity (95% CI)	% Specificity (95% CI)	Positive Likelihood Ratio	Negative Likelihood Ratio	Area Under ROC Curve*	95% CI†
CES-D	≥10 vs <10	76 (70–81)	79 (76–82)	3.6	0.30	0.87	0.84–0.89
PHQ-9	≥10 vs <10	54 (47–61)	90 (88–92)	5.4	0.51	0.86	0.84–0.89
PHQ-2	≥3 vs <3	39 (33–46)	92 (90–94)	4.9	0.66	0.84	0.82–0.87
Two items	≥1 vs 0	90 (86–94)	69 (66–73)	2.9	0.14	0.84	0.81–0.86

* Determined by the trapezoidal rule, a nonparametric estimate of the area under the curve. Area under the ROC curve was larger for the CES-D compared with the 2 items ($p = 0.02$) and for the PHQ-9 compared with the 2 items ($p = 0.04$). There was no difference in area under the ROC curve for the PHQ-2 compared with the 2-item instrument ($p = 0.70$).

† The 95% CI for area under the curve was calculated as area ± (1.96 × SE) using DeLong's formula for SE.

CES-D = Center for Epidemiological Studies Depression Scale; 95% CI = exact binomial 95% confidence intervals; ROC = receiver-operating characteristic.

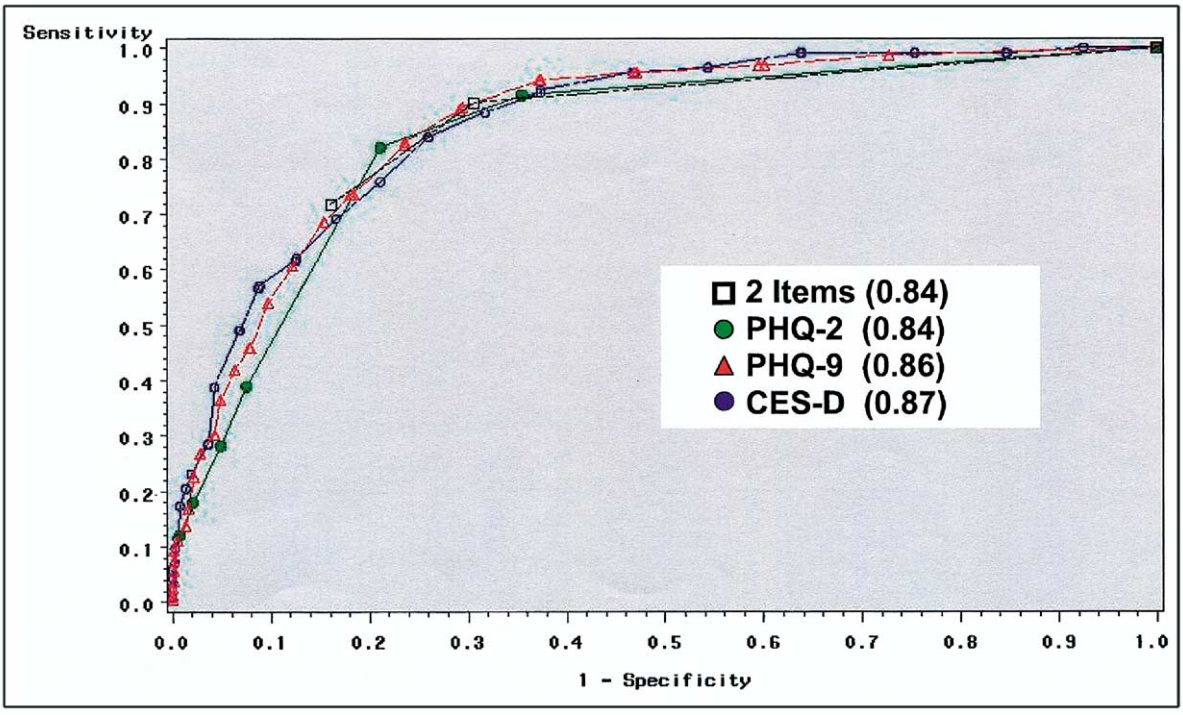

Figure 1. Areas under the receiver-operating characteristic curves for the PHQ-9, PHQ-2, CES-D, and 2-item screening instruments.

views was used to determine left ventricular ejection fraction. An echocardiogram was also obtained immediately after exercise, and inducible ischemia was defined as the presence of ≥1 new wall motion abnormality at peak exercise.

