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Changes in Depressive Symptoms and Mortality in Patients with Heart Failure: Effects of Cognitive-Affective and Somatic Symptoms

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Abstract

Objective—Depression is an independent predictor of adverse outcomes in patients with heart failure (HF). However, the effect of changes in cognitive-affective and somatic symptoms on mortality of HF patients is not known. The purpose of this study was to examine whether changes in cognitive-affective and somatic depressive symptoms over time were associated with mortality in HF.

Methods—In this secondary analysis of data from the REMOTE-HF clinical trial, we analyzed data from 457 HF patients (39% female, mean [SD] age, 65.6 [12.8] years) who survived at least 1 year and repeated the Patient Health Questionnaire (PHQ-9) at 1 year. Cognitive-affective and somatic depression scores were calculated, respectively, based on published PHQ-9 factor models. Using Cox proportional-hazards regression analyses, we evaluated the effect of changes in cognitive-affective and somatic symptoms from baseline to 1 year on cardiac and all-cause deaths.

Results—Controlling for baseline depression scores and other patient characteristics, the change in somatic symptoms was associated with increased risk of cardiac death during the subsequent 1-year period (hazard ratio [HR] = 1.24, 95% confidence interval [CI]: 1.07 – 1.44, p = .005), but the change in cognitive-affective symptoms was not (HR = 0.94, 95% CI: 0.81 – 1.08, p = .38). Similar results were found for all-cause mortality.

Conclusions—Worsening somatic depressive symptoms, not cognitive-affective symptoms, are independently associated with increased mortality of HF patients. The findings suggest that routine and ongoing assessment of somatic depressive symptoms in HF patients may help clinicians identify patients at increased risk for adverse outcomes.

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Keywords

Heart failure; depression; mortality; somatic depressive symptoms; cognitive-affective depressive symptoms

Introduction

Heart failure (HF) is a debilitating disease affecting more than 5 million individuals in the United States (1) and more than 15 million individuals in Europe (2). Moreover, its prevalence is expected to rise with the aging of the population (1, 2). Depression is common in HF patients. In a meta-analysis published in 2006, Rutledge et al. (3) reported that the prevalence of depression in HF patients ranged from 11% in patients with the New York Heart Association (NYHA) Class I to 42% in patients with Class IV. In more recent studies, the reported prevalence of depression in HF patients ranged from 30% to 46% (4–6). Depression has also been reported as a strong, independent predictor of death and cardiac events in patients with HF (4–8).

Depression is a dynamic process with fluctuations in symptoms over time (9). In a study that followed 611 HF patients, 229 (38%) were depressed at baseline (6). Of those 229 patients, 61% had remission within 18 months, while 39% remained depressed. An additional 19% of the 382 patients without depression at baseline developed depressive symptoms at 18 months. Therefore, a one-time assessment of depression may not be sufficient in evaluating the effect of depression on outcomes of HF patients. In an effort to address this problem, several investigators have examined the influence of changes in depressive symptoms on outcomes of HF patients. In a study with 147 HF patients, Sherwood et al. (10) reported that worsening depressive symptoms over 1 year were associated with increased risk of hospitalization or mortality in the subsequent 4 years, after controlling for baseline depression and risk factors. Johansson et al. (6) also reported an association of worsening depressive symptoms over 18 months with increased risk of hospitalization and mortality during the subsequent 18-month period after adjustment for baseline depression and risk factors among HF patients.

Depression is characterized by multidimensional symptoms, including cognitive-affective symptoms, such as sadness, loss of interest, irritability, hopelessness, concentration difficulties, guilt, and suicidal ideation, along with somatic symptoms, such as fatigue, sleep disturbances, psychomotor agitation or retardation, appetite changes, and body aches and pains (11). Differential effects of cognitive-affective versus somatic depressive symptoms on patient outcomes have been examined in cardiac populations (12–18). In multiple studies, somatic symptoms of depression, but not cognitive-affective symptoms, have been reported to be significantly associated with mortality in patients with coronary heart disease (12, 14–18) or HF (13).

Despite the dynamic nature of depression, the associations between changes in cognitive-affective and somatic symptoms of depression over time and patient outcomes have been examined in only one study with post-myocardial infarction (MI) patients (19) and have never been examined in HF patients. Therefore, we conducted this study to examine whether

changes in cognitive-affective and somatic symptoms of depression over time predict cardiac and all-cause mortality in patients with HF.

Methods

Study Design and Participants

This study was a secondary analysis of data from HF patients enrolled in a multicenter, randomized clinical trial designed to evaluate the effects of a focused education intervention on clinical outcomes of HF patients (Rural Education to Improve Outcomes in Heart Failure [REMOTE-HF] study) (20). The study was reviewed and approved by the Institutional Review Board of each participating institution. From multiple cardiology practices in rural areas of California, Kentucky, and Nevada, patients were recruited if they were 18 years or older, having a clinical diagnosis of HF, and lived in a rural area defined as a town of < 2,500 persons, a metropolitan center of < 50,000 persons, or open country (21). Other inclusion criteria were having been hospitalized for HF within the past 6 months, being able to read and write English, and living independently (i.e., not institutionalized). Patients who had a complicating serious co-morbidity (e.g., a psychiatric illness, untreated malignancy, or renal failure requiring dialysis), had a neurological disorder that impaired cognition, or were already participating in a HF disease management program were excluded.

