

Original Article



Health Status Trajectories Among Outpatients With Heart Failure

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Abstract

Context. Health status (i.e., symptoms, function, and quality of life) is an important palliative care outcome in patients with heart failure; however, patterns of health status over time (i.e., trajectories) are not well described.

Objectives. The objective of this study was to identify health status trajectories in outpatients with heart failure and assess whether depression, symptom burden, or sense of peace predict health status trajectory.

Methods. This is an observational study utilizing data from the Patient-Centered Disease Management for Heart Failure trial. Participants completed Kansas City Cardiomyopathy Questionnaires at baseline, three, six, and 12 months. Latent class growth analysis identified health status trajectories; multinomial logistic regression models identified predictors of trajectory membership.

Results. Patients ($n = 384$) were primarily men (97%) and older (mean age 67.6 ± 10.1). Three health status trajectories were identified. All three trajectories improved at three months; however, the marked improvement health status trajectory ($n = 19$) showed progressive improvement over one year, whereas the poor ($n = 119$) and moderate ($n = 246$) health status trajectories had little change after three months. In adjusted analyses, worse baseline depression (odds ratio 1.10; 95% confidence interval 1.01–1.20), symptom burden (1.45; 1.15–1.83), and sense of peace (0.41; 0.22–0.75) predicted membership in the poor vs. moderate health status trajectory.

Conclusion. We identified three one-year health status trajectories in patients with heart failure, with the two most common trajectories characterized by early improvement followed by limited change. Future research should assess these findings in nonveterans and women and explore whether treatment of depression, high symptom burden, and low sense of peace leads to improved long-term heart failure health status trajectory. *J Pain Symptom Manage* 2017;53:224–231. © 2016 American Academy of Hospice and Palliative Medicine. Published by Elsevier Inc. All rights reserved.

Key Words

Heart failure, health status, depression, symptom burden, spirituality, peace

Introduction

Heart failure is a prevalent, highly morbid disease that requires patients to cope with numerous chronic medications,¹ daily heart failure self-care,² and frequently, multiple comorbid illnesses.³ The disease

course for patients with heart failure is often unpredictable and uncertain,⁴ punctuated by hospitalizations that are difficult to anticipate or prevent.⁵ Furthermore, patients with heart failure suffer from depression, high symptom burden, and poor spiritual well-being at a rate comparable with those with

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advanced cancer.⁶ Palliative care clearly has a role in the care of patients with heart failure but to date is a relatively untapped resource for this population. Health status is a patient-reported measure of symptom burden, quality of life, and functional status⁷ and reflects palliative care needs in this population.⁶

Health status is not only an important measure of palliative care needs, it is also associated with outcomes in patients with heart failure. For example, one-year mortality and hospitalization rates were four and five times higher in outpatients with heart failure and very poor health status compared with those with very good health status.⁸ Short-term changes in health status also carry prognostic significance. In 6632 patients with ischemic heart disease, three-month changes in heart failure–specific health status were associated with subsequent mortality and hospitalization.⁹ Thus, besides being a measure of the patient experience, heart failure–specific health status is a powerful marker of prognosis and is useful for monitoring disease progression and response to therapy.¹⁰

Health status is a patient-centered outcome, that, despite appropriate use of guideline-concordant pharmacologic and device-based therapies,^{11,12} is challenging to improve. Understanding patterns of health status over time could help guide the development of tailored interventions designed to improve health status in patients with heart failure. Previous work has demonstrated significant interindividual differences in patterns of health status over time,^{13,14} whereas others demonstrate relatively stable mean health status in the outpatient setting when measured on a population level.^{15,16} One approach for characterizing patterns of health status over time is latent class methods, which identify otherwise unobserved subgroups of patients who are similar to one another but different from other subgroups in the population.¹⁷ Latent class analysis differs from simple regression of means over time because it allows for the possibility of more than one pattern of means over time by identifying subgroups based on trajectory patterns. Latent class analysis is, therefore, considered more effective at capturing clinical heterogeneity within a population.¹⁷ For example, latent class methods were used in the study of Alzheimer dementia to identify clinically distinct subgroups of patients with Alzheimer dementia^{18,19} and to identify phenotypes of asymptomatic patients at higher risk for developing cognitive impairment or dementia.²⁰