Statistical analysis: We calculated test characteristics for each of the 4 screening instruments compared with a computerized version of the Diagnostic Interview Schedule interview diagnosis of depression (criterion standard). Sensitivity, specificity, likelihood ratios, and positive predictive values were determined by standard formulas.[16] Exact binomial 95% confidence intervals were calculated for sensitivity and specificity. Each screening instrument was then converted to its continuous or ordinal scale and receiver-operating characteristic curves were generated. Areas under the receiver-operating characteristic curves were calculated by the trapezoidal rule, and 95% confidence intervals for the area under these curves were calculated as area ± (1.96 × SE) using DeLong's formula for SEs. We compared areas under the receiver-operating characteristic curves using the method of Hanley and McNeil.[17] We then performed analyses that were stratified by age, gender, history of depression, and substance abuse to further evaluate the test characteristics of the instrument with the highest sensitivity. Analyses were performed using SAS 8 (SAS Institute, Cary, North Carolina).

Results

Our sample of outpatients who had CHD consisted mostly of older men who were a mean age of 67 years (Table 1). Of the 1,024 participants, 224 (22%) had major depression as determined by the criterion standard com-

Table 3
Test characteristics of four depression screening instruments in 690 participants with coronary heart disease*

Screening Instruments	Cutpoint	% Sensitivity (95% CI)	% Specificity (95% CI)	Positive Likelihood Ratio	Negative Likelihood Ratio	Area Under ROC Curve†	95% CI‡
CES-D	≥10 vs <10	77 (69–84)	79 (75–82)	3.7	0.29	0.88	0.85–0.91
PHQ-9	≥10 vs <10	52 (44–61)	90 (88–93)	5.2	0.53	0.87	0.84–0.89
PHQ-2	≥3 vs <3	39 (30–47)	92 (89–94)	4.9	0.66	0.84	0.80–0.87
Two items	≥1 vs 0	91 (85–95)	71 (67–75)	3.1	0.13	0.85	0.81–0.89

* Excluded were 334 participants who had substance abuse (regular alcohol use or illicit drug use during previous year).
† Determined by the trapezoidal rule, a nonparametric estimate of the area under the curve. Area under the ROC curve for the CES-D, PHQ-9, and PHQ-2 were not statistically different from the 2-item test.
‡ The 95% CI for area under the curve was calculated as area ± (1.96 × SE) using DeLong's formula for SE.
Abbreviations as in Table 2.

Table 4
Test characteristic of two-item screening instrument, stratified by clinical variables

Variable	No. of Subjects	Depressed	% Sensitivity (95% CI)	% Specificity (95% CI)	Positive Likelihood Ratio	Negative Likelihood Ratio	Area Under ROC Curve	95% CI
Age (yrs) <65	421	33%	90 (84–94)	65 (59–70)	2.6	0.15	0.81	0.77–0.85
Age (yrs) 65–75	357	16%	91 (81–97)	72 (66–77)	3.3	0.13	0.85	0.80–0.90
Age (yrs) >75	245	11%	88 (70–98)	72 (66–78)	3.1	0.17	0.84	0.76–0.92
History of depression*	352	50%	90 (85–94)	50 (43–58)	1.8	0.20	0.75	0.70–0.80
No history of depression	671	7%	89 (77–96)	75 (71–78)	3.6	0.15	0.86	0.80–0.91
Men	839	19%	87 (81–92)	71 (68–75)	2.9	0.18	0.83	0.79–0.86
Women	184	36%	97 (90–100)	59 (50–68)	2.4	0.05	0.84	0.79–0.89
No substance abuse	689	20%	91 (85–95)	71 (67–75)	3.1	0.13	0.85	0.81–0.88
Substance abuse†	334	26%	88 (79–94)	65 (59–71)	2.5	0.18	0.81	0.77–0.86

* Self-reported history of depression or use of an antidepressant medication.
† Regular alcohol use or illicit drug use during previous year.
Abbreviations as in Table 2.

puterized version of the Diagnostic Interview Schedule. Overall, the screening instruments had sensitivities of 39% to 90% and specificities of 69% to 92% using standard cutpoints (Table 2). Areas under the receiver-operating characteristic curves were similar for all screening tests, with a range of 0.84 to 0.87 (Figure 1). The CES-D and PHQ-9 had larger areas under the receiver-operating characteristic curve than did the simple 2-item test ($p = 0.04$), but there was no difference in area under the receiver-operating characteristic curve between the PHQ-2 and the simple yes/no (2-item) instrument ($p = 0.70$). After excluding participants who demonstrated substance abuse, there were no detectable differences in areas under the receiver-operating characteristic curve across the 4 instruments (Table 3).

