Depression Outcome in Inpatients With Congestive Heart Failure

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**Background:** High rates of depression are found among hospitalized patients with congestive heart failure. Little is known about the outcome of depression in these patients or factors that influence that outcome.

**Methods:** To assess baseline patient characteristics as predictors of time to remission in depressed inpatients with congestive heart failure, consecutive patients older than 50 years admitted with congestive heart failure were screened for major and minor depression using a structured clinical interview. Patients with minor depression were reevaluated at 6 and 12 weeks, and those with major depression at 6, 12, 18, and 24 weeks using the Longitudinal Interview Follow-up Evaluation.

**Results:** Of a total of 473 depressed patients, 404 (247 with minor depression and 157 with major depression) were identified and followed up. Patients with minor depression were followed up for an average of 11.3 weeks, during which 64.0% went into remission; those with major depression were followed up for 20.2 weeks, during which 47.8% went into remission. Baseline predictors of shorter time to remission for minor depression were less severe depression (hazard ratio [HR], 0.95; 95% confidence interval [CI], 0.92-0.98) and fewer comorbid illnesses (HR, 0.92; 95% CI, 0.87-0.98); patients who were younger and had better physical functioning and those not treated with antidepressants also tended to go into remission faster. For major depression, less severe depression was the primary predictor (HR, 0.92; 95% CI, 0.88-0.96), although patients who were younger, male, without a history of depression, and with fewer comorbid medical disorders also tended to go into remission faster. Fewer than 50% of patients with major depression received treatment, and only 12% had psychiatric consultations.

**Conclusions:** The outcome of minor depression may be more dependent on physical stressors, whereas major depression seems more affected by intrinsic vulnerability. Many patients with major depression were not treated, and few had psychiatric consultations.

Arch Intern Med. 2006;166:991-996

**CONGESTIVE HEART FAILURE (CHF)** is the most frequent cause of hospitalization in older adults. Major depression is present in 17% to 37% of patients and minor depression in 16% to 22%. Nearly $5 billion of the total $20 billion cost of heart failure has been attributed to depression, and severely depressed patients show a 4-fold increase in mortality. A key question is whether depressive symptoms during hospitalization are a temporary adjustment reaction or an indication of a persistent depression. Many physicians believe that it is the severity of CHF that underlies depressive symptoms, and that if they treat heart failure adequately then depression will remit.

Although numerous studies have documented the effect of depression on outcomes in patients with CHF, few, if any, have examined factors during hospitalization that influence the course of depressive disorder following discharge. Because there are almost no data on the course of depression in inpatients with CHF, we do not know which of the many patients with depression during hospitalization need specific treatment or specialized psychiatric care.

Predictors of depression outcome can be grouped into 4 categories: vulnerability factors (both sociodemographic and psychological), situational stressors, coping resources, and depression treatments. Sociodemographic indicators of vulnerability include younger age, female sex, and less education and income. Psychological indicators of vulnerability are severity of depression, comorbid psychiatric disorders, and personal or family history. Situational stressors, both health related and non–health related, can likewise have an impact on the course of depression. Coping resources, such as social support, in turn, may act as a buffer against these life stressors.
With regard to depression treatments, previous studies\textsuperscript{12,13} have found that 16% to 26% of depressed patients with CHF receive antidepressant drugs, although such treatment is not without controversy, given concerns about efficacy, adverse effects, and adverse drug interactions in patients with cardiac disorders.\textsuperscript{14} Psychosocial treatments may also reduce the negative consequences of depression in patients with CHF,\textsuperscript{15} although rates and effects of psychotherapy are unknown.

The present study systematically identified patients with CHF and major or minor depression during a medical inpatient admission. The course of depression and predictors of time to remission were examined.

### METHODS

#### PROCEDURE

To recruit patients from academic and community settings, consecutive patients hospitalized at Duke University Medical Center, Durham, NC (>1000 beds), and 3 nearby community hospitals (102 to 369 beds) were evaluated. Inclusion criteria were age of 50 years or older, a diagnosis of CHF and major or minor depression, a score of 22 or higher on the Mini-Mental State examination,\textsuperscript{16} English speaking, and residence within 35 miles of the hospital. The admitting physician determined the diagnosis of CHF; this had to be documented as part of the active problem list but was not necessarily the primary reason for admission. Patients were not renumerated for participation.

