A Positive 2-Item Patient Health Questionnaire Depression Screen Among Hospitalized Heart Failure Patients is Associated With Elevated 12-Month Mortality

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ABSTRACT

Background: Given the association of depression with poorer cardiac outcomes, an American Heart Association Science Advisory has advocated routine screening of cardiac patients for depression using the 2-item Patient Health Questionnaire (PHQ-2) "at a minimum." However, the prognostic value of the PHQ-2 among HF patients is unknown.

Methods and Results: We screened hospitalized HF patients (ejection fraction [EF] <40%) that staff suspected may be depressed with the PHQ-2, and then determined vital status at up to 12-months follow-up. At baseline, PHQ-2 depression screen−positive patients (PHQ-2+; n = 371), compared with PHQ-2 screen−negative patients (PHQ-2−; n = 100), were younger (65 vs 70 years) and more likely to report New York Heart Association (NYHA) functional class III/IV than class II symptoms (67% vs. 39%) and lower levels of physical and mental health−related quality of life (all $P \leq .002$); they were similar in other characteristics (65% male, 26% mean EF). At 12 months, 20% of PHQ-2+ versus 8% of PHQ-2− patients had died ($P = .007$) and PHQ-2 status remained associated with both all-cause (hazard ratio [HR] 3.1, 95% confidence interval [CI] 1.4−6.7; $P = .003$) and cardiovascular (HR 2.7, 95% CI 1.1−6.6; $P = .03$) mortality even after adjustment for age, gender, EF, NYHA functional class, and a variety of other covariates.

Conclusions: Among hospitalized HF patients, a positive PHQ-2 depression screen is associated with an elevated 12-month mortality risk. (*J Cardiac Fail 2012;18:238−245*)

Key Words: Depression, heart failure, Patient Health Questionnaire, mortality.

Heart failure (HF) is a common and growing health problem that affects more than 5.7 million Americans, with more than 660,000 newly diagnosed cases, 277,000 deaths, and $39 billion in direct and indirect costs yearly.[1] HF is also the leading cause of hospitalization among Medicare patients, and its 5-year mortality rate following first hospitalization exceeds that of all cancers except lung.[2] Moreover, HF remains the only major cardiovascular disease whose mortality rate has been essentially unchanged over the past decade despite recent advances in its therapeutic management.[1]

One potential contributor to these persistently poor outcomes is the presence of unrecognized and inadequately treated depression. Depression is highly prevalent among HF patients,[3,4] and strong evidence has linked it to increased morbidity and mortality,[5−11] higher levels of health

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services utilization,[12] and reduced health-related quality of life (HRQoL) independent of disease severity[9,13,14] and even at subsyndromal elevations of mood symptoms.[8,9]

Several depression screening instruments have been validated for use in cardiac populations and found to have similar psychometric characteristics.[15] Given these similarities, a recent American Heart Association (AHA) Science Advisory has advocated a strategy of increased awareness and screening of coronary heart disease (CHD) patients for depression with the 2-item Patient Health Questionnaire (PHQ-2)[16] "at a minimum," followed by the 9-item PHQ (PHQ-9)[17] to investigate positive screens and provide a severity score that can be used to guide treatment selection and monitoring.[18] Unlike other instruments, the PHQ-2 requires nominal training and time to administer and is therefore feasible for routine use in clinical practice. However, its prognostic value among patients with HF is unknown. We addressed this question as part of a study to inform later development of a trial to examine the impact of screening and treating depression among patients with HF.

Methods

Study Setting

We screened HF patients for depression before hospital discharge at 4 university-affiliated Pittsburgh-area hospitals, implementing a protocol approved by the Institutional Review Board of the University of Pittsburgh before the start of patient enrollment.

Patient Population

We targeted enrollment of 372 PHQ-2+ subjects based on sample-size calculations designed to identify the predictive PHQ-9[17] cutpoint score for determining mortality using receiver operating characteristic (ROC) analyses by New York Heart Association (NYHA) functional class and sex (6 separate analyses) with 80% power, 70%−85% sensitivity, 50% minimum specificity, and 90% confidence.[19] For comparison purposes, we also planned to enroll a convenience sample of 100 PHQ-2− hospitalized HF patients who met all protocol-eligibility criteria.

