2012

SYMPTOM ASSESSMENT AND MANAGEMENT IN PATIENTS WITH HEART FAILURE

Kyoung Suk Lee
University of Kentucky, kyounglee7@gmail.com

STUDENT AGREEMENT:

I represent that my thesis or dissertation and abstract are my original work. Proper attribution has been given to all outside sources. I understand that I am solely responsible for obtaining any needed copyright permissions. I have obtained and attached hereto needed written permission statements(s) from the owner(s) of each third-party copyrighted matter to be included in my work, allowing electronic distribution (if such use is not permitted by the fair use doctrine).

I hereby grant to The University of Kentucky and its agents the non-exclusive license to archive and make accessible my work in whole or in part in all forms of media, now or hereafter known. I agree that the document mentioned above may be made available immediately for worldwide access unless a preapproved embargo applies.

I retain all other ownership rights to the copyright of my work. I also retain the right to use in future works (such as articles or books) all or part of my work. I understand that I am free to register the copyright to my work.

REVIEW, APPROVAL AND ACCEPTANCE

The document mentioned above has been reviewed and accepted by the student's advisor, on behalf of the advisory committee, and by the Director of Graduate Studies (DGS), on behalf of the program; we verify that this is the final, approved version of the student's dissertation including all changes required by the advisory committee. The undersigned agree to abide by the statements above.

Kyoung Suk Lee, Student

Dr. Debra K. Moser, Major Professor

Dr. Terry A. Lennie, Director of Graduate Studies

SYMPTOM ASSESSMENT AND MANAGEMENT IN PATIENTS WITH HEART FAILURE

DISSERTATION

A dissertation submitted in partial fulfillment of the
requirements for the degree of Doctor of Philosophy in the
College of Nursing
at the University of Kentucky

By
Kyoung Suk Lee

Lexington, Kentucky

Director: Dr. Debra K. Moser, Professor of Nursing

Lexington, Kentucky

2012

ABSTRACT OF DISSERTATION

SYMPTOM ASSESSMENT AND MANAGEMENT IN PATIENTS WITH HEART FAILURE

Patients with heart failure (HF) must monitor and recognize escalating symptoms to manage worsening HF in a timely manner. However, routine symptom monitoring is not commonly performed by this population.

Providing a symptom diary along with an education and counseling session may help HF patients promote symptom monitoring and interpretation. The accumulated information about changes in daily symptoms will allow patients to easily compare current symptom status to the past without depending on memory and can rapidly capture worsening HF. To date, few studies have tested the effect of a daily symptom diary.

The purpose of this dissertation was to develop and test a symptom diary intervention to improve outcomes in HF patients. Prior to testing the intervention, preliminary work included: (1) determining the impact of symptom clusters on cardiac event-free survival; (2) evaluating the quality of existing symptom measures designed for HF patients; (3) evaluating the effect of physical symptom items that were often included in a depressive symptom instrument on cardiac event-free survival; and (4) evaluating the association between symptom monitoring and self-care management. Based on this information, a randomized, controlled pilot study was conducted to test the effect of a symptom diary with an education and counseling intervention on prognosis, health-related quality of life (HRQOL), and self-care maintenance at 3 months follow-up.

A total of 44 hospitalized patients with HF were randomly assigned to either usual care or intervention providing a daily symptom diary with education and counseling. There were trends toward fewer HF events and improved self-care maintenance in the intervention group compared to the usual care group. However, there was no difference in HRQOL between the two groups.

The results of this dissertation suggest the importance of assessing symptom clusters and further studies to improve the quality of existing HF symptom measures. Results from this dissertation also provided the evidence of the advantages of regular symptom monitoring to facilitate early identification of worsening HF and initiation of

timely responses. However, further studies are needed to provide additional evidence of the positive impact of a use of daily symptom diary in patients with HF.

KEYWORDS: heart failure, symptoms and signs, symptom assessment, self-care, outcomes.

Kyoung Suk Lee
Student's Signature

April 19, 2012
Date

SYMPTOM ASSESSMENT AND MANAGEMENT IN PATIENTS WITH HEART FAILURE

By

Kyoung Suk Lee

Debra K. Moser, DNSc
Director of Dissertation

Terry A. Lennie, PhD
Director of Graduate Studies

April 19, 2012

This dissertation is dedicated to my family
and friends for all the support through this process.

ACKNOWLEDGMENTS

I would like to acknowledge my advisor, committee members, colleagues, study participants that made this dissertation possible. I would like to thank Dr. Debra K. Moser, my advisor and inspiration. Dr. Moser has been greatly helpful throughout my dissertation process with insightful feedback and profound support. I am grateful that Dr. Moser believed in me and provided me with many opportunities to develop my successful academic career. Her high quality of scholarship is exemplified by her careful mentorship and expertise, which is truly inspirational. I would also like to thank Dr. Terry A. Lennie, who was readily available and insightfully mentored me throughout my doctoral program. I would like to extend my special thanks to Dr. Sherry Warden, who provided me with incredible support and encouragement during my doctoral program. I have never forgotten her kindness that started from the first day of my school in the United States. I would also like to thank Dr. Joy Jacobs-Lawson with her insightful guidance and expertise. I am appreciative of Dr. Sujin Kim to serve as outside examiner on my committee.

In addition to my committee, several other colleagues assisted throughout the process. I would like to thank colleagues at the RICH heart team, whom I was privileged to work with and from whom I also learned much. Jeanine Vezie assisted me to schedule appointments with my study participants and worried about my safety during home visit. I would like to thank my fellow friends, Demetrius Abshire, Audrey Darville, and Amanda Fallin, who always offer valuable input and support as well as read my countless papers.

I would like to acknowledge the University of Kentucky P20 Center for Biobehavioral Research Research on Self-Management in Cardiopulmonary Disease, which granted me to access the existing data for my chapters two, four, and five. This study would not have been possible without the support and collaboration of the administration, nurses, and patients at the University of Kentucky Chandler Medical Center, the Saint Joseph Heart Institute, and the Ephraim McDowell Regional Hospital.

I would be remiss if I did not thank Dr. Kyungeh An for her continual support and encouragement. Without her, I would not able to able to dream on studying abroad and

study under Dr. Moser's guidance. She always listens to me with patience and shares my joys and sorrows.

Finally, I am genuinely grateful to my family, who lives far away. My parents and sister provide me with their unconditional love, support for my career aspirations, and prayers. I would especially like to thank my younger sister, who is always there for my parents while I am studying abroad.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

CHAPTER ONE

Introduction

Heart failure (HF) is a progressive and complex clinical syndrome manifested by multiple symptoms and signs. The prevalence of HF is increasing as longevity increases in the population and there is greater survival from acute coronary events.[1] In the United States, HF affects approximately 5.7 million adults and an additional 3 million adults will have HF by 2030.[2]

Despite advances in HF management, patients with HF experience a poor prognosis and compromised quality of life. Among Medicare beneficiaries from two large HF registries, three-month and one-year rehospitalization rates were 40% and 65%, respectively. In the same study, the one-year post-discharge mortality rate was 34%.[3] People with HF report poorer quality of life compared to those with cardiac conditions other than HF (e.g., angina and hypertension) or those without HF.[4-6] Symptom burden, from both physical (e.g., dyspnea and fatigue) and emotional (e.g., depressive symptoms) symptoms, contributes substantially to poorer quality of life.[7-9]

Symptom status is one of the most important factors associated with adverse outcomes in patients with HF. In a longitudinal study, quality of life at three months was predicted by physical symptom status at baseline.[10] Dyspnea was an independent predictor of increased risk for mortality, and fatigue independently predicted hospitalization due to HF exacerbation.[11] Patients with highly variable daily symptom patterns of dyspnea and edema were at substantially greater risks for hospitalization for HF or mortality from HF.[12] Thus, symptoms experienced by patients with HF should be properly assessed and managed to improve outcomes.

It is imperative that clinicians and researchers use valid and reliable symptom instruments to capture symptom experiences accurately and to evaluate changes in symptoms. Most symptom instruments used in the HF population were originally designed for other populations, such as patients who had cancer (e.g., the Memorial Symptom Assessment Scale)[13] or received palliative care (e.g., the Edmonton Symptom Assessment System).[14] Although cancer and palliative care patients are chronically ill like patients with HF, the critical symptoms that need to be addressed may be different.

Some HF investigators have used items from HF-specific quality of life measures (i.e., the Minnesota Living with HF and the Kansas City Cardiomyopathy Questionnaire) to assess symptom status in patients with HF.[15-17] There are a limited number of symptom instruments modified or designed for patients with HF; however, their psychometric properties have not been well demonstrated. A critical evaluation of the quality of symptom measures designed for and used in patients with HF is needed.

Dyspnea is the most frequently assessed and reported symptom in acute care settings, although patients with HF also experience atypical symptoms, such as palpitations, hot flashes, and nausea/ vomiting, prior to seeking medical care.[18-19] Although typical symptoms reflecting congestion are important markers for healthcare providers to assess and manage HF, addressing only these typical symptoms may limit our ability to understand patients' symptom experiences and provide comprehensive symptom management. It is critical to evaluate a full range of symptoms in patients with HF.

Symptoms occur concurrently rather than in isolation. Patients with HF report multiple symptoms with an average of 15 physical and psychological symptoms,[8] and the symptoms are associated with each other. For example, fatigue is associated with sleep difficulties, chest pain, weakness, and depressive symptoms.[20-21] Dyspnea increases as edema becomes severe.[22] Despite evidence that patients experience multiple symptoms simultaneously, few efforts to identify groups of symptoms (symptom clusters) and their impact on outcomes have been made in the HF population.

The presence of multiple, co-occurring symptoms impedes the ability of patients with HF to seek medical assistance in a timely manner.[23-24] Patients with HF have difficulty recognizing changes in any one or more symptoms. For example, about half of patients in one study reported that the recognition of critical symptoms (e.g., ankle swelling and dyspnea) reflecting HF exacerbation was challenging.[25] Only 5% of patients realized that their worsening symptoms were caused by HF when they visited the hospital.[19] Instead many patients associate their symptoms with other causes such as aging or other comorbid conditions.[19, 26-27] Failure to distinguish between sources of the symptoms may lead to delays in seeking assistance and receiving timely management.

The main reason for hospitalization in patients with HF is worsening symptoms of HF. According to a situation-specific theory of HF self-care,[28] self-care in HF is conceptualized as a naturalistic decision-making process, which consists of self-care maintenance to maintain physiological stability and self-care management to respond to altered symptom status. Self-care maintenance has two components, symptom monitoring and adherence to recommended regimens. Self-care management has three elements: recognizing symptoms, implementing treatment strategies, and evaluating the treatment strategies (Figure 1). By engaging in self-care maintenance and management, a delay in seeking care for worsening symptoms can be prevented.

Regular symptom monitoring is essential for patients with HF to take action in response to changes in symptom status, which may ultimately shorten time to seeking care or prevent recurrent hospitalizations.[29] One way to promote patients' engagement in symptom monitoring behaviors is by providing a symptom diary where patients can keep track of their daily symptom changes. By keeping a symptom diary, patients may effectively detect and compare changes in symptom status without relying on recall. In one study, monitoring daily weight was associated with a decrease in one-year mortality rates and time to first hospitalization during a one-year follow-up in patients with HF. However, changes in weight alone do not always reflect worsening HF.[30] A comprehensive symptom diary that includes weight and other HF symptoms and signs may substantially improve outcomes.

The purpose of this dissertation was to develop and test a symptom diary with an education and counseling intervention in order to improve self-care and outcomes in patients with HF. Each chapter of this dissertation illustrates part of a journey to develop a preliminary program of research focused on improving symptom management and outcomes in patients with HF.

In chapter two, results of a study to identify symptom clusters between men and women and determine the impact of symptom clusters on cardiac event-free survival are presented.[17] Although patients with HF report experiencing multiple symptoms simultaneously, investigators tend to focus on individual symptoms and their impact on outcomes. It is important to examine whether there are symptom clusters (co-occurring symptom groups) in patients with HF and explore gender differences in symptom clusters

on outcomes. It is also necessary to explore gender differences in symptom clusters as symptom experiences between men and women are dissimilar.[8, 31] To identify symptom clusters, hierarchical cluster analyses were conducted with seven symptoms that were commonly reported by patients with HF. Two identical symptom clusters were revealed in men and women: (1) a physical symptom cluster and (2) an emotional/ cognitive symptom cluster. Cox proportional hazards regression was used to determine whether the two symptom clusters predicted time to first cardiac event after adjusting for relevant demographic and clinical variables.

In chapter three of this dissertation, a systematic, critical review of the literature is presented to examine the quality of existing symptom measures designed for and used in patients with HF. From a systemic search, five instruments were identified that met inclusion and exclusion criteria: M.D Anderson Symptom Index-HF; Memorial Symptom Assessment Scale-HF; HF Signs and Symptoms Checklist; HF Symptom Checklist; and HF Symptom Survey. These five symptom instruments were evaluated according to the following five evaluation categories adapted and modified from a previous study:[32] (1) contents; (2) measuring scales; (3) psychometric properties; (4) completion process; and (5) information.

In chapter four, results are presented from a study that was conducted to determine whether physical depressive symptoms altered the association between depressive symptoms and cardiac event-free survival in patients with HF. Selecting psychometrically sound instruments is important to evaluate the impact of symptoms. Depressive symptoms are a risk factor for deleterious outcomes in patients with HF. Popular depressive symptom instruments, such as the Beck Depression Inventory and the Patient Health Questionnaire-9, include physical depressive symptoms, such as fatigue, sleep disturbances, or changes in appetite. These physical depressive symptoms are reported in up to 84% of patients with HF regardless of depression status.[8-9, 33] Patients who are symptomatic and in an advanced stage of HF are more likely to be judged to be depressed than patients who are asymptomatic.[33-35] When depressive symptoms are measured with instruments including physical depressive symptom items, the depressive symptom scores may reflect the severity of HF rather than depressive symptoms. This, in turn, may inflate the association between depressive symptoms and outcomes in patients

with HF. It is critical to evaluate whether the use of depressive symptom measures, including physical symptoms, influence the relationship between depressive symptoms and outcomes. Thus, we compared the predictive abilities of a depressive symptom measure (the Patient Health Questionnaire-9) with and without physical depressive symptom items for cardiac event-free survival.

In chapter five, the results of a study to examine the association between symptom monitoring behaviors and self-care management in patients with HF are presented. According to a situation-specific theory of HF self-care (Figure 1),[28] it is suggested that symptom monitoring behaviors are essential for patients to adequately perform self-care management behaviors. However, the empirical evidence to support that adherence to symptom monitoring may result in appropriate self-care management is lacking. In this study, we examined the relationship between adherence to regular symptom monitoring and self-care management in patients with HF.

Chapter six includes preliminary findings from a longitudinal, randomized, controlled pilot study to test the effect of a symptom diary with an education and counseling intervention on self-care maintenance, health-related quality of life, and prognosis in patients with HF at three months. Patients were invited to participate if they were diagnosed with HF and admitted to the hospital due to cardiovascular reasons (e.g., HF exacerbation and myocardial infarction). Baseline assessment was done within one month after the initial hospitalization and two additional follow-ups were made at one month and three months thereafter.

A total of 44 patients were randomized into either the intervention or usual care groups. Patients in the intervention group received a symptom diary with education and counseling for 90 minutes, which was developed based on the HF Society of America guideline, at baseline.[36] Additional biweekly booster sessions were done by the principal investigator via phone to discuss keeping the symptom diary, review important points from education and counseling sessions, and support patients. Heart failure events, which were defined as the composite of HF-related deaths and hospitalizations, and emergency department visits due to HF deterioration, were collected at three months via medical record reviews and interviews with patients or their families. Health-related quality of life, self-care maintenance, depressive symptoms, and New York Heart Association

functional class were measured at baseline, one month, and three months. The effectiveness of the intervention was evaluated by comparing group differences in changes in health-related quality of life and self-care maintenance, and the number of HF events for three months.

In chapter seven, summary and conclusions from the findings of prior chapters are presented. Clinical implications and recommendations for future research are suggested. It is anticipated that findings from each chapter will contribute to comprehensive evaluation of the symptom experience of patients with HF by clinicians and researchers by suggesting the importance of assessing co-occurring symptoms (symptom clusters) and addressing issues related to existing symptom instruments. Results from this dissertation will translate into significant benefits for patients with HF and healthcare providers by providing evidence of the advantages of regular symptom monitoring in order to facilitate early identification of worsening symptoms of HF and initiation of timely responses.

Figure 1.1. A specific-situation theory of heart failure self-care

Source: Riegel B, Dickson VV. A situation-specific theory of heart failure self-care. Journal of cardiovascular nursing 2008; 23:190-6

CHAPTER TWO

Symptom clusters in Men and Women with Heart Failure and Their Impact on Event-Free Survival

Introduction

Heart failure (HF) is a serious health problem worldwide. In the United States alone, HF afflicts around 5.7 million people.[37] Physical and emotional symptoms are a defining feature of HF. Patients with HF have reported experiencing an average of 15 physical and emotional symptoms.[38] Occurrence of multiple symptoms adversely affect patient lives by increasing psychological distress and decreasing quality of life.[10, 38-41]

To date, most researchers have focused on symptoms in isolation.[42] However, patients with HF commonly experience more than one symptom at a time.[38-41] The effect of multiple, concurrent symptoms on outcomes may be multiplicative.[43-46] Patients with more symptoms or a greater degree of symptom burden have worse outcomes.[38, 40, 44] Fatigue severity mediated the association between pain and performance status in patients with cancer.[44] Thus, the investigation of multiple symptoms as an interconnected experience is necessary to obtain a more complete picture of patient symptom experiences.

The consideration of symptom clusters, defined as two or more interrelated symptoms occurring together provides a novel approach to symptom assessment and management.[47] Patient's ability to recognize a change in condition that requires urgent attention from their healthcare providers may be facilitated by knowledge about symptom clusters.[48] Identifying the profiles of patients who are at risk for worse outcomes based on symptom clusters may support the development and delivery of effective, individualized strategies for specific groups of patients.[48]

Gender may play a role in the HF symptom experience because HF characteristics, including etiology and prevalence of HF symptoms, differ between men and women.[49] Women tend to present with more signs and symptoms related to HF (e.g., dyspnea, fatigue, lower extremity edema, third heart sound, jugular venous distension, and rales) than men.[50-51] Some symptoms, such as fatigue, depression, and anxiety, are reported to be more prevalent and severe in women than men.[38, 52-54] In addition, symptoms are an important determinant of outcomes, such as mortality and quality of

life.[10, 38-40, 55-56] Given that women with HF tend to have worse outcomes compared to men,[56-59] it is possible that symptom experiences are different between men and women.[50, 60] Thus, comparison of symptoms between genders may provide valuable information for tailoring interventions for patients with HF.

The purpose of this study was to compare symptom clusters between men and women with HF, differences in patient characteristics among symptom clusters, and the impact of these symptom clusters on outcomes. The specific aims were to: (1) determine whether different symptom clusters were present in men and women with HF, (2) compare patient characteristics of groups within symptom clusters, and (3) examine the impact of symptom clusters on event-free survival defined as time to first cardiac event (i.e., death, rehospitalization, or emergency department [ED] visit due to cardiac causes).

Methods

The data for this study were compiled from three prospective, longitudinal studies that had similar inclusion and exclusion criteria. Institutional Review Board approval was obtained for each study. Eligibility of patients who were referred to the investigators by nurses and physicians at each site was confirmed by the investigators or trained research nurses using medical record review. Patients who agreed to participate in the study provided written informed consent and completed the questionnaire packets during a visit to the General Clinical Research Center. Patients were followed for a median of 361 days to obtain cardiac event-free survival data.

Patients

A total of 331 patients were included in this study. Patients were recruited from HF outpatient clinics associated with six large community hospitals or academic medical centers in Kentucky, Georgia, and Indiana. Patients were included who: (1) had a confirmed diagnosis of HF with either preserved or non-preserved systolic function, (2) were receiving optimal medical therapy, (3) were able to read and speak English, and (4) had no obvious cognitive impairment that prevented completing the questionnaire packets and interview with research nurses. Patients were excluded if they had: (1) valvular heart disease as an etiology of their HF, (2) a myocardial infarction within the previous three months, (3) been referred for heart transplantation, or (4) major life-threatening

comorbidities such as end-stage renal or liver disease. Exclusion criteria for this study were selected because HF resulting from valvular heart disease may be correctable unlike HF from other etiologies. In addition, patients who had a myocardial infarction recently, been referred for heart transplantation or serious comorbidities are more likely to be hemodynamically unstable and have a shorter life expectancy.

Measures

Heart failure symptoms

Symptoms were identified using the Minnesota Living with Heart Failure Questionnaire (MLHF),[61] which consists of 21 items assessing health-related quality of life in patients with HF. The instrument contains the following eight items measuring distress from HF-related symptoms that are thought to influence health-related quality of life:[10, 40, 62-63] edema, dyspnea, fatigue/increased need to rest, fatigue/low energy, sleep disturbances, worrying, feeling depressed, and cognitive problems (difficulty concentrating or remembering things). Patients rated each item on a scale from 0 (no distress) to 5 (very severe distress). In this study the internal consistency of these eight items was demonstrated by a Cronbach's alpha of 0.89.

Demographic and clinical characteristics.

Demographic and clinical characteristics (e.g., age, gender, ethnicity, and body mass index [BMI]) were obtained using a demographic and clinical questionnaire. Total comorbidity scores were obtained from the Charlson Comorbidity Index.[64] The scores of the Charlson Comorbidity Index were weighted by taking into account the number and seriousness of comorbid illnesses. New York Heart Association (NYHA) functional classification was determined by trained research nurses via in-depth structured patient interviews.

Cardiac event-free survival.

Cardiac event-free survival was defined as time to first cardiac event which included death, rehospitalization, or ED visit due to cardiac reasons. The data were obtained by monthly follow-up calls to patients or family and by administrative review of medical records and public death records.

Statistical Analyses

Data were analyzed using SAS (version 9.1, SAS Institute Inc, Cary, NC). Descriptive statistics including frequency distributions, means, standard deviations, and ranges were used to describe the demographic and clinical characteristics of patients.

Cluster analysis was used to identify symptom clusters because this technique maximizes the homogeneity of variables within clusters while simultaneously maximizing the heterogeneity between clusters.[65] We used the hierarchical cluster agglomerative approach which begins with treating each variable as a separate cluster and then combines the variables into consecutively larger clusters based on their similarity. The Euclidean distance was used to measure the similarity of variables. Proximity between groups of variables was measured using Ward's method by which clusters were joined by minimizing the total within-cluster error sum of squares. Ward's method was chosen because it is sensitive to outliers and effective when identifying clusters compared to other inter-group proximity measures.[66]

The resulting clusters were pictorialized with dendrograms, which illustrate the proximity of variables to each other. Semi-partial R-squared scores were used to determine the degree of homogeneity of variables within the clusters, with larger values reflecting less similarity between clusters. To decide the optimal number of clusters we used dendrograms, the *pseudo-F* statistic, and the *pseudo-T* squared statistic.[66] To demonstrate the validity of the identified number of clusters, principal component analysis was conducted and the first and second principal component scores were plotted.[67]

Based on the identified symptom clusters, patients were divided in groups by the median split of total scores of each symptom cluster, which were calculated by summing distress scores of symptoms in each cluster. Analysis of variance (ANOVA) or the chi-square test was used to compare differences in demographic and clinical characteristics among four patient groups (i.e., low distress, physical distress, emotional/cognitive distress, and high distress). Post hoc analysis was done using the Bonferroni adjustment. Hierarchical Cox proportional hazards regression was used to determine whether total scores of symptom distress within symptom clusters predicted time to first cardiac event

(i.e., death, rehospitalization, or ED visit due to cardiac reasons) after controlling for age, gender, total comorbidity scores, BMI, and NYHA functional class.

Results

Sample Characteristics

The mean age of patients was 61years with a range of 24 to 87 years (Table 1). Patients were predominately male, Caucasian, married or cohabitating, and obese. The majority of patients had an ischemic HF etiology, and were in NYHA functional classes III and IV. A greater percentage of women were non-Caucasian (i.e., African-American and Hispanics), and had non-ischemic HF etiology (e.g., idiopathic and hypertension) than men ($p<0.05$).

Symptom distress scores from each individual symptom are illustrated in Table 2. All patients reported that among physical symptoms fatigue/low energy was the most distressful and edema the least (mean ± S.D 3.0 ±1.7 vs. 1.2 ± 1.5), while among emotional/cognitive symptoms, worrying was the most distressful and feeling depressed the least (mean ± S.D 1.7 ±1.8 vs. 1.5 ± 1.5). Women reported significantly higher levels of distress from fatigue/ increased need to rest, sleep disturbances, and feeling depressed than men, while all other symptoms were rated similarly by men and women.

Symptom Clusters

Three identical clusters were identified in men and women. The first cluster labeled the physical symptom cluster included dyspnea, fatigue/increased need to rest, fatigue/low energy, and sleep disturbances. The second cluster labeled the emotional/cognitive symptom cluster, included worrying, feeling depressed, and cognitive problems. Edema formed a third, single symptom cluster. The dendrograms and the *pseudo-F* and *pseudo-T* squared statistics indicated that three clusters were the optimal solution, which was also confirmed by the principal component analysis (Figures 1 and 2). Because the definition of a symptom cluster is two or more symptoms that occur simultaneously, edema was excluded from further analyses. Also, because gender differences in symptom clusters were not found, the whole sample was used for further analyses.

Characteristics of Symptom Cluster Groups

Patients were divided into four groups based on the median split of total symptom distress scores of the physical and emotional/cognitive symptom clusters. The "low distress" group included patients with low distress in both physical and emotional/cognitive symptom clusters. The "physical distress" group included patients with high distress scores in the physical symptom cluster and low distress scores in the emotional/cognitive symptom cluster. The "emotional/cognitive distress" group included patients with high distress scores in the emotional/cognitive symptom cluster and low distress scores in the physical symptom cluster. The "high distress" group included patients with high distress scores in both physical and emotional/cognitive symptom clusters.

Comparisons of characteristics among the four groups are summarized in Table 3. Patients in the physical distress and high distress groups consisted primarily of females and those in NYHA functional class III and IV. Patients in the emotional/cognitive distress and high distress groups were younger than patients in the low distress and physical distress groups. Patients in the high distress group had a greater comorbidity burden than those in the other three groups. Fewer beta blockers, angiotensin-converting enzyme inhibitors (ACE I), or angiotensin-receptor blockers (ARB) were taken by patients in the physical distress group compared to the other three groups.

Prediction of Cardiac Event-Free Survival

During a median follow-up period of 361 days, there were 82 cardiac events (Table 4): death 2% (2/82); hospitalization 81% (66/82); and ED visit 17% (14/82). The cardiac event rates of the four groups were 17.5% (22/126) in the low distress group, 16.7% (6/36) in the physical distress group, 32.6% (15/46) in the emotional/cognitive distress group, and 31.7% (39/123) in the high distress group. The results of the multivariate hierarchical Cox regression analysis for symptom clusters are summarized in Table 5. Because the total symptom distress scores in the physical and emotional/cognitive symptom clusters were significantly correlated (r=0.644, p<0.01), the interaction effect of the two symptom clusters was included in the analysis. The total symptom distress score in the emotional/cognitive symptom cluster, but not the physical symptom cluster, was an independent predictor of cardiac event-free survival after

adjusting for age, gender, total comorbidity scores, BMI, and NYHA functional class (p=0.007). Every one unit increment in distress scores in the emotional/cognitive symptom cluster was associated with an 18% increase in the risk for a cardiac event.

The four groups were entered as categorical variables into the multivariate hierarchical Cox regression to determine which group had a higher risk for a cardiac event. Figure 3 depicts the survival curves of the four groups after controlling for age, gender, total comorbidity score, BMI, and NYHA functional class. Patients in the emotional/cognitive distress (hazard ratio [HR]: 2.40, 95% confidence interval [CI] 1.31-4.41) and high distress groups (HR: 2.02, 95% CI 1.03-3.95) had a higher risk for a cardiac event compared to those in the low distress group. However, there were no differences in time to first cardiac event between patients in the physical distress and low distress groups.

Discussion

This was the first study to compare symptom clusters between genders in patients with HF and to determine whether symptom clusters predicted cardiac event-free survival. Contrary to what we hypothesized based on prior research, gender differences in HF symptom clusters were not found. Between the two symptom clusters, only the emotional/cognitive symptom cluster predicted higher risk for a cardiac event.

The relationships among individual symptoms and outcomes in patients with HF have been reported in previous studies.[55, 68-73] For example, in the study of Ekman and colleagues dyspnea severity was a predictor of increased death and all-cause rehospitalization and fatigue severity was a predictor of rehospitalization due to HF exacerbation.[55] Heart failure patients with depressive symptoms have also been reported to have up to a two-fold greater risk for death (HR=1.08-2.25).[68, 70-71] While these results are informative, they do not provide a full understanding of the relationship between symptoms and outcomes of patients with HF given that patients commonly experience multiple symptoms concurrently.

There are data suggesting that the presence of co-occurring symptoms may convey a higher risk for negative outcomes[43-45] that might be only identifiable when symptoms are considered together. The coexistence of anxiety and depressive symptoms in patients with coronary heart disease was associated with a higher risk for mortality

when compared with the presence of either symptom alone.[43] Advanced cancer patients with concurrent four symptoms were nine times more likely to die compared to those with one symptom.[45] Thus, exploring symptom clusters appears to be important for accurate risk assessment of patients with HF.