Once different trajectories are identified, predictors of trajectory membership can be determined. Such predictors may be useful as targets for interventions tailored to patients belonging to the clinically worst trajectories. In this study, we focused on three predictors: depression, symptom burden, and spiritual well-being (measured by patients' sense of peace) based on a

previously published conceptual model describing the relationship between them.²¹ Furthermore, depression, symptom burden, and sense of peace are core foci for a palliative care approach.²² In the conceptual model, symptom burden, depression and spiritual well-being contribute to health status, in addition to sociodemographic characteristics, comorbid illnesses, and clinical heart failure characteristics. Depression, high symptom burden, and poor spiritual well-being are commonly reported among patients with heart failure,⁶ are potentially modifiable, not directly attributable to heart failure severity, and have previously been linked to health status or quality of life in heart failure.^{23–30}

Therefore, the aims of the current observational study were to 1) identify whether latent classes could be used to represent one-year health status subgroups, or trajectories, in patients with heart failure in the outpatient setting and 2) assess whether potentially modifiable, patient-reported factors at baseline (depression, symptom burden, and spiritual well-being as measured by patients' sense of peace) are associated with trajectory membership.

Methods

We used data from The Patient-Centered Disease Management for Heart Failure trial (PCDM), which enrolled 392 outpatients from four Veterans Affairs Medical Centers with a new or existing diagnosis of heart failure with preserved or reduced ejection fraction, any New York Heart Association class, and a Kansas City Cardiomyopathy Questionnaire (KCCQ) overall summary score <60. The KCCQ is a reliable (Cronbach's $\alpha = 0.84$ in the current data set), validated, 23-item heart failure–specific health status questionnaire.³¹ The KCCQ overall summary score was used in both the PCDM trial and the present study. The overall summary score includes domains of physical limitation, symptoms, quality of life, and social limitation. It is scored from 0 to 100; lower scores indicate worse health status. Participants completed the KCCQ at study enrollment and at three, six, and 12 months.

A full description of the PCDM trial design³² and primary trial results¹⁴ are published elsewhere. Briefly, the PCDM trial randomized participants to a collaborative care model of symptom management or usual care. The primary outcome was improvement in KCCQ score at one year. There were no significant differences in baseline characteristics between the intervention ($n = 187$) and usual care ($n = 197$) groups, including KCCQ score (37.9 vs. 36.9, $P = 0.48$). Mean change in KCCQ at one year was 13.5 points and did not differ between the intervention and usual care group ($P = 0.97$). Because the PCDM intervention did not influence health status, this analysis includes all trial participants,

irrespective of randomization. All participants provided informed consent, and the institutional review board at each study site approved the study protocol.

Baseline Predictor Variables: Measurements

Depressive symptoms were assessed at study enrollment using the Patient Health Questionnaire-9 (PHQ-9), a reliable (Cronbach's $\alpha = 0.83$ in the current data set), validated, nine-item instrument designed to screen for depression.³³ The PHQ-9 is scored from 0 to 27; a positive screen for depression is a PHQ-9 score ≥ 10 .

At study enrollment, patients rated each of eight symptoms on a scale of 0–5, with 0 being “not at all bothersome” and 5 being “extremely bothersome.” Total symptom burden score was created by summing the number of symptoms each patient rated on this scale as ≥ 3 . The symptoms measured in this study (chest pain or pressure, other pain, dry mouth, numbness/tingling in the hands or feet, constipation, nausea, cough, and dizziness) were chosen because they are commonly reported in heart failure.^{27,28,34,35}

Sense of peace, a measure of spiritual well-being, was assessed at study enrollment as the patient's congruence with the statement “I feel at peace,” rated from 0 (not at all at peace) to 5 (completely at peace). This single item is a valid measure based on concurrent validity testing with other spiritual well-being measures.³⁶

Questions in the PHQ-9, symptom burden scale, and sense of peace measure do not overlap with questions in the KCCQ, with the exception of a single KCCQ item that assesses mood/depression and, therefore, overlaps with the PHQ-9. Removal of this item from the KCCQ did not have any influence on the reported results; therefore, we maintained the KCCQ in its original form for consistency with previous research.

Other Baseline Data

Baseline demographic characteristics were collected via survey. Medical history and clinical heart failure characteristics were ascertained by chart review. Each patient's medical conditions were summed to create a comorbidity score (maximum score of 10; medical conditions measured were: coronary artery disease, diabetes, hypertension, transient ischemic attack, chronic obstructive pulmonary disease, atrial fibrillation, peripheral vascular disease, alcohol abuse, other substance abuse including tobacco, and sleep apnea).

