Relationship of Depression to Increased Risk of Mortality and Rehospitalization in Patients With Congestive Heart Failure

Wei Jiang, MD; Jude Alexander, MD; Eric Christopher, MD; Maragatha Kuchibhatla, PhD; Laura H. Gaulden, NP; Michael S. Cuffe, MD; Michael A. Blazing, MD; Charles Davenport; Robert M. Califf, MD; Ranga R. Krishnan, MD; Christopher M. O’Connor, MD

Background: Patients with congestive heart failure (CHF) may have a high prevalence of depression, which may increase the risk of adverse outcomes.

Objective: To determine the prevalence and relationship of depression to outcomes of patients hospitalized with CHF.

Methods: We screened patients aged 18 years or older having New York Heart Association class II or greater CHF, an ejection fraction of 35% or less, or both, admitted between March 1, 1997, and June 30, 1998, to the cardiology service of one hospital. Patients with a Beck Depression Inventory score of 10 or higher underwent a modified National Institute of Mental Health Diagnostic Interview Schedule to identify major depressive disorder. Primary care providers coordinated standard treatment for CHF and other medical and psychiatric disorders. We assessed all-cause mortality and readmission (rehospitalization) rates 3 months and 1 year after depression assessment. Logistic regression analyses were used to evaluate the independent prognostic value of depression after adjustment for clinical risk factors.

Results: Of 374 patients screened, 35.3% had a Beck Depression Inventory score of 10 or higher and 13.9% had major depressive disorder. Overall mortality was 7.9% at 3 months and 16.2% at 1 year. Major depression was associated with increased mortality at 3 months (odds ratio, 2.5 vs no depression; \( P = .08 \)) and at 1 year (odds ratio, 2.23; \( P = .04 \)) and readmission at 3 months (odds ratio, 1.90; \( P = .04 \)) and at 1 year (odds ratio, 3.07; \( P = .005 \)). These increased risks were independent of age, New York Heart Association class, baseline ejection fraction, and ischemic etiology of CHF.

Conclusions: Major depression is common in patients hospitalized with CHF and is independently associated with a poor prognosis.

Arch Intern Med. 2001;161:1849-1856
SUBJECTS AND METHODS

PATIENT SAMPLE

Adult patients aged 18 years or older admitted to the cardiology service at Duke University Medical Center, Durham, NC, between March 1, 1997, and June 30, 1998, were eligible for enrollment if they had clinically diagnosed CHF, defined as New York Heart Association (NYHA) classification II or greater, an ejection fraction of 35% or less (by radionuclide study, echocardiography, or angiography), or both. The institutional review board approved the protocol; all study procedures were in accord with ethical standards outlined in the Helsinki Declaration of 1975, as revised in 1983. All participants provided informed consent according to review board guidelines. Exclusion criteria included pregnancy, active suicidal ideation, planned major surgery, and the inability to provide consent.

ASSESSMENTS

All participants first completed a self-administered questionnaire, the Beck Depression Inventory (BDI). The 21-item BDI was developed to assess the severity of depression in psychiatric patients diagnosed as having affective disorder. It also has been used to screen for depression in various other populations.7,18 The documented psychometric properties of the BDI support its use as a sensitive depression screening tool and a clinically useful scale to measure its severity.7,19 We chose a cutoff score of 10 to be consistent with prior diagnostic and prognostic studies.20

Patients who scored 10 or higher on the BDI questionnaire then underwent a structured interview using a modified version of the National Institute of Mental Health Diagnostic Interview Schedule (DIS). This tool screens for major depressive disorder according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV). The depression section of the DIS that we used was the modified version by Carney and Freedland21 for use in studies of depression in cardiac patients. Frasure-Smith et al2 also have used a modified DIS in studies of patients who have suffered myocardial infarction; DSM-II and Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition (DSM-III-R) depressive disorders were associated with significantly increased mortality in these studies. Patients with a positive DIS interview were classified as having major depression. Patients with a negative DIS interview and a score of 10 or higher on the BDI were classified as having mild depression.