After obtaining consent from patients’ physicians and written informed consent from patients, trained psychiatric research nurses identified depressive disorders using the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorder, Fourth Edition (DSM-IV), Axis I Disorders, version 2.0.\textsuperscript{17} Only the depressive disorder section of the instrument was administered. Depressive symptoms were counted using the inclusive approach.\textsuperscript{26} Major depression was defined as 2 or more weeks of depressed mood or anhedonia plus 4 or more additional symptoms (as defined by the DSM-IV\textsuperscript{19}) that cause significant dysfunction; minor depression was defined similarly but required only 1 to 3 additional symptoms. Depressed patients (only) then continued with the rest of the interview. Research nurses were retrained together every 6 months to ensure reliability of data collection. Institutional review boards at all hospitals approved the study.

#### BASELINE MEASURES

Sociodemographic indicators of vulnerability, such as age, sex, race, education, and income, were assessed in the usual manner. Psychological indicators were severity of depression, comorbid psychiatric illness, and history of psychiatric illness. Severity of depression was measured using the 17-item Hamilton Depression Rating Scale (HDRS).\textsuperscript{20} A DSM-IV checklist identified other concurrent comorbid Axis I psychiatric disorders. Previous episodes of depression similar to the current episode were identified. Psychiatric history (excluding depression) and family history of depression were obtained using the Duke Depression Evaluation Schedule.\textsuperscript{21}

Situational stressors included global and disease-specific measures. The Cumulative Illness Rating Scale assesses impairment of 12 major organ systems on a 0 to 4 scale of severity.\textsuperscript{22} Active comorbid medical illnesses were also identified from the medical records and classified into 31 categories according to the criteria of the International Classification of Diseases, Ninth Revision (ICD-9)\textsuperscript{23}; the Charlson Comorbidity Index was used to assign weights to each diagnosis to arrive at a total comorbidity score.\textsuperscript{24} Finally, physical functioning was measured using the Duke Activity Status Index, a 12-item self-rated scale designed for patients with cardiac disease that assesses activities of daily living.\textsuperscript{25} Three disease-specific measures were also administered. The Chronic Heart Failure Questionnaire measures 3 domains of functioning (dyspnea, fatigue, and emotional subcales).\textsuperscript{26} The Dyspnea subscale (the only domain assessed herein) examines on a 1 to 7 scale how much shortness of breath (from “extremely short of breath” to “not at all short of breath”) the patient had experienced in the previous 2 weeks while performing each of 5 important activities. Patients were also assigned a New York Heart Association (NYHA) classification of I through IV based on physical functioning assessed using the 20-item Specific Activity Scale, which uses metabolic equivalent tasks as anchor points.\textsuperscript{27} Finally, nurses rated global severity of CHF on a 1 to 10 scale. Stressful life events unrelated to health during the 12 months prior to the interview were also assessed.\textsuperscript{28}

As a measure of coping resources, the 11-item version of the Duke Social Support Index assessed 2 components of social support: social network and subjective support.\textsuperscript{29} Depression treatments were examined in 3 ways. First, subjects were asked if they were currently taking a medication for depression, how long they had taken that medication, and if antidepressant drug therapy had ever been prescribed in the past; psychotherapy was assessed similarly. Second, each subject’s medical records were reviewed for evidence of antidepressant drug therapy or psychotherapy. Third, intensity of antidepressant use was assessed by a modified version of a treatment intensity scale used in drug studies.\textsuperscript{30} This scale includes type of antidepressant, dosage, and duration of treatment and covers a wider range of old and new antidepressants. Medical records were reviewed for psychiatric consultations obtained during hospitalization.

#### CHANGES IN DEPRESSION

At 6, 12, 18, and 24 weeks after the baseline evaluation, research nurses interviewed patients by telephone or in their homes (alternating); patients with minor depression were evaluated only at 6 and 12 weeks, the time when symptoms change most for this disorder.\textsuperscript{16} The course of depression was assessed using the Longitudinal Interval Follow-up Evaluation,\textsuperscript{31} which collects information retrospectively on the course of depressive disorder as defined by the DSM-IV\textsuperscript{19} since the last contact and allows weekly tracking of symptoms. Weekly psychiatric status ratings for the Longitudinal Interval Follow-up Evaluation ranged from 1 (usual self) to 6 (definite criteria for severe depression).