Statistical Analyses

The initial goal of the analysis was to examine for heterogeneity in the KCCQ score trajectories over time. Eight participants dropped out of the study before collection of baseline data, yielding a final cohort of 384. Latent class growth models were estimated in Mplus, version 7.2, to examine whether

latent classes could best represent health status trajectories. Individuals belonging to a trajectory were expected to be similar to one another in regard to changes in KCCQ score over time but different from individuals in other trajectories.

Before carrying out the latent class growth analysis, an unconditional growth model was fit, without considering the presence of latent classes, to determine the shape of the growth trajectory over time. It was determined that the quadratic growth model demonstrated better fit to the data than the model with linear growth. Quadratic growth models with one, two, three, and four latent classes were estimated, and confidence in the final solution was based on several statistical indices of fit and the theoretical meaningfulness and conceptual interpretability of the class structure. Statistical fit criteria were the Bayesian information criterion (BIC), Akaike's information criterion (AIC), a significant Lo-Mendell-Rubin likelihood ratio test (LMR-LRT), and trajectory size greater than or equal to 5% of the sample.³⁷ Lower BIC and AIC values indicate a better fitting model; for the LMR-LRT, fit is determined by a significance test comparing the estimated model to a model with one fewer trajectory, where a significant value supports the model with a greater number of trajectories.

Once the final trajectory subgroup structure was determined, baseline depression, symptom burden, and sense of peace were examined as predictors of trajectory membership. Guided by the conceptual model, we controlled for other measures that may influence health status trajectory (age, race, burden of comorbid illnesses, and clinical heart failure characteristics as measured by ejection fraction) by including these variables as covariates in our multinomial logistic regression model. Although sex may influence health status trajectory, we did not adjust for it because our population was overwhelmingly men. We did conduct a sensitivity analysis using only male participants (data not shown), which showed similar results to the analyses of the full sample. One of the trajectories had few patients (5%); therefore, we only examined predictors of trajectory membership between the two major trajectories.

Missing data occurring as a result of attrition over time were addressed by estimating the growth models with all available data using full information maximum likelihood estimation; the small amount of missing data on the predictors and covariates was addressed using multiple imputation. A small number of patients ($n = 29$; 7.6%) died over the course of data collection; not surprisingly, nonparametric tests showed that these patients were older and had a reduced EF compared with those who were not deceased. The two patient groups did not differ in terms of KCCQ score, comorbidities, symptoms, depression, or sense of peace (data not shown). A sensitivity analysis was conducted

removing 29 patients who died over the course of data collection, with no changes to the observed conclusions. Results using available data for all participants are, therefore, reported.

Results

Reflective of the U.S. veteran population, our cohort was primarily Caucasian (81.8%) and men (96.6%), with a mean age of 67.6. Patients ($n = 384$) had on average very poor health status at baseline (mean KCCQ 37.4), and almost half of patients had heart failure with preserved ejection fraction (Table 1). Over one year, 29 (7.6%) died.

Based on the BIC, AIC, and LMR-LRT, there was support for both a two- and a three-trajectory model. Lower BIC and AIC values supported the three-trajectory model over the two-trajectory model, although there was no significant difference in fit between the two- and three-trajectory models based on the LMR-LRT ($P = 0.10$). Although the third trajectory reflects a small proportion of the sample (5%), it was theoretically unique from the first two trajectories. We, therefore, report the three-trajectory model.

The three-trajectory model is shown in Figure 1. The two most common trajectories (moderate health status and poor health status) showed initial improvement from baseline to three months, followed by little change throughout the rest of the follow-up period. These trajectories differed primarily in their baseline values, not their change over time. The marked improvement trajectory consisted of a small group of patients whose health status was initially very poor but improved substantially and progressively throughout the year.

Table 2 lists mean \pm SD values for predictor variables and covariates by most likely trajectory membership. After adjustment for patient characteristics (age, race, comorbidity score, and ejection fraction), worse depression, symptom burden, and sense of peace were associated with membership in the poor health status trajectory compared with the moderate health status trajectory (Table 2).