INITIAL DATA COLLECTION

Detailed demographic data were collected from medical records, including age, race, sex, primary reason for admission, concomitant illnesses, vital signs, physical examination results, NYHA class, ejection fraction (lowest measurement obtained during the index admission), and discharge medications.

FOLLOW-UP

All participants were contacted by mail at 3 months and 1 year after the initial assessment, to collect data on mortality and readmissions. We telephoned patients if information was not received 4 to 6 weeks after the initial mailing or for clarification of the information received. The Duke Databank for Cardiovascular Disease was used to obtain missing data and contact information. Follow-up data were 99.7% complete; only 1 patient was lost to follow-up at 1 year.

All patients received routine inpatient and post-discharge care from their primary care physicians and cardiologists during follow-up. If a patient met the modified DSM-IV criteria for major depressive disorder, we reported the DIS results to the primary care team for the index admission. Further intervention for depression was deferred to their clinical judgment. We specified no particular treatment plan for such patients because no evidence exists about the safety or efficacy of treatment of depression in this population.

STATISTICAL ANALYSIS

We examined the relationship of depression measures and all-cause mortality and readmission at 3 months and 1 year, after grouping patients in 2 ways according to BDI score and DIS result. The first approach placed patients into 1 of 3 categories: (1) those having no depression (BDI score, <10; hereafter referred to as the no depression group), (2) mild depression (BDI score, ≥10 but a negative DIS interview; hereafter referred to as the mild depression group), or (3) major depression (BDI score, ≥10 and a positive DIS interview; hereafter referred to as the major depression group). This was designed to assess how outcomes may differ by severity of depression. We also compared the rates of mortality and readmission based on a BDI score of less than 10 vs 10 or more, as in previous studies.7,22 Logistic regression analyses were performed to assess the relationships of depression with mortality and readmission. The independent ability of depression to predict mortality and readmission was examined by logistic regression models that adjusted for age, ejection fraction, and NYHA class. The cause of CHF (ischemic vs nonischemic) was added as a covariate to these models because of increased mortality and readmission noted in patients with an ischemic cause of CHF.21 Cox proportional hazards models were used to examine the association of depression with mortality over time. All analyses were performed using SAS software (Version 6.12, SAS, Cary, NC). Statistical significance was defined as $P<.05.$
RESULTS

PATIENTS

A total of 374 patients consented to participate in the survey (Figure 1). Of these, 357 patients completed the BDI questionnaire. We excluded 17 patients who provided consent but did not complete the questionnaire before discharge. A total of 126 (35.3%) of the 357 patients scored 10 or higher on the BDI. Of these, 26 did not complete the DIS interview because they refused further evaluation or were discharged before the interviewer could arrive, leaving 331 patients for analyses involving DIS measures (100 who completed the interview, plus the 231 patients with a BDI score <10). Of patients who underwent the DIS interview, 13.9% (46 of 331 patients) had a positive result and were considered to have major depressive disorder. Patients who did not meet the DSM-IV criteria for major depression but who had a BDI score of 10 or higher were considered to have mild depression. No patient who consented to participate expressed active suicidal ideation.

Age, race, previous infarction, cause of CHF, primary reason for admission, ejection fraction, and discharge medications were similar among groups (Table 1). The major depression group did include a greater proportion of women. Higher NYHA classes were observed in both the mild and major depression groups compared with the no depression group. The baseline characteristics for the 26 patients who had a BDI score of 10 or higher but did not complete the DIS interview also are summarized in Table 1.