We demonstrated a greater risk for shorter cardiac event-free survival time in patients with higher distress scores from the emotional/cognitive symptom cluster than the physical symptom cluster. A potential reason for this finding is that healthcare providers and patients often focus more on physical than psychological symptoms. Because the primary reasons for seeking health care are usually related to physical manifestations of HF, healthcare providers tend to treat physical symptoms and not explore psychological factors that might be an underlying cause of HF events.[74] For example, the ACC/AHA guideline for diagnosis and management of HF address physical signs and symptoms, but not patient emotional or cognitive symptoms.[75] Consequently, the assessment of emotional or cognitive symptom status might not often occur and subsequently not be managed appropriately.

The lack of an impact of physical symptom cluster on cardiac event-free survival may also be explained by the association between self-care and symptoms experienced by patients with HF. Heart failure patients whose symptoms are severe enough to impair daily activities have a better understanding of the importance of self-care.[76] Severe physical symptoms may also motivate patients to perform better self-care to prevent worsening symptoms. On the other hand, the negative impact of individual emotional/cognitive symptoms on engaging in self-care was reported in previous studies:[77-82] Patients who are depressed, anxious, or cognitively impaired tend to experience greater difficulty with and fewer benefits to the performance of self-care (e.g., taking medications as directed and monitoring symptoms regularly), difficulty remembering complex recommendations on medication, diet, or symptom monitoring, and have less ability to accurately interpret the changes in symptom status.

There is evidence that patients with depressive symptom often experience cognitive impairment simultaneously. Brain structural changes that involved in emotional and cognitive functions (e.g., hippocampus and caudate nuclei) were observed in patients with HF,[83] which may explain why they occur as a cluster. Other evidence to support this

conclusion includes the study by Alves and colleagues[84] in which depressive symptom scores predicted overall cognitive function in patients with HF. Cognitive function was improved by eight-week antidepressant treatment in HF patients with major depressive disorder.[84] Our data suggest that coexistence of both symptoms might magnify the detrimental impact of each symptom and worsen outcomes more than the presence of a single symptom. Thus, it is important to monitor and manage symptoms in cluster in patients with HF.

In the cluster analysis, edema was not included in either symptom cluster for either gender. This may be related to lower distress scores for edema compared to the other symptoms in this study. Given that clusters were constructed by minimizing the heterogeneity within clusters, the lower distress score for edema led to greater dissimilarity with other symptoms. Patients who experience edema commonly delay contacting their healthcare provider before acute cardiac decompensation;[85-86] this may occur because they are less likely to experience distress from edema.

Information about patient characteristics may be of value for healthcare providers to develop and deliver efficacious strategies, such as risk assessment, that may help to prevent potential adverse outcomes. Thus, we examined characteristics of patients according to symptom cluster groups. There were more women in the "physical distress" and "high distress" groups in which patients experienced more distress from physical symptoms. Similar results were reported in previous studies in which women experienced more physical impairment than men.[59, 87-88] Patients were primarily younger in the "high distress" and "emotional/cognitive distress" groups, which suggests that younger patients with HF experience greater distress from the emotional/cognitive symptom cluster regardless of the distress associated with the physical symptom cluster. This finding is in line with previous research reporting better physical and worse emotional status in younger patients with HF.[10, 71, 73, 89] Given that greater distress from the emotional/cognitive symptom cluster was associated with earlier cardiac events in this study, healthcare providers should focus attention on younger patients who have poor psychological status regardless of their physical status.

There were several limitations of this study. First, the results of this study may not be generalizable to all patients with HF, particularly older patients and ethnic groups

other than Caucasian. Second, the MLHF was used as the measure of symptom distress. This instrument is primarily a measure of health-related quality of life. However, given the demonstrated reliability and validity of the MLHF, using symptom data from this instrument was a scientifically sound approach to meet the aims of this study. Although patients with HF experience a wide range of symptoms, we only evaluated seven symptoms. The limited number of symptoms included might not fully capture patient symptom experiences. However, the symptoms included in this study are reported most frequently by patients with HF.[38-40] Third, we assessed only symptom distress levels. Additional symptom dimensions including frequency and intensity may also need to be considered. In cancer patients, symptom distress was relatively persistent over time compared to intensity[90] and baseline symptom distress predicted distress levels three and six months later.[91] Thus, symptom distress might be the best predictor of long-term outcomes like survival.

Conclusions

In this study we demonstrated that symptoms occur in clusters rather than in isolation. These findings provide a new perspective on symptom assessment and management in patients with HF by highlighting the importance of symptoms clusters. Identifying symptom clusters may guide and support the development of more comprehensive interventions.[48, 92] Teaching patients about symptom clusters might also improve symptom recognition by promoting greater patient self-awareness. If patients know that symptoms occur in clusters, awareness of one symptom may trigger self-assessment for presence of additional symptoms, which might facilitate health care-seeking behaviors for changes in symptom status in a timely manner. Thus, focusing on symptom clusters may lead to better patient outcomes.

Table 2.1. Sample characteristics (N=331)

Characteristics	Total	Male (n=216)	Female (n=115)	*p*-value
	Mean (± S.D) or N (%)			
Age, years	61 (± 11)	60 (± 11)	62 (±11)	0.233
Ethnicity				<0.001
Caucasian	269 (81%)	188 (87%)	81 (70%)	
Marital status				<0.001
Married/ cohabitate	181 (55%)	141 (65%)	40 (35%)	
Single/divorced/ widowed	150 (45%)	75 (35%)	75 (65%)	
Ischemic etiology of HF	179 (54%)	137 (65%)	42 (38%)	<0.001
NYHA class				0.203
I/II	128 (39%)	91 (42%)	37 (32%)	
III	145 (44%)	90 (42%)	55 (48%)	
IV	58 (18%)	35 (16%)	23 (20%)	
Body mass index (kg/m^2)	32 (± 7)	31 (± 7)	32 (± 8)	0.548
Charlson comorbidity index	3.4 (± 2.0)	3.4 (± 2.0)	3.4 (± 2.0)	0.837
ACE I or ARB	278 (84%)	186 (86%)	92 (80%)	0.078
Beta blocker	287 (87%)	185 (86%)	102 (89%)	0.630
Total scores of physical symptom cluster‡	10 (± 6)	10 (± 6)	12 (± 6)	0.004
Total scores of emotional/ cognitive cluster‡	5 (± 5)	5 (± 4)	5 (± 5)	0.453

Notes. ‡ Higher scores indicate greater distress
HF: heart failure; NYHA: New York Heart Association functional class; ACE I: angiotensin-converting enzyme inhibitors; ARB: angiotensin receptor blocking agents

Table 2.2. Symptom distress scores between men and women (N=331)

	Male (n=216)	Female (n=115)	*p*-value
Edema	1.1 (± 1.5)	1.4 (± 1.6)	0.130
Dyspnea	2.7 (± 1.8)	2.9 (± 1.7)	0.747
Fatigue/increased need to rest	2.0 (± 1.7)	2.8 (± 1.8)	0.011
Fatigue/low energy	2.9 (± 1.7)	3.3 (± 1.6)	0.150
Sleep disturbances	2.0 (± 1.8)	2.5 (± 1.9)	0.010
Worrying	1.7 (± 1.7)	1.7 (± 1.9)	0.305
Feeling depressed	1.4 (± 1.6)	1.6 (± 1.9)	0.021
Cognitive problems	1.6 (± 1.7)	1.8 (± 1.9)	0.213

Values are mean (± S.D)

Table 2.3. Characteristics of patients in symptom cluster groups (N=331)

	Low distress both	Physical distress	Emotional/ cognitive distress	High distress both	
	n= 126	n= 36	n= 46	n= 123	*p*-value
Age, years	64 (± 12)[a]	66 (± 8)[a]	58 (± 12)[b]	58 (± 10)[b]	<0.001
Female	35 (28%)	18 (50%)	11 (24%)	51 (42%)	0.011
Ethnicity					0.793
Caucasian	103 (82%)	29 (81%)	39 (85%)	98 (80%)	
Marital status					0.020
Married/ cohabitate	68 (54%)	12 (33%)	31 (67%)	70 (57%)	
Single/ divorced/ widowed	58 (46%)	24 (67%)	15 (33%)	53 (43%)	
Ischemic etiology of HF	69 (55%)	21 (58%)	29 (63%)	60 (49%)	0.451
NYHA class					<0.001
I/II	74 (59%)[a]	5 (14%)[a]	24 (52%)[b]	25 (20%)[a]	
III	37 (29%)[a]	22 (61%)[b]	20 (44%)[b]	66 (54%)[b]	
IV	15 (12%)[b]	9 (25%)[b]	2 (4%)[a]	32 (26%)[a]	
Body mass index (kg/m^2)	30 (± 8)	33 (± 7)	32 (± 7)	32 (± 7)	0.276
Charlson comorbidity index	3.1 (± 1.7)[a]	3.5 (± 1.6)	3.0 (± 1.5)	3.9 (± 2.2)[b]	0.004
ACE I or ARB	113 (90%)[a]	22 (61%)[b]	41 (89%)[a]	102 (83%)[a]	<0.001
Beta blocker	116 (92%)[a]	26 (72%)[b]	37 (80%)[a]	108 (88%)[a]	0.009
Total scores of physical symptom cluster	5 (± 3)[a]	14 (± 3)[b]	7 (± 2)[a]	16 (± 3)[b]	<0.001
Total scores of emotional/ cognitive symptom cluster	1 (± 1)[a]	1 (± 1)[a]	6 (± 2)[b]	10 (± 3)[b]	<0.001

Notes. Values are mean (± S.D) or N (%)
Low distress: low distress scores in both symptom clusters; Physical distress: high distress scores in physical symptom cluster; Emotional/cognitive distress: high distress scores in emotional/cognitive symptom cluster; and High distress: high distress scores in both symptom clusters
HF: heart failure; NYHA: New York Heart Association functional class; ACE I: angiotensin-converting enzyme inhibitors; ARB: angiotensin receptor blocking agents
Groups with different superscripts are significantly different from each other. Groups without superscript do not differ from one another.

Table 2.4. Cardiac events in symptom cluster groups (N=82)

	Low distress both	Physical distress high	Emotional/ cognitive distress high	High distress both
	n= 22	n= 6	n= 15	n= 39
Death	2 (2%)	0 (0%)	0 (0%)	0 (0%)
Rehospitalization	17 (13%)	5 (14%)	11 (24%)	33 (27%)
Emergency department visit	3 (2%)	1 (3%)	4 (9%)	6 (5%)

Notes. Values are N (%)
Low distress: low distress scores in both symptom clusters; Physical distress: high distress scores in physical symptom cluster; Emotional/cognitive distress: high distress scores in emotional/cognitive symptom cluster; and High distress: high distress scores in both symptom clusters

Table 2.5. Multivariate Cox regression analysis for symptom clusters (N=331)

	Hazard Ratio	*p*-value	95% Confidence Interval
Age	0.985	0.180	0.96-1.01
Female	1.633	0.059	0.98-2.72
NYHA			
NYHA I/II	1.000		
NYHA III	1.005	0.985	0.60-1.69
NYHA IV	0.800	0.542	0.39-1.64
Charlson Comorbidity Index	1.217	0.003	1.07-1.39
Body mass index (kg/m^2)	0.959	0.020	0.93-0.99
Emotional/Cognitive Symptom Cluster Score	1.184	0.021	1.03-1.37
Physical Symptom Cluster Score	1.039	0.285	0.97-1.12
Interaction between Emotional/Cognitive and Physical Symptom Cluster	0.990	0.052	0.98-1.00

Total model *p*-value=0.007

Figure 2.1. Symptom cluster dendrogram for men

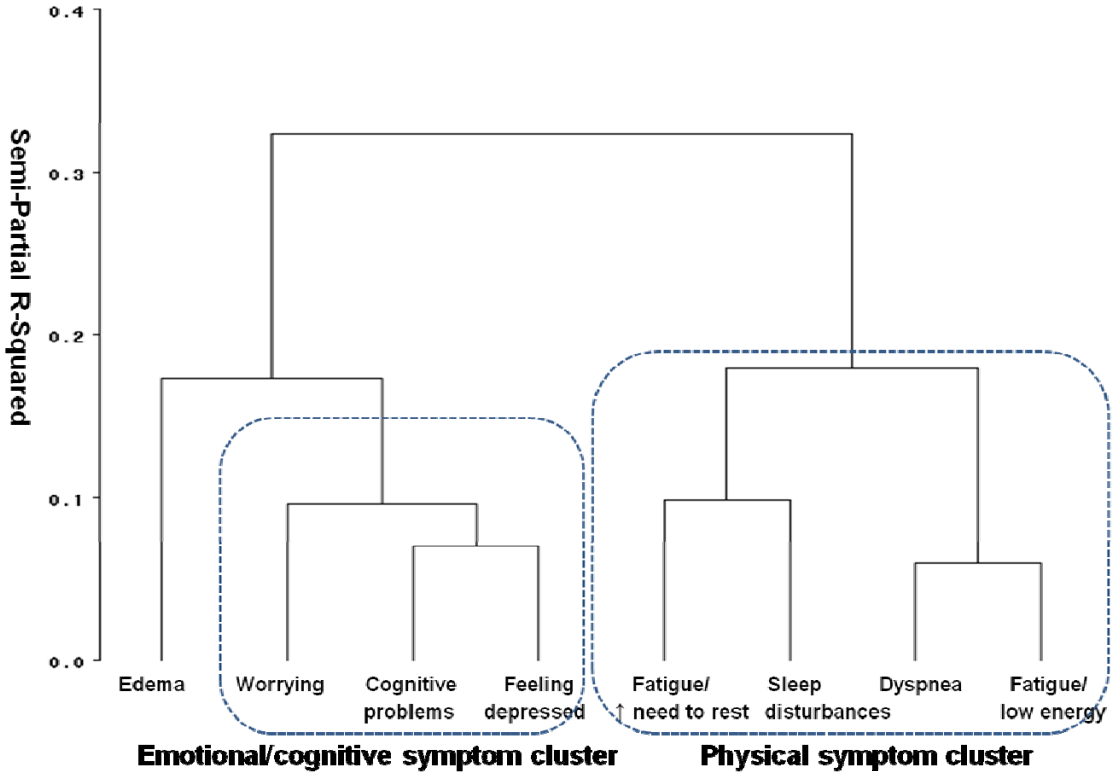


Figure 2.2. Symptom cluster dendrogram for women

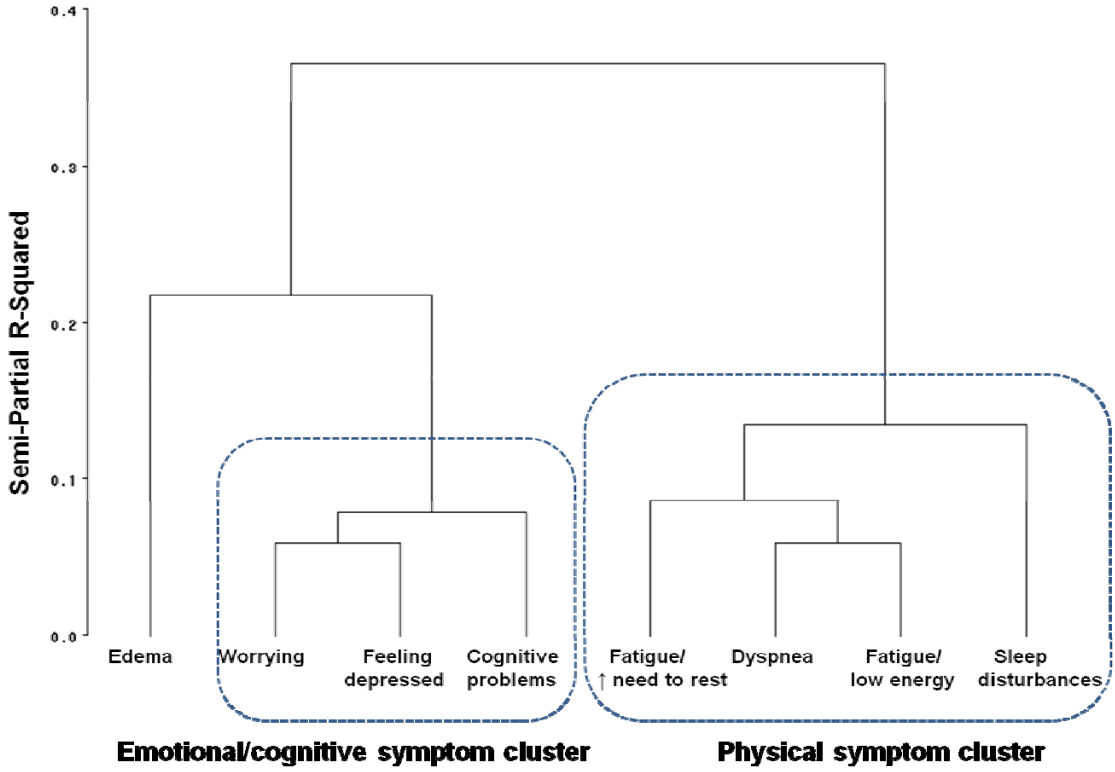
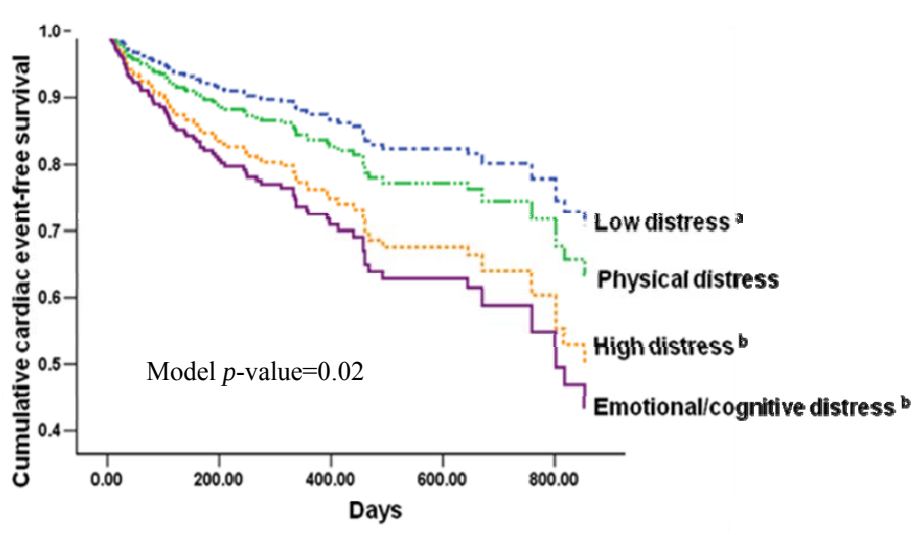


Figure 2.3. Cardiac event-free survival by four symptom cluster groups



The number of patients who were followed up in given time points

Low distress	126	97	57	34	20
Physical distress	36	26	14	8	2
Emotional/cognitive distress	123	73	39	21	11
High distress	46	33	22	16	2

Note. Groups with different superscripts are significantly different from each other. Groups without superscript do not differ from one another.

Low distress: low distress scores in both symptom clusters; Physical distress: high distress scores in physical symptom cluster; Emotional/cognitive distress: high distress scores in emotional/cognitive symptom cluster; and High distress: high distress scores in both symptom clusters

CHAPTER THREE

Heart Failure Symptom Measures: systematic review

Introduction

Heart failure (HF) is a progressive, irreversible clinical syndrome, characterized by a variety of symptoms.[16] Patients with HF report an average of nine physical symptoms even when they are not experiencing an exacerbation.[33] Dyspnea and fatigue, the most prevalent HF symptoms, are experienced by more than half and up to 94% of all patients with HF, respectively.[8, 33, 50, 93] The presence of multiple symptoms negatively affects functional status, quality of life, and survival.[8, 17, 93-94] Thus, it is essential to provide effective symptom assessment and management in the HF population.

One of the primary goals of HF management is reducing patient symptom burden. To achieve this goal, conducting a systematic symptom assessment is essential. It is important that healthcare providers inquire not only about the most common physical symptoms of HF such as dyspnea, but also psychological symptoms such as depressive symptoms. Comprehensive evaluation of symptoms allows healthcare providers to (1) help reduce symptom burden, a focus important to patients and (2) assess the effectiveness of interventions to improve symptoms. However, there are few symptom instruments developed for patients with HF that measure the full range of symptoms experienced by patients. Although the symptom experience is multi-dimensional, meaning that it includes not only presence or absence of symptoms, but frequency, severity, and distress related to symptoms, some instruments are designed to evaluate only one aspect of the symptom experience. Thus, in order to accurately assess the symptom experience in patients with HF, it is critical to evaluate commonly used instruments.

The purpose of this paper is to provide a critical review and analysis of self-reported symptom measures designed for and used in patients with HF. The specific aims of this paper are to (1) provide a conceptual definition of symptoms; (2) identify symptom instruments designed for HF patients; and (3) evaluate their quality with five criteria (i.e., content, measuring scale, psychometric properties, completion process, and information).

Conceptual Definitions of Symptoms

According to the Oxford English Dictionary, a symptom is defined as "bodily or mental phenomenon, circumstance, or change of condition arising from and accompanying a disease or affliction, and constituting an indication or evidence of it."[95] This definition is distinguished from that of a sign, which is "objective evidence or indication of disease."[96] Researchers commonly conceptualize symptoms as subjective phenomena indicating perceived alterations in normal function (e.g., biopsychosocial aspects, sensations, or cognition).[97-98] Symptoms are not merely the reflection of functional or structural abnormalities in body organs and systems. Rather, they are integrated and meaningful experiences that reflect the reality of the person experiencing them in the context of his or her cultural and personal situation.[99] Thus, symptoms change over time within a person and are experienced in a variety of ways among those with the same symptoms.[100]

Symptoms are multi-dimensional. Lenz and colleagues[46] suggested four dimensions of symptoms – quality, timing, intensity, and distress. Quality refers to symptom characteristics (e.g., throbbing or pounding pain), the location of a given sensation, and response to a particular intervention. Timing is the frequency and duration of symptoms. Intensity refers to symptom severity and is commonly used in clinical and research settings due to its relatively easy quantification.[46] Distress refers to the extent to which the person is bothered by a symptom. Although symptom occurrence, intensity, and distress are strongly inter-correlated, they are unique components of the symptom experience.[101]

People commonly experience multiple symptoms.[46, 98] The impact of co-occurring symptoms is multiplicative rather than additive. The coexistence of four symptoms in advanced cancer patients was associated with nine times higher risk for death compared to the presence of one symptom.[45] Therefore, symptoms are subjective, experiential, and multiplicative if several symptoms occur simultaneously.

Methods

A systematic search using the PubMed and Cumulative Index of Nursing and Allied Health Literature (CINAHL) databases (August 1978 to July 2011) was

undertaken. Search terms were selected by scanning search strategies of a systematic review on a similar topic[32] and examining index terms (e.g., subject headings). Combinations of key words and subject headings were used for the electronic database search. The key words searched in the two databases were (1) (Heart failure) AND (Signs and Symptoms) AND (Scale OR Instrument OR Checklist OR Inventory) AND (Evaluation OR Assessment OR Measurement OR Rating) AND (Distress OR Severity OR Frequency OR Prevalence); and (2) (Heart failure) AND (Signs and Symptoms) AND (Reliability OR Validity OR Psychometric). Because CINAHL yielded few citations, a new search using index terms was used: (Heart Failure-subheading: Symptoms) AND (Major heading: Symptoms OR Quality of life OR Self-care OR Palliative care OR Cardiac patients). References lists and bibliographies of all pertinent articles identified by online database searches were searched.

The search was limited to journal articles and proceedings which were published in English. Instruments were included in the review if they were primarily designed or modified for patients with HF to measure multiple symptoms (> two symptoms). Exclusion criteria included quality of life instruments or their modified versions; single-symptom item instruments; instruments measuring symptom perception (awareness) or functional status rather than symptoms; or diary-type instruments.

Instrument Evaluation

Instruments were evaluated based on five criteria, which we modified according to the criteria developed by Kirkova and colleagues[32] to rate the quality of the instrument. Because Kirkova and colleagues did not explicitly describe how to rate each category of an ideal instrument, we modified the original five evaluation categories with specific evaluation criteria for each category (Table 1). The five evaluation categories were: (1) contents (i.e., comprehensive assessment of symptoms included in the instruments); (2) measuring scale (i.e., simplicity and ease of use by subjects and suitability in clinical and research purposes); (3) psychometric properties (i.e., precision and accuracy); (4) completion process (i.e., burden of the instrument completion); and (5) information (i.e., usefulness to facilitate effective symptom management).

Results

The search strategies yielded 323 articles and proceedings. Of those, 13 articles[8, 102-111] and proceedings[112-113] met the inclusion and exclusion criteria for this review. Of the 13 articles and proceedings found, seven symptom measures developed for patients with HF that included three or more symptoms were identified (Table 2). However, the EuroHeart Failure Survey-Symptom[110] and the modified version of the Cardiac Symptom Survey[111] were excluded because information on these instruments (e.g., psychometric properties or how it was developed) was not available in the literature or from the corresponding authors. An article,[103] in which the Memorial Symptom Assessment Scale-HF (MSAS-HF) was used, was also excluded in this review. Although the authors claimed to use the MSAS-HF, only 10 out of 32 symptoms were used and patients were asked to report their symptom experience over the two weeks instead of seven days, which was the timeframe used in the MSAS-HF.

Of the five symptom instruments, three were modified based on symptom measures developed for patients with cancer or cardiac surgery (i.e., the HF Symptom Survey[112] from the Cardiac Symptom Scale, the M.D. Anderson Symptom Inventory-HF [MDASI-HF][108] from the M.D. Anderson Symptom Inventory, and MSAS-HF[113] from the MSAS).

The symptom measures reviewed in this paper included signs (e.g., weight gain and diarrhea) along with symptoms, despite the fact that the definitions of signs, defined as "objective evidence or indication of disease"[96] and symptoms, defined as "bodily or mental phenomenon, circumstance, or change of condition arising from and accompanying a disease or affliction, and constituting an indication or evidence of it"[95] are different and clearly describe distinct phenomenon. However, it was impossible to separate signs out from the measures and evaluate them. Thus, we reviewed symptom measures as they were.

Contents

The five instruments varied in the number of symptoms/ signs assessed (13-32 symptoms/ signs). Many symptoms overlapped, yet were not always included in all five measures (Table 3). The HF Signs and Symptoms Checklist,[107] the MDASI-HF,[108] and MSAS-HF[113] included not only typical HF symptoms related to fluid overload (e.g.,

fatigue and swelling) but also atypical symptoms (e.g., dry mouth and diarrhea). Three of the five instruments contained both physical and psychological symptoms, but the HF Symptom Checklist[102] and the HF Signs and Symptoms Checklist[107] did not. Orthopnea, paroxysmal nocturnal dyspnea, edema, and coughing were addressed in all five instruments. Psychological symptoms were not included in the HF Signs and Symptoms Checklist[107] and the HF Symptom Checklist[102], and fewer psychological than physical symptoms were included (2-5 psychological symptoms).The most frequently included psychological symptom was feeling depressed.

Symptoms were described with different descriptors. Coughing was further specified as "worsening cough,"[112] "nighttime cough,"[108] "dry and hacking cough,"[102] and "severe cough -keeping awake at night or chest hurts when coughing."[107] Symptoms items in the HF Signs and Symptoms Checklist were more descriptive than other instruments. For example, weight gain was also further specified as "greater than 2 pounds in a day or 5 pounds in a week" in the HF Signs and Symptoms Checklist,[107] while general terms were used in other measures such as "weight gain" in the MSAS-HF.[113]

Multiple symptom dimensions (e.g., frequency and severity) were addressed in three measures (i.e., the HF Symptom Survey, MDASI-HF, and MSAS-HF), while only presence or absence of symptoms was assessed in the HF Symptom Checklist[102] and the HF Signs and Symptoms Checklist.[107] Symptom frequency was the least frequently reported while severity and distress (or interference) were the most frequently included. There were no symptom measures that inquired about co-occurring symptoms to examine the presence of symptom clusters.

Measuring Scale

Reading levels of the instruments were not explicitly addressed. However, the authors who developed the HF Signs and Symptoms Checklist and the MDASI-HF mentioned their efforts to simplify wording of items in order to increase patients' understanding.[107-108]

Depending on the purpose of symptom instruments (e.g., daily symptom or intermittent symptom assessment), patients were asked to recall their symptom experience within a certain time period. Timeframes varied from "during last 24 hours"

[108] to "during previous two weeks,"[102] although most instruments measured symptoms that had been experienced over seven days.

With the exception of the two instruments (i.e., the HF Signs and Symptoms Checklist and HF Symptom Checklist) measuring the presence or absence of the symptoms (yes or no),[102, 107] numeric ratings were used in three instruments (i.e., the HF Symptom Survey, MDASI-HF, and MSAS-HF). [108, 112-113] In the HF Symptom Survey, patients were asked to write down the appropriate numeric values to indicate their symptom scores from 0 to 10, while response options in the MSAS-HF and the MDASI-HF were laid out and patients circled their rating. Each numeric point in the scale was labeled with adjectives (e.g., mild and severe) in the MSAS-HF, while adjectives were given at the anchors in the MDASI-HF.