#### STATISTICAL ANALYSIS

Frequency distributions and mean scores are presented in Table 1. The outcome variable, time to remission, was the interval between evaluation and the first time patients had a psychiatric status rating of 1 or 2 for 2 consecutive weeks.\textsuperscript{32} Patients whose depression did not remit during follow-up and those providing only partial follow-up data were censored at the time they were last known to be depressed. Bivariate and multivariate predictors of remission were examined using a Cox proportional hazards regression model. In bivariate analyses, individual variables were examined alone in the model (Table 2). In the multivariate analysis, variables significant at $P<.10$ in the bivariate analyses were added in blocks to the model in a hierarchical fashion: vulner-
Between November 1999 and December 2003, 289 patients with minor depression and 184 with major depression were identified. Follow-up data were obtained on 404 of these 473 patients at 6 weeks (85.4%), 394 at 12 weeks (83.3%), 118 at 18 weeks (64.1%), and 113 at 24 weeks (61.4%). At the 6-week follow-up, the 69 nonrespon-
dents differed from the 404 respondents in that they were older (72.2 vs 69.2 years), had less frequent history of depression (42.0% vs 59.3%), less frequent history of psychotherapy (8.8% vs 22.3%), and worse physical functioning (Duke Activity Status Index, 14.8 vs 16.3). At the 24-week follow-up, 71 nonrespondents differed from 113 respondents in that they were older (71.8 vs 66.4 years); had worse depression (HDRS, 18.6 vs 16.2); had less frequent history of depression (50.7% vs 74.4%), and history of psychotherapy (12.7% vs 31.9%); and had fewer stressful life events (12.0 vs 15.3). Baseline severity of CHF by NYHA class and Chronic Heart Failure Questionnaire score did not differ between nonrespondents and respondents.

Baseline characteristics of respondents are presented in Table 1, stratified by depression type. The NYHA class (based on the Specific Activity Scale available on 325 patients) was III or IV in 90.2%. Ratings by research nurses of cardiac system impairment (an item from the Cumulative Illness Rating Scale) were moderately severe to extremely severe in 92.1% of 404 patients. Of the patients assessed at baseline, chronic pulmonary disease was one of the most common medical comorbidities (65.4%).

REMISSION BY DEPRESSION TYPE

Depressive symptoms at baseline had been present for a mean duration of 17.0 (35.1) weeks for patients with...
Patients who went into remission more quickly
Baseline predictors of time to remission are presented in Table 2. Patients with minor depression (64.0%) went into remission; the mean time to remission was 5.4 (2.7) weeks. For patients with major depression, mean follow-up was 11.3 (1.9) weeks, during which 158 (64.0%) went into remission; the mean time to remission was 5.4 (2.7) weeks. For patients with major depression, mean follow-up was 20.2 (6.3) weeks, during which 75 (47.8%) went into remission; the mean time to remission was 11.7 (6.5) weeks. When follow-up is limited to 3 months, patients with minor depression were significantly more likely than those with major depression to go into remission (64.0% vs 29.3%; \( P < .001 \)); the time to remission was also shorter for those with minor depression (5.4 vs 7.2 weeks; \( P < .001 \)).

**MINOR DEPRESSION**

Baseline predictors of time to remission are presented in Table 2. Patients who went into remission more quickly (\( t = 1.2; P = .24 \)) were younger, had less severe depression and medical illness, better physical functioning, greater social support, and were not taking antidepressant drugs.

Multivariate predictors of shorter time to remission were younger age, less severe depressive symptoms, better physical functioning, fewer comorbid medical illnesses, and no antidepressant drug treatment (Table 3). Based on the level of statistical significance set for this analysis (\( P < .01 \)), however, only depression severity and medical comorbidity were independent and significant predictors. For every 1-point increase on the HDRS, there was a 5% slowing in the time to remission (HR, 0.95). Likewise, for every 1-point increase in the Charlson Comorbidity Index (range, 0–49), there was an 8% slowing in time to remission (HR, 0.92).

**MAJOR DEPRESSION**

In bivariate analyses, baseline characteristics that predicted shorter time to remission were younger age, male sex, less severe depression, no history of depression, and fewer comorbid medical illnesses. None of the other 19 baseline characteristics predicted time to remission at \( P < 0.10 \). In multivariate analyses, only severity of depression was a significant and independent predictor. For every 1-point increase on the HDRS, there was an 8% slowing in the time to remission (HR, 0.92). Age and history of depression were also marginally significant in their effects (for both, \( P = .02 \)), as was sex and comorbid illness (for both, \( P = .05 \)). Every year of increased age slowed time to remission by 3%; a history of depression slowed remission by 46%, female sex slowed remission by 38%, and each additional comorbid illness slowed remission by 9%.