GRADED DEPRESSION MEASURES AND MORTALITY

Overall mortality was 7.9% at 3 months and 16.2% at 1 year. Patients with major depression had the highest mortality rates at 3 months and 1 year (13.0% and 26.1%, respectively) (Table 2). Patients with mild depression had mortality rates of 7.4% at 3 months and 11.1% at 1 year, similar to those of patients whose BDI score was less than 10 (5.7% and 13.7%, respectively). Logistic regression revealed that patients with major depression had roughly twice the mortality risk at 1 year of those without depression (odds ratio [OR], 2.23; P = .04). Although the 3-month mortality rate in the major depression group also was high, more than twice the rate of the no depression group, the difference was not statistically significant (OR, 2.50; P = .08) (Table 3). Compared with the mild depression group, the major depression group had higher mortality at both intervals, but the differences likewise were not statistically significant (Table 4). Mortality did not differ significantly between patients with mild vs no depression (Tables 2 and 3).

The association of depression with mortality over 1 year derived from Cox modeling was similar to the results from logistic regression (Figure 2). With major depression vs no depression, the relative risk was 1.44 (95% confidence interval [CI], 1.033-2.011; P = .03); with major depression vs mild depression, the relative risk was 2.48 (95% CI, 0.929-6.596; P = .06); and with mild depression vs no depression, the relative risk was 0.83 (95% CI, 0.346-1.989; P = .68).

GRADED DEPRESSION MEASURES AND READMISSION

Of the entire cohort, 40.2% had 1 or more readmissions within 3 months and 60.5% by 1 year. Similar to the mortality results, the major depression group had the highest readmission rates at 3 months and 1 year (52.2% and 80.4%, respectively), followed by the mild depression group (42.6% and 55.6%) and the no depression group (36.5% and 52.3%) (Table 2). Compared with the no depression group, the major depression group had an OR of 1.90 for readmission at 3 months (P = .04) and 3.07 at 1 year (P = .005) (Table 3). Readmission in the major depression group was similar to that in the mild depression group at 3 months (OR, 1.47; P = .34) but was significantly elevated at 1 year (OR, 3.29; P = .009) (Table 4). The mild depression group had slightly higher rates of readmission at 3 months and 1 year compared with the no depression group, but not significantly so (P = .41 and .82, respectively) (Table 3).

BDI MEASURES AND MORTALITY AND READMISSION

A total of 357 patients completed the BDI questionnaire, of whom 126 (35.3%) scored 10 or higher. The 26 patients whose BDI score was 10 or higher but who did not complete the DIS interview were included in this analysis. Patients with a BDI score of 10 or higher had mortality rates of 11.9% at 3 months and 20.8% at 1 year vs 5.7% and 13.7%, respectively, for patients whose BDI score was less than 10 (Table 5). These differences were statistically significant at 3 months (P = .04), but not at 1 year (P = .08). Cox proportional hazards analysis yielded a relative mortality risk at 1 year of 1.62 with major depression vs no depression.
pression vs no depression (95% CI, 0.959-2.72; \( P = .07 \)). Of the patients with a BDI score of 10 or higher, 46.8% were readmitted by 3 months and 66.4% by 1 year, compared with readmission rates of 36.5% and 57.3%, respectively, for those with a BDI score less than 10 (\( P = .06 \) and \( P = .09 \), respectively).