Information about completion rates was unavailable except for the HF Symptom Survey. In a study using the HF Symptom Survey, 5% of patients (7/139) did not fill out all symptom dimensions of each symptom or responded in a contradictory manner (e.g., despite indicating not having a symptom, nonzero ratings of other symptom dimensions for the same symptom were given).[104] No more than 3% of responses per symptom were missing.[104]

Scores on each dimension (e.g., severity and frequency) were commonly derived by summing and/or averaging scores of each symptom. However, to compute total distress scores in the MSAS-HF its original distress scores, which ranged from 0-4, were rescaled with a 0.8 increase.[8] Composite scores of all the dimensions scored were formed in the MSAS-HF and the MDASI-HF. The total burden score in the MSAS-HF was determined by averaging scores in each dimension of symptoms (frequency, severity, and distress).[8] An overall symptom distress score in the MDASI-HF was computed based on the mean scores of six symptom interference items (i.e., how have your symptoms interfered with your life).[108] There were subscales for HF-specific symptoms in the MSAS-HF and the MDASI-HF that were scored by averaging scores of HF relevant symptoms, such as swelling, coughing, and palpitations.

The five symptom measures covered 13 to 32 symptoms/ signs, but the number of items that patients answered was often larger than the number of symptoms included in the measure. This occurs because multiple symptom dimensions were assessed with each

symptom item. For example, in the HF Symptom Survey, in which 14 symptoms were included and four dimensions were assessed in each symptom, patients answered a total of 56 items.

Psychometric Properties

Reliability. Reliability is the indicator of the extent to which measurements yield similar results on repeated testing with a population of individuals or groups.[114] The reliability coefficient is estimated based on subject variability and measurement error and can range from 0 to 1, with 1 indicating perfect reliability without measurement errors. There are two types of reliability measures: internal consistency and stability. Internal consistency reflects the correlations among all the items in the measures, which can be tested with Cronbach's alpha or split halves. Stability represents the reproducibility of a measure administered at different times, which can be expressed with inter-observer reliability or test-retest reliability.[114] Acceptable reliability coefficients are greater than 0.8 for internal consistency and greater than 0.5 for stability.[114] Internal consistency was reported in all instruments except for the HF Signs and Symptoms Checklist. Stability was not reported in any of the five symptom instruments reviewed in this paper.

The HF Symptom Survey. Good internal consistency across the four symptom dimensions (frequency, severity, interference with physical activity, and interference with enjoyment of life) was observed with Cronbach's alphas of 0.80-0.88.[112]

The HF Symptom Checklist. The Cronbach's alpha coefficient was 0.68,[102, 105-106] which is lower than the desirable values of the internal consistency (Cronbach's alpha coefficient $\geq$0.8).[114]

The M.D. Anderson Symptom Inventory-HF. Good reliability was observed for the 13 MDASI-HF core symptoms, eight HF symptoms, and six interference items with Cronbach's alphas of 0.89, 0.83, and 0.92, respectively.[108]

The Memorial Symptom Assessment Scale-HF. Internal consistency reliability of burden scores in each subscale was examined using Cronbach's alphas, which were 0.80 -0.87 for the physical symptom subscale; 0.83- 0.91 for the psychological symptom subscale; and 0.73- 0.85 for the HF symptom subscale.[8, 113]

Validity. Validity is the degree to which instruments measure what they purport to measure.[115] There are several types of validity testing, which are content, criterion

(concurrent and predictive), and construct (e.g., convergent and discriminant, discriminative, and factor structure analysis) validity.[115] Content validity addresses how well the items cover the construct of interest, which is determined based on the judgments of experts in the field. Criterion validity provides evidence about how well scores on a measure are correlated with other measures that have same or highly related constructs and has been used and accepted in the field as a gold standard. Construct validity is a judgment based on the accumulation of evidence demonstrating the relationship between the measure being evaluated and the variables known to be related or theoretically related to the construct measured by the instrument.[115]

The HF Symptom Survey. The 14 symptoms were identified by literature review. A HF expert panel consisting of four nurses examined its content validity.[104] Criterion validity was not reported. Construct validity was examined with convergent and discriminative validations. Moderate to strong correlations were found between the subscale scores of the HF Symptom Survey and the Kansas City Cardiomyopathy Questionnaire, which measures health-related quality of life in patients with HF (r = -0.62 to -0.78).[112] Symptom frequency and severity scores in the HF Symptom Survey increased significantly as New York Heart Association (NYHA) functional class increased from I to IV.[112]

The HF Signs and Symptoms Checklist. Content validity was evaluated by a panel of four HF experts (three advanced practice nurses and one master's prepared cardiac patient educator).[107] Lynn's method,[116] which consists of a two-stage content validity process (instrument development and quantification of content validity using Index of Content Validity), was used to ascertain content validity.

Criterion validity was not explored. Construct validity was supported by demonstrating the association between symptom scores (the number of symptoms reported by patients) and their functional status measured by NYHA functional class.[107] Patients in a hospital care setting experienced more symptoms than patients in an ambulatory care setting.[107]

The HF Symptom Checklist. The items in the HF Symptom Checklist were identified from HF symptoms listed in the Agency for Health Care Policy Research 1994 publication on HF practice guidelines.[102, 105-106] Two cardiac clinical nursing specialists

validated the items.[102, 105-106] High correlations were reported between the items in the HF Symptom Checklist and a symptom checklist which was developed for medical record reviews.[102, 105-106] No information about construct validity was available.

The M.D. Anderson Symptom Inventory-HF. Heart failure symptom items were generated by literature review, patient interviews, and HF experts and refined by a panel of HF experts (10 cardiologists and 10 advanced practice nurses with HF specialty).[108] To ensure content validity the panel of HF experts was carefully selected based on three criteria (cardiology practice for at least five years, at least one publication related to HF management, and considered an expert by the HF community). Index of Content Validity was used to rate the relevance of items by the expert panel.[108] Initially, 30 items were included in the MDASI-HF, and three items were removed (i.e., depression, anxiety, and limitation of physical activity) due to item redundancy identified via cluster analysis.[108]

Criterion validity using concurrent validation was supported by moderate correlations of two commonly used symptom measures with the MDASI-HF (r= 0.59-0.62 for NYHA functional class and r= 0.55-0.65 for the Eastern Cooperative Oncology Group, respectively).[108] Construct validity was evaluated by comparing differences in average severity and interference scores by B-type natriuretic peptide (BNP) categories formed using the cutoff point of 100 pg/mL, which reflects volume expansion and pressure overload in the left ventricle. Significant group differences were observed in symptom severity scores but not interference scores.[108] Factor analysis was performed using eight HF symptom items. Two underlying factors emerged: (1) overt HF symptoms (nighttime cough, paroxysmal nocturnal dyspnea, fatigue, orthopnea, and palpitations); and (2) covert HF symptoms (sudden weight gain, abdominal bloating, and edema).[108]

The Memorial Symptom Assessment Scale-HF. Information on the validity of the MSAS-HF was limited. Zambroski and colleagues modified the MSAS by adding five HF-specific symptoms and eliminating five cancer-specific symptoms from the MSAS. No information was available about the content validation (content relevance and representativeness) of the modified items in HF patients. Information supporting criterion validity was not reported. The construct validity was supported by demonstrating that patients with HF had higher scores in symptoms prevalence than healthy adults without HF.[113] Symptom burden and prevalence scores were significantly associated with scores

of the Minnesota Living with HF Questionnaire, which measures health-related quality of life.[8]

Completion Process

Completion time was not available except for the HF Symptom Checklist. It took approximately 10 minutes for patients to complete the 13-item HF Symptom Checklist.[106] All instruments were designed to be a paper-pencil format as opposed to a computerized format.

Information

There was limited information about changes in symptom scores in relation to symptom management. There was a small correlation (r=0.34) between scores of the HF Symptom Checklist administered during hospitalization with scores 4 to 6 weeks after the index hospitalization.[102] Most studies using the instruments reviewed were cross-sectional in nature, which limited the ability to examine how scores in symptom measures were responsive to treatment or changes.

The associations between scores in the symptom measures and outcomes (e.g., quality of life) and important factors associated with outcomes (e.g., depressive symptoms) were investigated in three studies.[8, 102, 108] In a study in which the MSAS-HF was used, the scores of total symptom prevalence and total symptom burden scores predicted health-related quality of life.[8] In another study in which the HF Symptom Checklist was used, symptom scores at baseline (during hospitalization) explained 13% of the variance in scores of depressive symptoms 4-6 weeks after the index hospitalization.[102] Symptom severity scores measured with the MDASI-HF were significantly different between patients who had high and low BNP levels.[108]

Discussion

We reviewed five symptom measures that have been designed for and used in the HF population. The challenge in this review was the dearth of information about the development process and psychometric properties of symptom measures. There were only one article [108] and two proceedings[112-113] aimed at exploring psychometric properties of symptom measures. None of the symptom measures reviewed in this paper provided sufficient information on all five criteria used to evaluate instrument quality.

The level of comprehensiveness of symptom measures varied among the five measures reviewed. The variability in content among symptom measures may be associated with instrument developers' views of the separateness of symptoms. In the HF Signs and Symptoms Checklist, "nausea, vomiting, diarrhea and/or loss of appetite," which are gastrointestinal-related problems, were assessed with one item. In the MSAS-HF feeling nervous and feeling irritable, which are the characteristics of anxiety,[117] were counted as separate symptoms. A possible problem with combining symptoms together is that healthcare providers are not able to figure out exactly which symptoms are experienced by patients without further probing. On the other hand, too fine a separation of symptoms may be unwarranted as patients are often unable to distinguish subtle differences between similar symptoms.

Another factor related to the content variability may be what kinds of symptoms (typical or atypical HF symptoms) instrument developers intended to measure. The HF Symptom Checklist consisted of typical HF physical symptoms, while the other four included typical as well as atypical HF symptoms. In an initial clinical assessment, instruments containing a variety of symptoms may be beneficial in order to gain a fuller picture of patients' symptom experiences. Given that multiple comorbid conditions and polypharmacy are common in patients with HF, patients often experience cardiac and non-cardiac symptoms.[33, 118] A comprehensive symptom instrument can serve as a prompt for patients to ensure that they provide information about all symptoms they are experiencing. After the initial assessment with a comprehensive symptom measure, healthcare providers may determine which symptom measures, either HF symptom-focused or full version, can be used for the follow-up visits depending on patients' symptom experiences.

Including different symptom dimensions also influences the variability in the content. The MSAS-HF and the HF Symptom Survey contained three dimensions while the HF Signs and Symptoms Checklist and the HF Symptom Checklist had one dimension (presence or absence of symptoms). A multi-dimensional approach to symptom assessment is important because simple presence or absence of symptoms does not fully describe symptom experiences.[119] However, there are issues with the length of multi-dimensional symptom measures and their potential use in a busy clinical setting,

given that the completion time for the 13 item-HF Symptom Checklist was approximately 10 minutes.[106]

Information about reading levels was not available for the five measures reviewed in this paper. Albert and colleagues addressed their efforts in selecting simple, easy wordings to describe symptom items in the HF Signs and Symptoms Checklist.[107] Also, the authors included operational definitions of symptom items. For example, sudden weight gain was defined as "a greater than 2 pounds in a day or 5 pounds in a week" in the HF Signs and Symptoms Checklist. Providing definitions helps patients understand the meaning of symptom items by increasing the clarity of items.[107] It is also beneficial for healthcare providers to obtain accurate, reproducible results by conveying a consistent meaning of symptom items to patients. However, it would be difficult to compare results among symptom instruments if each instrument developer defines similar symptoms differently. It is necessary to conduct critical evaluations of which definitions most properly describe symptoms.

Although the optimal schedule for assessing symptom experience is unknown, a shorter timeframe is appropriate because symptom status changes quickly.[32] The MDASI-HF can be used for daily symptom assessment, while the other four measures can be used for intermittent assessment.

Clear instructions to patients are important in order to obtain quality data. Inadequate instructions led to the problem of patients providing frequency or severity despite endorsing the absence of the same symptom.[104] Similar errors were also reported by Chang and colleagues[31] when they used the MSAS in the cancer population. Because the MSAS-HF used instructions similar to the MSAS, it is expected that this same problem may occur when the MSAS-HF is administered to HF patients.

Scoring for each of the symptom measures was relatively easy. There were subscales in the MDASI-HF and MSAS-HF (e.g., HF symptom and psychological symptom subscales), which may be convenient for healthcare providers to selectively administer depending on their needs. Symptom burden scores in the MSAS-HF were computed by averaging scores of the three symptom domains. This method assumed that patients were equally burdened by symptom severity, frequency, or distress.[120]

The psychometric properties of the five measures have not been extensively investigated or reported. Of the four measures in which internal consistency was examined, good internal consistency was supported in all measures except for the HF Symptom Checklist. Stability has not been investigated in any symptom measure reviewed, which may be related to relatively rapid changes in symptom status.

Four measures[102, 107-109] showed evidence of content validity. Rigorous content validation processes were described by instrument developers by conducting literature review, using the Index of Content Validity, or consulting with a panel of HF experts. However, there is no report available regarding content validity of the MSAS-HF.

Criterion validity was not commonly performed, which may be related to the fact that there is not a gold standard to measure symptoms in the HF population. Construct validity was demonstrated by convergent and discriminative validations (e.g., symptom score comparison by NYHA functional class) and factor analysis. However, as the validation process is ongoing, more validation studies about these measures are needed. Despite the dearth of information about psychometric properties, the MDASI-HF has been rigorously examined and showed sound psychometric properties.

Symptom measure scores should be helpful to make clinical decisions and facilitate symptom management. Only three studies[8, 102, 108] were identified and demonstrated that symptom scores were associated with outcomes. The limited information regarding clinical implications may be related to the fact that the five symptom measures were recently introduced (2001 to 2010).

Conclusion

Heart failure is a clinical syndrome which manifests a variety of symptoms. Symptom assessment and management are imperative to monitor the progress of illness and the impact of symptoms on outcomes. Symptom assessment is challenging as standardized symptom measures are lacking for patients with HF. Because existing symptoms measures are at a relatively early stage, the information regarding the criteria that we modified and amplified to examine the quality of symptom measures is not sufficient. More studies are needed to further validate existing HF symptom measures before one can be recommended for research and clinical use.

Table 3.1. Evaluation criteria of ideal symptom instruments categories

Category	Characteristics	Evaluation criteria
Contents	Comprehensiveness	• The number of symptoms included • Description of symptom items • Symptom dimensions assessed (i.e., prevalence, frequency, severity, and distress) • Symptom clusters (co-occurring symptoms)
Measuring scales	• Simplicity and ease of the instrument completion • Suitability in clinical and research purposes	• Reading level • Timeframe of symptoms experience • Completion rates • Complexity of scoring system • Brevity
Psychometric properties	• Accuracy • Precision	• Reliability (internal consistency and test-retest reliability) • Validity (content, criterion, and construct validity)
Completion process	Burden of the instrument completion	• Time to completion
Information	Clinical implications	• Association with prognosis (e.g., survival and quality of life) and important factors related to prognosis

Table 3.2. Symptom measures reviewed

Contents	Measuring Scale	Validity		Completion process	Information
		Reliability	**Validity**		
Heart Failure Symptom Survey[112]-Modified version of cardiac symptom scale					
Number of symptoms: 14 symptoms (12 physical and 2 psychological symptoms) Domain: • Frequency • Severity • Interference with physical activity • Interference with enjoyment of life Symptom Cluster: not addressed	Reading level: NA Number of items: 56 items Timeframe: during the past 7 days Incompletion rates: < 3% per symptom Scoring system: • An 11-point numeric rating scale • Averaging scores of each symptom	Internal consistency: Cronbach's α of 0.80-0.88 Stability: NA	Content validity: literature review and an expert panel Criterion validity: NA Construct validity: convergent and discriminative validity	NA	NA

Table 3.2 (continued)

Contents	Measuring Scale	Validity		Completion process	Information
		Reliability	Validity		
Heart Failure Signs and Symptoms Checklist[107]					
Number of symptoms: 12 symptoms (12 physical symptoms) and 9 signs Domain: Presence or absence Symptom Cluster: not addressed	Reading level: NA (considered wording of items in the process of the instrument development) Number of items: 29 items (24 to assess signs and symptoms, 4 to determine NYHA class, and 1 to assess additional symptoms/ signs that were not listed) Timeframe: during previous 7 days Completion rates: NA Scoring system: the number of symptoms reported	Internal consistency: NA Stability: NA	Content validity: literature review and an expert panel Criterion validity: NA Construct validity: discriminative validity	NA	NA

Table 3.2 (continued)

Contents	Measuring Scale	Validity		Completion process	Information
		Reliability	Validity		
Heart Failure Symptom Checklist[102]					
Number of symptoms: 13 symptoms (13 physical symptoms) Domain: Presence or absence Symptom Cluster: not addressed	Reading level: NA Number of items: 13 items Timeframe: during previous 2 weeks Completion rates: NA Scoring system: the number of symptoms reported	Internal consistency: Cronbach's α of 0.68 Stability: NA	Content validity: literature review Criterion validity: concurrent validity Construct validity: NA	Time to completion: 10 minutes	Small correlation (r=0.34) of the symptom scores before and after the treatment Symptom scores measured during hospitalization were explained 13% of the variance in depressive symptoms 4-6 weeks after the index hospitalization

Table 3.2 (continued)

Contents	Measuring Scale	Validity		Completion process	Information
		Reliability	Validity		
†M.D. Anderson Symptom Inventory-Heart Failure[108]- Modified version of the M. D. Anderson Symptom Inventory					
Number of symptoms: 21 symptoms (18 physical and 3 psychological symptoms) Domain: • Severity • Overall symptom interference Symptom Cluster: not addressed	Reading level: NA Number of items: 27 items (21 symptom severity items + 6 overall symptom interference items) Timeframe: during last 24 hours Completion rates: NA Scoring system: • An 11-point numeric rating scale • Averaging scores Subscales: HF symptoms, MDASI core symptoms, and symptom distress	Internal consistency: Cronbach's α of 0.83-0.92 Stability: NA	Content validity: literature review, an expert panel, and patient interviews Criterion validity: concurrent validity Construct validity: discriminative validity and factor structure analysis	NA	NA

Table 3.2 (continued)

Contents	Measuring Scale	Validity		Completion process	Information
		Reliability	Validity		
Memorial Symptom Assessment Scale-Heart Failure*[113]*- Modified version of the Memorial Symptom Assessment Scale					
Number of symptoms: 32 symptoms (27 physical and 5 psychological symptoms) Domain: • Presence or absence • Frequency • Severity • Distress Symptom Cluster: not addressed	Reading level: NA Number of items: 122 items (symptom frequency are not assessed in 6 symptoms) Timeframe: during the past 7 days Completion rates: NA Scoring system: • 4- or 5-point rating scale • Averaging scores of each symptom • Composite score: burden scores (the mean of the frequency, severity, and distress of each symptom) Subscales: HF, physical, and psychological symptom subscales	Internal consistency: Cronbach's α of 0.73-0.91 Stability: NA	Content validity: NA Criterion validity: NA Construct validity: convergent and discriminative validity	NA	Total symptom prevalence and total symptom burden predicted quality of life

Note. NA=not available; HF=heart failure; NYHA=New York Heart Association
† Targeting HF patients with cancer

Table 3.3. Symptoms included in the symptom measures

	HF Symptom Survey[112]	**HF Signs and Symptom Checklist**[107]	**HF Symptom Checklist**[102]	**M.D. Anderson Symptom Inventory-HF** [108]	**Memorial Symptom Assessment Scale-HF** [113]
Shortness of breath		or trouble breathing		X	X
Shortness of breath with activity	X		with exertion		
Shortness of breath at rest	X				
Shortness of breath when lying flat	X	need to use more than 1 pillow to sleep on at night; sleeps in a reclining position, shortness of breath (trouble breathing) when lying flat	X	difficulty sleeping without adding pillows	X
Waking up breathless at night	shortness of breath when you wake up during the night	wake up from a sound sleep & unable to breathe without sitting up in bed	X	X	X
Difficulty sleeping	X			X	X
Swelling	feet, ankles, or legs	or edema[a]	feet or ankles	ankle	arms or legs
Weight gain		sudden (> 2 lbs in a day or > 5 lbs in a week)	X	sudden	X
Weight loss		X			X

Table 3.3 (continued)

	HF Symptom Survey[112]	**HF Signs and Symptom Checklist**[107]	**HF Symptom Checklist**[102]	**M.D. Anderson Symptom Inventory-HF** [108]	**Memorial Symptom Assessment Scale-HF** [113]
Fatigue	or tiredness [b]	profound fatigue with exertion [c]	X	X	
Weakness		generalized [c]	X		
Lack of energy	X[b]			X	X
Cough	worsening	severe (keeps you awake at night or chest hurts when coughing)	dry and hacking	nighttime	X
Poor appetite		loss of appetite [d]	X	X	X
Change in the way food tastes					X
Dry mouth				X	X
Nausea		X [d]	X	X	X
Vomiting		X [d]		X	X
Feeling bloated	full or bloated feeling in your abdomen	right sided abdominal / belly fullness or discomfort & tenderness		X	X
Feeling drowsy				or sleepy	X
Dizziness	or lightheadedness	or lightheadedness	X		X
Palpitations		or feels like heart is racing in chest or you can feel your heart beating fast	X	X	X

Table 3.3 (continued)

	HF Symptom Survey[112]	**HF Signs and Symptom Checklist**[107]	**HF Symptom Checklist**[102]	**M.D. Anderson Symptom Inventory-HF** [108]	**Memorial Symptom Assessment Scale-HF** [113]
Irregular heartbeat	or fluttering feeling in chest	or feels like heart beat is skipping			
Chest pain	pressure or heaviness in chest	X	X		X
Pain				X	X
Sweats					X
Constipation					X
Diarrhea		X[d]			X
Problem with urination		change in urine output compared to normal (darker color, voiding less often or in smaller amounts)			X
Problems with sexual interest or activity					X
Numbness/tingling in hands/feet				numbness	X
Itching					X
Wheezing		X			
Worrying					X
Feeling nervous					X
Feeling sad	depressed or feeling down			X	X

Table 3.3 (continued)

	HF Symptom Survey[112]	**HF Signs and Symptom Checklist**[107]	**HF Symptom Checklist**[102]	**M.D. Anderson Symptom Inventory-HF** [108]	**Memorial Symptom Assessment Scale-HF** [113]
Feeling distress				X	
Feeling irritable					X
Difficulty concentrating	X[e]				X
Restlessness		or confusion			
Difficulty remembering	forgetfulness [e]			X	
Decreased ability to exercise or carry out activities		X			
Low blood pressure or low blood pressure when sitting or standing		X			
Feel like you are going to faint or actually fainted (black out)		X			
Cool, pale, or mottled skin		X			
Heart rate < 60 beats per minute or > 120 beats per minute		X			

Note. HF=Heart failure
a Patients are asked to check the box to indicate the swelling sites (ankles or legs; abdomen; or all over)
b Fatigue, tiredness or lack of energy were assessed with one item
c Profound fatigue with exertion or generalized weakness were assessed with one item
d Nausea, vomiting, diarrhea and/or loss of appetite were assessed with one item.
e Difficulty concentrating or forgetfulness was assessed with one ite

CHAPTER FOUR

Association of Physical versus Affective Depressive Symptoms with Cardiac Event-Free Survival in Patients with Heart Failure

Introduction

Heart failure (HF) is a growing health care concern associated with adverse outcomes and staggering health care expenditures.[37] In addition to traditional risk factors (e.g., age and comorbidities),[121-122] psychological status is recognized as a significant predictor of outcomes.[63, 70-71, 122] Depressive symptoms are related to poor prognosis and quality of life in patients with HF.[63, 70-71, 73, 122-123] Thus, it is important for health care providers to recognize and manage depressive symptoms appropriately in the HF population.

Depressive symptoms are common in patients with HF, with a prevalence from 30% to 51%.[71, 73, 123-126] This large variability might be related to the selection of instruments to measure depressive symptoms and their cut points for defining varying levels of depressive symptoms.[127] Instruments used to measure the levels of depressive symptoms often include physical depressive symptoms, such as changes in appetite, sleep disturbances, or fatigue. However, these symptoms are frequently reported by patients with HF.[39, 124] This poses a challenge for health care providers to accurately screen and monitor depressive symptoms because these physical depressive symptoms may reflect the severity of HF rather than depressive symptom status.[128]

Patients in more advanced stages of HF have greater physical symptom prevalence and burden than those in less advanced stage of HF.[50] Patients with depressive symptoms experience more physical symptoms of HF (dyspnea, fatigue, sleep disturbance, and loss of appetite) than patients without depressive symptoms.[124] Thus, the inclusion of physical symptoms might reflect HF severity, inflate the severity of depressive symptoms, and in turn, artificially increase their impact on outcomes in HF.

Researchers have expressed concern about measuring depressive symptoms in patients with HF using instruments that include physical symptoms.[34, 129] One way to address this concern is to use an established depressive symptom instrument such as the Patient Health Questionnaire (PHQ-9) that includes physical and affective depressive symptoms to compare the predictive ability between versions of the instrument with and

without physical depressive symptoms. The purpose of this study was to determine whether the presence of physical depressive symptoms on the PHQ-9 over-estimates the relationship of depressive symptoms to cardiac event-free survival. The specific aim was to compare the predictive ability for cardiac event-free survival of the full PHQ-9 with versions that contain just the physical and just the affective depressive symptoms after adjusting for health status and clinical and socio-demographic variables.

Methods

Design, Setting, and Procedure

This study was a prospective, longitudinal investigation. Patients with HF were recruited from outpatient clinics associated with two academic medical centers in Georgia and Kentucky from August 2004 to March 2009. This study was approved by the Institutional Review Boards at each study site. Patients with HF were identified by referral from their nurses and physicians, and their eligibility was confirmed by trained research nurses. Signed, informed consent was obtained from patients who agreed to participate in the study during a visit to the General Clinical Research Center (GCRC). Patients were interviewed to collect demographic and clinical data and completed questionnaire packets during the visit to the GCRC. Patients were followed up over a median of 360 days (2 – 1826 days) to determine cardiac events.

Participants

Patients who met the following criteria were eligible for this study: (1) diagnosis of HF by a cardiologist using the Framingham criteria [130]; (2) no myocardial infarction within the previous three months; (3) taking consistent doses of HF medications at the time of study participation; and (4) able to read and speak English. Patients who had valvular heart disease as an etiology of their HF, were referred for heart transplantation, had obvious cognitive impairments, or had major life-threatening comorbidities (e.g., end-stage renal or liver disease or cancer other than skin cancer) were excluded.

Measurement

Depressive symptoms. Depressive symptoms were assessed using the PHQ-9, which consists of nine items (Table 1).[131] Each item corresponds to one of the nine symptoms of the major depressive disorder criteria of the Diagnostic and Statistical

Manual of Mental Disorders-IV (DSM-IV). Patients rate items based on how often they experience these symptoms over two weeks on a 4-point Likert scale ranging from 0 (not at all) to 3 (nearly every day). The scores were summed and ranged from 0 to 27, with scores of $\geq 5, \geq 10, \geq 15$, and ≥ 20, representing mild, moderate, moderately severe, and severe levels of depression symptoms, respectively. The validity of the PHQ-9 has been demonstrated to screen for depression in patients with cardiac disease with high specificity and predictive value.[132] Its brevity makes its use in clinical settings or research desirable.[133]

Three items related to sleep disturbance, fatigue, and appetite change were classified as comprising the PHQ-9 physical depressive symptom dimension in this study because these are often experienced by patients with HF.[38-39] The remaining six items of anhedonia, depressed mood, negative feelings about oneself, concentration problems, psychomotor agitation/ retardation, and suicidal ideation were classified as comprising the PHQ-9 affective depressive symptom dimension. The reliability of the scores for the two dimensions of depressive symptoms in this study was measured using Cronbach's α: 0.764 for physical depressive symptom and 0.814 for affective depressive symptom dimensions.

Health status and Clinical, socio-demographic characteristics. Health status in this study was operationally defined as comorbidity burden measured with the Charlson Comorbidity Index and functional status measured with New York Heart Association (NYHA) functional classification. The Charlson Comorbidity Index was used to measure comorbidity burden which is weighted by taking into account comorbid illnesses (i.e., the number and seriousness).[64] New York Heart Association functional classification was determined to assess limitations of physical activities resulting from symptoms by in-depth structured interviews by a trained research nurse. Clinical and socio-demographic characteristics (e.g., medication and marital status) were collected via patient interviews and medical record reviews.

Cardiac events. Cardiac events were defined as the composite end point of cardiac-related death, cardiac-related hospitalization, or emergency department (ED) visit attributable to cardiac reasons (e.g., worsening HF symptoms). The data were obtained by

monthly follow-up calls to patients and their families and confirmed by reviewing medical records and public death records.