Factors such as education, income, and social support did not independently predict time to remission for either minor or major depression (nor did measures of CHF severity).

**DEPRESSION TREATMENTS AND CONSULTATIONS**

Given the lack of effect (or negative effect) of antidepressant drug therapy on course of depression, further analyses were conducted. As Table 1 indicates, 26.4% of patients with minor depression and 44.6% of those with major depression received antidepressants. For patients with minor depression, the same antidepressant drug had been taken for a mean (SD) of 2.3 (3.8) years; for major depression, mean duration was 2.4 (3.3) years. Duration, however, was unrelated to depression course (HR, 1.00; \( n = 60 \)). Patients receiving antidepressant drug therapy also tended to be in the current depressive episode longer than those not receiving it (22.9 vs 16.4 weeks; \( P = .06 \)) and had more severe depression (HDRS, 16.1 vs 14.0; \( P < .001 \)). Psychiatric consultations were obtained for 4.6% of patients with minor depression and 11.6% with major depression. Thus, depressed patients treated with antidepressant drug therapy had more severe and somewhat more persistent depression. However, despite

**Table 3. Proportional Hazards Multivariate Model of Time to Remission**

<table>
<thead>
<tr>
<th>Baseline Variable</th>
<th>Minor Depression (n = 246)</th>
<th>Major Depression (n = 157)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (95% CI)</td>
<td>( 0.99 (0.97-1.00)^* )</td>
<td>( 0.97 (0.95-1.00)^* )</td>
</tr>
<tr>
<td>Age, y</td>
<td>( 0.95 (0.92-0.98)^* )</td>
<td>( 0.92 (0.89-0.96)^* )</td>
</tr>
<tr>
<td>Female sex</td>
<td>( 0.95 (0.87-0.98)^* )</td>
<td>( 0.91 (0.83-1.00)^* )</td>
</tr>
<tr>
<td>HDRS</td>
<td>( 0.95 (0.92-0.98)^* )</td>
<td>( 0.92 (0.88-0.96)^* )</td>
</tr>
<tr>
<td>History of depression, yes</td>
<td>( 0.95 (0.92-0.98)^* )</td>
<td>( 0.92 (0.88-0.96)^* )</td>
</tr>
<tr>
<td>Degree of stress</td>
<td>( 0.95 (0.92-0.98)^* )</td>
<td>( 0.92 (0.88-0.96)^* )</td>
</tr>
<tr>
<td>Ability to perform ADLs</td>
<td>( 0.95 (0.92-0.98)^* )</td>
<td>( 0.92 (0.88-0.96)^* )</td>
</tr>
<tr>
<td>Comorbid medical illnesses</td>
<td>( 0.95 (0.92-0.98)^* )</td>
<td>( 0.92 (0.88-0.96)^* )</td>
</tr>
<tr>
<td>Treatment variables</td>
<td>( 0.95 (0.92-0.98)^* )</td>
<td>( 0.92 (0.88-0.96)^* )</td>
</tr>
<tr>
<td>Baseline antidepressant drug treatment,</td>
<td>( 0.95 (0.92-0.98)^* )</td>
<td>( 0.92 (0.88-0.96)^* )</td>
</tr>
<tr>
<td>Model likelihood ratio, ( \chi^2 ) (df)</td>
<td>( 38.2 (5)^\ddagger )</td>
<td>( 30.6 (5)^\ddagger )</td>
</tr>
</tbody>
</table>

*Indicates variable was not significant (\( P = .10 \)) in that particular model.

Abbreviations: ADLs, activities of daily living; CI, confidence interval (values >1.00 indicate increased speed of remission); HR, hazard ratio; HDRS, Hamilton Depression Rating Scale.

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ongoing depression, many had taken the same drug for more than 2 years and seldom received psychiatric consultation during hospitalization.

**COMMENT**

This study, conducted in a naturalistic setting and including a mixture of patients from academic and community hospitals, examines the course of depression and predictors of remission. Minor depression fully remitted in 64% of patients within 3 months, and average time to remission was 5.4 weeks. Major depression fully remitted in 48% of patients within 6 months, and among those who went into remission, average time to remission was 11.7 weeks. When the follow-up time for both disorders was limited to 3 months, a higher percentage of patients with minor depression went into remission compared with those with major depression (64% vs 29%), and depression remitted faster (5.4 vs 7.1 weeks).