Discussion

Three distinct one-year health status trajectories were identified in 384 outpatients with heart failure. The two most common trajectories were characterized by initial improvement followed by little change over the rest of the follow-up period and were distinguished primarily by their baseline values. A third health status trajectory with few patients was characterized by marked and progressive improvement in health status over the one-year follow-up period. Worse depression, symptom burden, and sense of

Table 1
Baseline Characteristics: Data Are Presented as Number (%) or Mean \pm SD Unless Otherwise Noted

Variable	All Patients ($n = 384$ Unless Otherwise Noted)
Age	67.6 \pm 10.1
Male	370 (96.6%) ($n = 383$)
Non-Caucasian race	70 (18.2%)
Ejection fraction	($n = 348$)
Normal ($\geq 50\%$)	162 (46.6%)
Mildly reduced (40%–49%)	68 (19.5%)
Moderately reduced (30%–39%)	78 (22.4%)
Severely reduced ($<30\%$)	40 (11.5%)
NYHA class	($n = 369$)
I/II	194 (52.6%)
III/IV	175 (47.4%)
Comorbidities	
Total comorbidity count	3.4 \pm 1.4
Coronary artery disease (history of myocardial infarction, percutaneous coronary intervention or coronary artery bypass surgery)	207 (53.8%)
Diabetes mellitus	192 (50.0%)
Hypertension	317 (82.6%)
Transient ischemic attack or stroke	33 (8.6%)
Chronic obstructive pulmonary disease	116 (30.2%)
Atrial fibrillation	143 (37.2%)
Peripheral vascular disease	48 (12.5%)
Alcohol abuse	60 (15.6%)
Other substance abuse, including tobacco	28 (7.3%)
Sleep apnea	168 (43.8%)
Patient-reported variables	
Symptoms ^a	
Total number of bothersome symptoms ^b	2.8 \pm 1.7
Non-chest pain	264 (68.9%) ($n = 383$)
Numbness/tingling	223 (58.2%) ($n = 383$)
Dry mouth	198 (51.7%) ($n = 383$)
Dizziness	130 (33.9%) ($n = 383$)
Constipation	120 (31.4%) ($n = 382$)
Cough	113 (29.5%) ($n = 383$)
Chest pain	111 (29.0%) ($n = 383$)
Nausea	48 (12.6%) ($n = 382$)
Depression (PHQ-9 score) ^c	9.0 \pm 5.5
Positive depression screen (PHQ score ≥ 10)	155 (40.9%) ($n = 379$)
Sense of peace ^d	3.2 \pm 1.1
Baseline KCCQ ^e	37.4 \pm 14.0

KCCQ = Kansas City Cardiomyopathy Questionnaire; NYHA = New York Heart Association; PHQ-9 = Patient Health Questionnaire-9.

^aPatients rated each symptom ranging from “not at all bothersome” to “extremely bothersome” over the past two weeks. Results are reported as n (%) of patients rating each symptom as at least “moderately bothersome” (≥ 3 on a six-point Likert scale ranging from 0 to 5).

^bSum of the number of symptoms rated as “bothersome” (≥ 3 on a six-point Likert scale ranging from 0 to 5).

^cPHQ-9 score range 0–27; higher scores indicate worse depression.

^dCongruence with the phrase “I feel at peace” rated from 0 (not at all at peace) to 5 (completely at peace).

^eKCCQ score ranges from 0 to 100; higher scores indicate better health status.

peace were associated with membership in the poor health status trajectory, in support of the health status conceptual model.²¹

Health Status Trajectories

Mean KCCQ score increased by 15–20 points in the moderate and poor trajectories between baseline and