Statistical Analyses

Data were analyzed using SAS software version 9.2 (SAS Institute Inc, Cary, North Carolina). Unadjusted Cox proportional hazards regressions were performed separately for physical and affective depressive symptom dimensions of the PHQ-9 in order to examine predictive ability for time to first cardiac event. Two series of multivariable analyses were done. Health status (the Charlson Comorbidity Index and NYHA class) was entered as covariates in the first model and health status and clinical, socio-demographic variables (age, gender, etiology of HF, body mass index [BMI], and anti-depressant medication therapy) were entered together in the second model. Covariates included in the models were selected *a priori* based on previous studies.[34, 73, 121, 129, 134]

The seven covariates included in our survival analysis models resulted in a ratio of seven events per predictors, which is lower than the recommended 10 events per predictor for survival analysis. To determine whether models with seven covariates provided reliable prediction, we ran progressive models in which the least significant predictors were removed one by one and compared information criteria values (e.g., Akaike's information criterion) among the models. The information criteria values in the reduced models were similar to the full model with seven covariates. Therefore, given that all covariates were identified as important in prior research we included all seven covariates in the analyses.

The proportional hazards assumptions were evaluated with graphical displays of deviations between the observed cumulative martingale residuals and the values of each explanatory variable from 20 random simulations. The Kolmogorov-type supremum tests from 1000 simulated patterns also were used. Both methods indicated that there was not a gross violation of the model assumption.

Results

Sample Characteristics

A total of 210 patients with HF participated in the study (Table 2). The majority of patients were male, Caucasian, and married or cohabitating. Ischemia was the most common HF etiology. The median score of the PHQ-9 was 4 (the first and third quartiles: 1 and 9, respectively). Patients having moderate to severe depressive symptoms (PHQ-9 scores ≥ 10) were 23% (49/210) of total participants. Of these patients having moderate to severe depressive symptoms, 41% (20/49) were prescribed anti-depressants.

Patients were grouped by the median split of PHQ-9 scores for physical depressive symptom and affective depressive symptom dimensions (Table 2). The high PHQ-9 physical depressive symptom group (scores > 3) had a greater proportion in NYHA functional classes III and IV, higher comorbidity burden scores, and a greater number of prescribed anti-depressants than the low PHQ-9 physical depressive symptom group (scores ≤ 3). The high PHQ-9 affective depressive symptom group (scores >1) were younger and had a greater proportion in NYHA functional classes III and IV, higher comorbidity burden scores, and a greater number of prescribed anti-depressants compared to the low PHQ-9 affective depressive symptom group (scores ≤ 1).

Cardiac Events

During the follow-up period, 59 cardiac events occurred: 2% (4/210) were cardiac death, 23% (48/210) were cardiac-related hospitalizations, and 3% (7/210) were ED visits due to cardiac causes.

Prediction of Cardiac Event-free Survival

Full version of the PHQ-9. The total scores of the PHQ-9 predicted cardiac event-free survival in the unadjusted and adjusted analyses (Table 3). The association between total scores of the PHQ-9 and time to first cardiac event remained significant after adjusting for the covariates (unadjusted hazard ratio [HR] = 1.08, 95% confidence interval [CI] =1.03 – 1.13; adjusted HR for health status [the Charlson Comorbidity Index and NYHA functional class] = 1.07, 95% CI =1.03 – 1.13). Every one point increase in total PHQ-9 score was associated with a 6% increase in the risk for a cardiac event after

controlling for all covariates (adjusted HR for all covariates = 1.06, 95% CI =1.01 – 1.12).

PHQ-9 physical depressive symptom dimension. In the unadjusted Cox regression analysis scores of the PHQ-9 physical depressive symptom dimension were a predictor for cardiac event (unadjusted HR = 1.11, 95% CI =1.02 – 1.21). Scores of the PHQ-9 physical depressive symptom dimension did not predict cardiac event-free survival after adjusting for health status. Neither the Charlson Comorbidity Index nor NYHA functional class predicted cardiac event-free survival.

After entering all covariates, the association between scores of the PHQ-9 physical depressive symptom dimension and cardiac event-free survival was not significant (Table 4). Only anti-depressant medication therapy was an independent predictor of cardiac event-free survival (adjusted HR = 1.98, 95% CI =1.06 – 3.71). Patients prescribed anti-depressants had nearly double the risk for a cardiac event than patients not prescribed anti-depressants.

PHQ-9 affective depressive symptom dimension. The scores of the PHQ-9 affective depressive symptom dimension predicted cardiac event-free survival in both unadjusted and adjusted models (unadjusted HR = 1.14, 95% CI =1.06 – 1.22). In the two series of multivariable analyses the association between scores of the PHQ-9 affective depressive symptom dimension and cardiac event-free survival remained significant. In the first model adjusting for health status, scores of the PHQ-9 affective depressive symptom dimension was the only predictor of cardiac event-free survival (adjusted HR for health status = 1.13, 95% CI = 1.05 – 1.21). In the second model adjusting for all covariates, scores of the PHQ-9 affective depressive symptom dimension independently predicted cardiac event-free survival (Table 5). Every one point increase in the scores of the PHQ-9 affective depressive symptom dimension was associated with a 12% increase in the risk for a cardiac event (adjusted HR for all covariates = 1.12, 95% CI = 1.03 – 1.22).

Discussion

We found different predictive outcomes for the PHQ-9 physical and affective depressive symptom dimensions in patients with HF. Both affective and physical depressive symptom dimensions were predictive of a cardiac event in unadjusted models.

However, affective depressive symptoms, but not physical depressive symptoms, persistently predicted time to cardiac event in adjusted models controlling for health status (the Charlson Comorbidity Index and NYHA functional class) and clinical, socio-demographic factors. These results suggest that physical depressive symptoms may largely reflect health status, and the relationship between depressive symptoms and risk for a cardiac event is limited to affective depressive symptoms.

There is evidence that affective depressive symptoms may be a useful indicator to detect levels of depressive symptoms. In the study of Holzapfel and colleagues affective depressive symptoms (e.g., depressed mood and worthless/ guilty) were more often reported by depressed patients with HF than those without HF, while the frequency of physical depressive symptom experience did not differ [128]. In a study in which depressive symptoms were measured with the Beck Depression Inventory (BDI)-II, somatic depressive symptom scores were not different between patients with post acute myocardial infarction and psychiatric outpatients matched on age, gender, and cognitive/affective depressive symptom scores.[135] Simon and Von Korff demonstrated that the overall pattern of physical symptoms, such as weight and appetite changes, fatigue, and sleep disturbances, was similar to depressed patients with and without chronic illness.[136] The removal of overlapping physical symptoms from self-report depressive symptom instruments does not improve the discriminating ability for the presence of depression using diagnostic interview based on the DSM-IV criteria for major depressive episode in patients with chronic pain.[137-138]

In the study of Azevedo and colleagues in which the association between depressive symptoms, which were measured with the BDI, and HF stages, which were defined by the American College of Cardiology and American Heart Association, patients with a higher stage (more advanced HF) had higher levels of depressive symptoms. This relationship between HF stages and depressive symptom levels remained significant after deleting physical symptom items (i.e., fatigue, sleep disturbance, and changes in appetite) from the BDI.[34]

We found that the unique contribution of the physical depressive symptoms to risks for a cardiac event disappeared with the inclusion of health status (comorbidities and NYHA functional class) in regression models. This might indicate the significant

association between health status and physical depressive symptoms. There are several studies in which the relationship between health status and physical depressive symptoms was demonstrated. In a previous study in which the BDI was used to measure depressive symptoms in patients with HF scores of the BDI somatic/affective depressive symptom dimension (e.g., irritability, crying, fatigue, and sleep disturbances), but not scores of the BDI cognitive/ affective symptom dimension (e.g., sense of failure, self-accusation, and suicidal ideas), were different by NYHA classes.[139] Significant differences in depressive symptom levels between patients with and without HF were observed only when using a depressive symptom measure incorporating physical symptoms (the Centers for the Epidemiological Studies of Depression Questionnaire), but not measures free of physical symptoms (Profile of Mood States-Short form dejection-depression and the Hospital Anxiety and Depression Scale-depression).[140]

Similarly, the BDI somatic/affective symptoms, but not the BDI cognitive/affective symptoms, were significantly related to the Charlson Comorbidity Index in patients with myocardial infarction.[141] Watkins and colleagues also showed a stronger relationship of comorbidities, which were measured by the Charlson Comorbidity Index, with the BDI physical depressive symptoms (r=0.24) than the BDI cognitive symptoms (r=0.06) in patients after acute myocardial infarction.[142]

Barefoot and colleagues demonstrated the important role of affective depressive symptoms in predicting cardiac death among patients with coronary artery disease.[143] Hazard ratios of four depressive symptom dimensions, which were measured with the Zung Self-rating Depression Scale (SDS), were compared between unadjusted models and an adjusted model in which all depressive symptom dimensions were entered simultaneously. The hazard ratio of the SDS affective symptoms (e.g., sadness, irritability, restlessness, and suicidal ideas) remained similarly while the hazard ratios of the others including somatic (e.g., tiredness and sleep difficulties) and well-being (e.g., satisfaction and optimism) dimensions substantially reduced. Similarly, affective depressive symptoms were associated with cardiac mortality in patients after coronary artery bypass surgery while physical depressive symptoms were not.[144] This result suggests that the relationship between depressive symptom levels and cardiac mortality is not altered by physical symptoms due to disease conditions.[144]

Conflicting findings that physical depressive symptoms, not affective depressive symptoms, predict cardiac outcomes (e.g., mortality or hospitalizations) are observed in previous studies in patients with coronary heart diseases, such as acute myocardial infarction.[145-147] The significant relationship between physical depressive symptoms and all-cause mortality was also reported in the HF population.[139] Schiffer and colleagues reported that the BDI somatic/affective symptom dimension (e.g., irritability, crying, fatigue, and sleep disturbances) was an independent predictor of all-cause mortality while the BDI cognitive/affective symptom dimension (e.g., sense of failure, self-accusation, and suicidal ideas) was not in patients with HF.[139] This conflicting finding with the current study may be related to different outcome variables. The outcome of their study was all-cause mortality while ours was the combined end point of mortality, hospitalization, and ED visit related to cardiac reasons. The majority of cardiac events in this study were hospitalizations. It is possible that factors related to death are different from factors related to hospitalizations. For instance, left ventricular ejection fraction or NYHA functional class was an independent predictor of mortality, but not hospitalization.[148-149]

The use of different measures to assess depressive symptoms may contribute to the inconsistent findings. The items in the BDI and the PHQ-9 are different although there are some items that are overlapped between the two measures including anhedonia, suicidal ideation, psychomotor agitation/ retardation, and fatigue. Physical and affective depressive symptom dimensions were defined with different items between the study of Schiffer et al. and ours. An item indicating psychomotor agitation/ retardation was categorized as the BDI somatic/affective symptom dimension in the study of Schiffer et al. while the item was categorized as the PHQ-9 affective depressive symptoms in our study.

One interesting finding in this study is the association between being prescribed anti-depressants and higher risk for cardiac events. The prescription of anti-depressants was a significant predictor of a cardiac event in the multivariable model which included the PHQ-9 physical symptom dimension. However, this relationship was not significant in the adjusted models using total PHQ-9 scores or PHQ-9 affective symptom dimension scores. We extrapolate that the impact of taking anti-depressants differs by dimensions of

depressive symptoms. However, we cannot determine from out data whether patients prescribed anti-depressants actually took the medication or that the dose prescribed was adequate to treat depressive symptoms. Therefore, our results should be interpreted as demonstrating that prescribing anti-depressants was associated with an increased risk for a cardiac event. Our results do, however, suggest that simply prescribing anti-depressants is not sufficient and without proper follow-up to assure adequate treatment, it may increase the risk for a cardiac event.

It is important to acknowledge the differential influence of physical and affective depressive symptoms on cardiac event-free survival in patients with HF. The use of the measures including physical depressive symptoms does not inflate the association between depressive symptoms and cardiac event-free survival.

There are limitations that should be noted in this study. The sample may not be representative of the HF population because men and Caucasians predominated. Because this was an observation study, no definitive inferences can be drawn regarding causal relationships. The number of covariates include in our multivariable models exceeded the recommended number of covariates per event. However, our model testing demonstrated that the full model provided as reliable prediction as models with fewer covariates without causing an overfitting issue. Therefore, the full model, which had empirical support, was the optimal model to include in the analyses.

Conclusion

The accurate assessment of depressive symptoms in patients with HF has been a critical issue because of their adverse effects on outcomes. However, shared physical symptoms between HF and depressive symptoms are barriers to prevent evaluating the severity of depressive symptoms in HF. In this study we demonstrated a distinctive prognostic ability between physical and affective depressive symptoms to outcomes in patients with HF. Affective depressive symptoms were associated with cardiac event-free survival independent of health status, but not physical depressive symptoms. The use of depressive symptom measures including physical symptoms does not inflate the relationship of depressive symptoms to cardiac event-free survival. Thus, clinicians can use instruments that contain physical depressive symptoms to assess depressive

symptoms in their patients with HF without concern that the instruments over-estimate the relationship between depressive symptoms and outcomes.

Table 4.1. Items of the Patient Health Questionnaire-9

Items of the PHQ-9 physical depressive symptom dimension
1. Trouble falling/staying asleep, sleeping too much
2. Feeling tired or having little energy
3. Poor appetite or overeating
Items of the PHQ-9 affective depressive symptom dimension
1. Little interest or pleasure in doing things
2. Feeling down, depressed, or hopeless
3. Feeling bad about yourself – or that you are a failure or have let yourself or your family down
4. Trouble concentrating on things, such as reading the newspaper or watching television
5. Moving or speaking so slowly that other people could have noticed. Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual
6. Thoughts that you would be better off dead or of hurting yourself in some way

Table 4.2. Sample characteristics (N=210)

	Total	PHQ-9 physical symptom dimension		PHQ-9 affective symptom dimension	
		Low scores (n=115)	High scores (n=95)	Low scores (n=126)	High scores (n=84)
	Mean (S.D) or N (%)				
Age, years [b]	61 (11)	63(12)	60 (10)	64 (11)	58 (11)
Female	55 (26.2%)	26 (22.6%)	29 (30.5%)	29 (23.0%)	26 (31.0%)
Ethnicity					
Caucasian	169 (80.5%)	91 (79.1%)	78 (82.1%)	100 (79.4%)	69 (82.1%)
Others	41 (19.5%)	24 (20.9%)	17 (17.9%)	26 (20.6%)	15 (17.9%)
Marital Status					
Married/ cohabitate	117 (55.7%)	65 (56.5%)	52 (54.7%)	72 (57.1%)	45 (53.6%)
Single/ divorced/ widowed	93 (44.3%)	50 (43.5%)	43 (45.3%)	54 (42.9%)	39 (46.4%)
Body mass index (kg/m^2)	31.6 (7.4)	31.1 (7.8)	32.2 (7.0)	31.4 (7.8)	31.9 (6.8)
Charlson Comorbidity Index [a, b]	3.4 (2.1)	3.1 (2.0)	3.7 (2.1)	3.2 (2.0)	3.6 (2.3)
Ischemic etiology of HF	158 (75.2%)	83 (72.2%)	75 (79.0%)	94 (74.6%)	64 (76.2%)
NYHA class [a, b]					
I/ II	105 (50.0%)	70 (60.9%)	35 (36.8%)	74 (58.7%)	31 (36.9%)
III/ IV	105 (50.0%)	45 (39.1%)	60 (63.2%)	52 (41.3%)	53 (63.1%)
Medications					
Anti-depressant [a, b]	43 (20.5%)	12 (10.4%)	31 (32.6%)	15 (11.9%)	28 (33.3%)
ACE I or ARB (n=209)	172 (81.9%)	97 (85.1%)	75 (79.0%)	107 (84.9%)	65 (78.3%)
Beta blocker (n=209)	184 (87.6%)	104 (91.2%)	80 (84.2%)	110 (88.0%)	74 (88.1%)

[a] Significant differences between groups with low and high scores of the PHQ-9 physical symptom dimension (median split), p-value < .05
[b] Significant differences between groups with low and high scores of the PHQ-9 affective symptom dimension (median split), p-value < .05

Note. HF: Heart failure; NYHA: New York Heart Association functional class; PHQ-9: the Patient Health Questionnaire-9; ACE I: Angiotensin-converting enzyme inhibitors; ARB: Angiotensin receptor blocking agents

Table 4.3. Multivariable Cox regression analysis using the total scores of the PHQ-9 (N=210)

	Hazard Ratio	*p*-value	95% Confidence Interval
Age	0.99	.41	0.97-1.01
Female	0.85	.61	0.46-1.59
Charlson Comorbidity Index	1.05	.53	0.91-1.20
Ischemic etiology	2.14	.07	0.95-4.82
NYHA Class (I/II vs. III/IV)	0.91	.76	0.51-1.64
Body mass index (kg/m^2)	0.96	.07	0.92-1.00
Anti-depressant use	1.80	.07	0.96-3.36
Total scores of the PHQ-9	**1.06**	**.019**	**1.01-1.12**

Total model *p*-value =.001
Note. NYHA: New York Heart Association functional class; PHQ-9: the Patient Health Questionnaire-9

Table 4.4. Multivariable Cox regression analysis using scores of PHQ-9 physical depressive symptoms (N=210)

	Hazard Ratio	*p*-value	95% Confidence Interval
Age	0.99	.21	0.96-1.01
Female	0.80	.48	0.42-1.50
Charlson Comorbidity Index	1.06	.49	0.93-1.22
Ischemic etiology	2.09	.08	0.93-4.71
NYHA Class (I/II vs. III/IV)	0.96	.88	0.53-1.72
Body mass index (kg/m^2)	0.96	.06	0.92-1.00
Anti-depressant use	**1.98**	**.033**	**1.06-3.71**
PHQ-9 physical scores	1.07	.18	0.97-1.19

Total model *p*-value =.007
Note. NYHA: New York Heart Association functional class; PHQ-9: the Patient Health Questionnaire-9

Table 4.5. Multivariable Cox regression analysis using scores of PHQ-9 affective depressive symptoms (N=210)

	Hazard Ratio	*p*-value	95% Confidence Interval
Age	0.99	.62	0.97-1.02
Female	0.94	.83	0.50-1.75
Charlson Comorbidity Index	1.04	.57	0.91-1.20
Ischemic etiology	2.22	.06	0.98-5.02
NYHA Class (I/II vs. III/IV)	0.94	.82	0.52-1.67
Body mass index (kg/m^2)	0.96	.08	0.92-1.00
Anti-depressant use	1.83	.06	0.99-3.38
PHQ-9 affective scores	**1.12**	**.006**	**1.03-1.22**

Total model *p*-value <.001
Note. NYHA: New York Heart Association functional class; PHQ-9: the Patient Health Questionnaire-9

CHAPTER FIVE

The Association between Regular Symptom Monitoring and Self-Care Management in Patients with Heart Failure

Introduction

Heart failure (HF) is a serious health concern in the United States, with high mortality and rehospitalization rates. Approximately half of the patients who are diagnosed with HF will die within five years.[2] Although HF rehospitalization rates have decreased over 10 years from 1998 to 2008,[150] HF remains the most common reason for rehospitalizations among Medicare beneficiaries.[151] A majority of rehospitalizations due to worsening HF are preventable with active engagement in self-care, such as following a low sodium diet.[152-153] According to Annema and colleagues, up to 18% of HF rehospitalizations can be attributed to a delay in seeking help for escalating symptoms.[152] If patients monitor their symptoms on a regular basis and are aware of early symptoms and signs of HF exacerbation, HF readmission may be avoidable.

Self-care is conceptualized as a naturalistic decision making process by patients to maintain physiological stability (self-care maintenance) and respond to changes in their symptom status (self-care management).[29] Self-care maintenance consists of two components, monitoring symptoms and adhering to treatment regimens. Self-care management includes the following processes: recognizing altered symptom status, evaluating the changes in symptoms, deciding what actions to take, performing treatment strategies, and evaluating the results of actions taken.[29] It is suggested that patients who monitor symptoms are able to detect and interpret escalating symptoms in a timely manner and initiate successful self-care management.[29] However, the empirical evidence demonstrating the relationship between adherence to symptom monitoring behaviors and engagement in self-care management is lacking.

The purpose of this study was to examine the relationship of adherence to regular symptom monitoring, which is defined as always checking weights and lower extremity edema, with adequate self-care management among HF patients who experienced dyspnea or edema in the past month. We hypothesized that adequate self-care management would be predicted by adherence to regular symptom monitoring behaviors. The first specific aim was to compare differences in self-care management behaviors

among three groups of patients based on adherence to two types of symptom monitoring behaviors (i.e., monitoring weights and lower extremity edema): patients who were adherent to (1) both symptom monitoring behaviors; (2) either of the symptom monitoring behaviors; and (3) neither of the symptom monitoring behaviors. The second specific aim was to examine whether membership in one of the three symptom monitoring adherence groups predicted adequacy of self-care management.

Methods

The investigation was a cross-sectional, observational examination of the association between adherence to regular symptom monitoring and adequate self-management in patients with HF. Patients were enrolled from HF clinics from six large community hospitals and academic medical centers in Kentucky, Georgia, and Indiana. Institutional Review Board approval was obtained at all sites. All patients who agreed to participate in the study provided signed, informed consent and visited the General Clinical Research Center to complete questionnaire packets and interviews.

Patients

Prospectively patients were identified by physicians and nurse practitioners. Research nurses approached eligible patients, explained the study in detail, and obtained informed consent if the patients agreed to participate in the study. Patients who met the following criteria were eligible for the study: (1) confirmed diagnosis of HF; (2) dyspnea and/or edema over the past one month; (3) stable dosage of medications for at least three months; (4) no myocardial infarction within the three months prior to starting the study; (5) no referral for heart transplant; (6) free of noncardiac serious or life-threatening comorbid conditions (e.g., end-stage renal or liver disease); (7) free of obvious cognitive impairment that prevented providing informed consent and completing the questionnaire packets; and (8) English-speaking.

Measurements

Symptom Monitoring Behaviors. In this study, symptom monitoring behaviors were defined as monitoring weight and lower extremity edema, and assessed with two items from the self-care maintenance subscale of the Self-Care of Heart Failure Index (SCHFI).[154] Patients were asked how frequently they weighed themselves and checked

lower extremity swelling in the last month and could rate these items on a scale of 1 (never or rarely) to 4 (always). Patients were considered adherent to symptom monitoring if they reported monitoring always. The following three patient groups were created based on levels of adherence to the two items (weight and lower extremity edema monitoring): adherent to (1) both items (i.e., adherent group); (2) either of the items (i.e., partially adherent group); and (3) neither of the items (i.e., non-adherent group).

Self-Care Management. Self-care management was measured with the self-care management subscale of the SCHFI. The self-care management subscale is comprised of six items capturing symptom recognition (i.e., shortness of breath or edema), implementation of treatment strategies (i.e., taking an extra diuretic dose, restricting fluid and sodium intake, and seeking advice from healthcare providers), and treatment strategy evaluation. Patients could rate items related to the implementation of treatment strategies on a 4-point Likert scale and items related to symptom recognition and treatment strategy evaluation on a 5-point Likert scale. The scores were standardized to range from 0 to 100, with higher scores indicating better self-care management. A score of 70 or greater (based on prior evidence) was considered adequate self-care management.[154] Its reliability and validity have been supported in previous studies.[154]

*Functional Capacity.*Functional capacity was measured with the Duke Activity Status Index (DASI), which is a 12-item self-administered questionnaire.[155] The items in the DASI represent daily activities (e.g., personal care, ambulation, and household tasks). Each item is weighted by the estimated metabolic equivalents of task (MET) level associated with the activity in the item. Total scores can range from 0 to 58.2, with higher scores indicating fewer physical limitations and greater functional capacity.

Sociodemographic and Clinical data. Data on age, gender, ethnicity, marital status, and medication regimens were collected via patient interview and medical records review. The interview format of the Charlson Comorbidity Index was used to obtain total comorbidity scores by taking into account the number and seriousness of comorbid conditions.[156] Data on left ventricular ejection fraction (LVEF) and HF etiology were collected from the medical records. Patients were categorized as having either non-preserved systolic function (LVEF $\leq$ 40%) or preserved systolic function (LVEF > 40%)

with a cutoff of 40%. New York Heart Association (NYHA) functional classification was determined by trained research nurses via in-depth structured patient interviews.

Statistical Analyses

Data were analyzed by SAS (version 9.3). Descriptive statistics including frequency distributions, means, and standard deviations were used to describe sociodemographic and clinical characteristics. Chi-square tests or Fisher's exact tests of independence for categorical variables and one-way analysis of variance (ANOVA) for continuous variables were used to compare the differences in sociodemographic and clinical characteristics among three symptom monitoring adherence groups (i.e., adherent, partially adherent, and non-adherent groups). Bonferroni post-hoc test was performed if F-tests for ANOVA were significant (p-value < 0.05).

Univariable and multivariable logistic regression analyses were conducted to explore the association between the levels of symptom monitoring adherence and the adequacy of self-care management. An outcome variable (self-care management) was dichotomized for binary variables with the cutpoint of 70.[154] The confounding factors that were included in the multivariable model were age, gender, marital status, ethnicity, the Charlson Comorbidity Index, NYHA functional class, etiology of HF, LVEF, functional capacity measured with the DASI, and diuretic medication therapy. Receiver Operating Characteristic curves were used to assess model fit.

Results

Sample Characteristics

The sample (N= 311) was predominantly male, white, and married or cohabitating (Table 1). More than half of the sample were in NYHA functional class III/IV and had non-preserved systolic function with LVEF ≤ 40%. Average levels of self-care management were generally low with the mean score of below 70, which is the cutpoint for the adequacy of self-care management.[154] Less than half the total sample reported that they always monitored their weights (72/311) and lower extremity edema (112/311) (Figure 1). As described previously, three adherence groups were formed based on adherence to two symptom monitoring behaviors. A total of 15.1% (47/311) of patients

were in the adherent group, 28.9% (90/311) in the partially adherent group, and 56.0% (174/311) in the non-adherent group.

The demographic and clinical variables that differentiated among the three groups were ethnicity and etiology of HF. Patients in the adherent group were more likely to be White and have ischemic heart disease as the underlying etiology of HF than patients in the partially adherent and non-adherent groups. Diuretics were prescribed more often in patients in the adherent group than patients in the other two groups. Self-care management scores were significantly different among groups. The percentage of patients who performed adequate self-care management (self-care management scores of ≥ 70) were 38.3% (18/47) in the adherent, 25.6% (23/90) in the partially adherent, and 13.2% (23/174) in the non-adherent group.

Comparison of Self-care Management among Symptom Monitoring Adherence Groups

Of the total sample, 13% of patients failed to identify changes in symptoms (Table 2). None of the patients in the adherent group failed to recognize their symptoms, while approximately one out of five patients in the non-adherent group did not recognize symptom changes.

Among four possible treatment strategies to ameliorate worsening symptoms, reduced sodium intake was most likely to be performed while taking an extra diuretic was the least likely to be done by all patients. There were significant group differences with regard to limitation of sodium and fluid intake, and taking extra diuretics; however, there was no group difference in obtaining medical advice from healthcare providers (Table 2).

When dyspnea or lower extremity edema was experienced, one of five patients did not do anything. Only half of the patients who took actions to relieve worsening symptoms were sure or very sure of the effectiveness of their actions. Compared to patients in the partially adherent or non-adherent groups, more patients in the adherent group responded to altered symptom status and reported that they were sure or very sure of the effectiveness of their actions.

Association between Symptom Monitoring Adherence Groups and Adequate Self-care Management

Adequacy of self-care management was significantly associated with membership in one of the three symptom monitoring adherence groups. In a univariate model, compared to patients in the non-adherent group, the odds of performing adequate self-care management were two times and four times higher in patients in the partially adherent (odds ratio [OR] 2.27; 95% confidence interval [CI] 1.19 - 4.33) and adherent groups (OR 4.10; 95% CI 1.97 – 8.54), respectively.

A full multivariable logistic regression model was presented in Table 3. Symptom monitoring adherence group, diuretic therapy, and NYHA functional class were significant independent predictors of adequate self-care management. The adjusted odds of performing adequate self-care management were increased by 240% (95% CI 1.19-4.81) and 347% (95% CI 1.55-7.74) for the partially adherent and adherent groups, respectively. Patients who were prescribed diuretics were at six times higher odds of engaging in adequate self-care management than patients who were not, after adjusting for other variables in the model (95% CI 1.76 - 20.64). Patients in NYHA functional class III/IV had a 2.2-fold increase (95% CI 1.09 - 4.57) in their odds of performing adequate self-care management after controlling for other variables.

Discussion

Results of this study contribute to the body of literature suggesting the importance of regular symptom monitoring to adequate self-care management. Adequacy of self-care management was predicted by adherence to symptom monitoring behaviors measured by always monitoring weight and lower extremity edema. Patients who engaged in both symptom monitoring behaviors were more likely to identify altered symptom status, implement treatment strategies to relieve worsening HF status, and evaluate the effectiveness of their responses.

Monitoring signs and symptoms for congestion is important because one of the most common reasons for hospitalizations in patients with HF is volume overload. Because weight gain does not always reflect HF deterioration,[30] it is important to simultaneously monitor a range of signs and symptoms of volume overload, including weight gain and lower extremity edema. However, of 311 patients in this study only 15%

reported that they performed daily weight and lower extremity edema monitoring. More than half of the patients did not monitor their symptoms on a daily basis even though they experienced dyspnea or lower extremity edema during the past month.

