Feasibility and Utility of Screening for Depression and Anxiety Disorders in Patients With Cardiovascular Disease

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Background—Depression and anxiety in patients with cardiac disease are common and independently associated with morbidity and mortality. We aimed to explore the use of a 3-step approach to identify inpatients with cardiac disease with depression, generalized anxiety disorder (GAD), or panic disorder; understand the predictive value of individual screening items in identifying these disorders; and assess the relative prevalence of these disorders in this cohort.

Methods and Results—To identify depression and anxiety disorders in inpatients with cardiac disease as part of a care management trial, an iterative 3-step screening procedure was used. This included a 4-item (Coping Screen) tool in nursing data sets, a 5-item screen for positive Coping Screen patients (Patient Health Questionnaire-2 [PHQ-2], GAD-2, and an item about panic attacks), and a diagnostic evaluation using PHQ-9 and the Primary Care Evaluation of Mental Disorders anxiety disorder modules. Overall, 6210 inpatients received the Coping Screen, 581 completed portions of all 3 evaluation steps, and 210 received a diagnosis (143 depression, 129 GAD, 30 panic disorder). Controlling for age, sex, and the other screening items, PHQ-2 items independently predicted depression (little interest/pleasure: odds ratio [OR]=6.65, P<0.001; depression: OR=5.24, P=0.001), GAD-2 items predicted GAD (anxious: OR=4.09, P=0.003; unable to control worrying: OR=10.46, P<0.001), and the panic item predicted panic disorder (OR=49.61, P<0.001).

Conclusions—GAD was nearly as prevalent as depression in this cohort, and GAD-2 was an effective screening tool; however, panic disorder was rare. These results support the use of 2-step screening for depression and GAD beginning with a 4-item scale (GAD-2 plus PHQ-2).

Clinical Trial Registration—Unique Identifier: NCT01201967. URL: http://www.clinicaltrials.gov/ct2/show/NCT01201967.

Key Words: anxiety ◼ cardiovascular disease ◼ depression ◼ screening

Depression in patients with cardiac disease is highly prevalent and independently associated with adverse cardiovascular consequences that include worse health-related quality of life, impaired functional status, recurrent cardiac events, and higher rates of mortality.1–3 Given these facts, the American Heart Association (AHA) has recommended a 2-step screening process to detect depression among all patients with cardiac disease. This process first uses the 2-item Patient Health Questionnaire-2 (PHQ-2), followed by further assessment with the 9-item PHQ-9 for patients with positive PHQ-2 scores.4,5 These screening recommendations have been controversial, given the burden and questionable impact of screening alone, along with questions of generalizability to real-world clinical settings.6

Anxiety and specific anxiety disorders, such as generalized anxiety disorder (GAD) and panic disorder (PD), are also common and linked to adverse outcomes in patients with cardiovascular disease.7 GAD, in particular, has been linked in some studies to recurrent events and mortality in patients with cardiac disease to an extent similar to that of depression.8 Furthermore, brief screening tools, such as the GAD-2 scale, have been found to be sensitive and specific for a diagnosis of GAD in medical settings.9 Despite these links, systematic screening for anxiety disorders has not been investigated on a large scale in patients with cardiac disease.

Our group previously investigated the feasibility and utility of systematic depression screening on inpatient cardiac units as part of a depression care management trial in this patient population.10 As part of a new care management trial, we initiated a 3-stage screening process for combined depression and anxiety disorder screening that used questions already used in clinical care for prescreening, followed by more formal 2-step screening using validated items.

In this article, we aim to: (1) describe the overall feasibility and utility of this approach to identify inpatients with cardiac disease with depression, GAD, or PD; (2) understand the ability of individual screening items to predict these mood and anxiety disorders in this cohort; and (3) identify the relative prevalence of these 3 disorders among patients hospitalized for heart disease.
WHAT IS KNOWN

- Given the association between depression and poor cardiac outcomes, the American Heart Association has recommended a screening protocol to identify depression in patients with cardiovascular disease. However, despite similar associations between anxiety and cardiac outcomes, no recommendation exists for anxiety screening or combined depression/anxiety screening.