### Table 1. Baseline Characteristics by Severity of Depression

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No Depression (n = 231)</th>
<th>Mild Depression (n = 54)</th>
<th>Major Depression (n = 46)</th>
<th>BDI ( \geq 10 ), No DIS Assessment (n = 26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± SD, y</td>
<td>64 ± 13</td>
<td>63 ± 13</td>
<td>63 ± 13</td>
<td>61 ± 16</td>
</tr>
<tr>
<td>Male sex, %</td>
<td>64</td>
<td>63</td>
<td>54</td>
<td>77</td>
</tr>
<tr>
<td>Race, %</td>
<td>White</td>
<td>71</td>
<td>72</td>
<td>67</td>
</tr>
<tr>
<td>Black</td>
<td>23</td>
<td>24</td>
<td>31</td>
<td>34</td>
</tr>
<tr>
<td>Other</td>
<td>6</td>
<td>4</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>New York Heart Association class, %</td>
<td>II</td>
<td>56</td>
<td>39</td>
<td>37</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>37</td>
<td>50</td>
<td>52</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>7</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>Prior bypass surgery, %</td>
<td>35.1</td>
<td>27.8</td>
<td>27.8</td>
<td>30.4</td>
</tr>
<tr>
<td>Prior infarction, %</td>
<td>31.6</td>
<td>25.9</td>
<td>26.1</td>
<td>30.8</td>
</tr>
<tr>
<td>Ischemic origin of CHF, %</td>
<td>54.6</td>
<td>48.2</td>
<td>48.2</td>
<td>57.7</td>
</tr>
<tr>
<td>Ejection fraction, mean ± SD, %</td>
<td>30 ± 13</td>
<td>27 ± 13</td>
<td>33 ± 15</td>
<td>28 ± 11</td>
</tr>
<tr>
<td>BDI score, mean ± SD</td>
<td>4.5±2.8</td>
<td>14.2±4.8</td>
<td>21.1±8.1</td>
<td>16.8±5.9</td>
</tr>
<tr>
<td>Reason for index admission, %</td>
<td>Worsening CHF</td>
<td>32.0</td>
<td>48.2</td>
<td>43.5</td>
</tr>
<tr>
<td></td>
<td>Myocardial infarction</td>
<td>21.2</td>
<td>14.8</td>
<td>15.2</td>
</tr>
<tr>
<td></td>
<td>Unstable angina</td>
<td>22.9</td>
<td>22.2</td>
<td>28.3</td>
</tr>
<tr>
<td></td>
<td>Arrhythmia</td>
<td>19.9</td>
<td>9.3</td>
<td>8.7</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>3.9</td>
<td>5.6</td>
<td>4.4</td>
</tr>
<tr>
<td>Discharge medications, %</td>
<td>β-Blockers</td>
<td>58.0</td>
<td>57.4</td>
<td>54.4</td>
</tr>
<tr>
<td></td>
<td>Calcium blockers</td>
<td>17.8</td>
<td>24.1</td>
<td>21.7</td>
</tr>
<tr>
<td></td>
<td>ACE inhibitors</td>
<td>77.9</td>
<td>77.8</td>
<td>69.6</td>
</tr>
<tr>
<td></td>
<td>Diuretics</td>
<td>68.0</td>
<td>75.9</td>
<td>71.7</td>
</tr>
<tr>
<td></td>
<td>Nitrates</td>
<td>64.9</td>
<td>63.0</td>
<td>67.4</td>
</tr>
<tr>
<td></td>
<td>Antidepressants</td>
<td>12.1</td>
<td>22.2</td>
<td>26.1</td>
</tr>
<tr>
<td></td>
<td>Anticoagulants</td>
<td>6.1</td>
<td>14.8</td>
<td>8.7</td>
</tr>
</tbody>
</table>

*CHF indicates congestive heart failure; ACE, angiotensin-converting enzyme.
†Patients were classified into the following groups: no depression, Beck Depression Inventory (BDI) score less than 10; mild depression, BDI score 10 or more with a negative Diagnostic Inventory Schedule (DIS) result; major depression, BDI score 10 or more with a positive DIS result.

### Table 2. Rate of All-Cause Mortality and Readmission by Severity of Depression

<table>
<thead>
<tr>
<th>Variable</th>
<th>No Depression (n = 231)</th>
<th>Mild Depression (n = 54)</th>
<th>Major Depression (n = 46)</th>
<th>BDI ( \geq 10 ), No DIS Assessment (n = 26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At 3 mo</td>
<td>5.7</td>
<td>7.4</td>
<td>13.0</td>
<td>19.2</td>
</tr>
<tr>
<td>At 1 y</td>
<td>13.7</td>
<td>11.1</td>
<td>26.1</td>
<td>32.0</td>
</tr>
<tr>
<td>Readmission, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At 3 mo</td>
<td>36.5</td>
<td>42.6</td>
<td>52.2</td>
<td>46.2</td>
</tr>
<tr>
<td>At 1 y</td>
<td>52.3</td>
<td>55.6</td>
<td>80.4</td>
<td>64.0</td>
</tr>
</tbody>
</table>

*For an explanation of the patient classifications see the second footnote in Table 1.

