

Original Research Reports

The Association of Co-morbid Symptoms of Depression and Anxiety With All-Cause Mortality and Cardiac Rehospitalization in Patients With Heart Failure

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Background: Patients with heart failure (HF) experience multiple psychologic symptoms. Depression and anxiety are independently associated with survival. Whether co-morbid symptoms of anxiety and depression are associated with outcomes in patients with HF is unknown. **Objective:** To determine whether co-morbid symptoms of depression and anxiety are associated with all-cause mortality or rehospitalization for cardiac causes in patients with HF. **Method:** A total of 1260 patients with HF participated in this study. Cox regression analysis was used to determine whether co-morbid symptoms of depression and anxiety independently predicted all-cause mortality and cardiac rehospitalization. Anxiety and depression were treated first as continuous-level variables, then as categorical variables using standard published cut points. Patients were then divided into 4 groups based on the presence of

anxiety and depression symptoms. **Results:** When entered as a continuous variable, the interaction between anxiety and depression (hazard ratio = 1.02; 95% CI: 1.01–1.03; $p = 0.002$) was a significant predictor of all-cause mortality in patients with HF. When entered as a categorical variable, co-morbid symptoms of depression and anxiety (vs no symptoms or symptoms of anxiety or depression alone) independently predicted all-cause mortality (hazard ratio = 2.59; 95% CI: 1.49–4.49; $p = 0.001$). None of the psychologic variables was a predictor of cardiac rehospitalization in patients with HF whether using the continuous or categorical level of measurement. **Conclusion:** To improve mortality outcomes in patients with HF, attention must be paid by health care providers to the assessment and management of co-morbid symptoms of depression and anxiety.

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INTRODUCTION

In the United States, heart failure (HF) is a major public health problem that affects approximately 5.7 million patients, with 670,000 newly diagnosed patients each year.¹ The total costs of HF in the United States are estimated to be \$37 billion each year.¹

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All-Cause Mortality and Cardiac Rehospitalization

Although there have been significant therapeutic advances in the pharmacologic and surgical treatment of HF, the 1-year mortality rate of patients with HF who had progressive symptoms still approaches 40%, which is the same for some types of aggressive cancer.^{2,3} Even patients who have less serious HF symptoms usually experience impaired quality of life.³ The high mortality and morbidity rates associated with HF are still not well explained.⁴ Patients with HF simultaneously experience multiple psychological symptoms that affect health outcomes such as symptoms of depression and anxiety.

Depression is a mood disorder that interferes with an individual's ability to perform daily life activities.^{5,6} Depression is characterized by specific symptoms, such as changes in appetite, sleep disturbance, fatigue, agitation, feelings of guilt or worthlessness, and concentration problems.⁷⁻⁹ Depression is a significant clinical problem that is found in a substantial number of patients with HF; approximately 20% of outpatients who have HF have major depression, and up to 48% of outpatients experience clinically-significant depressive symptoms.¹⁰ Furthermore, patients with HF who are depressed are 2 times more likely to be hospitalized and face death than those who are not depressed.¹¹ Depression is associated with unhealthy behaviors, like smoking, and unsatisfactory patient compliance.^{12,13} Moreover, depression is associated with pathophysiologic mechanisms that negatively affect cardiac conditions, such as hypercortisolemia, impaired platelet function, and reduced heart rate variability.¹⁴⁻¹⁷

Anxiety is a negative emotional state resulting from the perception of threat and is described as the result of a perceived inability to predict, control, or gain from the threatening situation.^{5,7} Anxiety is significantly associated with a higher occurrence of adverse cardiac events and cardiac death in the general population and in patients with coronary artery disease.^{5,18} Anxiety also has been linked to pathophysiologic mechanisms that could mediate negative outcomes, such as reduced heart rate variability and baroreflex cardiac control, cardiac arrhythmias, and sudden death.¹⁹⁻²¹ Patients with HF have a 60% higher level of anxiety compared with that of healthy elders; 40% of patients have significant anxiety.^{7,22,23} In addition, patients with HF tend to have higher levels of anxiety compared with other patients who have cardiac disease or even those with cancer and lung disease. However, there are contradictory results

about the association between anxiety and health outcomes in patients with HF.^{24,25}

Individually, depression and anxiety are associated with survival in patients with HF; however, the association of co-morbid symptoms of anxiety and depression with morbidity and mortality in patients with HF is unknown. Thus, the purpose of this study was to examine whether co-morbid symptoms of depression and anxiety are associated with all-cause mortality or rehospitalization for cardiac causes in patients with HF.

METHOD

Design, Sample, and Setting

Data from this study were from the Heart Failure Health-Related Quality of Life Collaborative Registry, housed at the University of Kentucky College of Nursing.²⁶ This is a longitudinal database that includes data from patients from across the United States and from several international sites ($n = 4076$). From this database, we analyzed data from all patients who had information on anxiety, depression, and mortality and rehospitalization outcomes ($n = 1260$). The demographics (i.e., age, sex, and ethnicity) and New York Heart Association (NYHA) class of the sample used in the current study were compared statistically with those in the registry who did not have data on anxiety, depression, and outcomes. There were no differences between both these groups on these 4 variables. The database was accessed through the Research and Interventions for Cardiovascular Health program at the University of Kentucky. The inclusion criterion for the original database was patients with a confirmed diagnosis of HF with impaired or preserved left ventricular systolic function. Patients were excluded if they had valvular heart disease, were referred for heart transplantation, had a history of cerebrovascular accident or myocardial infarction in the past 6 months, or had a co-existing terminal illness. Data on mortality and rehospitalization were collected over 12 months.^{27,28}

Measures

Symptoms of Depression and Anxiety

Depressive Symptoms. The Patient Health Questionnaire (PHQ-9) was used to measure depressive symptoms in this study.^{29,30} The PHQ-9 is a 9-item, self-reported measure of depression that reflects the

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