WHAT THE STUDY ADDS

- This is the first article to describe systematic 3-stage screening for anxiety disorders and depression in hospitalized patients with cardiac disease.
- In this cohort, generalized anxiety disorder was nearly as prevalent as depression. Given the links between anxiety and poor cardiac outcomes, this study provides support for systematic screening for generalized anxiety disorder in this population. In contrast, panic disorder was rare.
- The results of this study support the use of a 2-step screening process for depression and generalized anxiety disorder: (1) a 4-item screen for generalized anxiety disorder and depression for initial screening, and (2) the Patient Health Questionnaire-9 and Generalized Anxiety Disorder-7 for diagnostic evaluation as appropriate.

Screening Process

Coping Screen

As part of routine clinical care, all patients admitted to the cardiac units at the Massachusetts General Hospital are asked 4 yes/no questions referred to as the Coping Screen by the admitting nurse to evaluate the presence or absence of fear, depression, anxiety, and irritability. Patients who endorse ≥1 of these symptoms are considered to have a positive Coping Screen; currently, no systematic clinical interventions are in place for patients who have a positive screen.

To facilitate the integration of our study screening process into clinical care, we used this Coping Screen as the initial step to identify patients with our disorders of interest. Members of the study team systematically reviewed admission nursing evaluations on the 2 cardiac inpatient units to determine which patients had a positive Coping Screen.

5-Item Screen

All patients with a positive Coping Screen were then evaluated by a study social work care manager to determine whether they were suffering from clinically significant depression, GAD, or PD via 2 additional steps. First, a 5-item screening tool (here referred to as the 5-item Screen) was developed and used; this tool comprised PHQ-2, GAD-2, and a question about the presence of panic attacks.

PHQ-2, frequently used in patients with cardiac disease and the first step of the AHA-recommended depression screening procedure, inquires about (1) feeling down, depressed, or hopeless; and (2) having little interest or pleasure in doing things in the past 2 weeks. Items were posed as yes/no questions, as in previous screening evaluations. GAD-2 inquires about (1) feeling nervous, anxious, or on edge; and (2) being unable to stop or control worrying in the past 2 weeks. These inquiries were also posed as yes/no questions. GAD-2 was selected because of its brevity and because it was found to be both feasible and effective in identifying GAD in medical settings. Finally, we added the question on panic attacks (“In the last 4 weeks, have you had an anxiety attack—suddenly feeling fear or panic?”) given its successful use in primary care patients via the Depression and Anxiety Detector for primary care patients. A positive screen on the 5-item Screen was defined as an affirmative response to ≥1 of the items.

Diagnostic Evaluation (PHQ-9 and Primary Care Evaluation of Mental Disorders)

Patients with a positive 5-item Screen underwent disorder-specific screening with PHQ-9 and the Primary Care Evaluation of Mental Disorders (PRIME-MD) anxiety modules for GAD and PD to determine whether the patient met criteria for clinical depression or formal Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) criteria for GAD or PD. PHQ-9 consists of the 9 DSM-IV diagnostic criteria for major depressive disorder (MDD), each scored on a scale of 0 to 3 based on the frequency of symptoms (from not at all to nearly every day) for a total score of 0 to 27. For a diagnosis of clinical depression, we required that patients have ≥5 of the 9 symptoms, including either depressed mood or anhedonia, present on more than half the days in the past 2 weeks. This definition was chosen instead of a simple cutoff score to more closely mirror the DSM-IV diagnosis of MDD and to avoid diagnosing depression based only on somatic symptoms. PHQ-9 was chosen to diagnose depression because (1) this scale has been used in nearly all previous collaborative care studies, (2) it is recommended by the AHA, (3) it was efficient and effective in our previous study on these units, and (4) depressive symptoms slightly less than full MDD still seem to adversely impact outcomes in this cohort.