Procedure

Details regarding the study design and procedure have been described elsewhere (20). After written informed consent was obtained, data on sociodemographics and depressive symptoms were collected using self-administered structured questionnaires. Clinical data were abstracted from medical records using a standardized form. Echocardiograms were ordered if not available in the patient record.

After completing the baseline questionnaires, patients were randomized into one of three groups: usual care (control) or one of two intervention groups (Fluid Watchers LITE [LITE] or Fluid Watchers PLUS [PLUS]). Patients in the two intervention groups received different levels of education about HF. Data were collected again at 12 and 24 months by a research nurse either in the patient's home or the physician's office or clinic. All patients received $25 per visit as compensation. Patient screening was conducted from September 2006 through December 2010, and the last two-year follow-up was completed in January 2012.

Measurements

Depressive symptoms—Patients' depressive symptoms were measured with the nine-item Patient Health Questionnaire (PHQ-9), a valid screening tool for depression (22, 23). The nine items in the PHQ-9 correspond with the nine diagnostic criteria for depressive disorder in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) (22). Each item is scored on a scale from 0 (not at all) to 3 (nearly every day) with a total score ranging from 0 to 27. A PHQ-9 score of 10 or greater suggest clinical depression (23). Good internal consistency of the PHQ-9 in the present study was reflected in a Cronbach's alpha of .87.

The two-dimensional structure of depressive symptoms (i.e., cognitive-affective symptoms and somatic symptoms) has been evaluated previously using the PHQ-9 in patients with heart disease (14, 16, 24). Five items related to feeling depressed, loss of interest, feeling of worthlessness, trouble concentrating, and suicidal thoughts are classified as cognitive-affective symptoms, while four items related to change in appetite, sleep problems, psychomotor agitation or retardation, and fatigue are classified as somatic symptoms (24). Internal consistency of both dimensions was acceptable in our sample with Cronbach's alphas for cognitive-affective symptoms and somatic symptoms of .81 and .75, respectively.

Other measures—The functional status of patients was assessed with the NYHA classification system (25), which has been widely used in both clinical practice and research. Based on the extent to which symptoms limit their level of physical activity, patients are classified into one of four classes with class IV being the worst (25). Patients' NYHA class was determined by the patient's physician or research nurse prior to randomization. Data on patients' comorbidities were collected from medical records using the Charlson Comorbidity Index (26). The Charlson index is a widely used, valid tool designed to measure the number and severity of comorbid diseases based on 19 major disease categories (26).

Endpoints—The primary endpoint for this study was cardiac deaths that occurred between 1 and 2 years of follow-up. At each data collection point, mortality was determined by a combination of medical record review, discussion with patients' family member and/or physician, and review of the Social Security Death Index. In all cases, copies of the death certificates were obtained. All-cause mortality was also considered as a secondary endpoint.

Statistical Analysis

Data were analyzed using IBM-SPSS 21.0. Characteristics of HF patients and other study variables were described using descriptive statistics including means, standard deviations, frequencies, and ranges. The characteristics of the study sample and the patients who died during the first year of the study follow-up (and therefore were excluded from the main analysis) were compared using student's t-tests, Mann-Whitney tests, and chi-square tests depending on the type and distribution of the data. All assumptions for each statistical test were checked.

Based on published PHQ-9 factor models (24), cognitive-affective and somatic scores were calculated, respectively. The change in cognitive-affective and somatic scores was calculated by subtracting the baseline score from the 1-year score for each dimension separately. Therefore, positive values represent worsening of depressive symptoms. Correlations among depressive symptom variables were assessed using Pearson's correlation coefficients.

Univariate (unadjusted) Cox proportional-hazards regression analyses were conducted first to evaluate the effect of each depressive symptom variable on cardiac and all-cause deaths occurred between 1 and 2 years of follow-up. Following the univariate analyses, multivariate Cox proportional-hazards regression analyses were performed to evaluate how changes in cognitive-affective and somatic symptoms of depression over a 1-year period were related to cardiac and all-cause deaths occurred during the subsequent 1-year follow-up

period, after controlling for baseline cognitive-affective and somatic depressive symptoms and selected sociodemographic and clinical characteristics (i.e., age, gender, ejection fraction [EF], NYHA class, and study group). The PHQ-9 total score and change in the total score were included in the univariate models to evaluate whether the effects of depressive symptoms differ with and without the two-dimensional structure. The covariates were selected because of their known influence on outcomes of HF patients. The study group variable was included to control for the intervention effects on outcome variables. The statistical significance level was set at $p < .05$.