From December 2007 to April 2009, study nurse-recruiters approached hospital personnel to inquire if they were caring for any patients with HF who had a cardiac ejection fraction (EF) of $<40\%$ and they suspected might be depressed, and if so to ask for the patient's verbal agreement permitting the recruiter to approach. If the patient agreed, our nurse-recruiter explained our study to the patient, reviewed our enrollment criteria, and then obtained the patient's signed informed consent to undergo our screening procedure. We required all patients to: 1) have a documented EF $<40\%$ as determined by echocardiogram, cardiac catheterization, or multiple gated acquisition scan; 2) have NYHA functional class II-IV cardiac symptoms; 3) have no current alcohol dependence or other substance abuse disorder; 4) score ≥ 24 on the Folstein Mini-Mental State Examination[20] to ensure mental capacity to provide informed consent and reliable responses to our assessment instruments; 5) be medically stable and not have another medical condition known to be fatal within 6 months; 6) be discharged home or to short-term rehabilitation; and 7) be English speaking, have no communication barrier, and have a household telephone. Patients prescribed antidepressant pharmacotherapy at baseline were included in our PHQ-2 depression screen−positive cohort if they screened positive on the PHQ-2 and met all other eligibility criteria; they were excluded from our PHQ-2 screen−negative cohort.

Baseline Assessment

The PHQ-2 assesses for the presence of the 2 cardinal symptoms of depression over the past 2 weeks: "little interest or pleasure in doing things" and "feeling down, depressed, or hopeless."[16] We defined a positive PHQ-2 depression screen (PHQ-2+) as patient endorsement of 1 or both of its items, and a negative screen (PHQ-2−) when the patient responded negatively to both of these items. This classification has 90% sensitivity and 69% specificity for the diagnosis of major depression among CHD patients when measured against the gold-standard Diagnostic Interview Schedule.[21]

Before a study subject's hospital discharge, our nurse-recruiters administered the PHQ-9[17] to ascertain the severity of mood symptoms, the SF-12 to assess mental (SF-12 MCS) and physical (SF-12 PCS) HRQoL,[22] and the PRIME-MD Anxiety Module to determine the presence of an anxiety disorder[23] and conducted a chart review to collect baseline sociodemographic and clinical data. After the baseline assessment, the recruiters distributed a National Institute of Mental Health brochure entitled "Depression and Heart Disease"[24] to all screened patients to heighten their awareness of the impact of mood disorders on heart disease. We also encouraged PHQ-2 screen−positive patients via telephone and by mailed letter to contact their primary care physicians (PCPs) to discuss this clinical finding, and we sent a similar letter to their PCPs also encouraging follow-up.

Vital Status

We ascertained vital status via telephone contact with patients and/or their designated secondary contacts (e.g., spouse, adult child). A study physician classified cause of death (cardiovascular or other) through a review of medical records, obituary notices, and/or written summaries of interviews with secondary contacts and discussions with subjects' physicians as necessary.

Statistical Analyses

We compared baseline sociodemographic, diagnostic, symptom severity, functional status, and current treatment for depression by PHQ-2 status with the use of *t*-tests for continuous data and chi-square analyses for categoric data. We used Kaplan-Meier analyses to calculate incidence of all-cause and cardiovascular deaths by PHQ-2 status, with log-rank tests to evaluate these differences for statistical significance and Cox models to adjust for differences in baseline covariates. To control for possible confounders of the relationship between mood symptoms and mortality, we adjusted for several recognized predictors of HF mortality.[25,26] They included the presence of anemia (hemoglobin <10 g/dL), diabetes, hyponatremia (sodium <136 mEq/L), renal insufficinecy (creatinine >1.7 mg/dL), systolic and diastolic blood pressure, use of an angiotensin-converting enzyme inhibitor (ACE-I) or angiotensin receptor blocker (ARB) medication, and use of coumadin. Because antidepressant medication use could affect mortality risk,[27,28] we repeated our multivariate analyses excluding those PHQ-2+ patients using antidepressants at baseline. All analyses were performed with SAS statistical software.