The PRIME-MD anxiety modules for GAD and PD are structured interview assessments that inquire about the presence of symptoms meeting DSM-IV criteria for GAD and PD. In the GAD module, a diagnosis of GAD typically requires feeling nervous, anxious, and on edge; worrying a lot about different things; and suffering from 3 associated symptoms, present for more than half the days, during the past 4 weeks. However, we required such symptoms for 6 months to match DSM-IV criteria and to account for normative anxiety in the setting of medical illness. PD was diagnosed when a patient reported sudden and recurrent
panic attacks, accompanied by ≥4 associated symptoms, and with anxiety about future attacks or their implications, all consistent with DSM-IV criteria. This module has been used in previous GAD/PD studies in primary care patients and was rapid and effective in the diagnosis of these disorders. In all cases, care was taken to ensure that mood and anxiety symptoms met full criteria for the disorder rather than being present for brief periods in the context of an acute medical hospitalization.

Data Collection and Statistical Analysis

For all patients admitted to the cardiac units from September 2010 through August 2012, age, sex, and date of admission were recorded, in addition to the screening data described earlier. Furthermore, if a patient did not continue to a subsequent step of screening (eg, because of patient refusal or discharge), then the reasons for not continuing to the next step were recorded when available. Patients also were not screened further if it was determined that they met 1 of the exclusion criteria for the MOSAIC study.

Statistical analyses were performed using Stata (version 11.0, StataCorp College Station, TX). Descriptive statistics were used to calculate proportions of positive screens at each step, means regarding age and sex, and numbers of patients identified with each disorder. Comparisons of age and sex between those undergoing and not undergoing screening were performed using independent sample t tests and χ² analysis, respectively. Multivariate logistic regression was performed to assess which items on the Coping Screen were associated with a diagnosis of depression, GAD, or PD, independent of one another and age and sex. A similar logistic regression was performed to assess which 5-item Screen items were independently associated with a positive disorder diagnosis. All statistical tests were 2-tailed, and statistical significance was set at P<0.0167 to control for multiple comparisons (ie, for each of the 3 disorders) in both of the statistical analyses.

Figure. Patient flow through screening process. *Not appropriate=did not meet inclusion criteria for study or met an exclusion criterion for study (eg, active psychosis, bipolar disorder). **Medical acuity=medical illness was so severe that it prevented evaluation (eg, intubated). GAD indicates generalized anxiety disorder; MDD, major depressive disorder; and PD, panic disorder.
## Results

### Patients

During the period of observation, 10,115 patients were admitted to the inpatient cardiac units. The majority (n=6,431; 63.6%) of these patients was male, and the average age was 66.8 years (±14.7 years). Admissions were divided relatively evenly between the cardiac step-down unit (n=4,487; 47.9%) and the general inpatient cardiology unit (n=5,268; 52.1%).

Of the patients admitted to the inpatient cardiac units during the study period, 6,210 received the initial Coping Screen, and 581 patients completed portions of all 3 steps of the screening procedure. As in the overall sample, most patients who received the Coping Screen were male (n=3,957; 63.7%), and the average age was 66.5 years (±14.5 years). Of the 3,905 patients with incomplete screening on the Coping Screen, the most common cause was the omission of screening questions during the admission interview (n=2,017; 52% of missed screens). Although most nurses did not indicate on the Coping Screen as to why screening was not performed, a significant portion of these patients (n=1,346; 34% of missed screens) would not have been appropriate for the MOSAIC study (eg, the patients were boarding on the cardiac units but were not patients with cardiac disease, the patients did not speak English). The most common causes for lack of screening with the 5-item Screen included patient ineligibility for the study (n=496; 36%), patient discharge before evaluation (n=424; 31%), and patient refusal (n=212; 15%). The most common cause for lack of depression-screening specific with PHQ-9 was evaluator decision. Our definition of depression required an endorsement of either depressed mood or anhedonia (ie, the 2 depression items on the 5-item Screen, which were identical to the first 2 items of PHQ-9). Therefore, if patients did not endorse either of those 2 items on the 5-item Screen, our evaluator deferred PHQ-9 administration because it would be impossible for those patients to meet our criteria for a diagnosis of depression. There were no significant differences in age or sex between patients who did or did not receive the Coping Screen (age: mean of screened patients=66.5±14.5 years, mean of unscreened patients=67.1±15.1 years, P=0.07; sex: 3,957 [63.7%] of screened patients were male, 2,474 [63.4%] of unscreened patients were male, χ²=0.14, P=0.71).