Results

Baseline characteristics

As presented in Figure 1, 614 patients were enrolled and randomized. Of these, 12 patients were lost to follow-up prior to 3-month assessment with no data on clinical outcomes. Out of the 602 remaining patients, 66 patients died during the first year of follow-up and 42 patients were lost to follow-up prior to 1-year assessment. Of the 494 patients who remained in the study at 1 year, 37 patients did not complete the PHQ-9. Therefore, data from 457 patients, who survived at least 1 year and repeated the PHQ-9, were analyzed for this study.

Table 1 presents sociodemographic and clinical characteristics of the study sample (n = 457). Among the 457 patients included in the present study, 386 patients (84.5%) were non-Hispanic white, 28 (6.1%) were black, and 20 (4.4%) were Hispanic. Fifty-three percent of the study sample (240 patients) had an EF of less than 40%. Of the 66 patients who died during the first year of follow-up, 37 died of cardiac causes. Compared with the study sample, the patients who died before follow-up at 1 year were significantly older ($p < .001$), were more likely to be non-Hispanic white ($p = .040$), were less likely to be employed ($p = .004$), had a higher NYHA class ($p < .001$), and had more severe comorbid conditions ($p = .007$). They were also more likely to have a prior history of coronary artery bypass graft surgery ($p = .008$), more likely to be sedentary ($p < .001$), less likely to have a body mass index (BMI) greater than 25 Kg/m^2 ($p < .001$), and less likely to be on a beta-blocker ($p = .001$) compared with the study sample. In addition, the patients who died during the first year of follow-up had higher scores on the PHQ-9 at baseline (mean total score 9.71, SD 6.50; mean cognitive-affective symptom score 4.15, SD 3.83; mean somatic symptom score 5.56, SD 3.48) than the study sample (mean total score 6.78, SD 6.21, $t_{521} = 3.56$, $p < .001$; mean cognitive-affective symptom score 2.79, SD 3.44, $t_{521} = 2.96$, $p = .003$; mean somatic symptom score 3.99, SD 3.24, $t_{521} = 3.65$, $p < .001$).

Depressive symptoms

At baseline, 127 patients (27.8%) had a PHQ-9 score of 10 or greater, suggesting clinical depression. At 1-year follow-up, 48.8% of these patients remained clinically depressed, while 51.2% remitted. Out of 330 patients who had a PHQ-9 score less than 10 at baseline, 12.1% had newly developed depressive symptoms with a PHQ-9 score of 10 or greater at 1 year. On average, the patients had a 0.77-point (SD 5.89) reduction in the PHQ-9 total scores, a 0.34-point (SD 3.38) reduction in cognitive-affective symptom scores, and a 0.43-point (SD 3.19) reduction in somatic symptom scores from baseline to 1-year follow-up. The

changes in cognitive-affective and somatic symptom scores ranged from a 12-point reduction to a 15-point increase and from an 11-point reduction to a 12-point increase, respectively. The baseline cognitive-affective and somatic symptom scores were strongly correlated (r = .73, p < .001), and baseline scores were strongly correlated with their own change scores (baseline cognitive-affective score and change in cognitive affective scores: r = −0.52, p < .001; baseline somatic score and change in somatic scores: r = -0.52, p < .001). There was also a strong correlation between changes in cognitive-affective and somatic symptom scores from baseline to 1-year follow-up (r = .61, p < 001).

Relationships of changes in cognitive-affective and somatic depressive symptoms to cardiac and all-cause mortality

During the subsequent 1-year follow-up period, 50 patients (10.9%) died, of which 35 deaths (7.7% or 70% of the deaths) were attributable to a cardiac cause. In univariate Cox proportional-hazards regression analyses to test the effect of each depressive symptom variable (i.e., the PHQ-9 total, cognitive-affective and somatic depressive symptom scores at baseline and changes in the PHQ-9 total, cognitive-affective and somatic depressive symptom scores) on cardiac and all-cause deaths, only the change in somatic symptoms of depression was found to be significantly associated with increased risk of cardiac death during the subsequent 1-year period (Table 2). Increased risk of all-cause death during the subsequent 1-year period was found to be associated with the changes in the PHQ-9 total and somatic symptom scores (Table 2). Baseline depressive symptom scores and the change in cognitive-affective depressive symptoms were not significant in these models.

Table 3 shows results from multivariate Cox proportional-hazards regression analyses that predict cardiac and all-cause deaths during the subsequent 1-year follow-up period. In these models, baseline depression scores (cognitive-affective and somatic scores) were not significant. The change in somatic symptoms of depression, as indicated by increased somatic PHQ-9 scores over a 1-year period, remained significantly associated with increased risk of cardiac death during the subsequent 1-year period (hazard ratio [HR] = 1.24, 95% confidence interval [CI]: 1.07 to 1.44, p = .005), after adjustment for baseline cognitive-affective and somatic scores and demographic and clinical characteristics selected a priori (i.e., age, gender, EF, NYHA class, and study group). However, the change in cognitive-affective symptoms was not significant (HR = 0.94, 95% CI: 0.81 to 1.08, p = .38). After controlling for the same covariates, the change in somatic symptoms of depression remained significantly associated with increased risk of all-cause death during the subsequent 1-year period (HR = 1.25, 95% CI: 1.11 to 1.42, p < .001), but the change in cognitive-affective symptoms was not significant in the model (HR = 0.93, 95% CI: 0.82 to 1.05, p = .24).