Poor adherence to symptom monitoring has been demonstrated in previous studies. More than half of patients with HF do not weigh themselves daily.[157-163] Only 9% of patients who were recently discharged from the hospital due to decompensated HF reported monitoring for symptoms of worsening HF.[160]

Reasons for not monitoring signs and symptoms of congestions may be related to a lack of knowledge and motivation. Less than 40% of patients with HF were unaware that swelling of the legs and ankles, waking up at night due to shortness of breath, and weight gain were signs and symptoms of worsening HF.[164] Patients simply do not know that they should monitor their weight or are not informed of the importance of daily weight monitoring by their healthcare providers.[157, 159] Patients decide not to weigh themselves because they do not know how to use the information, even if they are aware of the importance of this behavior.[159, 165] Gallagher suggests that poor adherence to symptom monitoring is related to patients' misconception about HF, which is perceived as an acute illness. [166] As patients believe HF is present when symptoms are present, they may not value daily symptom monitoring when they do not experience symptoms limiting their daily activities.

The notion that adhering to symptom monitoring facilitates self-care management behaviors to relieve altered symptom status is supported by this study. Patients in the adherent symptom monitoring group were more likely to recognize changes in symptoms (dyspnea or lower extremity edema) in a timely manner, respond to those changes, and evaluate the effectiveness of the responses as compared to patients in the partially adherent and non-adherent groups in this study. Dickson and colleagues introduced and defined three types of patients based on their self-care capacities: patients who are novice, inconsistent, and expert in self-care.[167] A self-care expert is characterized as one who routinely performs "body listening," makes a link between altered symptom status and its causes, chooses rational decisions about the changes, depends on lessons learned from previous experiences of symptom management, and reassesses the effectiveness of the actions taken.[168]

According to this self-care typology, patients in the adherent group in this study can be categorized as self-care experts because they performed adequate self-care management when symptoms of worsening HF occurred. Patients who vigilantly monitor their symptoms may have sufficient knowledge of HF mechanisms and causes of HF symptoms, and a good understanding of what to do to prevent HF exacerbation; however, it is beyond the purpose of this study to show whether patients in the adherent group had a better understanding of HF as compared to patients in the partially adherent and non-adherent groups in this study.

Adequate self-care management was associated with poor functional status in this study. Patients experiencing limited daily activities due to HF symptoms were more likely to perform adequate self-care management to avert an exacerbation of HF. Poor functional status due to HF symptoms may drive patients with HF to engage in self-care maintenance (e.g., symptom monitoring) and management (e.g., decreasing sodium intake) in order to maintain physical stability and/or ameliorate worsening HF.[169-170]

One interesting finding in this study is the association between prescribed diuretics and self-care management. Diuretic prescription was an independent predictor of adequate self-care management, although the 95% CI for diuretic prescription in the logistic regression was wide. Diuretics are considered the first-line treatment for patients with HF to achieve symptom control by preventing fluid overload. Flexible diuretic titration by capable patients is recommended in HF guideline and consensus statements.[36,171] Patients in the adherent group were prescribed diuretics more and were more likely to take extra diuretics if changes in symptoms occurred than patients in the partially adherent and non-adherent groups in this study. Patients who were prescribed diuretics might have learned about flexible diuretic regimens from their healthcare providers and adjusted their diuretic dosage based on their symptoms, although this is speculation as we did not collect information on flexible diuretic titration by patients.

Limitations of this study include limited generalizability. The sample in this study, which was predominantly male and white, makes it difficult to draw inferences from this study sample to all HF patients. Symptom monitoring behaviors and self-care management were assessed based on self-reporting, which may be subject to recall or social desirability bias. We used monitoring weight and lower extremity edema as a

measure of symptom monitoring behaviors. As weight gain and lower extremity edema are commonly experienced by patients with HF and have objective measures, patients may be able to compare and detect daily changes compared to changes in dyspnea, which may be affected by the degree of activities.

Conclusion

Adherence to regular symptom monitoring was associated with adequate self-care management. This result supports the conclusion that engaging in symptom monitoring is the first step in recognition of altered body states that prompts patients to proceed to appropriate self-care management in order to mitigate worsening symptoms. This, in turn, may decrease preventable hospitalizations due to failure to seek care in a timely manner. It is important to understand that lower extremity edema or weight gain alone cannot provide a complete picture of clinical deterioration. Thus, healthcare providers stress the importance of monitoring a group of relevant signs and symptoms of HF exacerbation to patients.

Table 5.1. Sample characteristics (N=311)

	Total (N = 311)	**Non-adherent (N = 174)**	**Partially adherent (N = 90)**	**Adherent (N = 47)**	***p*-value**
Age, years	60 (11.9)	59 (12.5)	61 (10.2)	63 (11.9)	0.06
Gender					0.50
Male	201 (64.6%)	117 (67.2%)	54 (60.0%)	30 (63.8%)	
Female	110 (35.4%)	57 (32.8%)	36 (40.0%)	17 (36.2%)	
Marital Status					0.05
Single/divorced/ widow	126 (40.5%)	63 (36.2%)	46 (51.1%)	17 (36.2%)	
Married/co-habitating	185 (59.5%)	111 (63.8%)	44 (48.9%)	30 (63.8%)	
Ethnicity					0.01
White	206 (66.2%)	105 (60.3%)	61 (67.8%)	40 (85.1%)	
Minority	105 (33.8%)	69 (39.7%)	29 (32.2%)	7 (14.9%)	
NYHA class					0.78
I/II	112 (36.0%)	62 (35.6%)	31 (34.4%)	19 (40.4%)	
III/IV	199 (64.0%)	112 (64.4%)	59 (65.6%)	28 (59.6%)	
Ischemic etiology of Heart Failure	220 (70.7%)	113 (64.9%)	68 (75.6%)	39 (83.0%)	0.03
Ejection fraction					0.16
≤ 40%	200 (64.3%)	107 (61.5%)	57 (63.3%)	36 (76.6%)	
> 40%	111 (35.7%)	67 (38.5%)	33 (36.7%)	11 (23.4%)	
Duke Activity Status Index scores	11.4 (11.8)	12.2 (13.2)	10.1 (10.2)	10.6 (8.2)	0.35
Chalson Comorbidity Index	3.3 (1.9)	3.2 (1.8)	3.6 (2.0)	3.5 (2.1)	0.15
Self-care Management†	55.5 (20.5)	49.4 (19.4)	59.9 (19.3)	70.0 (17.6)	<.001
Medications					
ACEI or ARB (n=310)	254 (81.9%)	148 (85.1%)	71 (79.8%)	35 (74.5%)	0.20
Beta Blocker (n=309)	267 (86.4%)	149 (85.6%)	75 (85.2%)	43 (91.5%)	0.54
Diuretics	245 (78.8%)	124 (71.3%)	75 (83.3%)	46 (97.9%)	<.001

Note. Values are mean (SD) or n (%). † Significant group difference among all three groups
NYHA=New York Heart Association; ACEI = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker

Table 5.2. Self-care management behaviors by symptom monitoring adherence groups (N=311)

	Total (N = 311)	**Non-adherent (N = 174)**	**Partially adherent (N = 90)**	**Adherent (N = 47)**	***p*-value**
Symptom Recognition					<.001
Not recognized	41 (13.2%)	33 (19.0%)	8 (8.9%)	0 (0.0%)	
Not quickly	30 (9.6%)	22 (12.6%)	5 (5.6%)	3 (6.4%)	
Somewhat quickly	44 (14.1%)	23 (13.2%)	15 (16.7%)	6 (12.8%)	
Quickly	85 (27.3%)	52 (29.9%)	25 (27.8%)	8 (17.0%)	
Very quickly	111 (35.7%)	44 (25.3%)	37 (41.1%)	30 (63.8%)	
Restrict Sodium Intake					0.011
Not likely	29 (9.3%)	21 (12.1%)	7 (7.8%)	1 (2.1%)	
Somewhat likely	64 (20.6%)	40 (23.0%)	18 (20.0%)	6 (12.8%)	
Likely	79 (25.4%)	51 (29.3%)	16 (17.8%)	12 (25.5%)	
Very likely	139 (44.7%)	62 (35.6%)	49 (54.4%)	28 (59.6%)	
Restrict Fluid Intake					<.001
Not likely	95 (30.5%)	66 (37.9%)	24 (26.7%)	5 (10.6%)	
Somewhat likely	65 (20.9%)	40 (23.0%)	19 (21.1%)	6 (12.8%)	
Likely	74 (23.8%)	40 (23.0%)	17 (18.9%)	17 (36.2%)	
Very likely	77 (24.8%)	28 (16.1%)	30 (33.3%)	19 (40.4%)	
Take an Extra Diuretics					0.030
Not likely	112 (36.0%)	67 (38.5%)	34 (37.8%)	11 (23.4%)	
Somewhat likely	44 (14.1%)	30 (17.2%)	10 (11.1%)	4 (8.5%)	
Likely	63 (20.3%)	36 (20.7%)	19 (21.1%)	8 (17.0%)	
Very likely	92 (29.6%)	41 (23.6%)	27 (30.0%)	24 (51.1%)	
Call HealthCare Providers for Guidance					0.265
Not likely	93 (29.9%)	53 (30.5%)	28 (31.1%)	12 (25.5%)	
Somewhat likely	57 (18.3%)	27 (15.5%)	19 (21.1%)	11 (23.4%)	
Likely	67 (21.5%)	46 (26.4%)	13 (14.4%)	8 (17.0%)	
Very likely	94 (30.2%)	48 (27.6%)	30 (33.3%)	16 (34.0%)	
Evaluation of Treatment Strategies (helpful or not)					<.001
Did not try anything	62 (19.9%)	43 (24.7%)	12 (13.3%)	7 (14.9%)	
Not sure	48 (15.4%)	33 (19.0%)	12 (13.3%)	3 (6.4%)	
Somewhat sure	74 (23.8%)	49 (28.2%)	19 (21.1%)	6 (12.8%)	
Sure	67 (21.5%)	27 (15.5%)	22 (24.4%)	18 (38.3%)	
Very sure	60 (19.3%)	22 (12.6%)	25 (27.8%)	13 (27.7%)	

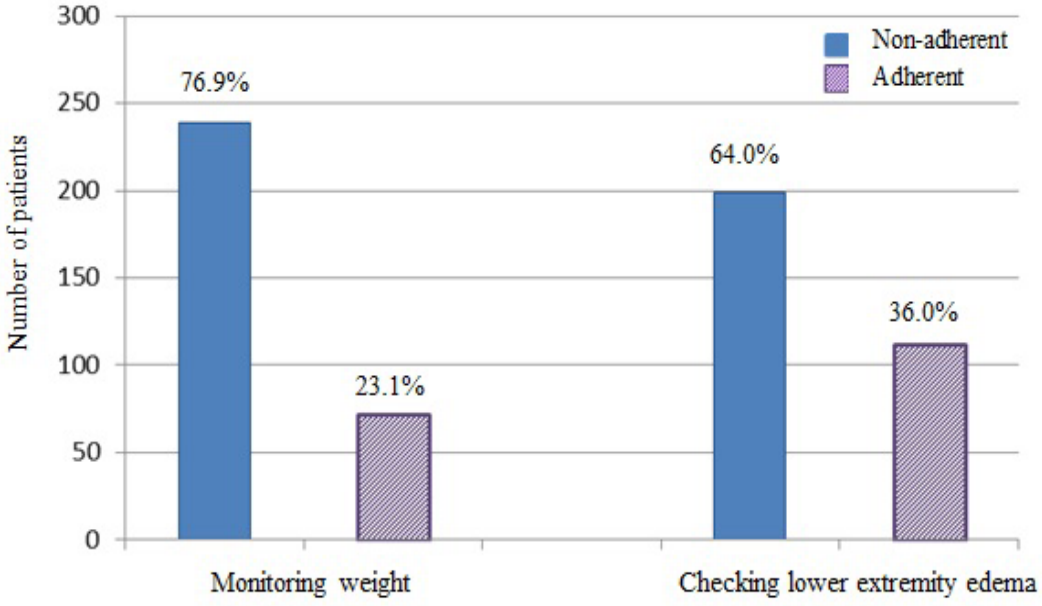
Note. Values are n (%).

Table 5.3. Logistic regression (N=311)

	Odds Ratio	**95% Confidence Interval**	***p*-value**
Age	1.01	0.99 - 1.04	0.350
Gender (Female vs. Male)	0.83	0.42 - 1.64	0.586
Marital Status (Married/co-habitating vs. Single/separated/widowed)	1.39	0.74 - 2.62	0.302
Ethnicity (White vs. Minority)	1.44	0.73 - 2.84	0.296
Chalson Comorbidity Index	0.93	0.79 - 1.10	0.396
NYHA Class (III/IV vs. I/II)	**2.23**	**1.09 - 4.57**	**0.028**
Etiology of Heart Failure (Non-ischemic vs. Ischemic)	0.77	0.37 - 1.61	0.487
Ejection Fraction (≤ 40% vs. > 40%)	1.72	0.86 - 3.45	0.128
Duke Activity Status Index scores	1.02	0.99 - 1.05	0.130
Diuretic Prescription	**6.02**	**1.76 - 20.64**	**0.004**
Symptom Monitoring Adherence Groups			**0.005**
Partially Adherent Group	**2.40**	**1.19 - 4.81**	**0.014**
Adherent Group	**3.47**	**1.55 - 7.74**	**0.003**

Note. NYHA=New York Heart Association
Model *p*-value <0.001

Figure 5.1. Adherence to symptom monitoring behaviors (N=311)



CHAPTER SIX

A Symptom Diary Intervention to Improve Outcomes in Patients with HF: A Pilot Study

Introduction

Patients with heart failure (HF) must monitor for and recognize escalating symptoms in order to take action to relieve symptoms in a timely manner and decrease preventable hospitalizations. However, routine symptom monitoring is not commonly performed by patients with HF.[172-175] For example, monitoring daily weight as a measure of fluid overload is performed by less than 50% of patients and only 5%-26% of these patients notice weight gain prior to requiring admission.[85-86, 173, 175-176] When patients fail to monitor symptoms routinely they do not recognize the need to take action early (e.g., taking extra diuretics or consulting their healthcare provider) that could prevent emergent hospitalization.

A delay in seeking care can occur when patients ignore or fail to recognize changes in HF symptoms.[177] Patients who experience a gradual increase in symptoms (e.g., edema and dyspnea) wait up to seven days or more before seeking treatment, which can ultimately result in hospitalization for acute decompensated HF.[27, 74, 85-86, 178] Other reasons for slow patient response time when experiencing worsening HF symptoms include a belief that chronic, non-specific HF symptoms are unimportant or are due to other causes, such as stress, aging or comorbid conditions.[85-86, 178-179] Thus, it is essential that tools be developed to promote regular monitoring of symptoms by patients with HF.

One tool that can promote symptom monitoring and recognition is a daily symptom diary. In one randomized controlled study testing the effect of using a weight diary in patients with HF, rates of one-year mortality were significantly lower in weight diary users versus non-users.[180] When patients record presence and severity of symptoms on a daily basis, it may be easier for them to compare current symptom status to the past without relying on memory alone. In this way, patients may more rapidly recognize signs and symptoms of worsening HF.

The aim of this study was to test the effect of a daily symptom diary intervention that included education and counseling about HF symptoms, how to recognize them, and what to do with escalating symptoms. The outcomes tested at 3-month follow-up were HF event-free survival, health-related quality of life (HRQOL), and self-care

maintenance. In this randomized controlled trial, I hypothesized that patients who received the intervention would have longer HF event-free survival and better HRQOL and be more adherent to self-care maintenance compared to patients who did not receive the intervention. Additionally, I used changes in depressive symptoms as covariate because depressive symptoms are associated with outcomes of interest in this study. In this paper, I describe the design and intervention and report preliminary results of the trial.

Methods

Design and Procedure

This pilot study was conducted using a two-group, randomized, repeated measures experimental design. Patients were recruited during their inpatient stay in one academic medical center and two community hospitals in Kentucky. Patients were identified from the hospital daily HF reports, in which patients' names and locations were listed and were screened for their eligibility by hospital staff and the investigator. The investigator obtained signed, informed consent from all patients who agreed to participate in the study. A baseline assessment (within six weeks of hospital discharge) and two additional follow-ups at one month and three months from the baseline were done at either the College of Nursing at the University of Kentucky or patients' houses by the investigator. Data stable over three months (e.g., age, gender, and living arrangement) were collected only at baseline. Data expected to change over three months (i.e., HRQOL, self-care maintenance, depressive symptoms, and New York Heart Association [NYHA] functional class) were collected at baseline, one month, and three months. Data about HF events were collected at three months. Patients were followed until death, loss to follow-up, or study completion. Patients voluntarily participated in this study without monetary compensation.

Sample

Patients who were diagnosed with HF and hospitalized for a cardiac-related reason were screened for their eligibility to this study. The study cohort was composed of patients who were 21 years or older, diagnosed as having HF with either preserved or non-preserved systolic function, able to read and speak English, and lived within two-

hours driving distance from Lexington, KY. Exclusion criteria were: (1) currently using any type of symptom monitoring instruments; (2) having severe or life-threatening comorbidities (e.g., cancers, liver failure, or end stage renal failure); (3) awaiting cardiac transplantation; (4) not having a telephone; or (5) having cognitive impairment that prevented provision of informed consent, or inability to respond questions and fill out questionnaires.

Randomization

A random sequence was generated by a random number generating program. In order to ensure a good balance of participants in each group, a permuted block of four was used. When each patient's baseline was scheduled, the investigator assigned them to the intervention or usual care group according to the randomization list. Patients and the investigators were not blinded to the group assignment of patients.

Intervention Group

Patients in the intervention group received the initial education and counseling session with introduction of the symptom diary in the College of Nursing at the University of Kentucky or their home, depending on their preference. The intervention was provided after initial data collection was completed. Thereafter, patients received a total of 5 booster sessions (i.e., supporting patients and reviewing education) via biweekly phone calls for three months.

The face-to-face education and counseling session consisted of a simplified explanation of HF and how it causes symptoms, causes of worsening symptoms in relation to fluid retention and diet, how to monitor symptoms, what to do about worsening symptoms, and a review of the medication regimen. Symptoms of HF exacerbation (e.g., increased swelling, shortness of breath, and weight gain) were listed in the symptom diary. Information about how to manage altered symptom status was also provided (e.g., when to call their healthcare providers or criteria for taking extra diuretics, if they were prescribed) based on the HF Society of America guidelines.[36]

Patients in the intervention group received a symptom diary to track their daily symptoms and record their weight for monitoring purposes. The symptom diary was a ledger type and had four sections: (1) daily weight; (2) rating the severity of each of seven symptoms (i.e., swelling of feet, hands, or abdomen; shortness of breath with

activity; shortness of breath at rest; difficulty sleeping; difficulty breathing when lying flat; waking up breathless at night; and feeling nervous); (3) rating the degree of activity limitation due to symptom status during a day (How much did you have to cut down your activity because of symptoms?); and (4) personal comments for noting symptoms other than the ones listed and actions taken to relieve symptoms. Patients were instructed to weigh themselves daily in the morning after the first urination in similar clothing before eating or drinking. A 6-point rating scale was used to rate symptom severity (0=no symptom to 5= extremely severe) and change in activity level (0=not at all to 5=stopped almost all activities). The adequacy of format and contents of the diary was confirmed by an expert panel (three experts in nursing and HF and one gerontology expert).

After baseline, five booster sessions were done by the investigator. Patients received biweekly calls to discuss their experience with keeping the symptom diary, review changes in symptoms of HF, and subsequent actions that patients might have taken. The investigator encouraged patients to keep the symptom diary daily.

Usual Care Group

Usual care in the institutions used in this study included giving patients a discharge education booklet describing HF, a low sodium diet recommendation, and instructions to take medications as prescribed. Tools for symptom monitoring, such as a symptom diary, were not provided by healthcare providers as part of routine care.

Measures

Heart failure event-free survival. In this study, HF event-free survival was defined as the composite end point of time to first event of HF-related death or hospitalization, or emergency department visit for HF. Experts in HF and the investigator considered HF-related events as any hospital admission or emergency department visit related to worsening HF as a primary diagnosis, including acute on chronic HF, volume overload requiring intravenous diuretic therapy, dyspnea not primarily caused by pulmonary diseases, internal cardiac defibrillator (ICD) or biventricular pacemaker placement due to severe HF, ICD firing, or sudden cardiac arrest. The data on these events were obtained from patients or their family at three months and confirmed with medical records.

Health-related quality of life. Health-related quality of life was measured with the Minnesota Living with HF Questionnaire (MLHFQ).[181] The MLHFQ, a disease-specific HRQOL instrument, assesses a patient's perception of the impact of HF and HF treatment on physical, psychological, and social aspects of life. The MLHFQ contains 21 items rated by the patient using a 6-point Likert scale (0-5 points). Items are totaled to give a HRQOL score. The range of possible scores was 0 to 105, with higher scores indicating a worse HRQOL. This instrument is the most widely used measure of HRQOL in HF research. Reliability and validity of the instrument have been demonstrated multiple times in a variety of HF samples.[182-184] In this study, Cronbach's alpha coefficient for HRQOL scores at baseline was .93.

Self-care maintenance. Self-care maintenance was quantified with the self-care maintenance subscale of the Self-Care of HF Index. The self-care maintenance subscale consists of 10 items, two items about monitoring symptoms for congestion (i.e., weight and lower extremity edema), and eight items about adherence to the recommended therapeutic regimens (e.g., doing physical activity, following low sodium diet, taking medications as directed, and keeping an appointment with healthcare providers). Scores on the self-care maintenance subscale were standardized to 100, with higher scores reflecting better self-care maintenance. The reliability and validity of the Self-Care of HF Index in patients with HF has been supported.[185] The internal consistency of the self-care maintenance subscale measured with Cronbach's alpha coefficient at baseline was .59 in this study.

Depressive symptoms. The nine-item Patient Health Questionnaire (PHQ-9) was used to assess depressive symptoms. Items on the PHQ-9 reflect diagnostic criteria for major depression as described in the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition.[131] Patients were asked to rate each item on a 4-point Likert scale (0–3) to indicate how often they have experienced the item from not at all (0) to nearly every day (3) over the last two weeks. Scores could range from 0 to 27, with higher scores indicating more depressed. Scores of 5, 10, 15, and 20 represent thresholds, indicating mild, moderate, moderately severe, and severe levels of depression symptoms, respectively. The psychometric soundness of the PHQ-9 has been demonstrated with

patients with cardiac disease.[132, 186] Good internal consistency with Cronbach's alpha coefficient of 0.85 was observed in this study.

New York Heart Association functional class. New York Heart Association functional class is a simple summary measure of a patient's functional limitation resulting from characteristic symptoms of HF (e.g., dyspnea and fatigue). Patients' functional status is categorized into four functional classes: class I (i.e., no limitation of ordinary physical activity due to HF symptoms), class II (i.e., slight limitation of physical activity), class III (marked limitation of physical activity), and class IV (inability to carry on any physical activity without discomfort).[187] The investigator determined patients' NYHA functional class via in-depth structured interview.

Socio-demographic and clinical characteristics. Data about age, gender, education levels, ethnicity, and living arrangements were collected using a standard investigator-developed sociodemographic questionnaire. Medical records were reviewed to obtain medication regimens. Comorbidities at enrollment were assessed with the Charlson Comorbidity Index.[64] Scores can range from 0 to 34, with higher scores indicating higher burden from comorbid conditions.

Statistical Analyses

Data were analyzed with SAS (version 9.3). Analyses were undertaken on an intention-to-treat basis. Baseline sociodemographic and clinical variables were compared between intervention and usual care groups with summary descriptive statistics. Comparisons of continuous variables between groups were made with independent t-tests and discrete variables with chi-square tests as appropriate.

Kaplan–Meier curves with the log rank test were used to compare group differences in time to first HF event. Cox proportional hazards regression was also conducted to examine the effect of the intervention on HF event-free survival independent of baseline self-care maintenance scores. According to the Kolmogorov-type supremum tests, there was no violation of the assumption of proportional hazards. All patients who had baseline data were included in these survival analyses.

Linear mixed models were conducted to examine the relationship between groups and changes in HRQOL and self-care maintenance over three months, after adjusting for NYHA functional class (time-variant covariate) and depressive symptom scores (time-

variant covariate). Fixed effects were groups (i.e., intervention vs. usual care), time (i.e., at baseline, one month, and three months), the group-by-time interaction. Unstructured covariate structure was used as a pattern of within-subject autocorrelation among times due to unequal spaced follow-up times. I also used the same statistical method to examine the changes in depressive symptoms by group without adjusting for covariates. Only patients who had at least two observations were included in linear mixed model analyses.

I calculated the post-hoc statistical power of the present investigation using nQuery Advisor 6.0 (version 4.0) to estimate a sufficient sample size for a future large-scale study. The power analyses were done using a two-tailed test at the .05 significance level.

Results

Sample Characteristics

Figure 1 reflects the flow of patients through the study and includes the number of patients screened, enrolled, and included in the analyses at each time point. A total of 44 patients completed baseline assessment (23 patients in the intervention and 21 patients in the usual care groups). Of these 44 patients, two (4.5%) died and eight (18.2%) dropped out of the study during the three-month follow-up period. Except for ethnicity, there were no significant differences in baseline sociodemographic and clinical characteristics, and scores of HRQOL, self-care maintenance, and depressive symptoms between patients who dropped out of the study and patients who did not. There was a higher proportion of African Americans than Caucasians in patients who dropped out of the study compared to patients who did not (70.0% vs. 29.4%, p-value < .05).

Baseline characteristics of patients in the intervention group are compared to those of patients in the usual care group in Table 1. The mean age of the total sample was 60 years and ranged from 28 to 86 years. Patients were predominantly Caucasian and the majority lived with someone. The mean depressive symptom score was 9.5, indicating moderate depressive symptoms. Patients in the intervention group did not significantly differ in sociodemographic or clinical characteristics, scores of HRQOL or depressive symptom scores from patients in the usual care group.

Table 2 presents the baseline characteristics of a subset of patients who had at least two follow-ups (N=36). There were no significant differences between patients in

this subset (n=36) and in patients with only one follow-up (n=8; four from intervention and four from usual care groups) with regard to all baseline sample characteristics.

Primary Findings

Heart Failure Event-free Survival. There were 14 HF events that occurred in eight patients (two patients in the intervention group vs. six patients in the usual care group) during the study: two deaths, nine hospitalizations, and three emergency department visits. The eight patients who had HF events were in NYHA functional class III or IV. A total of 11 HF events occurred in the usual care group (i.e., two deaths, six hospitalizations, and three emergency department visits), while three HF events occurred in the intervention group (i.e., three hospitalizations).

The HF event-free survival curves by group are shown in Figure 2. Although not statistically significant, a trend is evident for patients in the intervention group to experience longer HF event-free survival compared to patients in the usual care group (*p*-value =.07). Heart failure event-free survival was 91.3% (21/23) in the intervention group vs. 71.4% (15/21) in the usual care group. Cox regression analysis was performed to examine the association between HF event-free survival and intervention after adjusting for baseline self-care maintenance; however, the model was not significant.

Health-related Quality of Life. The mean scores of HRQOL decreased over time (*p*-value < .01) in both the intervention and usual care groups (Figure 3). There were no differences in changes in HRQOL scores between groups over three months. When depressive symptoms and NYHA functional class were entered in the model as time-variant covariates, the relationship between time and changes in HRQOL was no longer significant (*p*-value= .09); however, an increase in depressive symptoms was significantly associated with increases in HRQOL scores over three months (*p*-value < .001).

Self-care Maintenance. There was an interaction between group and follow-up time in changes in self-care maintenance scores over three months (Figure 4). Self-care maintenance scores in the intervention group increased over time, while self-care maintenance scores in the usual care group decreased over time (*p*-value= .05). The interaction effect of group by follow-up time on changes in self-care maintenance scores

no longer remained significant (*p*-value= .06), after adjusting for depressive symptoms and NYHA functional class.

Secondary Finding

Depressive symptoms. There was an interaction effect of group by follow-up time (*p*-value= .02) on changes in depressive symptom scores (Figure 5). Depressive symptom scores in patients in the intervention group increased with time, while depressive symptom scores in patients in the usual care group decreased over time.

Post-hoc Power Analysis

Post-hoc power analyses were done to estimate power to detect group differences and estimate a sufficient sample size for future study based on the preliminary findings. The rate of HF events in the intervention group was 91.3% compared to 71.4% in the usual care group. The present study had a power of 35% to detect the group differences in HF event-free survival with a constant hazard ratio of 3.70 using a .050 level two-sided log-rank test for equality of survival curves. A total of 128 patients (64 per group) is required to detect the group differences in HF event-free survival with hazard ratio of 3.70 with a power of .80.

The estimated effect sizes (i.e., proportion of the variance attributed to the fixed effect of interest) of HRQOL and self-care maintenance with partial eta were .14 and .01, respectively. The post-hoc power analyses indicated that we had 15% and 5% of power to detect the group differences in HRQOL and self-care maintenance, respectively. If we increase sample size of 64 per group, which was estimated from the post-hoc power analysis for HF event-free survival, the power to detect the group differences in HRQOL will increase to 75%, while the power in self-care maintenance will be the same as 5%.