Admission cardiac diagnoses were well distributed among individuals with a psychiatric diagnosis (17% with myocardial infarction, 26% with unstable angina, 30% with heart failure, and 28% with arrhythmia). Using χ² analysis, we found no significant associations between cardiac and psychiatric diagnoses (depression: χ²=5.11, P=0.16; GAD: χ²=6.84, P=0.08; PD: χ²=6.42, P=0.09).

### Association of Screening Questions With Psychiatric Disorders

See Figure for full details of patient flow through the screening process. A total of 210 patients received a psychiatric diagnosis (143 depression, 129 GAD, 30 PD). This figure represented 30% of patients screened with the 5-item Screen and 36% of those patients who went through disorder-specific screening. The Coping Screen had a positive predictive value (PPV) of 6% for depression, 7% for GAD, and 1% for PD, whereas the 5-item Screen (as a whole) had a PPV of 20% for depression, 18% for GAD, and 4% for PD. When the 5-item Screen was broken down to its component scales (ie, PHQ-2, GAD-2, and panic attack item), the PPV of the scale improved: the PHQ-2 items had a PPV of 32% for depression, GAD-2 items had a PPV of 20% for GAD, and the panic attack item had a PPV of 27% for PD.

On multivariate logistic regression, when controlling for age and sex, endorsement of depressed mood on the Coping Screen was associated with a diagnosis of depression (odds ratio [OR]=2.25, 95% confidence interval [CI], 1.36–3.71; P=0.002; Tables 1 and 2). The remaining Coping Screen items were not associated with any psychiatric diagnoses. In contrast, all items of the 5-item Screen were associated with the diagnosis of a psychiatric disorder. Little interest/pleasure and depressed mood were associated with clinical depression (little interest/pleasure: OR=6.65, 95% CI, 3.78–11.71, P<0.001; depressed mood: OR=5.24, 95% CI, 2.00–13.71, P=0.001; Tables 1 and 3); little interest/pleasure, anxiety, and inability to stop worrying were associated with GAD (little interest/pleasure: OR=2.12, 95% CI, 1.27–3.54, P=0.004; anxiety: OR=4.09, 95% CI, 1.62–10.32, P=0.003; inability to stop worrying: OR=10.46, 95% CI, 5.22–20.96, P<0.001; Tables 1 and 2).

### Table 1. Significant Associations Between Individual Screening Items and Psychiatric Disorders

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Any Disorder</th>
<th>MDD</th>
<th>GAD</th>
<th>PD</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHQ-2 items</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have you felt anxious/nervous?</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have you felt depressed?</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have you felt fearful?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have you felt irritable?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GAD-2 items</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Little interest/pleasure</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Down, depressed, hopeless</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nervous, anxious, on edge</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unable to stop or control worrying</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PD items</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxiety attack</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Findings were considered significant if P<0.0167 (corrected for multiple comparisons). GAD indicates generalized anxiety disorder; MDD, major depressive disorder; and PD, panic disorder.