Advanced age was significantly associated with increased mortality at 3 months (OR, 1.05 for each 1-year increase; 95% CI, 1.011-1.091; \( P = .01 \)) and at 1 year (OR, 1.035; 95% CI, 1.009-1.062; \( P = .01 \)). Age also was associated with increased readmissions at 3 months, but not at 1 year (OR, 1.03; 95% CI, 1.012-1.05; \( P = .002 \) and OR, 1.008; 95% CI, 0.99-1.025; \( P = .39 \), respectively). Although the NYHA class was not associated with either outcome at 3 months, it was associated with increased risks for both at 1 year (for death: OR, 1.846 for each higher class; 95% CI, 1.208-2.821; \( P = .005 \); for readmission: OR, 1.773; 95% CI, 1.245-2.525; \( P = .002 \)). Ejection fraction (as a continuous variable and dichotomized as \( \leq 20\% \) vs. \( > 20\% \)) was not associated with mortality or readmission. The prevalence of depression was similar by the cause of CHF, but patients with an ischemic origin had significantly increased mortality and readmission rates at both intervals (Table 6).

The relationships between major depression and mortality and readmission were attenuated when risk fac-
Major depression may play a significant role in increased mortality and readmissions in patients with CHF. Overall mortality in this population was 7.9% at 3 months and 16.2% at 1 year, comparable with the finding of previous studies in such populations. Patients with CHF who have major depression were more than twice as likely as nondepressed patients to die or be readmitted within 3 months to 1 year after hospitalization. Consistent with the findings of previous studies, advanced age and higher NYHA class were associated with higher mortality and readmissions during the 12 months of the current study. These factors might have attenuated the prognostic ability of major depression with regard to mortality at 3 months and 1 year, and for readmission at 3 months, but a trend persisted after adjustment for age, NYHA class, and baseline ejection fraction. The adjusted readmission rate at 1 year was almost 3 times higher in patients with major depression vs their nondepressed and mildly depressed counterparts, a statistically significant difference. Thus, the prognostic ability of major depression for poor short-term outcomes in these patients seems not to depend on the effects of traditional risk factors such as age and deteriorated cardiac function. The prognostic ability of major depression likewise showed no interaction with the adverse effects of ischemic heart disease.

Most studies examining the prognostic value of depression in patients with cardiovascular disease have
used questionnaires for its assessment. Frasure-Smith et al\textsuperscript{6-7} are the exception, using psychiatry-oriented, individual interviews and self-administered BDI questionnaires to establish a clinical diagnosis of major depression after acute myocardial infarction. In 222 such patients, they noted a significant, negative prognostic effect of major depression at 6 months, but not at 18 months. An elevated BDI score (\(\geq 10\)) in their study had significant prognostic value at 18 months, independent of traditional risk factors after myocardial infarction.\textsuperscript{7} The relationship between BDI measures and survival at 6 months, however, was not reported. They also reported a similarly poor prognosis at 1 year with BDI scores of 10 or higher in a larger population that included the 222 original patients.\textsuperscript{22} In our study, a BDI score of 10 or higher had significant prognostic value for 3-month outcomes and showed a trend toward poorer outcomes at 1 year. When we divided the cohort into patients with no depression, mild depression, or major depression, however, the mild depression group (patients with a BDI score \(\geq 10\) but a negative DIS result) showed mortality and readmission rates only slightly higher than those of patients with a BDI score less than 10. Significantly increased mortality and readmission were found only in the major depression group. The group with a BDI score of 10 or higher included patients with a positive DIS result and patients who did not complete the DIS interview, who were excluded in the graded depression analysis model. Our study distinguished different prognoses of patients with a BDI score of 10 or higher and a positive DIS for major depression from those with a BDI score of 10 or higher and a negative DIS result. The use of standardized psychiatric diagnostic measures may be necessary to identify patients with CHF at higher risk for death or readmission.