Discussion

To our knowledge, this is the first study in which the differential effects of changes in cognitive-affective and somatic symptoms of depression on mortality of HF patients were examined. In the present study, we found that the change in the PHQ-9 total scores from baseline to 1-year follow-up was significantly associated with all-cause mortality during the subsequent 1-year follow-up, but not with cardiac mortality. When the differential effects

were examined, worsening somatic depressive symptoms over a 1-year period were associated with increased cardiac and all-cause mortality among HF patients during the subsequent 1-year follow-up, while cognitive-affective symptoms were not. Specifically, a 1-point increase in PHQ-9 somatic symptom scores from baseline to 1-year follow-up was associated with a 24% increase in risk for cardiac mortality and a 25% increase in risk for all-cause mortality for the next 12 months, even after controlling for baseline cognitive-affective and somatic symptom scores and demographic and clinical characteristics, including HF disease severity.

Only one previous study exists where the differential effect of changes over time in cognitive-affective and somatic depressive symptoms on mortality was examined in patients with cardiac disease (19). Consistent with our findings, Roest et al. (19) reported that improvement in somatic symptoms over a 6-month period, but not cognitive-affective symptoms, was independently associated with reduced risk of recurrent MI and mortality in post-MI patients. Despite the strong evidence that depression increases the risk of mortality in patients with HF (4–8), little is known about the mechanism underlying this relationship. Several psychobiological mechanisms have been proposed to describe the relationship between depression and HF, including inflammation, autonomic nervous system dysregulation, and health behaviors (27, 28). Patients with HF have higher levels of pro-inflammatory cytokines, which may contribute to development of HF (29). Higher levels of inflammatory markers are also found in patients with depression (30). Thus, inflammation has been suggested as a mediator between HF and depression (27, 28). However, findings from previous studies are inconsistent regarding the relationship between levels of inflammatory markers and changes in depressive symptoms over time in HF patients (31, 32), which warrants additional prospective research. Low heart rate variability, suggesting autonomic nervous system dysregulation, is another potential mechanism that has been suggested to link depression and increased cardiac mortality (27, 28). In patients with stable coronary artery disease (33) or with a recent myocardial infarction (34), low heart rate variability has been reported to be a strong independent predictor of mortality. The differential associations of cognitive-affective and somatic depressive symptoms with increased mortality have also been examined in relation to heart rate variability. Analyzing data from the Heart and Soul study with 863 outpatients with stable coronary heart disease, de Jonge et al. (24) reported a significant association of somatic depressive symptoms, but not cognitive-affective symptoms, with lower heart rate variability. These previous findings suggest a possibility that the significant association found in our study between worsening somatic depressive symptoms and increased cardiac mortality may be mediated by autonomic dysregulation. Health behaviors may also explain the relationship between depression and adverse outcomes in HF patients (27). Depressed patients are less adherent to HF self-care, such as diet and fluid restrictions and weight monitoring (35), which leads to worsening of HF (27). Yet, future research is needed to determine the mechanism underlying our findings by carefully examining these potential mediators.

In other previous studies, the association of cognitive-affective and somatic depressive symptoms measured at one time point (baseline) with patient outcomes was examined. In these studies, baseline somatic depressive symptoms, but not baseline cognitive-affective symptoms, were an independent predictor of mortality in patients with coronary heart

disease (12, 14–17) or HF (13). However, in a study by Lee et al. (36) of patients with HF, baseline cognitive-affective depressive symptoms were associated with increased risk of cardiac events, while baseline somatic/physical symptoms were not. The inconsistent findings may be attributable to the differences in the method used to assess depressive symptoms and the length of follow-up. The PHQ-9 was used in the study by Lee et al. (36), while the Beck Depression Inventory was used in the majority of other studies (12, 13, 15, 17). Moreover, symptoms were classified differently among the studies where the PHQ-9 was used. While Lee et al. (36) classified three symptoms (i.e., change in appetite, sleep problems, and fatigue) as somatic/physical symptoms because these symptoms are frequently experienced by HF patients, four symptoms, including psychomotor agitation or retardation, were classified as somatic symptoms in our study and other previous studies (14, 16) based on factor analysis by de Jonge et al. (24). The length of follow-up also varied among these previous studies, ranging from 1 year to 6 years. Interestingly, in our study, the patients who died before follow-up at 1 year had higher cognitive-affective and somatic symptom scores at baseline than the study sample (i.e., patients who survived at least 1 year and repeated the PHQ-9). However, baseline cognitive-affective and somatic symptom scores were not significantly associated with cardiac or all-cause mortality during the subsequent 1-year follow-up period. These findings suggest while symptoms of depression assessed at one time point (baseline) are helpful in predicting mortality over a relatively short period of time, repeated assessments of depressive symptoms are more useful in predicting mortality for a longer period.