### Table 2. Multivariate Logistic Regression Assessing Variables From Coping Screen Associated With Clinical Depression

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Odds Ratio</th>
<th>Standard Error</th>
<th>P Value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.99</td>
<td>0.01</td>
<td>0.11</td>
<td>0.97–1.00</td>
</tr>
<tr>
<td>Sex</td>
<td>1.19</td>
<td>0.27</td>
<td>0.44</td>
<td>0.76–1.87</td>
</tr>
<tr>
<td>Have you felt anxious/nervous?</td>
<td>1.32</td>
<td>0.37</td>
<td>0.32</td>
<td>0.76–2.27</td>
</tr>
<tr>
<td>Have you felt depressed?</td>
<td>2.25</td>
<td>0.58</td>
<td>0.002*</td>
<td>1.36–3.71</td>
</tr>
<tr>
<td>Have you felt fearful?</td>
<td>1.13</td>
<td>0.48</td>
<td>0.78</td>
<td>0.49–2.59</td>
</tr>
<tr>
<td>Have you felt irritable?</td>
<td>0.95</td>
<td>0.44</td>
<td>0.91</td>
<td>0.38–2.35</td>
</tr>
</tbody>
</table>

C-statistic=0.6204. CI indicates confidence interval.

*Findings were considered significant if P<0.0167 (corrected for multiple comparisons).
Having experienced an anxiety attack was associated with a diagnosis of PD (anxiety attack: OR=49.61, 95% CI, 13.63–180.53, P<0.001; Tables 1 and 5).

**Discussion**

Although we were able to identify >200 patients with clinical depression, GAD, PD, or their combination, this 3-stage screening process for anxiety and depression was suboptimal. A substantial proportion of patients were discharged before completing all 3 stages of the evaluation, and the initial Coping Screen questions—although appealing because they were already embedded in the nursing initial evaluation—have not been validated and were much less predictive of a disorder than the more structured and studied 5-item Screen questions. In contrast, the items from PHQ-2 and GAD-2, and the PD question, were strongly linked to a subsequent diagnosis of their corresponding disorder.

These findings were mirrored in the PPVs found for the different steps of our screening procedure. The Coping Screen had relatively low PPVs (ranging from 1% to 6%), suggesting that it is a relatively poor screening tool for depression, GAD, and PD in this population. However, compared with other studies, the 5-item Screen performed well, with the PHQ-2 items having a PPV of 32% for MDD, the GAD-2 items having a PPV of 20% for GAD, and the panic attack item having a PPV of 27% for PD. Although to our knowledge there is no published PPV for GAD-2, our PPVs for PHQ-2 and panic attack items were comparable with, or better than, the PPVs previously published in medically ill patients.5,11,22

Of the disorders for which we screened, depression was the most prevalent (20.5% of patients with a positive 5-item Screen), followed closely by GAD (18.5% of patients with a positive 5-item Screen). In contrast, PD was much less common, representing only 4.3% of patients with a positive 5-item Screen. Given the strong association between PHQ-2 screen (as part of the 5-item Screen) and a subsequent depression diagnosis made via PHQ-9, this study seems to confirm the use of the 2-stage screening for depression recommended by the AHA (PHQ-2 and PHQ-9). However, such screening should still only be used when a management protocol is in place for all patients found to have depression. Systematic screening, when linked to a program of depression management, has been associated with improved patient outcomes,16,18,23 but there is no evidence for any benefit associated with routine depression screening if there is no such mechanism for ongoing assessment and treatment.6

Most importantly, to our knowledge, this is the first study to assess systematic screening for anxiety disorders in patients with acute cardiac disease. A key finding was that GAD was almost as prevalent as depression in this population. Just as depression in patients with cardiac disease has been associated with adverse functional and medical outcomes,1–3 anxiety in general—and GAD specifically—has been associated with cardiac complications and mortality in this patient population.24–27 However, unlike depression, GAD screening is relatively uncommon and has not been recommended by the AHA or other organizations. The high prevalence rate of GAD in our study suggests that additional study of its use in this population is warranted.
We also evaluated patients for PD. Despite the strong links between the panic question and a subsequent diagnosis of PD, the absolute prevalence of PD diagnosis was very low and was highly comorbid with MDD and GAD (23 [77%] of the patients with PD had MDD or GAD). Given these facts, the lack of a validated screening instrument for this disorder, and weaker links to cardiovascular outcomes, screening for PD in patients with cardiovascular disease seems to be low yield.