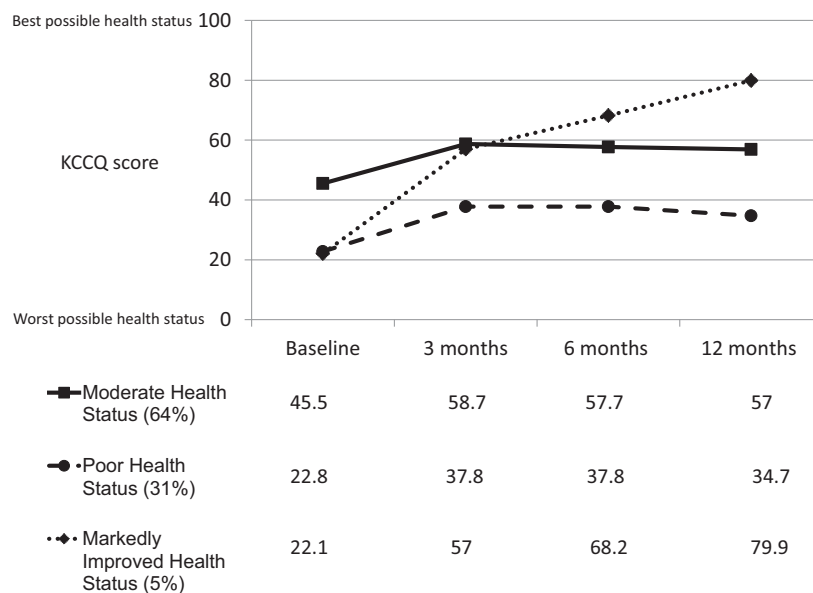


Fig. 1. KCCQ trajectories. Mean KCCQ score for each trajectory at each time point is indicated in the table below the figure. KCCQ score of 0 = worst possible health status; KCCQ of 100 = best possible health status. KCCQ = Kansas City Cardiomyopathy Questionnaire.

three months, which is consistent with a large clinical change.¹⁰ However, there was very little change over the rest of the one-year follow-up period. One possible explanation for the initial improvement in health status is regression toward the mean. One of the study inclusion criteria was poor health status (KCCQ < 60); therefore, the trial may have selected for patients who, although not hospitalized, had transient worsening in their heart failure severity, leading to a temporary drop in health status that qualified them for the study. The plateau in health status from months 3 to 12 is consistent with the results of Peters et al., who found little change in mean health status measured at study enrollment and one year later in 155 outpatients with heart failure.¹⁵ A retrospective analysis of 1458 patients hospitalized for heart failure found little change in mean health status score between one week and six months after admission.¹⁶ These studies, and the KCCQ patterns in our study in months 3–12, all suggest that for much of the time over one year, the natural, temporal variation of health status in the outpatient setting is on average, modest.

The marked improvement trajectory is an intriguing group of patients. The marked improvement and poor health status trajectories started with similar baseline KCCQ scores but diverged by the three-month measurement. Because the number of patients in the marked improvement trajectory was small, it would be premature to make inferences based on differences in baseline characteristics. Rather, these data can be used to test hypotheses in subsequent studies, such as whether those who have improved health status over time start with lower

comorbidities, less depression and symptom burden, and higher sense of peace. Future studies should attempt to replicate the finding of a group of patients with marked improvement and determine correlates of such a trajectory.

These results are relevant to patient-provider conversations about the natural history of health status for patients with heart failure as most patients with poor health status may have some short-term improvement, but reduced health status generally persists. If replicated in additional studies with other populations, this information may help in setting realistic expectations over time and guiding shared decision making. Additionally, the marked improvement trajectory, if confirmed in future studies with larger sample size, may help identify and characterize reversible causes of poor health status.

Factors Associated With Health Status Trajectories

Providing high-quality palliative care to patients with heart failure is challenging, in part because there are few data to guide clinical practice. Identifying and addressing reversible, patient-centered clinical factors associated with poor health status trajectory is one approach that may help palliative care clinicians focus their interventions. In the present study, we identified worse depression, greater symptom burden, and poor sense of peace as predictors of membership in the poor health status trajectory vs. the moderate health status trajectory. This has two important implications: first, although not tested in the present study, it is possible that addressing these domains will help patients improve to a better health status trajectory. Second, these findings

Table 2

Estimated Baseline Depression, Symptom Burden, and Sense of Peace Scores Based on Most Likely Trajectory Membership and Association Between Depression, Symptom Burden, and Sense of Peace With Trajectory Membership After Adjustment for Age, Race, Comorbidity Score, and Ejection Fraction

	Moderate Health Status Trajectory (<i>n</i> = 246)	Poor Health Status Trajectory (<i>n</i> = 119)	Marked Improvement Health Status Trajectory (<i>n</i> = 19)	Odds Ratio (95% CI) ^a
Baseline predictors				
PHQ-9 score ^b	7.7 ± 4.8	11.8 ± 3.6	9.1 ± 5.9	1.10 (1.01–1.20)
Symptom burden ^c	2.5 ± 1.7	3.6 ± 1.6	2.1 ± 1.2	1.45 (1.15–1.83)
Sense of peace score ^d	3.5 ± 0.9	2.7 ± 1.1	3.1 ± 1.3	0.41 (0.22–0.75)
Baseline covariates				
Age in years	68.0 ± 10.1	66.9 ± 10.2	65.9 ± 10.0	—
Non-Caucasian race	46 (18.3%)	20 (17.0%)	4 (28.6%)	—
Comorbidity score ^e	3.4 ± 1.4	3.6 ± 1.5	2.6 ± 0.8	—
Ejection fraction	<i>n</i> = 227	<i>n</i> = 108	<i>n</i> = 13	—
Normal (≥50%)	93 (41.0%)	62 (57.4%)	7 (53.9%)	—
Mildly reduced (40–49%)	47 (20.7%)	18 (16.7%)	3 (23.1%)	—
Moderately reduced (30–39%)	59 (26.0%)	17 (15.7%)	2 (15.4%)	—
Severely reduced (<30%)	28 (12.3%)	11 (10.2%)	1 (7.7%)	—