In the only other prospective study,\(^3^4\) of depressed patients with CHF, 55% of 44 patients with depressive disorder (type not specified) went into remission by 1 month and 75% by 6 months. In 129 general medical inpatients with minor or major depression, reductions of 20% and 28%, respectively, in symptoms were seen by 6 weeks, and reductions of 41% and 43% by 12 weeks (remission rates not reported).\(^1^8\) Follow-up for an additional 8 months found that further improvement was uncommon.

In addition, a primary focus of this report was to identify characteristics influencing time to remission. Patients with CHF and minor depression who went into remission faster were those with less severe depression and fewer comorbid medical illnesses. Depression tended to remit faster in those who were younger, had better physical functioning, and did not take antidepressants. Thus, degree of vulnerability (less severe depression and younger age) and degree of stress (better physical functioning and fewer comorbid disorders) both reduced time to remission.

Those with major depression who went into remission more quickly had less severe depression and tended to be younger, male, and with no history of depression and fewer comorbid disorders (4 of 5 characteristics indicating greater vulnerability). Female sex and previous episodes of depression have long predicted worse depression outcomes in older patients.\(^6\) Chronic depression may also be more common in older persons,\(^3^5\) and older age at onset may impede recovery.\(^5^6\) Younger patients with CHF may have more psychological reserve or cognitive flexibility that enables them to cope better with health stressors; alternatively, hypoxemia from longstanding CHF in older patients may result in more cases of chronic depression. Finally, stress from physical health problems tended to have less impact on the course of major depression than on minor depression. There is evidence that severity of medical illness has little effect on the responsiveness of major depression to treatment.\(^3^7\)

In the present study, however, treatment did not reduce time to remission; if anything, it predicted longer time to remission (at least for minor depression). Little is known about the effectiveness of antidepressant drug therapy in patients with CHF, although a large clinical trial is ongoing (the Sertraline AntiDepressant Heart Attack Randomized Trial in Heart Failure?) and will provide important information on safety and efficacy. There are reasons, however, why treatment in this study did not seem helpful. Treatment with antidepressant drug therapy may have indicated more severe and chronic depression because patients had often been taking these drugs for years. Lack of efficacy could have developed owing to drug resistance in some cases. Although length of treatment with antidepressant drug therapy was not a predictor of depression course, there was little evidence that drug effectiveness had been reviewed recently, at least in terms of seeking a psychiatric consultation (only 1 of 10 patients).

**LIMITATIONS**

Several factors limit generalizability. First, dropouts occurred nonrandomly during follow-up; these patients were older and had worse physical functioning and more severe depression, factors among responders that predicted slower time to remission. Thus, the effects of these factors on outcome may have been underestimated. Second, different lengths of follow-up were chosen for minor and major depression, limiting comparison between these disorders; however, a shorter follow-up for minor depression was chosen because previous work\(^1^8\) indicated that most change in symptoms occurs during the first 3 months after discharge. Third, no specific criteria were used for the diagnosis of CHF, which was not always the primary reason for admission; however, more than 90% of patients were classified as NYHA stage III or IV based on metabolic equivalent tasks, and the mean (SD) score (10.3 [5.9]) on the Chronic Heart Failure Questionnaire indicated severe disease. Despite these limitations, strengths include the systematic sampling method, the mix of patients from academic and community settings, well-established measures of predictors, the use of the Structured Clinical Interview for DSM-IV to diagnose depressive disorders, the Longitudinal Interval Follow-up Evaluation to assess outcome, and the high follow-up rate (85%).

**CLINICAL IMPLICATIONS**

Are depressive symptoms during hospitalization a temporary adjustment reaction that can be ignored, or do they indicate a persistent depression that needs treatment? In this study, severity of CHF had little impact on the course of either minor or major depression. Treating the CHF alone, then, is unlikely to result in depression improvements. Rather, focus should be on the type of depression present. Clinicians should be aware that minor depression is related more to the patient's current medical condition and will resolve soon after discharge in two thirds of cases (especially in those of younger age with milder symptoms and few comorbid illnesses). Waiting until the patient returns for follow-up to see if depression persists is reasonable. For those with major depression, whose depression may be driven more by an inherent vulnerability and less likely to resolve soon after
Accepted for Publication: November 12, 2005.

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Author Contributions: Dr Koenig had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Financial Disclosure: None.

Funding/SUPPORT: This study was funded by National Institute of Mental Health grant R01-MH57662.

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