Several limitations of the present study warrant discussion. The study sample was recruited from rural areas with limited economic resources and minimal access to specialized HF care, and the sample was predominantly non-Hispanic white. Therefore, the generalizability of our findings is limited. Due to the nature of secondary analysis, some important covariates were not included in the analysis. For example, data on treatment for depression were not collected in the REMOTE-HF trial. Therefore, we were unable to determine how many patients remitted spontaneously or after treatment or how many patients had treatment resistant depression. In addition, antidepressant use was found to be associated with increased mortality in HF patients in a few studies (4, 37), while others did not find such relationship (38, 39). Thus, antidepressant use needs to be taken into account in future studies that examine the relationship between depressive symptoms and mortality in HF patients. Also, data on inflammatory markers or changes in HF severity during the first year of follow-up were not collected in our study. Due to the possibilities for shared pathways and feedback loops between depression and HF (27, 28), these covariates should be controlled in future research. Additional research with a longer follow-up period is also needed to confirm our findings. Also, our multivariate models may be overfitted. However, when nested models were compared, the overall results, including parameter estimates, did not change with addition of variables. Therefore, we decided the models with variables selected a priori were the optimal model to describe the effect of changes in cognitive-affective and somatic depressive symptoms over time on cardiac and all-cause mortality in HF patients.

Conclusion

We found that worsening somatic symptoms of depression, not cognitive-affective symptoms of depression, were associated with increased cardiac and all-cause mortality of HF patients, after controlling for the severity of HF at baseline. Our findings suggest that routine and ongoing assessment of somatic depressive symptoms (i.e., appetite problems, sleeping difficulties, psychomotor agitation or retardation, and fatigue) may be useful for identifying HF patients who are at increased risk for adverse outcomes.

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List of Abbreviations

HF	heart failure
MI	myocardial infarction
REMOTE-HF	Rural Education to Improve Outcomes in Heart Failure study
PHQ-9	nine-item Patient Health Questionnaire
NYHA	New York Heart Association
EF	ejection fraction
BMI	body mass index
HR	hazard ratio
CI	confidence interval