The simple 2-item screening test was 90% sensitive with a negative likelihood ratio of 0.14 and a negative predictive value of 0.96 (95% confidence interval 0.94 to 0.98). These values were similar in groups stratified by age, gender, history of depression, and substance abuse (Table 4). In post hoc analyses, we observed similar test characteristics for a PHQ-9 cutpoint ≥4 (94% sensitive, 63% specific), a PHQ-2 cutpoint ≥1 (91% sensitive, 65% specific), and a 10-item CES-D score ≥7 (92% sensitive, 63% specific). The standard cutpoint of ≥10 on the PHQ-9 was 54% sensitive and 90% specific, with a positive likelihood ratio of 5.4.

Discussion

We found that a simple 2-item instrument was an effective tool for identifying major depression in patients who had CHD and had similar test characteristics to 3 other more time-consuming screening instruments for depression. A "no" response to the 2 items made depression highly unlikely, with a negative likelihood ratio of 0.14 and a posterior probability of 4%. Our results suggest that a simple 2-item instrument can be used to screen for depression in a diverse population of patients who have CHD. A negative test result effectively rules out depression so that no further screening is necessary.

Sensitivity should be maximized when choosing a screening instrument for depression so that cases are not missed. We found that the 2-item instrument was 90% sensitive for identifying major depression. However, its low specificity and low positive predictive value mean that less than half of patients who have a positive result on the 2-item screen will ultimately meet criteria for major depression. Thus, any patient who has a positive result on the depression

screen should have a follow-up diagnostic interview to confirm the diagnosis of depression.[18]

A diagnostic interview for depression can be performed quickly and safely by a cardiologist. Major depression is defined by depressed mood or loss of interest in nearly all activities for ≥2 weeks (the 2 symptoms asked in the 2-item instrument), accompanied by ≥3 or 4 of the following symptoms (for a total of 5 symptoms all together): insomnia or hypersomnia, feelings of worthlessness or excessive guilt, fatigue or loss of energy, decreased ability to think or concentrate, change in appetite or weight, psychomotor agitation or retardation, and recurrent thoughts of death or suicide.[18]

If practitioners find that the 2-step process of administering the 2-item screen followed by a diagnostic interview is not feasible, an alternative approach is to administer the PHQ-9 alone. A cutpoint ≥10 on the PHQ-9 is only 54% sensitive, but its 90% specificity and high positive predictive value mean that patients who screen positive need not undergo a follow-up diagnostic interview to confirm the diagnosis of depression. The PHQ-9 is a simple self-report instrument that can be completed in <2 minutes while the patient is in the waiting room or having vital signs measured. Because the PHQ-9 misses 46% of cases, we prefer to use the 2-item instrument and to confirm any positive screening result with a diagnostic interview for depression. However, because of the high prevalence of unrecognized depression in patients who have CHD,[1,2] administering the PHQ-9 allows for identification of >50% of depression cases without the need for further confirmation.

It has been estimated that up to 30% of patients who have stable heart disease also have depression,[1,2] and in our sample, 22% of subjects had major depression by the diagnostic interview. Depression is increasingly recognized as a strong predictor of morbidity and mortality in patients who have CHD.[4] Studies have demonstrated that, although primary providers can provide effective therapy (without referral) for up to 75% of patients who have depression, most cases of depression are unrecognized or inappropriately treated.[19,20] Therapies for depression are safe and effective in patients who have coronary disease. Selective serotonin reuptake inhibitors have been proved safe in patients who have CHD and may even have cardioprotective effects.[21,22] In addition, when referral is necessary, psychosocial interventions can improve psychological functioning[23] and decrease cardiovascular morbidity and mortality in patients who have CHD.[24,25]

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