The significant prognostic ability of a high BDI score (\(\geq 10\)) reported by Frasure-Smith et al\textsuperscript{6} was not evident in our population. These disparate results may reflect that our patients differed from those studied by Frasure-Smith et al\textsuperscript{6,7,22} First, most of our patients were admitted because of exacerbation of heart failure, unstable angina, or arrhythmia. Second, symptoms of depression (using BDI measures) may have differed between the populations. Patients with CHF may score higher on the BDI because of chronic physical deconditioning, which may lead to symptoms similar to the neurovegetative signs of depression—fatigue, reduced energy, sleep disturbance, and weight changes—rather than a truly depressed state. This may explain the decreased prognostic ability of the BDI score of 10 or higher in our patients. Alternatively, a much larger sample size might be needed to show the significantly increased mortality and readmission with mild depression in patients with CHF. The association of higher BDI scores with longer-term prognosis (\(\geq 1\) year) in this population needs further study.

Two studies have reported no relationship of depression with prognosis in patients with CHF. One study used self-reporting, the Center for Epidemiological Study Depressive Symptomatology Questionnaire, to screen for depression. The investigators found that depressive symptoms assessed before admission were not independently associated with cardiovascular events in 292 hospitalized patients who later were diagnosed as having CHF.\textsuperscript{11} The major concern with this study, however, is that depression assessment occurred long before CHF was diagnosed. Koenig,\textsuperscript{9} in 1998, reported a high prevalence (36.5\%) of major depression by DSM-IV criteria in 107 elderly patients (\(\geq 60\) years old) with CHF admitted to general medicine, cardiology, or neurology services.\textsuperscript{9} Mortality was not significantly higher during a median 46 weeks of follow-up in these patients compared with such patients without depression or with only minor depression (28.2\%, 20.0\%, and 30.4\% mortality, respectively). In his study, most patients (57.5\%) met criteria for either major or minor depression, and the population had a higher overall mortality rate (24.3\%). We speculate that the discrepancies between this and the current study result from differences in populations and sample sizes.

The mechanism for the poorer outcomes in patients with depression who have CHF may reflect several factors. First, patients with depression in our study were in higher NYHA classes than nondepressed patients, which may represent a greater deterioration in cardiopulmonary function, increased fluid retention, or both. This finding could explain reports of greater somatic symptoms and diminished functional status in patients with depression. Patients with depression have been reported to have poor social contacts and support network\textsuperscript{10,30-34} and to be noncompliant with treatment,\textsuperscript{35,36} which could adversely affect outcomes. Evidence suggests that platelet activity is high in patients with depression, especially those with concomitant vascular dis-
Accepted for publication January 18, 2001.

This study was supported in part by grant 5P60AG11268 from the National Institute on Aging, National Institutes of Health, Bethesda, Md; Claude D. Pepper Older Americans Independence Centers (Dr Jiang).

We thank Rebekka Arias, Christopher Simons, and Yan Zhang for their technical contributions and Pat French for editorial assistance.

Reprints: Wei Jiang, MD, 3203 Winfield Dr, Durham, NC 27707 (jiang001@mc.duke.edu).

REFERENCES


CONCLUSIONS

Depression is common in patients with CHF and may play a significant role in their short-term prognosis. The adverse effect of depression on prognosis seems to be independent of traditional risk factors. Recognition and clinical management of depression in this population is important. Whether treatment of depression can reduce mortality and readmissions is unknown, but this issue must be explored.

Correction

Misspelled Reviewer’s Name. In the December 11/25, 2000, issue of the ARCHIVES (2000;160:3503-3507), the name of one of our reviewers, Juliana Chan, was misspelled. We regret the error.