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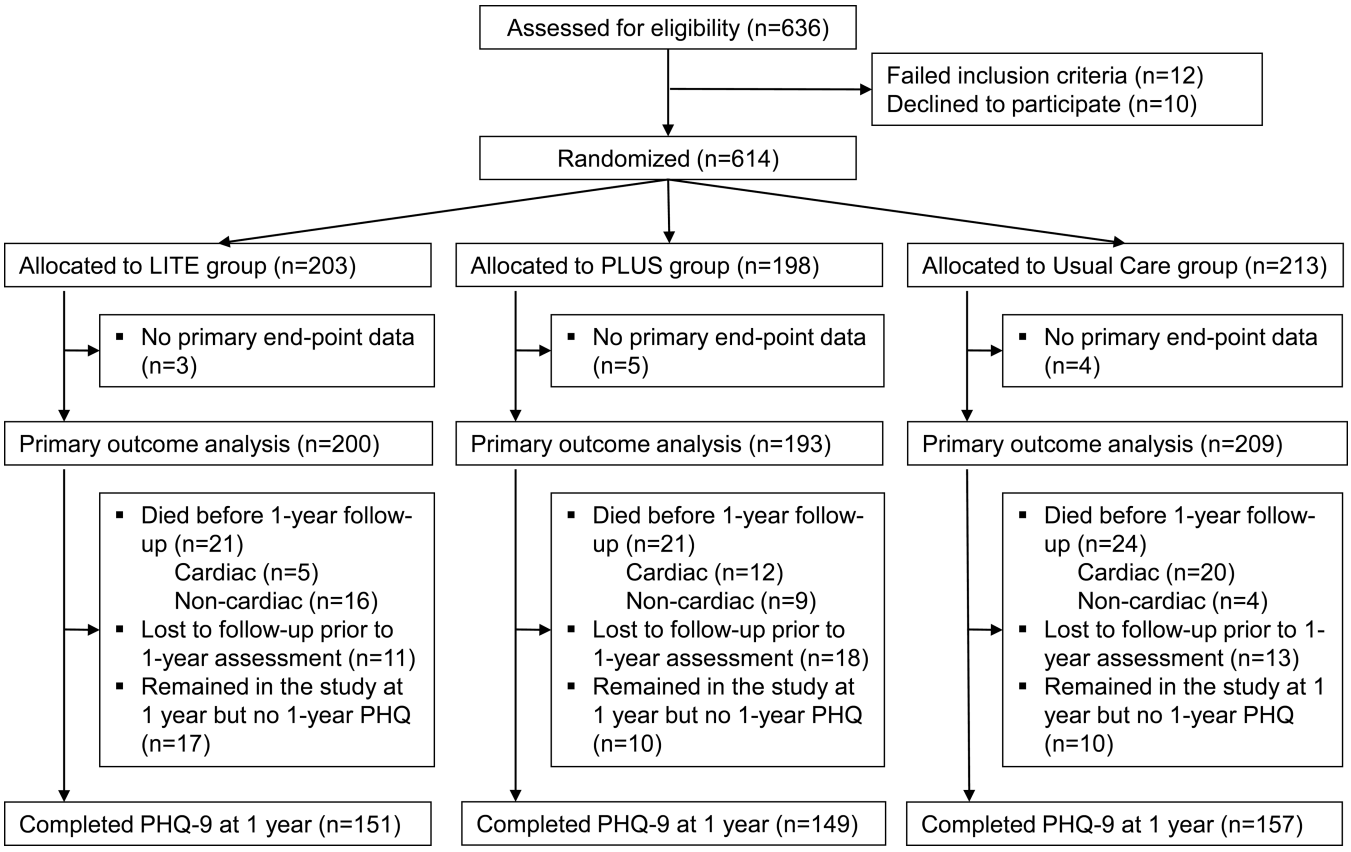
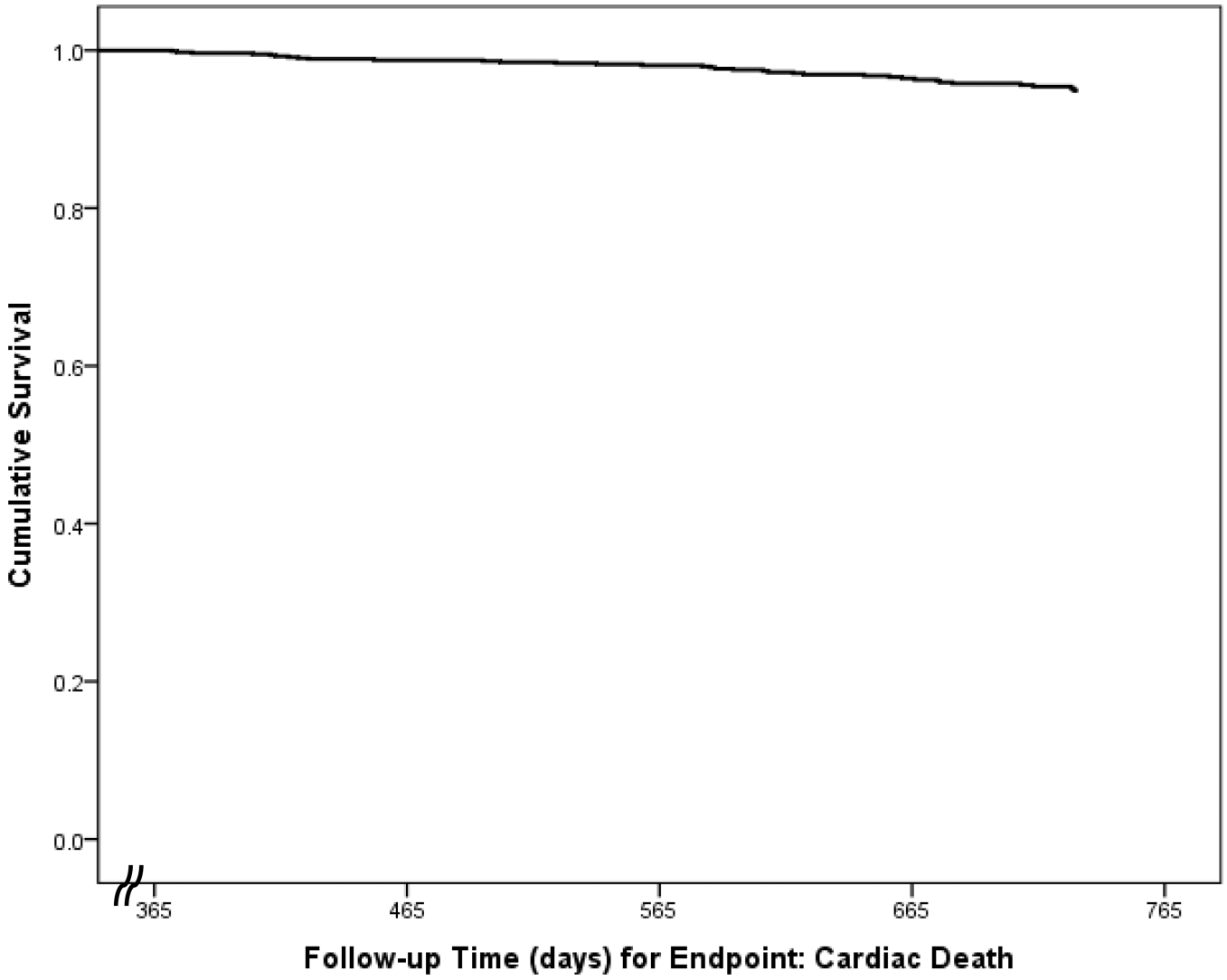


Figure 1.