Based on the above, in settings where ongoing assessment and management are available, we recommend screening patients with cardiac disease for both depression and GAD, but not PD. To streamline the screening process, we would remove the first screening step and the Coping Screen questions used here and would instead use a 2-step screening process via PHQ-4\(^26\): PHQ-2 plus GAD-2. These 4 items were predictive of MDD and GAD in this study, could be performed in the same amount of time as the less effective 4-item Coping Screen, have been used and validated for the screening of GAD and MDD in other medical populations,\(^28,29\) and may help to increase the rates of identification of GAD and MDD in this high-risk population.\(^28,30\) PHQ-4, as a combined tool, has been validated in primary care settings.\(^28\) When scoring the frequency of each item on a scale of 0 to 3 (0=not at all, 1=several days, 2=more than half the days, 3=nearly every day), a total score of ≥6 should signal clinicians to investigate the symptoms further.\(^30\) Confirmation of diagnosis could then be completed via PHQ-9 and GAD-7\(^11\) (a 7-item screen analogous to PHQ-9) or by the PRIME-MD modules for MDD and GAD.

This study confirms and expands on the current screening literature in several ways. First, it demonstrates the feasibility of performing a multistep screening procedure for the identification of depression in inpatients with cardiac disease, a finding that is consistent with other studies evaluating the 2-step screening process recommended by the AHA in inpatients with cardiac disease.\(^20,22\) Second, this study expands the breadth of screening to include anxiety disorders, which are important to identify and may impact both medical and psychiatric outcomes in this high-risk cohort. Third, this study also illustrates some of the challenges of screening in a busy inpatient setting. Similar to previous research,\(^10,22\) our study found that implementing a multistep screening procedure on a cardiac inpatient unit is complicated, and there are several barriers (eg, acceptance by unit staff, short lengths of stay, patients’ concerns about stigma with psychiatric illness) to overcome before it can be fully integrated into clinical practice. Although our study demonstrated the feasibility of the procedure, further refinement of the process and education of clinical staff may be necessary to improve rates of screening and successful identification and treatment of disorders.

There were a number of limitations to this work. First, we were unable to determine true prevalence rates of clinical depression, GAD, and PD in this population because those patients who did not meet inclusion criteria for the larger study or did not endorse any of the Coping Screen items were not screened fully; this also meant that we could not calculate the sensitivity or specificity of the screening items. Furthermore, that the 5-item Screen was performed only in patients with a positive Coping Screen may have led to an overestimation of the predictive power of the 5-item Screen and may limit the generalizability of the findings. Second, nurses are not trained to administer the items of the Coping Screen; this potentially could have led to variability in its administration and may have contributed to the suboptimal rates of its administration on admission. Third, GAD-2 and PHQ-2 were administered in a yes/no format instead of using a scale of 0 to 3 for each item. Although this made the administration of the items more efficient and potentially more acceptable to staff and patients, it may weaken the validity of those scales. Of note, however, PHQ-2—when administered in a yes/no fashion—has been linked with a diagnosis of depression\(^20\) and mortality\(^12\) in patients with cardiac disease, suggesting the effectiveness of these instruments when used in this format. Finally, the study was performed at an academic center on 2 inpatient cardiac units with a largely white population; these could limit the generalizability of the findings.

Despite these limitations, our study was able to show that screening with brief, validated tools can identify a substantial number of patients with depression and anxiety disorders in inpatients with cardiac disease. In addition, we found that GAD was nearly as prevalent as depression in this population, highlighting the potential use of screening for GAD in addition to depression, given the high prevalence of GAD and its impact on medical and psychiatric outcomes. Finally, it allows us to recommend a 4-item scale comprising GAD-2 and PHQ-2, which could be studied more extensively for the identification of GAD and depression in this high-risk population of patients with heart disease.

Disclosures

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