Feasibility and Acceptability

This pilot study provided evidence of the feasibility of using a daily symptom diary in HF patients. No patients dropped out because they found the diary too hard to use. The time to complete the diary daily was about up to 15 minutes according to patients. Patients said that examples in the diary helped them to understand how to use the diary. According to some patients, forgetting, traveling, feeling depressed, or being hospitalized were reasons that symptoms and weights were not monitored using the diary.

A 30-day diary adherence score was computed based on a formula created by White and colleagues:[188] dividing the number of days patients rated symptoms or weighed themselves by 30 days. The mean adherence scores in each item in the diary ranged from 87.6% to 90.3%. These adherence scores were higher than adherence scores of daily weight reported in the study of White and colleagues (79.4%).[188] These high adherence scores suggest that patients adhered well to the diary.

Patients in the intervention group made positive comments about using the daily symptom diary. One patient said that information about daily symptoms and weight enabled him to distinguish weight gain from retaining fluid rather than weight gain due to adiposity and understand the relationship between his dietary habits and fluid retention. Another patient mentioned that monitoring daily weight and symptoms became her routine because of the diary.

Discussion

This randomized, controlled trial was a pilot study to test the feasibility of using a daily symptom diary with education and counseling sessions in patients with HF, aimed at the improvement of outcomes in patients with HF, prior to designing a future large-scale study. I found no statistically significant differences between the intervention and usual care groups in HF event-free survival, and changes in HRQOL and self-care maintenance. However, I did find a trend for improvement in the intervention group in HF event-free survival and self-care maintenance over time. Despite the small sample size, which limited power to detect a statistical significance, findings from this study suggest a potential positive impact of daily symptom diary use along with education and counseling sessions on outcomes in patients with HF.

The post-hoc power analysis was done to plan for a future study. As expected, the power to detect the group differences in HF event-free survival between the two groups was 35%. Although this pilot study was underpowered, there were promising trends toward improved outcomes in HF event-free survival and self-care maintenance. I calculated the effect size and can now accurately determine the sample size needed for an adequately powered full scale randomized controlled trial.

Keeping a symptom diary helps patients pay attention to their bodily changes and detect early symptoms of HF exacerbation,[7] which may decrease preventable

hospitalizations.[180, 189] The advantages of keeping a diary on prognosis were observed in previous studies.[180, 189] Patients with HF who used a weight diary had a fewer number of readmissions and more days alive without repeated hospitalizations than patients who did not use a weight diary.[180]

I did not find a significant association between the intervention and HF event-free survival. However, the survival curves began to separate by approximately 25 days after baseline. There were five patients who had their first HF event within 30 days; of these five patients, four were in the usual care group while one was in the intervention group.

High NYHA class is associated with high rates of mortality and hospitalization in patients with HF,[190-192] which was consistently found in this study. In this study, only patients in NYHA functional class III and IV had HF events. Patients in the intervention group had fewer HF events than patients in the usual care group, despite the fact that there were no group differences in the proportion of patients in NYHA functional class. This finding suggests that the intervention in this study could negate the adverse impact of high NYHA functional class, a well-established risk factor for poor prognosis, although further investigation is required.

To be an expert in HF self-care, two types of skills are required: tactical skills, which involves the "how to" of adhering to the recommended regimens, and situational skills, which involves action plans of "what to do when."[193] The intervention in this study may benefit patients to build these skills by providing a symptom diary (i.e., tactical skills for symptom monitoring) with clear instructions in the diary about what to do when changes in symptoms are noticed (i.e., situational skills). In addition to this, deliberate efforts of monitoring and recording symptoms may help patients make associations between symptoms and their behaviors (e.g., diet)[189] and recognize precipitating factors of HF exacerbation. Once patients learn these associations, they may be more adherent to recommended regimens, such as following a low sodium diet and taking medication as directed, to prevent escalating symptoms of HF. These possible benefits of keeping a diary were observed in this study. At three months after the intervention, the mean score of self-care maintenance (i.e., symptom monitoring and adherence to therapeutic regimens) in patients in the intervention group was above 70 (75.6 ± 9.6), indicating adequate self-care maintenance,[185] while the mean score in patients in the usual care

group was below 70 (68.0 ± 11.1), indicating inadequacy of self-care maintenance. However, this difference was not statistically significant and further investigation with an adequate sample size is needed before conclusions can be reached.

The positive effects of keeping a diary on self-care behaviors were found in previous studies, in which adequate sample sizes were used. Caldwell and colleagues provided HF patients with a weight diary and one-time education focusing on symptom recognition and fluid weight management at baseline and a phone call at one month for reinforcement.[194] In this study, patients in the intervention group were more likely to be knowledgeable about HF and adherent to daily weight monitoring than patients in the control group at three months after the intervention. Wright and colleagues also demonstrated the benefits of keeping a diary.[180] Patients who used weight diaries, defined as weight monitoring at least once a week, were more likely to call their healthcare provider, compared to those who did not use weight diaries.[180] Thus, a daily symptom diary may be beneficial as a guide and reminder for patients to perform self-care activities.

Natural improvement in HRQOL after hospital discharge was observed in many previous studies, and highlights the importance of including control groups in intervention trials over simply using pre-post test designs.[195-196] This trend for improved HRQOL was found in both groups at one-month follow-up in this study.

To examine the effect of outliers on HRQOL scores, an additional analysis was done without adjusting for depressive symptoms and NYHA functional class after patients (n=7), whose HRQOL scores were in the high and low tenth percentiles, were removed. Without outliers, there was a trend for patients in the intervention group to report better HRQOL than patients in the usual care group over time.

There are several limitations in this pilot study. The main weakness of this study was its relatively small sample size which limited the power to detect a statistically significant effect on outcomes. However, I believe that the sample size achieved has allowed us to demonstrate that this approach to using a daily symptom diary is a feasible method to employ with patients with HF and further investigation of the intervention in an adequately powered study is warranted. Because of limited resources, the investigator delivered the intervention and collected outcome variables. In order to minimize possible

bias from doing the intervention and data collection by one person who was not blinded to group assignment, HF events were predefined by the investigator and an HF expert. Any ambiguity related to HF event was discussed with the HF expert.

Future Study

To improve this pilot study, three elements will be added. B-type natriuretic peptide (BNP), which is a cardiac neurohormone secreted from the ventricles in response to volume expansion and pressure overload, will be included as an outcome measure. By measuring BNP levels, I may evaluate the effectiveness of keeping a symptom diary in an objective way.

Motivational interviewing will be used to improve patients' adherence to keeping a symptom diary. Motivational interviewing is a one-to-one client-centered counseling technique known to increase patients' self-efficacy and support patients' autonomy.[197] There is evidence showing that adopting motivational interviewing as a way of delivering the intervention is effective in promoting behavioral changes.[197-198]

I will include patients' healthcare providers in a future intervention because they are influential in promoting patients' adherence to a symptom diary. I encouraged study participants to show their symptom diaries to healthcare providers. One patient made the copy of his diary and showed it to his doctor. However, his doctor did not look at his diary with him and told him that he would read it later. The patient was so disappointed and upset with his doctor's attitude. Another patient who showed her diary to her doctor received positive feedback on keeping the diary. She was motivated to continue keeping her symptom diary. Although these are anecdotal evidence, there are studies illustrating similar observations. In a previous study, patients did not perform symptom or blood pressure monitoring because the data were not reviewed by their healthcare providers and thus patients did not know how to use the data.[199] By including healthcare providers in a future study, we may increase adherence to the diary.

Conclusions

Optimal management of HF can be achieved with active self-care engagement by patients, as the majority of HF care, such as daily symptom monitoring and medication adherence, is performed by patients at home. The intervention used in this study was

designed to promote patients' symptom monitoring behaviors by providing a daily symptom diary with education and counseling sessions. Patients in the intervention group took an active role in their care and demonstrated a trend toward the improvement in self-care maintenance and fewer HF events. Based on the results of this study, I plan a full-scale randomized controlled trial with an adequate sample size.

Table 6.1. Characteristics of sample by groups (N=44)

	Total (N = 44)	**Usual care group (N = 21)**	**Intervention group (N = 23)**	***p*-value**
		N (%) or mean ± SD		
Age, years	60 ± 12	61 ± 13	60 ± 12	0.94
Gender				0.55
Male	23 (52.3%)	10 (47.6%)	13 (56.5%)	
Female	21 (47.7%)	11 (52.4%)	10 (43.5%)	
Living alone	15 (34.1%)	6 (28.6%)	9 (39.1%)	0.46
Ethnicity				0.49
African American	17 (38.6%)	7 (33.3%)	10 (43.5%)	
Caucasian	27 (61.4%)	14 (66.7%)	13 (56.5%)	
Education				0.50
< High school	3 (6.8%)	2 (9.5%)	1 (4.3%)	
≥ High school	41 (93.2%)	19 (90.5%)	22 (95.7%)	
Comorbidity	4.1 ± 2.4	4.6 ± 2.6	3.8 ± 2.2	0.31
NYHA class				0.37
I/II	22 (50.0%)	9 (42.9%)	13 (56.5%)	
III/IV	22 (50.0%)	12 (57.1%)	10 (43.5%)	
Left ventricular ejection fraction, %	38.7 ± 15.9	37.7 ± 16.5	39.7 ± 15.6	0.69
Ischemic etiology of HF	16 (36.4%)	6 (28.6%)	10 (43.5%)	0.31
Medication therapy				
ACEI or ARB	25 (56.8%)	10 (47.6%)	15 (65.2%)	0.24
Beta Blocker	35 (87.5%)	17 (89.5%)	18 (85.7%)	0.72
Diuretics	32 (80.0%)	15 (78.9%)	17 (81.0%)	0.87
Self-care maintenance	66.9 ± 15.9	71.4 ± 14.0	62.7 ± 15.2	0.06
Health-related quality of life	66.6 ± 24.6	68.4 ± 22.8	64.9 ± 26.5	0.65
Depressive symptoms	9.5 ± 6.5	10.1 ± 6.4	9.0 ± 6.6	0.57

Note. NYHA=New York Heart Association; HF= Heart Failure; ACEI = angiotensin converting enzyme inhibitor; and ARB = angiotensin receptor blocker

Table 6.2. Subset sample characteristics by groups (N=36)

	Total (N = 36)	**Usual care group (N = 17)**	**Intervention group (N = 19)**	***p*-value**
		N (%) or mean ± SD		
Age, years	62 ± 12	62 ± 12	62 ± 12	0.98
Gender				0.52
Male	19 (52.8%)	8 (47.1%)	11 (57.9%)	
Female	17 (47.2%)	9 (52.9%)	8 (42.1%)	
Living alone	12 (33.3%)	5 (29.4%)	7 (36.8%)	0.64
Ethnicity				0.64
African American	12 (33.3%)	5 (29.4%)	7 (36.8%)	
Caucasian	24 (66.7%)	12 (70.6%)	12 (63.2%)	
Education				0.22
< High school	2 (5.6%)	2 (11.8%)	0	
≥ High school	34 (94.4%)	15 (88.2%)	19 (100%)	
Comorbidity	4.0 ± 2.5	4.3 ± 2.7	3.7 ± 2.4	0.48
NYHA class				0.30
I/II	16 (44.4%)	6 (35.3%)	10 (52.6%)	
III/IV	20 (55.6%)	11 (64.7%)	9 (47.4%)	
Left ventricular ejection fraction, %	38.1 ± 16.3	37.6 ± 16.8	38.5 ± 16.3	0.87
Ischemic etiology of HF	12 (33.3%)	4 (23.5%)	8 (42.1%)	0.24
Medication therapy				
ACEI or ARB	21 (58.3%)	8 (47.1%)	13 (68.4%)	0.19
Beta Blocker	29 (85.3%)	14 (87.5%)	15 (83.3%)	0.73
Diuretics	27 (79.4%)	12 (75.0%)	15 (83.3%)	0.55
Self-care maintenance	67.7 ± 15.1	72.1 ± 13.9	63.7 ± 15.4	0.09
Health-related quality of life	67.4 ± 23.7	67.1 ± 24.7	67.8 ± 23.5	0.93
Depressive symptoms	9.8 ± 6.2	10.2 ± 6.3	9.4 ± 6.3	0.70

Note. NYHA=New York Heart Association; HF=heart failure; ACEI = angiotensin converting enzyme inhibitor; and ARB = angiotensin receptor blocker

Figure 6.1. Study flow diagram

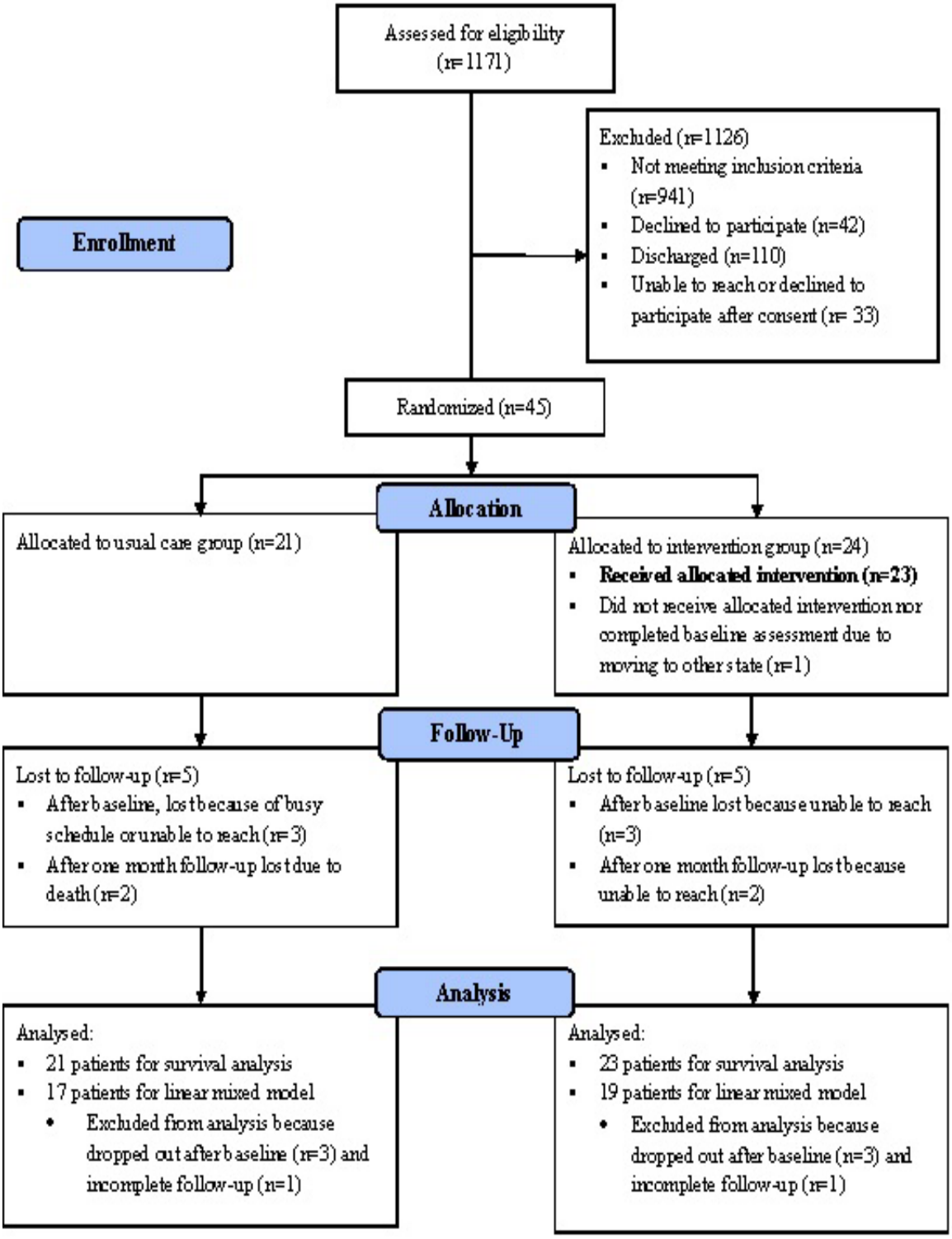


Figure 6.2. Kaplan–Meier curves (N=44)

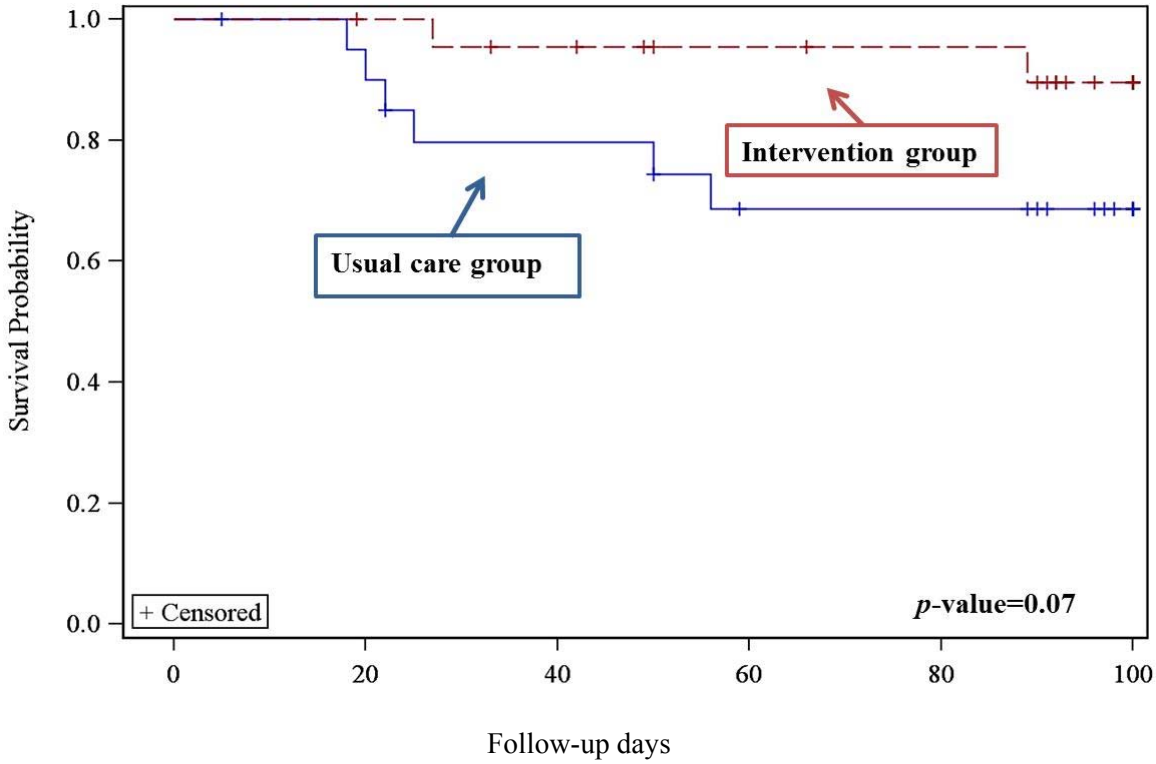
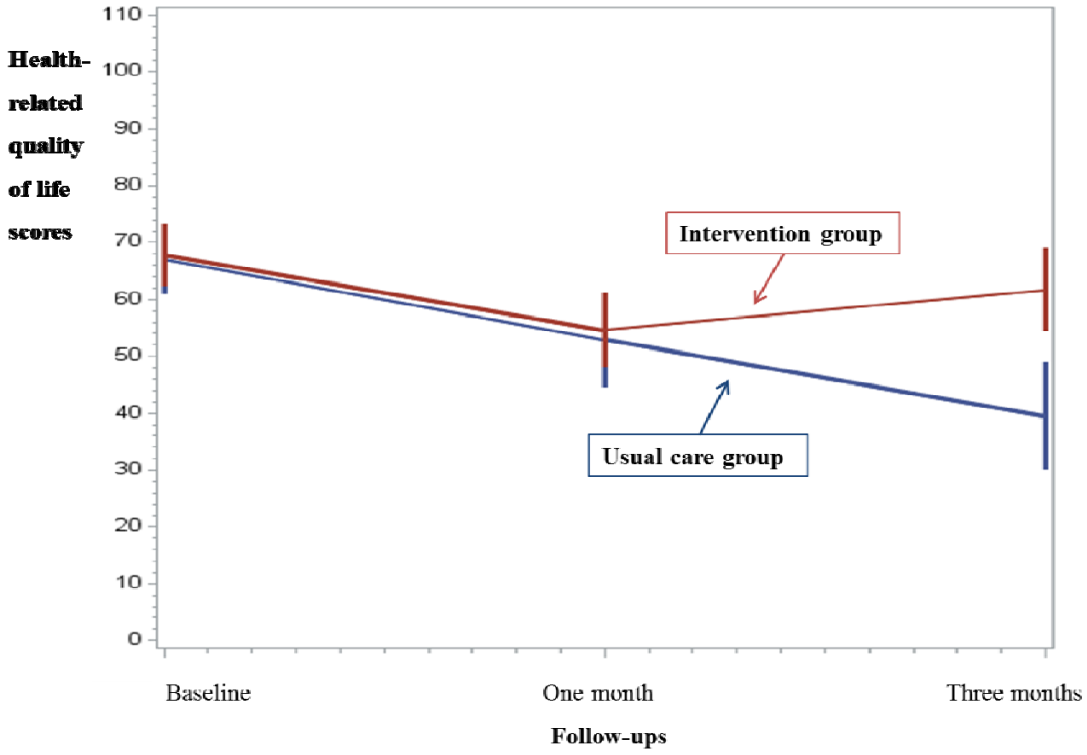


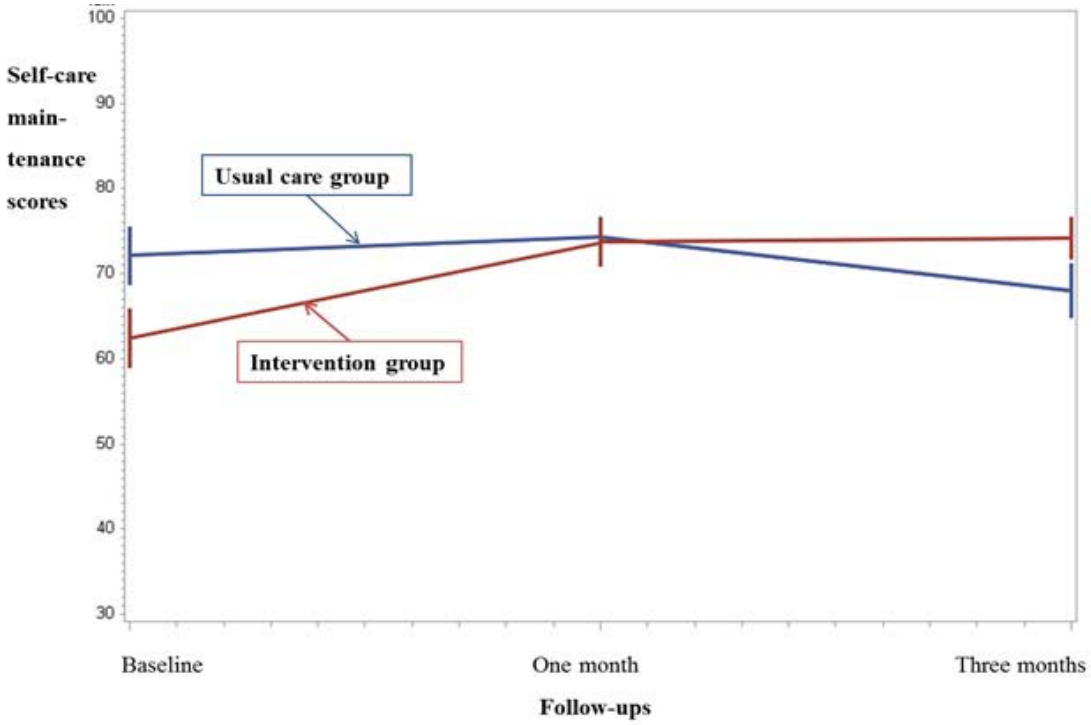
Figure 6.3. Changes in health-related quality of life by group (N=36)



Note. Higher scores indicate worse health-relate quality of life.

According to the linear mixed model, follow-up time (*p*-value= .09), group (*p*-value= .29), and interaction group by follow-up time (*p*-value= .86) were not significantly associated with changes in health-related quality of life scores over three months, after adjusting for changes in depressive symptom scores (*p*-value < .001) and New York Heart Association functional class (*p*-value= .62).

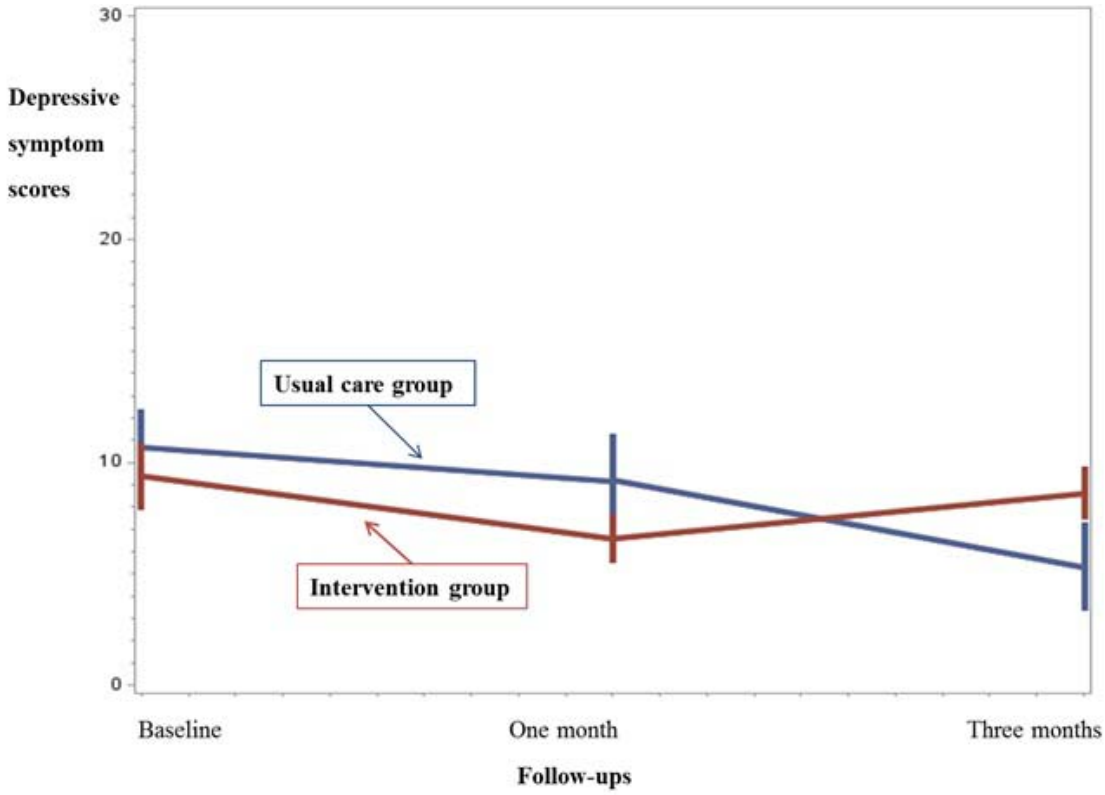
Figure 6.4. Changes in self-care maintenance by group (N=36)



Note. Higher scores indicate better self-care maintenance.

According to the linear mixed model, there was not an interaction effect of group by follow-up time (*p*-value=.06) on changes in self-care maintenance scores, after adjusting for changes in depressive symptom scores and New York Heart Association functional class.

Figure 6.5. Changes in depressive symptoms by group (N=36)



Note. Higher scores indicate more depressed.

According to the linear mixed model, there was an interaction effect of group by follow-up time (*p*-value=.02) on changes in depressive symptom scores.

CHAPTER SEVEN

Conclusions and Discussion

The purpose of chapter seven is to summarize and synthesize the findings of this dissertation and provide implications for clinicians and researchers. Symptoms are a distinctive feature of heart failure (HF) and substantially influence outcomes.[10, 55, 200-201] Despite the importance of symptoms in this population, there are few investigations regarding how, and with which instruments, to accurately assess patients' symptom experiences. This symptom measurement issue was addressed in three of five papers in this dissertation: (1) "Symptom Clusters in Men and Women with Heart Failure and Their Impact on Cardiac Event-Free Survival"; (2) "Heart Failure Symptom Measures: Systematic Review; and (3) "Association of Physical versus Affective Depressive Symptoms with Cardiac Event-Free Survival in Patients with Heart Failure."

Worsening symptoms of HF are the main reason for patients with HF to be hospitalized. It is believed that regular symptom monitoring with accurate measures enables patients to quickly recognize cues of worsening HF and take action, which may reduce preventable hospitalizations. However, it is not well studied whether patients who monitor worsening symptoms of HF are able to adequately respond to altered symptom status. If regular symptom monitoring leads to successful symptom management, developing a tool to assist patients' regular symptom monitoring is essential because there are no such tools and patients have considerable difficulty monitoring and recognizing symptoms on their own.[176, 202] The relationship between adherence to regular symptom monitoring and effective self-care management was investigated in chapters four and five: "Association between Regular Symptom Monitoring and Self-Care Management in Patients with HF" and "A Symptom Diary Intervention to Improve Outcomes in Patients with HF: a Pilot Study."