Flow of patient inclusion and follow-up

PHQ-9 = nine-item Patient Health Questionnaire



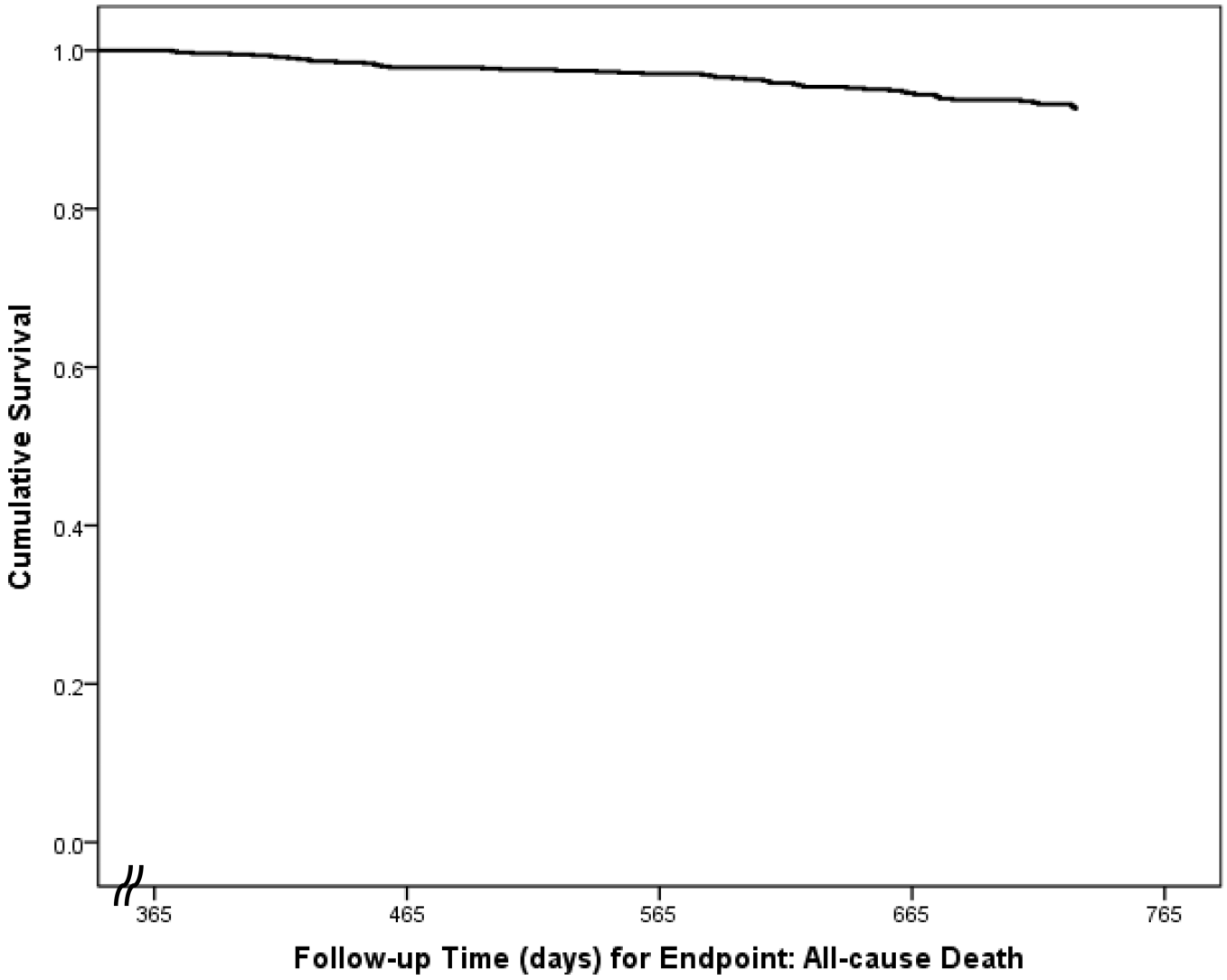


Figure 2.

Survival curves for 1-year cardiac and all-cause mortality (between 1 and 2 years of follow-up). Analysis includes adjustment for age, gender, ejection fraction, NYHA class, study group, baseline cognitive-affective and somatic symptoms, and changes in cognitive-affective and somatic symptoms.

Table1

Characteristics of the study population

Characteristic	Study sample (N = 457)
	N (%)
Study group	
Usual Care	157 (34.4%)
Fluid Watchers LITE group	151 (33.0%)
Fluid Watchers PLUS group	149 (32.6%)
Sociodemographics	
Age (Mean ± SD, in years)	65.63 ± 12.82
Gender	
Female	180 (39.4%)
Race/Ethnicity	
Non-Hispanic white	386 (84.5%)
Education level	
< High school	84 (18.4%)
Completed high school	220 (48.1%)
> High school	153 (33.5%)
Household income ($)	
< 20,000	164 (35.9%)
20,000 – 40,000	129 (28.2%)
40,000 – 75,000	80 (17.5%)
> 75,000	39 (8.5%)
Missing/decline to state	45 (9.8%)
Marital status	
Currently married/cohabitating	258 (56.5%)
Living situation	
Living alone	101 (22.1%)
Employment	
Employed	75 (16.4%)
Clinical characteristics	
Cause of heart failure	
Ischemic/myocardial infarction/ coronary artery disease	215 (47.0%)
Hypertension	104 (22.8%)
Cardiomyopathy	93 (20.4%)