CI = confidence interval; PHQ-9 = Patient Health Questionnaire-9.

Data are presented as mean ± SD or *n* (%).

^aPoor vs. moderate trajectory.

^bPHQ-9 score range 0–27; higher scores indicate worse depression.

^cSum of the number of symptoms rated as “bothersome” (≥3 on a six-point Likert scale ranging from 0 to 5).

^dCongruence with the phrase “I feel at peace” from 0 (not at all at peace) to 5 (completely at peace).

^eSum of up to 10 comorbid medical conditions: coronary artery disease, diabetes, hypertension, transient ischemic attack, chronic obstructive pulmonary disease, atrial fibrillation, peripheral vascular disease, alcohol abuse, other substance abuse including tobacco, and sleep apnea.

suggest that health status in heart failure patients is influenced by a variety of mechanisms, many of them unrelated to heart failure severity.

The link between depression and health status in patients with heart failure is well described in observational studies,^{23–25} but there are few data to guide management of depression in these patients. Clinical trials evaluating sertraline and escitalopram found that they did not improve outcomes in patients with heart failure;^{38,39} however, a recent, single-center randomized clinical trial evaluated the effect of cognitive behavioral therapy on patients with heart failure and comorbid depression. Patients in the cognitive behavioral therapy arm not only had improved depression scores but also improved KCCQ scores compared with the usual care arm.⁴⁰ These results support a causal link between depression and health status in patients with heart failure. Whether improving depression can improve the trajectory of health status remains to be seen.

Patients with heart failure suffer diverse symptoms with significant symptom burden, often comparable with those with advanced cancer.^{6,41} Total symptom burden has been linked to health status in patients with heart failure in cross-sectional studies.^{27,28,35} Our study expands on these findings by showing that higher total symptom burden is associated with worse one-year health status trajectory. Together, these data suggest that symptom-based management may be an effective approach to improving health status in patients with heart failure.

Spirituality is an important component to a patient's feeling of purpose in life and can play a

significant role in how patients experience a chronic, debilitating disease, such as heart failure.⁴² Spirituality has been linked to health status in cross-sectional studies of patients with heart failure.^{29,30} These findings were expanded on in the present study, which found that low sense of peace was associated with worse health status trajectory over one year. Potential interventions aimed at improving sense of peace are sparse but may include dignity therapy,⁴³ acknowledgment of the therapeutic benefits of prayer,⁴² and consultation with a chaplain or other religious leader. Further study is required to confirm the efficacy of such interventions in patients with heart failure and the effect they may have on health status trajectory.

Future Directions

Future studies should evaluate whether these findings are applicable in women and nonveterans and identify effective treatments for symptom burden and sense of peace in patients with heart failure and assess the impact of these treatments, in addition to treatments for depression, on health status trajectory. Future work should also focus on understanding the relative influence of depression, symptom burden, and sense of peace on health status trajectory. Finally, subsequent studies should also explore other potentially modifiable predictors of heart failure-specific health status.

Limitations

This study should be considered in the context of several limitations. First, the study population was

reflective of the veteran population, limiting application of these findings to female and nonwhite patients. Second, a larger sample size and longer follow-up period may have afforded more statistical power to detect and further characterize more dynamic trajectories, such as our marked improvement trajectory. Third, patients may have had improvements or declines in health status at time points not measured during the study.

Conclusions

We identified three one-year health status trajectories, with the two most common trajectories characterized by early improvement in health status followed by limited change. Worse baseline depression, higher symptom burden, and worse sense of peace predicted membership in the lowest health status trajectory. Future research should explore whether these findings apply outside the veteran population and whether treatment of depression, high symptom burden, and poor sense of peace in patients with heart failure leads to improvement in health status trajectory.

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