The motive for the first paper[17] was the inadequacy of the current practice and/or research in which symptoms are considered as individual, isolated entities, when patients with HF usually experience a wide range of symptoms simultaneously. Investigations of individual symptoms help increase our understanding of the particular symptoms; however, this approach may not illustrate the complete picture of patients' symptom experiences and can decrease our ability to appreciate the possible synergistic effects of

co-occurring symptoms on outcomes. Thus, I examined how symptoms clustered together and how symptom clusters affected outcomes.

I found that two distinct symptom clusters emerged from seven individual physical and psychological HF symptom items: (1) a physical symptom cluster and (2) an emotional/cognitive symptom cluster. The emotional/cognitive symptom cluster was associated with increased risk of a cardiac event while the physical symptom cluster was not. Characteristics among groups formed according to high and low scores of the two symptom clusters were also compared. Patients in the high distress group from the emotional/cognitive symptom cluster were younger and more symptomatic than patients in other groups.

Findings from this chapter suggested that healthcare providers should assess symptom clusters and pay special attention to patients who are at risk for poor outcomes (e.g., younger patients) in relation to symptom clusters. Healthcare providers should teach patients to monitor multiple symptoms together to effectively recognize changes in HF status. As early symptoms of HF exacerbation lack specificity,[203] it may be hard for patients with HF, especially those with comorbid conditions, to link these non-specific symptoms to their cardiac condition. Of 12 physical symptoms of HF, fatigue, weight gain, and dyspnea on exertion were grouped in a cluster in the study of Jurgens and colleagues.[204] Patients may not consider feeling tired as a manifestation of worsening HF, unless they notice other symptoms of congestion, such as weight gain and dyspnea on exertion.[203] The knowledge of symptom clusters may assist patients to discern whether symptoms are attributed to HF or other conditions.

One challenge to adequately assessing symptoms or identifying symptom clusters is the lack of symptom instruments that include a variety of symptoms. There is no "gold standard" symptom instrument in the HF population. To assess symptoms some investigators[15-17] used items related to symptoms from HF-specific quality of life measures. Others[9, 33, 205] used symptom measures developed for other populations, yet did not fully examine their psychometric properties in the HF population.

In chapter three, symptom measures that were developed for and used in patients with HF were identified and examined for their quality in five evaluation categories (i.e., contents, measuring scales, psychometric properties, completion process, and

information). Five symptom instruments were included: the M.D Anderson Symptom Index-HF, the Memorial Symptom Assessment Scale-HF, the HF Signs and Symptoms Checklist, the HF Symptom Checklist, and the HF Symptom Survey. In this chapter, it was concluded that all five symptom instruments did not satisfactorily meet the evaluation categories. This may have occurred because the five symptom instruments reviewed were recently developed or revised for patients with HF and have not yet been rigorously examined for their psychometric properties. No instrument had the capability of assessing for symptom clusters. In this chapter, ongoing validation of the five symptom instruments was recommended to demonstrate their reliability and validity. Contents of symptom measures should be evaluated by experts and patients. Consensus among experts is necessary in order to capture symptoms in a measurable way to promote effective symptom management. In some measures, similar symptom items were assessed separately, while in others these symptom items were combined. It is necessary to study how well patients can differentiate similar symptom items (e.g., feeling nervous from feeling anxious), which may serve as a guide to develop or modify symptom items.

Chapter four also addressed a measurement issue regarding the possible over estimation of the relationship between depressive symptoms and outcomes due to overlapping physical depressive symptoms and typical HF symptoms. One issue in assessing depressive symptoms is that established, popular depressive symptom measures include physical depressive symptoms, which are frequently reported HF symptoms. This calls into question the association between poor outcomes and depressive symptom scores measured with instruments that include physical depressive symptoms, because depressive symptom scores may be a reflection of HF severity rather than a depressed mood.

In chapter four, I evaluated whether the presence of physical depressive symptoms on the Patient Health Questionnaire-9 (PHQ-9), an established depressive symptom measure, exaggerated the association between depressive symptoms and cardiac event-free survival. In chapter four, it was concluded that physical depressive symptoms were not an independent predictor of cardiac event-free survival, but affective depressive symptoms were. This finding suggested that therelationship between depressive symptoms and risk for a cardiac event is not altered by the presence of

physical depressive symptoms. Outcomes can be accurately predicted based on depressive symptom scores using an instrument containing physical depressive symptoms.

As HF is a chronic condition, patients with HF are in the best position to monitor and recognize their own worsening symptoms, and regular symptom monitoring may result in proper, timely response to altered symptom status. In chapters five and six, investigations concerning patients' symptom assessment as a part of self-care maintenance were conducted.

Although it is suggested that regular symptom monitoring facilitates patients' actions to mitigate worsening symptoms, it is questionable whether patients who are adherent to daily symptom monitoring are able to adequately perform self-care management behaviors to alleviate symptoms. In a study by Nieuwenhuis and colleagues,[206] adherence to regular weight monitoring was not an independent predictor of seeking timely medical care. This finding suggested that patients do not follow recommendations for appropriate responses even if they recognize symptom changes and thus, miss the opportunity for timely intervention. Thus, in chapter five, the association between symptom monitoring behaviors (i.e., weight and lower extremity edema monitoring) and self-care management (i.e., response to changes in symptom status) was examined among HF patients who experienced dyspnea and lower extremity edema over the past month. I found that adequacy of self-care management was predicted by adherence to symptom monitoring behaviors. This finding suggested that regular symptom monitoring promotes the performance of subsequent self-care management, which may prevent hospitalizations in patients with HF.

The findings from chapter five gave me the confidence to develop an intervention to improve symptom monitoring behaviors in patients with HF in order to improve outcomes. In chapter six, a randomized controlled pilot study was conducted to test the effect of a symptom diary intervention (providing a symptom diary, self-care education, and counseling) on HF event-free survival, health-related quality of life (HRQOL), and self-care maintenance (i.e., symptom monitoring behaviors and adherence to therapeutic regimens) in patients with HF at 3-month follow-up. A total of 44 HF patients recently discharged from the hospital were randomly assigned into usual care or intervention

groups. There were trends toward the improvement in HF event-free survival and self-care maintenance over time in the intervention group, although these relationships did not reach statistical significance. There was no impact on HRQOL of the intervention. These findings suggest that a use of a simple daily symptom diary may promote patients' symptom monitoring behaviors, which enhances patients' self-care ability and facilitates timely intervention if symptom changes occur. Most importantly, these findings provide effect size data for use to determine the sample size needed for an adequately powered randomized controlled trial of the intervention.

Implications

This dissertation contributes to the science of HF management that focuses on symptoms by: (1) questioning the current practice of HF symptom assessment by healthcare providers and/ or researchers; (2) suggesting possible approaches to how symptom assessment can be effectively conducted; (3) providing evidence that daily symptom monitoring behaviors promote appropriate actions to respond altered symptom status; and (4) providing a potential strategy to enhance routine symptom monitoring behaviors in patients with HF. There are two major implications for HF symptom assessment: how we assess symptom experiences of HF patients in a meaningful way and how we facilitate patients' routine symptom monitoring behaviors to improve outcomes.

Implications for Researchers

One of the purposes of symptom assessment in HF is to understand patients' symptom experiences, in order to develop and/or administer effective interventions to effectively manage symptoms. The current symptom instruments used in the HF population may not fulfill this purpose. Symptom clusters are not addressed in symptom instruments, despite the significant association between symptom clusters and outcomes. It is necessary to develop proper ways of addressing symptom clusters in HF symptom measures.

One way to assess symptom clusters may be to conduct (1) a qualitative study with patients who recently had HF exacerbation to explore their symptom experiences focusing on the presence of symptom clusters; and (2) a quantitative study with the same population to conduct cluster analyses, based on results from symptom assessments using

a symptom instrument including a wide range of symptoms. By comparing results from the qualitative and quantitative studies, the presence and types of symptom clusters can be identified. The validity of the identified symptom clusters can be demonstrated by examining the association between the symptom clusters and outcomes, such as cardiac events and HRQOL, and by determining whether these symptom clusters are common in other HF patient populations, including subgroups such as patients with diabetes.

Some symptom instruments include multiple items, which appear to measure a similar symptom. However, it is unknown how well patients can differentiate these similar symptom items. In addition, symptoms are operationalized in a variety of ways, which opens the question about how this information can be compared among different symptom measures or meaningfully used to promote symptom management. Thus, it is essential that researchers in the field discuss these issues in order to modify existing symptom measures or develop new measures . For example, in international meetings, such as annual American Heart Association and HF Society of America conferences, HF experts can discuss this issue related to effective symptom assessment. The consensus from HF experts needs to be validated with clinicians and patients.

This dissertation demonstrated, in an observational study, that regular symptom monitoring is associated with the appropriate self-care management, which ultimately contributes to outcome improvement in HF. However, the results from chapter six, an intervention pilot, showed trends toward reduced rates of HF events and enhanced self-care maintenance after using a daily symptom diary. Due to the small sample size in this pilot study, there was limited power to detect the effect of the intervention. Further studies with a larger sample size are needed to support the effectiveness of a daily symptom diary use in patients with HF. Such studies are worthy of the attention of researchers given the preliminary findings in this study and the results of prior studies.

Implications for Clinicians

The concept of symptom clusters has an important implication for clinicians because symptoms occur together and symptom clusters are associated with outcomes. In clinical settings, clinicians should address the presence of symptom clusters when teaching patients. With knowledge of symptom clusters, patients can be aware of the fact that worsening symptoms of HF occur simultaneously, and monitor symptoms relevant to

HF together. It may help patients to take action in a timely manner before emergent interventions are required.

It is too early to recommend which symptom clusters should be addressed because science of symptom cluster analysis in the HF population is at an early stage. There are few studies focusing on identifying symptom clusters and evaluating their impact on outcomes. Also, symptom measures used in previous research had a limited number of symptom items. Although more studies are needed regarding symptom clusters, it is important for clinicians to address the concept of symptom clusters when teaching patients.

The median risk-adjusted 30-day readmission and mortality after hospitalization for HF were 24% and 11%, respectively.[207] As patients with HF are vulnerable to poor outcomes during the period following discharge, increased surveillance of patients' condition is essential.

The findings from the pilot study in chapter six also offer a strategy to help patients monitor symptoms on a daily basis.

One approach may be providing a daily symptom diary to patients as routine HF care. Patients would be able to quickly recognize and react to HF deterioration with the information in the symptom diary, which may result in better outcomes. The information from the diary is also beneficial for clinicians to understand daily symptom experience and patients' self-care practice at home and provide individualized advice regarding symptom management and self-care. Another merit of a daily symptom diary is that it is simple and easy to use regardless of patients' education and not resource-intensive to administer. Thus, a daily symptom diary is a viable option for clinicians to routinely use in their HF care.

Conclusions

Accurate symptom assessment and management in HF are important because symptom status has serious consequences. The results of this dissertation revealed that existing symptom instruments in HF were not satisfactory to capture accurate symptom experiences and address symptom clusters. Collaborative efforts among researchers, clinicians, and patients are required to advance HF symptom assessment.

Routine symptom monitoring is important for patients to properly manage altered symptom status and prevent a delay in seeking care. The pilot study in this dissertation offers a promising strategy, a daily symptom diary, to enhance patients' regular symptom monitoring behaviors. In this pilot study, daily symptom diary users tended to have fewer HF events and better self-care maintenance compared to daily symptom diary non-users. This simple diary is easy to implement by clinicians and acceptable by patients. However, more studies are needed to demonstrate a positive impact of a daily symptom diary use on outcomes in HF.

References

1. Alla F, Zannad F, Filippatos G. Epidemiology of acute heart failure syndromes. Heart Fail Rev 2007;12:91-5.
2. Roger VL, Go AS, Lloyd-Jones DM, et al. Heart Disease and Stroke Statistics--2012 Update: A Report From the American Heart Association. Circulation 2012;125:e2-e220.
3. Greiner MA, Hammill BG, Fonarow GC, et al. Predicting Costs Among Medicare Beneficiaries With Heart Failure. Am J Cardiol 2011.
4. Lesman-Leegte I, Jaarsma T, Coyne JC, Hillege HL, Van Veldhuisen DJ, Sanderman R. Quality of life and depressive symptoms in the elderly: a comparison between patients with heart failure and age- and gender-matched community controls. J Card Fail 2009;15:17-23.
5. Heo S, Moser DK, Lennie TA, Zambroski CH, Chung ML. A comparison of health-related quality of life between older adults with heart failure and healthy older adults. Heart Lung 2007;36:16-24.
6. Hobbs FD, Kenkre JE, Roalfe AK, Davis RC, Hare R, Davies MK. Impact of heart failure and left ventricular systolic dysfunction on quality of life: a cross-sectional study comparing common chronic cardiac and medical disorders and a representative adult population. Eur Heart J 2002;23:1867-76.
7. Heo S, Doering LV, Widener J, Moser DK. Predictors and Effect of Physical Symptom Status on Health-Related Quality of Life in Patients With Heart Failure. Am J Crit Care 2008;17:124-32.
8. Zambroski CH, Moser DK, Bhat G, Ziegler C. Impact of symptom prevalence and symptom burden on quality of life in patients with heart failure. Eur J Cardiovasc Nurs 2005;4:198-206.
9. Blinderman CD, Hornel P, Billings JA, Portenoy RK, Tennstedt SL. Symptom distress and quality of life in patients with advanced congestive heart failure. J Pain Symptom Manage 2008;35:594-603.
10. Heo S, Doering LV, Widener J, Moser DK. Predictors and effect of physical symptom status on health-related quality of life in patients with heart failure.

American journal of critical care : an official publication, American Association of Critical-Care Nurses 2008;17:124-32.

11. Ekman I, Cleland JG, Swedberg K, Charlesworth A, Metra M, Poole-Wilson PA. Symptoms in patients with heart failure are prognostic predictors: insights from COMET. J Card Fail 2005;11:288-92.
12. Moser DK, Frazier SK, Worrall-Carter L, et al. Symptom variability, not severity, predicts rehospitalization and mortality in patients with heart failure. Eur J Cardiovasc Nurs 2010.
13. Portenoy RK, Thaler HT, Kornblith AB, et al. The Memorial Symptom Assessment Scale: an instrument for the evaluation of symptom prevalence, characteristics and distress. Eur J Cancer 1994;30A:1326-36.
14. Bruera E, Kuehn N, Miller MJ, Selmser P, Macmillan K. The Edmonton Symptom Assessment System (ESAS): a simple method for the assessment of palliative care patients. J Palliat Care 1991;7:6-9.
15. Barnes S, Gott M, Payne S, et al. Prevalence of symptoms in a community-based sample of heart failure patients. J Pain Symptom Manage 2006;32:208-16.
16. Jurgens CY, Moser DK, Armola R, Carlson B, Sethares K, Riegel B. Symptom clusters of heart failure. Res Nurs Health 2009;32:551-60.
17. Lee KS, Song EK, Lennie TA, et al. Symptom clusters in men and women with heart failure and their impact on cardiac event-free survival. J Cardiovasc Nurs 2010;25:263-72.
18. Albert N, Trochelman K, Li JB, Lin SH. Signs and Symptoms of Heart Failure: Are You Asking the Right Questions? Am J Crit Care 2010;19:443-52.
19. Patel H, Shafazand M, Schaufelberger M, Ekman I. Reasons for seeking acute care in chronic heart failure. Eur J Heart Fail 2007;9:702-8.
20. Friedman MM, King KB. Correlates of fatigue in older women with heart failure. Heart Lung 1995;24:512-8.
21. Smith OR, Michielsen HJ, Pelle AJ, Schiffer AA, Winter JB, Denollet J. Symptoms of fatigue in chronic heart failure patients: clinical and psychological predictors. Eur J Heart Fail 2007;9:922-7.

22. Webel AR, Frazier SK, Moser DK, Lennie TA. Daily variability in dyspnea, edema and body weight in heart failure patients. Eur J Cardiovasc Nurs 2007;6:60-5.
23. Nieuwenhuis MM, Jaarsma T, van Veldhuisen DJ, van der Wal MH. Factors associated with patient delay in seeking care after worsening symptoms in heart failure patients. J Card Fail 2011;17:657-63.
24. Friedman MM. Older adults' symptoms and their duration before hospitalization for heart failure. Heart Lung 1997;26:169-76.
25. Carlson B, Riegel B, Moser DK. Self-care abilities of patients with heart failure. Heart Lung 2001;30:351-9.
26. Horowitz CR, Rein SB, Leventhal H. A story of maladies, misconceptions and mishaps: effective management of heart failure. Social Science & Medicine 2004;58:631-43.
27. Jurgens CY, Hoke L, Byrnes J, Riegel B. Why do elders delay responding to heart failure symptoms? Nursing research 2009;58:274-82.
28. Riegel B, Dickson VV. A situation-specific theory of heart failure self-care. The Journal of cardiovascular nursing 2008;23:190-6.
29. Riegel B, Dickson VV. A situation-specific theory of heart failure self-care. J Cardiovasc Nurs 2008;23:190-6.
30. Lewin J, Ledwidge M, O'Loughlin C, McNally C, McDonald K. Clinical deterioration in established heart failure: what is the value of BNP and weight gain in aiding diagnosis? Eur J Heart Fail 2005;7:953-7.
31. Ekman I, Ehrenberg A. Fatigue in chronic heart failure--does gender make a difference? Eur J Cardiovasc Nurs 2002;1:77-82.
32. Kirkova J, Davis MP, Walsh D, et al. Cancer symptom assessment instruments: a systematic review. J Clin Oncol 2006;24:1459-73.
33. Bekelman DB, Havranek EP, Becker DM, et al. Symptoms, depression, and quality of life in patients with heart failure. J Card Fail 2007;13:643-8.
34. Azevedo A, Bettencourt P, Frioes F, et al. Depressive symptoms and heart failure stages. Psychosomatics 2008;49:42-8.

35. Rutledge T, Reis VA, Linke SE, Greenberg BH, Mills PJ. Depression in heart failure a meta-analytic review of prevalence, intervention effects, and associations with clinical outcomes. J Am Coll Cardiol 2006;48:1527-37.
36. Lindenfeld J, Albert NM, Boehmer JP, et al. HFSA 2010 Comprehensive Heart Failure Practice Guideline. Journal of cardiac failure 2010;16:e1-194.
37. Lloyd-Jones D, Adams R, Carnethon M, et al. Heart disease and stroke statistics--2009 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation 2009;119:480-6.
38. Zambroski CH, Moser DK, Bhat G, Ziegler C. Impact of symptom prevalence and symptom burden on quality of life in patients with heart failure. Eur J Cardiovasc Nurs 2005;4:198-206.
39. Blinderman CD, Homel P, Billings JA, Portenoy RK, Tennstedt SL. Symptom distress and quality of life in patients with advanced congestive heart failure. J Pain Symptom Manage 2008;35:594-603.
40. Bekelman DB, Havranek EP, Becker DM, et al. Symptoms, depression, and quality of life in patients with heart failure. J Card Fail 2007;13:643-8.
41. Lesman-Leegte I, Jaarsma T, Sanderman R, Hillege HL, van Veldhuisen DJ. Determinants of depressive symptoms in hospitalised men and women with heart failure. Eur J Cardiovasc Nurs 2008;7:121-6.
42. Miaskowski C, Aouizerat BE, Dodd M, Cooper B. Conceptual issues in symptom clusters research and their implications for quality-of-life assessment in patients with cancer. J Natl Cancer Inst Monogr 2007:39-46.
43. Doering LV, Moser DK, Riegel B, et al. Persistent comorbid symptoms of depression and anxiety predict mortality in heart disease. Int J Cardiol 2009.
44. Ferreira KA, Kimura M, Teixeira MJ, et al. Impact of cancer-related symptom synergisms on health-related quality of life and performance status. J Pain Symptom Manage 2008;35:604-16.
45. Teunissen SC, de Graeff A, de Haes HC, Voest EE. Prognostic significance of symptoms of hospitalised advanced cancer patients. Eur J Cancer 2006;42:2510-6.
46. Lenz ER, Pugh LC, Milligan RA, Gift A, Suppe F. The middle-range theory of unpleasant symptoms: an update. ANS Adv Nurs Sci 1997;19:14-27.

47. Kim HJ, McGuire DB, Tulman L, Barsevick AM. Symptom clusters: concept analysis and clinical implications for cancer nursing. Cancer Nurs 2005;28:270-82; quiz 83-4.
48. Ryan CJ, DeVon HA, Horne R, et al. Symptom clusters in acute myocardial infarction: a secondary data analysis. Nurs Res 2007;56:72-81.
49. Azevedo A. Gender differences in heart failure. Heart 2008;94:264-5.
50. Barnes S, Gott M, Payne S, et al. Prevalence of symptoms in a community-based sample of heart failure patients. J Pain Symptom Manage 2006;32:208-16.
51. Azevedo A, Bettencourt P, Pimenta J, et al. Clinical syndrome suggestive of heart failure is frequently attributable to non-cardiac disorders--population-based study. Eur J Heart Fail 2007;9:391-6.
52. Gottlieb SS, Khatta M, Friedmann E, et al. The influence of age, gender, and race on the prevalence of depression in heart failure patients. J Am Coll Cardiol 2004;43:1542-9.
53. Ekman I, Ehrenberg A. Fatigue in chronic heart failure--does gender make a difference? Eur J Cardiovasc Nurs 2002;1:77-82.
54. Hagglund L, Boman K, Olofsson M, Brulin C. Fatigue and health-related quality of life in elderly patients with and without heart failure in primary healthcare. Eur J Cardiovasc Nurs 2007;6:208-15.
55. Ekman I, Cleland JG, Swedberg K, Charlesworth A, Metra M, Poole-Wilson PA. Symptoms in patients with heart failure are prognostic predictors: insights from COMET. Journal of cardiac failure 2005;11:288-92.
56. Lewis EF, Lamas GA, O'Meara E, et al. Characterization of health-related quality of life in heart failure patients with preserved versus low ejection fraction in CHARM. Eur J Heart Fail 2007;9:83-91.
57. Johansson P, Dahlstrom U, Alehagen U. Depressive symptoms and six-year cardiovascular mortality in elderly patients with and without heart failure. Scand Cardiovasc J 2007;41:299-307.
58. Cline CM, Willenheimer RB, Erhardt LR, Wiklund I, Israelsson BY. Health-related quality of life in elderly patients with heart failure. Scand Cardiovasc J 1999;33:278-85.

59. Riedinger MS, Dracup KA, Brecht ML, Padilla G, Sarna L, Ganz PA. Quality of life in patients with heart failure: do gender differences exist? Heart Lung 2001;30:105-16.
60. Ekman I, Boman K, Olofsson M, Aires N, Swedberg K. Gender makes a difference in the description of dyspnoea in patients with chronic heart failure. Eur J Cardiovasc Nurs 2005;4:117-21.
61. Rector TS, Kubo SH, Cohn JN. Patients' self-assessment of their congestive heart failure, Part 2: Content, reliability and validity of a new measure, the Minnesota Living with Heart Failure Questionnaire. Heart failure 1987;3:198-209.
62. Brostrom A, Stromberg A, Dahlstrom U, Fridlund B. Sleep difficulties, daytime sleepiness, and health-related quality of life in patients with chronic heart failure. J Cardiovasc Nurs 2004;19:234-42.
63. De Jong M, Moser DK, Chung ML. Predictors of health status for heart failure patients. Prog Cardiovasc Nurs 2005;20:155-62.
64. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373-83.
65. Everitt BS. Cluster analysis: a brief discussion of some of the problems. Br J Psychiatry 1972;120:143-5.
66. Everitt BS, Landau S, Leese M. Cluster analysis. 4 ed. New York: Arnold, a member of the Hodder Headline Group; 2001.
67. Dunteman GH. Use of principal components in cluster analysis. In: Principal Components Analysis. 1st ed: Sage Publications, Inc; 1989:78-9.
68. Murberg TA, Bru E, Svebak S, Tveteras R, Aarsland T. Depressed mood and subjective health symptoms as predictors of mortality in patients with congestive heart failure: a two-years follow-up study. Int J Psychiatry Med 1999;29:311-26.
69. Zuccala G, Pedone C, Cesari M, et al. The effects of cognitive impairment on mortality among hospitalized patients with heart failure. Am J Med 2003;115:97-103.

70. Friedmann E, Thomas SA, Liu F, Morton PG, Chapa D, Gottlieb SS. Relationship of depression, anxiety, and social isolation to chronic heart failure outpatient mortality. Am Heart J 2006;152:940 e1-8.
71. Jiang W, Kuchibhatla M, Clary GL, et al. Relationship between depressive symptoms and long-term mortality in patients with heart failure. Am Heart J 2007;154:102-8.
72. Jiang W, Kuchibhatla M, Cuffe MS, et al. Prognostic value of anxiety and depression in patients with chronic heart failure. Circulation 2004;110:3452-6.
73. Sherwood A, Blumenthal JA, Trivedi R, et al. Relationship of depression to death or hospitalization in patients with heart failure. Arch Intern Med 2007;167:367-73.
74. Goldberg RJ, Goldberg JH, Pruell S, et al. Delays in seeking medical care in hospitalized patients with decompensated heart failure. Am J Med 2008;121:212-8.
75. Hunt SA, Abraham WT, Chin MH, et al. 2009 focused update incorporated into the ACC/AHA 2005 Guidelines for the Diagnosis and Management of Heart Failure in Adults: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines: developed in collaboration with the International Society for Heart and Lung Transplantation. Circulation 2009;119:e391-479.
76. Rockwell JM, Riegel B. Predictors of self-care in persons with heart failure. Heart Lung 2001;30:18-25.
77. Luyster FS, Hughes JW, Gunstad J. Depression and anxiety symptoms are associated with reduced dietary adherence in heart failure patients treated with an implantable cardioverter defibrillator. J Cardiovasc Nurs 2009;24:10-7.
78. van der Wal MH, Jaarsma T, Moser DK, Veeger NJ, van Gilst WH, van Veldhuisen DJ. Compliance in heart failure patients: the importance of knowledge and beliefs. Eur Heart J 2006;27:434-40.
79. Bennett SJ, Cordes DK, Westmoreland G, Castro R, Donnelly E. Self-care strategies for symptom management in patients with chronic heart failure. Nurs Res 2000;49:139-45.
80. Moser DK, Watkins JF. Conceptualizing self-care in heart failure: a life course model of patient characteristics. J Cardiovasc Nurs 2008;23:205-18.

81. Morgan AL, Masoudi FA, Havranek EP, et al. Difficulty taking medications, depression, and health status in heart failure patients. J Card Fail 2006;12:54-60.
82. van der Wal MH, Jaarsma T, Moser DK, van Gilst WH, van Veldhuisen DJ. Unraveling the mechanisms for heart failure patients' beliefs about compliance. Heart Lung 2007;36:253-61.
83. Woo MA, Kumar R, Macey PM, Fonarow GC, Harper RM. Brain injury in autonomic, emotional, and cognitive regulatory areas in patients with heart failure. J Card Fail 2009;15:214-23.
84. Alves TC, Rays J, Telles RM, et al. Effects of antidepressant treatment on cognitive performance in elderly subjects with heart failure and comorbid major depression: an exploratory study. Psychosomatics 2007;48:22-30.
85. Friedman MM. Older adults' symptoms and their duration before hospitalization for heart failure. Heart Lung 1997;26:169-76.
86. Jurgens CY. Somatic awareness, uncertainty, and delay in care-seeking in acute heart failure. Research in nursing & health 2006;29:74-86.
87. Friedman MM. Gender differences in the health related quality of life of older adults with heart failure. Heart Lung 2003;32:320-7.
88. Chin MH, Goldman L. Gender differences in 1-year survival and quality of life among patients admitted with congestive heart failure. Med Care 1998;36:1033-46.
89. Moser DK, Watkins JF, Heo S, et al. Changed Expectations: Why Health-Related Quality of Life is Better in Elderly Patients with Heart Failure than in Younger Patients. In: the 2008 Scientific Sessions of the American Heart Association. New Orleans, LA: Circulation; 2008:S_666.
90. Tishelman C, Degner LF, Rudman A, et al. Symptoms in patients with lung carcinoma: distinguishing distress from intensity. Cancer 2005;104:2013-21.
91. Cooley ME, Short TH, Moriarty HJ. Symptom prevalence, distress, and change over time in adults receiving treatment for lung cancer. Psychooncology 2003;12:694-708.
92. Smith OR, Gidron Y, Kupper N, Winter JB, Denollet J. Vital exhaustion in chronic heart failure: symptom profiles and clinical outcome. J Psychosom Res 2009;66:195-201.