Characteristic	Study sample (N = 457)
	N (%)
Idiopathic/viral/other	44 (9.6%)
Ejection fraction (%) (Mean ± SD)	38.92 ± 15.14
NYHA functional class	
I	49 (10.7%)
II	265 (58.0%)
III	132 (28.9%)
IV	10 (2.2%)
Charlson comorbidity index Total score (Mean ± SD)	3.28 ± 1.75
Cardiac history	
Prior angina	208 (45.5%)
Prior acute myocardial infarction	233 (51%)
Prior angioplasty	161 (35.2%)
Prior coronary artery bypass graft	140 (30.6%)
Prior heart valve surgery	52 (11.4%)
Risk factors	
Current smoker	56 (12.3%)
High cholesterol	314 (68.7%)
High blood pressure	377 (82.5%)
Sedentary	205 (44.9%)
Body mass index > 25	353 (77.2%)
Cardiac medications	
Diuretic	377 (82.5%)
Digitalis	109 (23.9%)
Angiotensin-converting enzyme inhibitor	263 (57.5%)
Beta blocker	378 (82.7%)
Anticoagulant	370 (81.0%)
Angiotensin II receptor blocker	86 (18.8%)

Characteristic	**Study sample (N = 457)**
	N (%)
Aldosterone inhibitor	104 (22.8%)
Baseline PHQ-9 score (Mean ± SD)	
Total score	6.78 ± 6.21
Cognitive-affective symptom score	2.79 ± 3.44
Somatic symptom score	3.99 ± 3.24

Note. Data on some characteristics were not available for all subjects. Due to rounding, not all percentages total 100. The PHQ-9 total scores can range from 0 to 27; cognitive-affective symptom scores, from 0 to 15; somatic symptom scores, from 0 to 12. NYHA = New York Heart Association; PHQ-9 = Patient Health Questionnaire 9-items.

Table2

Univariate Cox proportional-hazards models of 1-year mortality

	Cardiac mortality			All-cause mortality		
Variables	**HR**	**95% CI**	***p*-value**	**HR**	**95% CI**	***p*-value**
Baseline depressive symptoms (PHQ-9 total score)	1.02	0.97 – 1.07	.56	1.00	0.96 – 1.05	.91
Baseline cognitive-affective symptoms	1.01	0.92 – 1.11	.81	0.98	0.90 – 1.07	.64
Baseline somatic symptoms	1.05	0.95 – 1.15	.39	1.03	0.95 – 1.12	.49
Change in depressive symptoms (1 year PHQ-9 total score – baseline PHQ-9 total score)	1.04	0.99 – 1.10	0.11	1.05	1.01 – 1.10	.02
Change in cognitive-affective symptoms (1 year score – baseline score)	1.05	0.95 – 1.15	.36	1.06	0.98 – 1.15	.13
Change in somatic symptoms (1 year score – baseline score)	1.11	1.00 – 1.23	.048	1.12	1.03 – 1.22	.008

NYHA = New York Heart Association

HRs for changes in cognitive-affective and somatic symptoms refer to one unit increase in the PHQ-9 scores.

Table3

Multivariate Cox proportional-hazards models of 1-year mortality

	Cardiac mortality			All-cause mortality		
Variables	**HR**	**95% CI**	***p*-value**	**HR**	**95% CI**	***p*-value**
Age	1.04	1.01 – 1.07	.017	1.04	1.02 – 1.07	.002
Female	1.06	0.50 – 2.23	.88	0.93	0.50 – 1.73	.81
Ejection fraction	0.99	0.96 – 1.01	.23	1.00	0.98 – 1.02	.65
NYHA class	3.11	1.88 – 5.17	< .001	2.86	1.87 – 4.36	< .001
Study group			.71			.49
LITE vs. Usual Care	0.74	0.33 – 1.68	.48	0.71	0.36 – 1.42	.33
PLUS vs. Usual Care	0.76	0.34 – 1.70	.50	0.70	0.36 – 1.39	.31
Baseline cognitive-affective symptoms	0.95	0.81 – 1.11	.52	0.92	0.81 – 1.05	.23
Baseline somatic symptoms	1.15	0.96 – 1.37	.12	1.17	1.01 – 1.35	.036
Change in cognitive-affective symptoms (1 year score – baseline score)	0.94	0.81 – 1.08	.38	0.93	0.82 – 1.05	.24
Change in somatic symptoms (1 year score – baseline score)	1.24	1.07 – 1.44	.005	1.25	1.11 – 1.42	< .001

NYHA = New York Heart Association

HRs for changes in cognitive-affective and somatic symptoms refer to one unit increase in the PHQ-9 scores.