93. Blinderman CD, Homel P, Billings JA, Portenoy RK, Tennstedt SL. Symptom distress and quality of life in patients with advanced congestive heart failure. J Pain Symptom Manage 2008;35:594-603.
94. Opasich C, Gualco A, De Feo S, et al. Physical and emotional symptom burden of patients with end-stage heart failure: what to measure, how and why. J Cardiovasc Med (Hagerstown) 2008;9:1104-8.
95. "Symptom, n.1a" The Oxford English Dictionary 2nd ed. OED Online Oxford University Press, 1989 (Accessed 5, March, 2010, at http://dictionary.oed.com/cgi/entry/50245187?query_type=word&queryword=symptom&first=1&max_to_show=10&sort_type=alpha&result_place=1&search_id=g8zh-QjAdUa-3126&hilite=50245187.)
96. "Sign, n. f" The Oxford English Dictionary 2nd ed. OED Online Oxford University Press, 1989. (Accessed 5, March, 2010, at http://dictionary.oed.com/cgi/entry/50224578?query_type=word&queryword=sign&first=1&max_to_show=10&sort_type=alpha&result_place=2&search_id=g8zh-5TSTWa-3257&hilite=50224578.)
97. Rhodes VA, Watson PM. Symptom distress--the concept: past and present. Semin Oncol Nurs 1987;3:242-7.
98. Dodd M, Janson S, Facione N, et al. Advancing the science of symptom management. J Adv Nurs 2001;33:668-76.
99. Good B, Good M-J. The meaning of symptoms: a cultural hermeneutic model for clinical practice. In: Eisenberg L, Kleinman A, eds. The Relevance of Social Science for Medicine. Dordrecht Holland: D. Reidel Publishing Company; 1981:165-96.
100. Ekman I, Cleland JG, Andersson B, Swedberg K. Exploring symptoms in chronic heart failure. Eur J Heart Fail 2005;7:699-703.
101. Portenoy RK, Thaler HT, Kornblith AB, et al. The Memorial Symptom Assessment Scale: an instrument for the evaluation of symptom prevalence, characteristics and distress. Eur J Cancer 1994;30A:1326-36.

102. Friedman MM, Griffin JA. Relationship of physical symptoms and physical functioning to depression in patients with heart failure. Heart & Lung 2001;30:98-104.
103. Song EK, Moser DK, Rayens MK, Lennie TA. Symptom clusters predict event-free survival in patients with heart failure. J Cardiovasc Nurs 2010;25:284-91.
104. Hertzog MA, Pozehl B, Duncan K. Cluster analysis of symptom occurrence to identify subgroups of heart failure patients: a pilot study. J Cardiovasc Nurs 2010;25:273-83.
105. Friedman MM. Gender differences in the health related quality of life of older adults with heart failure. Heart Lung 2003;32:320-7.
106. Friedman MM, Quinn JR. Heart failure patients' time, symptoms, and actions before a hospital admission. J Cardiovasc Nurs 2008;23:506-12.
107. Albert N, Trochelman K, Li J, Lin S. Signs and symptoms of heart failure: are you asking the right questions? Am J Crit Care 2010;19:443-52.
108. Fadol A, Mendoza T, Gning I, et al. Psychometric testing of the MDASI-HF: a symptom assessment instrument for patients with cancer and concurrent heart failure. J Card Fail 2008;14:497-507.
109. Quinn C, Dunbar SB, Higgins M. Heart failure symptom assessment and management: can caregivers serve as proxy? J Cardiovasc Nurs 2010;25:142-8.
110. Ingle L, Shelton RJ, Rigby AS, Nabb S, Clark AL, Cleland JG. The reproducibility and sensitivity of the 6-min walk test in elderly patients with chronic heart failure. Eur Heart J 2005;26:1742-51.
111. Todero CM, LaFramboise LM, Zimmerman LM. Symptom status and quality-of-life outcomes of home-based disease management program for heart failure patients. Outcomes Manag 2002;6:161-8.
112. Pozehl B, Duncan K, Hertzog M. Heart Failure Symptom Survey: Validity and reliability. J Card Fail 2006;12:S100-S.
113. Zambroski CH, Lennie T, Chung ML, Heo S, Smoot T, Ziegler C. Use of the memorial symptom assessment scale-heart failure in heart failure patients. Circulation 2004;110:739-.

114. Steiner DL, Norman GR. Basic Concepts. In: Health Measurement Scales: A Practical Guide to Their Development and Use. 4th ed. New York, NY: Oxford University Press; 2008:5-15.
115. Steiner DL, Norman GR. Validity. In: Health Measurement Scales: A Practical Guide to Their Development and Use. 4th ed. New York, NY: Oxford University Press; 2008:247-76.
116. Lynn MR. Determination and Quantification of Content Validity. Nurs Res 1986;35:382-5.
117. Derogatis LR, Melisaratos N. The Brief Symptom Inventory: an introductory report. Psychol Med 1983;13:595-605.
118. Opasich C, Gualco A. The complex symptom burden of the aged heart failure population. Curr Opin Support Palliat Care 2007;1:255-9.
119. Walke LM, Byers AL, McCorkle R, Fried TR. Symptom assessment in community-dwelling older adults with advanced chronic disease. J Pain Symptom Manage 2006;31:31-7.
120. Broberger E, Tishelman C, von Essen L. Discrepancies and similarities in how patients with lung cancer and their professional and family caregivers assess symptom occurrence and symptom distress. J Pain Symptom Manage 2005;29:572-83.
121. Pocock SJ, Wang D, Pfeffer MA, et al. Predictors of mortality and morbidity in patients with chronic heart failure. Eur Heart J 2006;27:65-75.
122. O'Connor CM, Abraham WT, Albert NM, et al. Predictors of mortality after discharge in patients hospitalized with heart failure: an analysis from the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF). Am Heart J 2008;156:662-73.
123. Parissis JT, Nikolaou M, Farmakis D, et al. Clinical and prognostic implications of self-rating depression scales and plasma B-type natriuretic peptide in hospitalised patients with chronic heart failure. Heart 2008;94:585-9.
124. Lesman-Leegte I, Jaarsma T, Sanderman R, Linssen G, van Veldhuisen DJ. Depressive symptoms are prominent among elderly hospitalised heart failure patients. Eur J Heart Fail 2006;8:634-40.

125. Freedland KE, Rich MW, Skala JA, Carney RM, Davila-Roman VG, Jaffe AS. Prevalence of depression in hospitalized patients with congestive heart failure. Psychosom Med 2003;65:119-28.
126. Jiang W, Alexander J, Christopher E, et al. Relationship of depression to increased risk of mortality and rehospitalization in patients with congestive heart failure. Arch Intern Med 2001;161:1849-56.
127. Rutledge T, Reis VA, Linke SE, Greenberg BH, Mills PJ. Depression in heart failure a meta-analytic review of prevalence, intervention effects, and associations with clinical outcomes. J Am Coll Cardiol 2006;48:1527-37.
128. Holzapfel N, Muller-Tasch T, Wild B, et al. Depression profile in patients with and without chronic heart failure. J Affect Disord 2008;105:53-62.
129. Jiang W, Alexander J, Christopher E, et al. Relationship of depression to increased risk of mortality and rehospitalization in patients with congestive heart failure. Archives of Internal Medicine 2001;161:1849-56.
130. McKee PA, Castelli WP, McNamara PM, Kannel WB. The natural history of congestive heart failure: the Framingham study. N Engl J Med 1971;285:1441-6.
131. Spitzer RL, Kroenke K, Williams JB. Validation and utility of a self-report version of PRIME-MD: the PHQ primary care study. Primary Care Evaluation of Mental Disorders. Patient Health Questionnaire. JAMA 1999;282:1737-44.
132. McManus D, Pipkin SS, Whooley MA. Screening for depression in patients with coronary heart disease (data from the Heart and Soul Study). The American journal of cardiology 2005;96:1076-81.
133. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. Journal of general internal medicine 2001;16:606-13.
134. Muzzarelli S, Leibundgut G, Maeder MT, et al. Predictors of early readmission or death in elderly patients with heart failure. Am Heart J 2010;160:308-14.
135. Thombs BD, Ziegelstein RC, Pilote L, et al. Somatic symptom overlap in Beck Depression Inventory-II scores following myocardial infarction. Br J Psychiatry 2010;197:61-6.
136. Simon GE, Von Korff M. Medical co-morbidity and validity of DSM-IV depression criteria. Psychol Med 2006;36:27-36.

137. Turk DC, Okifuji A. Detecting depression in chronic pain patients: adequacy of self-reports. Behav Res Ther 1994;32:9-16.
138. Geisser ME, Roth RS, Robinson ME. Assessing depression among persons with chronic pain using the Center for Epidemiological Studies-Depression Scale and the Beck Depression Inventory: a comparative analysis. Clin J Pain 1997;13:163-70.
139. Schiffer AA, Pelle AJ, Smith ORF, Widdershoven JW, Hendriks EH, Pedersen SS. Somatic Versus Cognitive Symptoms of Depression as Predictors of All-Cause Mortality and Health Status in Chronic Heart Failure. J Clin Psychiat 2009;70:1667-73.
140. Redeker NS. Somatic symptoms explain differences in psychological distress in heart failure patients vs a comparison group. Prog Cardiovasc Nurs 2006;21:182-9.
141. de Jonge P, Ormel J, van den Brink RH, et al. Symptom dimensions of depression following myocardial infarction and their relationship with somatic health status and cardiovascular prognosis. Am J Psychiatry 2006;163:138-44.
142. Watkins LL, Schneiderman N, Blumenthal JA, et al. Cognitive and somatic symptoms of depression are associated with medical comorbidity in patients after acute myocardial infarction. Am Heart J 2003;146:48-54.
143. Barefoot JC, Brummett BH, Helms MJ, Mark DB, Siegler IC, Williams RB. Depressive symptoms and survival of patients with coronary artery disease. Psychosom Med 2000;62:790-5.
144. Connerney I, Sloan RP, Shapiro PA, Bagiella E, Seckman C. Depression is associated with increased mortality 10 years after coronary artery bypass surgery. Psychosom Med 2010;72:874-81.
145. Hoen PW, Whooley MA, Martens EJ, Na B, van Melle JP, de Jonge P. Differential associations between specific depressive symptoms and cardiovascular prognosis in patients with stable coronary heart disease. J Am Coll Cardiol 2010;56:838-44.
146. Martens EJ, Hoen PW, Mittelhaeuser M, de Jonge P, Denollet J. Symptom dimensions of post-myocardial infarction depression, disease severity and cardiac prognosis. Psychol Med 2010;40:807-14.
147. Linke SE, Rutledge T, Johnson BD, et al. Depressive symptom dimensions and cardiovascular prognosis among women with suspected myocardial ischemia: A

report from the National Heart, Lung, and Blood Institute-sponsored Women's Ischemia Syndrome Evaluation. Arch Gen Psychiatry 2009;66:499-507.

148. Faris R, Purcell H, Henein MY, Coats AJ. Clinical depression is common and significantly associated with reduced survival in patients with non-ischaemic heart failure. Eur J Heart Fail 2002;4:541-51.
149. Rodriguez-Artalejo F, Guallar-Castillon P, Pascual CR, et al. Health-related quality of life as a predictor of hospital readmission and death among patients with heart failure. Arch Intern Med 2005;165:1274-9.
150. Chen J, Normand SL, Wang Y, Krumholz HM. National and regional trends in heart failure hospitalization and mortality rates for Medicare beneficiaries, 1998-2008. Jama 2011;306:1669-78.
151. Jencks SF, Williams MV, Coleman EA. Rehospitalizations among patients in the Medicare fee-for-service program. N Engl J Med 2009;360:1418-28.
152. Annema C, Luttik ML, Jaarsma T. Reasons for readmission in heart failure: Perspectives of patients, caregivers, cardiologists, and heart failure nurses. Heart Lung 2009;38:427-34.
153. Bennett SJ, Huster GA, Baker SL, et al. Characterization of the precipitants of hospitalization for heart failure decompensation. Am J Crit Care 1998;7:168-74.
154. Riegel B, Lee CS, Dickson VV, Carlson B. An update on the self-care of heart failure index. J Cardiovasc Nurs 2009;24:485-97.
155. Hlatky MA, Boineau RE, Higginbotham MB, et al. A brief self-administered questionnaire to determine functional capacity (the Duke Activity Status Index). Am J Cardiol 1989;64:651-4.
156. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373-83.
157. van der Wal MH, Jaarsma T, Moser DK, Veeger NJ, van Gilst WH, van Veldhuisen DJ. Compliance in heart failure patients: the importance of knowledge and beliefs. Eur Heart J 2006;27:434-40.

158. Lupon J, Gonzalez B, Mas D, et al. Patients' self-care improvement with nurse education intervention in Spain assessed by the European Heart Failure Self-Care Behaviour Scale. Eur J Cardiovasc Nurs 2008;7:16-20.
159. Ni H, Nauman D, Burgess D, Wise K, Crispell K, Hershberger RE. Factors influencing knowledge of and adherence to self-care among patients with heart failure. Arch Intern Med 1999;159:1613-9.
160. Moser DK, Doering LV, Chung ML. Vulnerabilities of patients recovering from an exacerbation of chronic heart failure. Am Heart J 2005;150:984.
161. Holst M, Willenheimer R, Martensson J, Lindholm M, Stromberg A. Telephone follow-up of self-care behaviour after a single session education of patients with heart failure in primary health care. Eur J Cardiovasc Nurs 2007;6:153-9.
162. Artinian NT, Magnan M, Sloan M, Lange MP. Self-care behaviors among patients with heart failure. Heart Lung 2002;31:161-72.
163. Gary R. Self-care practices in women with diastolic heart failure. Heart Lung 2006;35:9-19.
164. Baker DW, Asch SM, Keesey JW, et al. Differences in education, knowledge, self-management activities, and health outcomes for patients with heart failure cared for under the chronic disease model: the improving chronic illness care evaluation. J Card Fail 2005;11:405-13.
165. Jaarsma T, Abu-Saad HH, Dracup K, Halfens R. Self-care behaviour of patients with heart failure. Scand J Caring Sci 2000;14:112-9.
166. Gallagher R. Self management, symptom monitoring and associated factors in people with heart failure living in the community. Eur J Cardiovasc Nurs 2010;9:153-60.
167. Dickson VV, Deatrick JA, Riegel B. A typology of heart failure self-care management in non-elders. European journal of cardiovascular nursing : journal of the Working Group on Cardiovascular Nursing of the European Society of Cardiology 2008;7:171-81.
168. Riegel B, Lee CS, Dickson VV. Self care in patients with chronic heart failure. Nat Rev Cardiol 2011;8:644-54.

169. Rockwell JM, Riegel B. Predictors of self-care in persons with heart failure. Heart Lung 2001;30:18-25.
170. Cameron J, Worrall-Carter L, Page K, Riegel B, Lo SK, Stewart S. Does cognitive impairment predict poor self-care in patients with heart failure? Eur J Heart Fail 2010;12:508-15.
171. Dickstein K, Cohen-Solal A, Filippatos G, et al. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2008: the Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2008 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association of the ESC (HFA) and endorsed by the European Society of Intensive Care Medicine (ESICM). Eur Heart J 2008;29:2388-442.
172. Riegel B, Carlson B. Facilitators and barriers to heart failure self-care. Patient Educ Couns 2002;46:287-95.
173. Artinian NT, Magnan M, Sloan M, Lange MP. Self-care behaviors among patients with heart failure. Heart Lung 2002;31:161-72.
174. Horowitz CR, Rein SB, Leventhal H. A story of maladies, misconceptions and mishaps: effective management of heart failure. Soc Sci Med 2004;58:631-43.
175. Moser DK, Doering LV, Chung ML. Vulnerabilities of patients recovering from an exacerbation of chronic heart failure. Am Heart J 2005;150:984.
176. Patel H, Shafazand M, Schaufelberger M, Ekman I. Reasons for seeking acute care in chronic heart failure. European journal of heart failure 2007;9:702-8.
177. Riegel B, Moser DK, Anker SD, et al. State of the science: promoting self-care in persons with heart failure: a scientific statement from the American Heart Association. Circulation 2009;120:1141-63.
178. Evangelista LS, Dracup K, Doering LV. Treatment-seeking delays in heart failure patients. J Heart Lung Transplant 2000;19:932-8.
179. Gary R. Self-care practices in women with diastolic heart failure. Heart Lung 2006;35:9-19.
180. Wright SP, Walsh H, Ingley KM, et al. Uptake of self-management strategies in a heart failure management programme. Eur J Heart Fail 2003;5:371-80.

181. Rector TS, Cohn JN. Assessment of patient outcome with the Minnesota Living with Heart Failure questionnaire: reliability and validity during a randomized, double-blind, placebo-controlled trial of pimobendan. Pimobendan Multicenter Research Group. American heart journal 1992;124:1017-25.
182. Bennett SJ, Oldridge NB, Eckert GJ, et al. Comparison of quality of life measures in heart failure. Nursing research 2003;52:207-16.
183. Ni H, Toy W, Burgess D, et al. Comparative responsiveness of Short-Form 12 and Minnesota Living With Heart Failure Questionnaire in patients with heart failure. J Card Fail 2000;6:83-91.
184. Heo S, Moser DK, Riegel B, Hall LA, Christman N. Testing the psychometric properties of the Minnesota living with heart failure questionnaire. Nurs Res 2005;54:265-72.
185. Riegel B, Lee CS, Dickson VV, Carlson B. An update on the self-care of heart failure index. The Journal of cardiovascular nursing 2009;24:485-97.
186. Stafford L, Berk M, Jackson HJ. Validity of the Hospital Anxiety and Depression Scale and Patient Health Questionnaire-9 to screen for depression in patients with coronary artery disease. General hospital psychiatry 2007;29:417-24.
187. The Criteria Committee of the New York Heart Association. Nomenclature and Criteria for Diagnosis of Diseases of the Heart and Great Vessels. 9th ed. Boston, Mass: Little, Brown & Co; 1994.
188. White MM, Howie-Esquivel J, Caldwell MA. Improving heart failure symptom recognition: a diary analysis. The Journal of cardiovascular nursing 2010;25:7-12.
189. Eastwood CA, Travis L, Morgenstern TT, Donaho EK. Weight and symptom diary for self-monitoring in heart failure clinic patients. J Cardiovasc Nurs 2007;22:382-9.
190. Muntwyler J, Abetel G, Gruner C, Follath F. One-year mortality among unselected outpatients with heart failure. Eur Heart J 2002;23:1861-6.
191. Holland R, Rechel B, Stepien K, Harvey I, Brooksby I. Patients' Self-Assessed Functional Status in Heart Failure by New York Heart Association Class: A Prognostic Predictor of Hospitalizations, Quality of Life and Death. Journal of cardiac failure 2010;16:150-6.

192. Ahmed A, Aronow WS, Fleg JL. Higher New York Heart Association classes and increased mortality and hospitalization in patients with heart failure and preserved left ventricular function. American heart journal 2006;151:444-50.
193. Dickson VV, Riegel B. Are we teaching what patients need to know? Building skills in heart failure self-care. Heart Lung 2009;38:253-61.
194. Caldwell MA, Peters KJ, Dracup KA. A simplified education program improves knowledge, self-care behavior, and disease severity in heart failure patients in rural settings. Am Heart J 2005;150:983.
195. Moser DK, Yamokoski L, Sun JL, et al. Improvement in health-related quality of life after hospitalization predicts event-free survival in patients with advanced heart failure. J Card Fail 2009;15:763-9.
196. Riegel B, Moser DK, Glaser D, et al. The Minnesota Living With Heart Failure Questionnaire: sensitivity to differences and responsiveness to intervention intensity in a clinical population. Nursing research 2002;51:209-18.
197. Rubak S, Sandbaek A, Lauritzen T, Christensen B. Motivational interviewing: a systematic review and meta-analysis. The British journal of general practice : the journal of the Royal College of General Practitioners 2005;55:305-12.
198. Riegel B, Dickson VV, Hoke L, McMahon JP, Reis BF, Sayers S. A motivational counseling approach to improving heart failure self-care: mechanisms of effectiveness. The Journal of cardiovascular nursing 2006;21:232-41.
199. Seto E, Leonard KJ, Cafazzo JA, Masino C, Barnsley J, Ross HJ. Self-care and Quality of Life of Heart Failure Patients at a Multidisciplinary Heart Function Clinic. Journal of Cardiovascular Nursing 2011;26:377-85.
200. Lee KS, Lennie TA, Riegel B, et al. Concrete Symptom Clusters are Identifiable and Identical in Women and Men with Heart Failure, and Predict Health Outcome. Circulation 2008;118:S824-S.
201. Moser DK, Frazier SK, Worrall-Carter L, et al. Symptom variability, not severity, predicts rehospitalization and mortality in patients with heart failure. European Journal of Cardiovascular Nursing 2011;10:124-9.
202. Carlson B, Riegel B, Moser DK. Self-care abilities of patients with heart failure. Heart & lung : the journal of critical care 2001;30:351-9.

203. Jurgens CY, Moser DK, Armola R, Carlson B, Sethares K, Riegel B. Symptom clusters of heart failure. Res Nurs Health 2009;32:551-60.
204. Jurgens CY, Fain JA, Riegel B. Psychometric testing of the heart failure somatic awareness scale. J Cardiovasc Nurs 2006;21:95-102.
205. Walke LM, Gallo WT, Tinetti ME, Fried TR. The burden of symptoms among community-dwelling older persons with advanced chronic disease. Arch Intern Med 2004;164:2321-4.
206. Nieuwenhuis MM, Jaarsma T, van Veldhuisen DJ, van der Wal MH. Factors associated with patient delay in seeking care after worsening symptoms in heart failure patients. J Card Fail 2011;17:657-63.
207. Heidenreich PA, Hernandez AF, Yancy CW, Liang L, Peterson ED, Fonarow GC. Get With The Guidelines Program Participation, Process of Care, and Outcome for Medicare Patients Hospitalized With Heart Failure. Circ-Cardiovasc Qual 2012;5:37-43.

Vita

Date of Birth 11/06/1981

Place of Birth Kyunggido, South Korea

Education:

Institution	Degree or Diploma	Dates	Field(s) of Study
Seoul National University Seoul, Korea	BSN	2000-2004	Nursing
University of Kentucky Lexington, KY	MSN	2007-2009	Nursing
University of Kentucky Lexington, KY	MPH	2009-2011	Biostatistics

Professional Experience:

Dates	Institution and Location	Position
05/08-present	University of Kentucky College of Nursing Lexington, KY	Research assistant
08/07-05/08	College of Nursing University of Kentucky Lexington, KY	Teaching assistant
06/06-12/06	Acupuncture Meridian Science Research Center Kyung Hee University Suwon, Korea	Research assistant
01/04-06/06	Seoul National University Hospital Cardio-thoracic surgery intensive care unit Seoul, Korea	Staff Nurse

Teaching Experience

Date	Position	Course
2012	Lecturer	Analysis, Interpretation, and Presentation of Quantitative Data
2012	Lecturer	Doctoral Seminar
2011	Preceptor	Synthesis of Clinical Knowledge for Nursing Practice
2008	Teaching Assistant	Advanced Health Assessment

Awards and Honors:

2000-2001	Scholarship for Academic Excellence, Seoul National University
2003	Scholarship for Academic Excellence, Seoul National University
2002	College of Nursing Alumni Association Scholarship, Seoul National University
2004	Graduated with honors
2009	Finalist for the Nursing Research Award at the Heart Failure Society of America Annual Scientific Meeting in Boston, MA, September 2009
2010	Top student poster session at the 2010 Southern Nursing Research Society Conference in Austin, TX, February 2010
2010	First place for the Young Investigator Award at the Heart-Brain Summit Conference in Las Vegas, NV, September 2010
2011	Summer School 2011at University of Basel, Institute of Nursing Science - Applied Patient Safety: real data, real tools, real solutions
2011	Nursing Research Award from the Delta Psi Chapter of Sigma Theta Tau
2011	Late Breaker poster session at the 2011 Southern Nursing Research Society Conference in Jacksonville, FL, February 2011
2011	Best Graduate Poster session at the 2011Student Scholarship Showcase, the College of Nursing at the University of Kentucky, March 2011
2011	Finalist for the Nursing Research Award at the Heart Failure Society of America Annual Scientific Meeting in Boston, MA, September 2011
2008-07/2010	RICH Heart Program Predoctoral Fellowship, University of Kentucky
07/2010-07/2011	University of Kentucky Graduate School Academic Year Non-service Fellowship non-service Dissertation Year Fellowship
07/2011-present	University of Kentucky Graduate School non-service Dissertation Year Fellowship

Membership in Professional Organizations:

2008-present	American Heart Association, Council on Cardiovascular Nursing
2008-present	Southern Nursing Research Society
2009-present	Sigma Theta Tau International Honor Society of Nursing
2010-present	Council for the Advancement of Nursing Science

Publications

Journal articles:

Lee KS, Lennie TA, Heo S, Moser DK. (2012). Association of Physical versus Affective Depressive Symptoms with Cardiac Event-Free Survival in Patients with Heart Failure. Psychosomatic Medicine. (74)

Lee KS, Song EK, Frazier SK, Lennie TA, Chung ML, Heo S, Wu J, Rayens MK, Riegel B, Moser DK. (2011). Concrete symptom clusters are identifiable and identical in women and men with heart failure, and predict health outcome. Journal of Cardiovascular Nursing.(25) 263-72.

Moser DK, Frazier SK, Worrall-Carter L, Biddle MJ, Chung ML, **Lee KS**, Lennie, TA. (2010). Symptom variability, not severity, predicts rehospitalization and mortality in patients with heart failure. European Journal of Cardiovascular Nursing. S1474-5151

Published Abstracts:

Lee KS, Lennie TA, Dunbar SB, Pressler SJ, Heo S, Moser DK. (2011). Low levels of depressive symptoms predict the combined outcome of good health-related quality of life and no cardiac events in patients with heart failure. Cleve Clin J Med,78, S82

Lee KS, Lennie TA, Dunbar SB, Pressler SJ, Heo S, Moser DK. (2011). Regular Monitoring of Lower Extremity Edema Predicts Cardiac Event-free Survival in Patients with Heart Failure. J Card Fail, 17, S5

Lee KS, Lennie TA, Chung ML, Heo S, Wu J, Moser DK. (2009). Comparison of the impact of PHQ-9 scores with and without physical symptom items on event-free survival in heart failure. J Card Fail, 15, S5

Lee KS, Lennie TA, Riegel B, Heo S, Wu J, Chung ML, Rayens MK, Moser DK. (2008). Concrete symptom clusters are identifiable and identical in women and men with heart failure, and predict health outcome. Circulation, 118 S824.

Presentations

Moser DK, Wu J, Welsh D, Lennie TA, Chung ML, Abshire D, Dekker R, **Lee KS.** (2012) *Precipitants of Hospital Admission for Exacerbation of Heart Failure*. Paper presented at the 2012 World Congress of Cardiology Scientific Sessions, Dubai, United Arab Emirates

Lee KS, Lennie TA, Dunbar SB, Pressler SJ, Heo S, Moser DK. (2011) *Regular Monitoring of Lower Extremity Edema Predicts Cardiac Event-free Survival in Patients with Heart Failure.* Paper presented at the 2011 Scientific Sessions of the Heart Failure Society of America, Boston, MA.

Poynter PS, **Lee KS,** Bush HM, Crofford L. (2011) *Comparative Impact of Autoimmune Diseases on Health Status and Health Care Utilization.* Poster presentation at the 2011 ACR/ARHP Annual Scientific Meeting, Chicago, IL.

Lee KS, Guo J, Crofford L, Bush HM. (2011) *The Impact of Perceived Obesity Levels on Health Status in Women.* Poster presentation at the 6th Annual Center for Clinical and Translational Science Spring Conference, Lexington, KY.

Poynter PS, Crofford L, Bush HM, **Lee KS**. (2011) *Impact of Autoimmune Disease on Health Status and Health Care Utilization: Cross-sectional Data from the Kentucky Women's Health Registry.* Poster presentation at the 6th Annual Center for Clinical and Translational Science Spring Conference, Lexington, KY

Lee KS, Lennie TA, Dunbar SB, Pressler SJ, Heo S, Moser DK. (2011) *Regular Monitoring of Lower Extremity Edema Predicts Cardiac Event-free Survival in Patients with Heart Failure.* Poster presentation at the 2011 Southern Nursing Research Society Conference, Jacksonville, FL.

Lee KS, Lennie TA, Dunbar SB, Pressler SJ, Heo S, Moser DK. (2010) *Low Levels of Depressive Symptoms Predict the Combined Outcome of Good Health-Related Quality of Life and No Cardiac Events in Patient with Heart Failure.* Oral and poster presented at the 2010 Heart-Brain Summit Conference, Las Vegas, NV.

Lee KS, Lennie TA, Chung ML, Heo S, Song EK, Wu JR, Moser DK. (2010) *Depressive Symptoms Mediate the Relationship between Health-related Quality of Life and Cardiac Event-free Survival.* Poster presented at the 2010 Southern Nursing Research Society Conference, Austin, TX.

Lee KS, Lennie TA, Chung ML, Heo S, Wu J, Moser DK. (2009). *Comparison of the impact of PHQ-9 scores with and without physical symptom items on event-free survival in heart failure*. Paper presented at the 2009 Scientific Sessions of the Heart Failure Society of America, Boston, MA.

Lee KS, Moser DK, Heo S, Chung ML, Song EK, Dunbar SB, Pressler SJ, Lennie TA. (2009). *The Relationship of body composition with quality of life in patients with heart failure*. Poster presented at the 2009 Southern Nursing Research Society Conference, Baltimore, MD.

Lee KS, Lennie TA, Riegel B, Heo S, Wu J, Chung ML, Rayens MK, Moser DK. (2008). *Concrete symptom clusters are identifiable and identical in women and men with heart failure, and predict health outcome*. Paper presented at the 2008 Scientific Sessions of the American Heart Association, New Orleans, LA.

Kyoung Suk Lee

Signature