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Heart failure symptom clusters and quality of life

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ABSTRACT

Background: Heart failure (HF) is a progressive symptomatic illness with reports suggesting that patients experience multiple symptoms. Symptom clusters constitute symptoms that co-occur, are related, and influence outcomes.
Objectives: The specific aims of this study were to (1) examine prevalent symptoms experienced by persons with HF, (2) identify symptoms forming clusters, and (3) evaluate the impact of HF symptom clusters on quality of life (QOL).
Methods: 117 participants (62% male; 50% black; age = 56) were recruited. Prevalent symptoms were evaluated; principle components analysis (PCA) was used to extract symptom clusters; regression analysis was used to evaluate factors influencing QOL, defined as life satisfaction.
Results: Three symptom clusters—sickness behavior, discomforts of illness, and GI distress—were extracted. Sickness behavior significantly influenced QOL (β = −0.603 p = 0.0001), explaining 40% of the variance (F = 75.12; R^2 = 0.404; p = 0.0001).
Conclusions: The Sickness Behavior cluster had a negative impact on QOL and suggests that incorporating an evaluation of these symptoms may facilitate identification and treatment of symptoms having an additive and detrimental influence on QOL. Studies to examine the stability of the clusters are warranted.

Introduction

Heart failure is characterized by a constellation of signs and symptoms and, although medical treatment is aimed at reversing pathologic responses to decreased cardiac output, the major treatment target is symptom reduction.[1,2] Symptoms of chronic illnesses may occur singly but multiple co-occurring symptoms may also characterize the symptom experience.[3,4] In HF, symptoms often co-exist.[5–17] Evaluation of the clinical significance of a symptom cluster may include assessment of the effect of that symptom cluster on patient outcomes[18] such as cardiac-related re-hospitalization and mortality.[19] Numerous investigators have examined the impact of HF symptoms on quality of life[20–25] (QOL); however, the relationship of a cluster or clusters of HF symptoms to QOL has been studied to a more limited extent.[26,27] The purpose of this study, therefore, was to examine the presentation of symptom clusters in individuals who have HF and evaluate the relationship of these clusters to QOL. Specific aims were to: (1) Examine prevalent symptoms experienced by persons with HF, (2) identify symptoms that form clusters, and (3) evaluate the impact of HF symptom clusters on QOL.

Conceptual framework

The Theory of Unpleasant Symptoms (TUS)[28] illustrates the experience of concurrent symptoms. That is, symptoms occurring during the same period of time—for example, dyspnea, fatigue, and edema in an individual who has HF.[4] The symptoms must be related, co-occur, and yet be independent of other groups (clusters) of symptoms. In addition, the symptoms in a symptom cluster *may be related to a common source* such as a disease, treatment, life transition, or co-morbid conditions.[5] The influence of a symptom cluster on one or more outcomes may be useful in determining whether the cluster is clinically significant.[19] Model concepts include *influencing factors* (e.g., physiologic, psychologic, and situational factors) that may shape the symptom experience, the *symptoms* experienced by an individual, and the *consequences* of those symptoms. The model includes age and co-morbidity as *influencing factors*, prevalent *symptoms* experienced by individuals with HF, and QOL, a *consequence* of the symptom experience, defined as life satisfaction.[29]

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Methods

Design, sample and setting

A convenience sample of individuals with a confirmed diagnosis of HF was recruited to participate. Potential participants in this cross-sectional study were 18 years of age or older, NYHA functional class 2–4, had been receiving standard therapy for HF for at least 3 months, and were able to speak/read English well enough to provide informed consent and complete questionnaires. Exclusion criteria included a diagnosis of dementia.

Data collection procedures

The study was approved by the Virginia Commonwealth University Institutional Review Board. All patients meeting inclusion criteria ($n = 151$) were referred to study staff by HF clinicians. After obtaining informed consent, 146 participants were enrolled and received a packet containing instructions for completing study questionnaires. Participants completed the questionnaires during their clinic visit. Medical record reviews were then conducted by study staff. A total of 117 patients completed questionnaires.

Variables and measures

Table 1 includes descriptions of the instruments used to measure the variables. Validity and reliability of each instrument as reported in previous studies (if available) and the present study are included.

Statistical analysis

Demographic and clinical variables were used to characterize the sample. For continuous variables, the mean, standard deviation (*SD*), and range are reported. Mean total scale and subscale scores were calculated for each instrument. For the Quality of Life Index, which includes some questions to which some participants were not expected to respond, a proportional score was calculated by dividing participants' total and subscale scores by the maximum possible score, converting the score to a scale with a range of 0.00–1.00. Proportional scores were then returned to the original metric for use in analysis.

For categorical variables and symptom prevalence, frequency and percent were included. Correlation analysis using Pearson's r was used to evaluate relationships among model variables.

Principle components analysis (PCA) was used to identify symptom clusters. Direct oblimin rotation was used because symptoms were assumed to be correlated as well as to obtain simple and interpretable factors.[41]

Assumptions of regression were examined and multiple regression was performed with QOL as the dependent variable. We used a backward stepwise elimination model-building approach[42] to trim the model of non-significant variables.

Results

Sample characteristics

Participants ($n = 117$) were 62% male, 50% black and 56 years old. Less than half (42%) were receiving disability. Etiology of HF was primarily non-ischemic (51.3%). Mean left ventricular ejection fraction (EF) was 25% by echocardiogram. On average, time since onset of HF was 5.26 years. The majority were NYHA Class 3 and 4 (60%). Twenty-six (13.6%) had only HF. Over half of the participants (62%) had an Implantable Cardiac Defibrillator (ICD); 9% were receiving home intravenous inotrope infusions. Twenty-nine (24.8%) were wait-listed or being evaluated for transplantation, and 10 (8.5%) were being evaluated for mechanical circulatory support. See Tables 2 and 3 for demographic and clinical characteristics.

Descriptive statistics of symptoms experienced

Table 4 summarizes the descriptive statistics for the symptoms experienced. These symptoms represent prevalent symptoms experienced by HF patients.

Principle components analysis

A three-component solution was identified by PCA: sickness behavior, discomforts of illness, and gastrointestinal (GI) distress. Each symptom loaded on only one component with eigenvalues >1.0 and loadings ≥ 0.73 (Table 5). A Scree plot confirmed this solution. After identification of the symptom clusters, a composite score was calculated for each by multiplying each symptom score mean by the loading and summing the products of the calculation.

Descriptive statistics for model variables

Co-morbidities. On average, the co-morbidity burden was 3.21 (*SD* = 1.9; range 1–11). Other than HF, the most frequently identified co-morbidity was diabetes mellitus ($n = 51$; 44.3%).

Sickness Behavior. The sickness behavior cluster (mean = 58.89; *SD* = 25.16) included anxiety, depression, daytime sleepiness, cognitive impairment, and fatigue. The TUS states that symptoms in a cluster must be related.[28] In this cluster, the most highly correlated symptoms were depression and fatigue ($r = 0.652$, $p \leq 0.0005$) and depression and anxiety ($r = 0.648$, $p \leq 0.0005$). Depression was also correlated with daytime sleepiness ($r = 0.513$, $p = 0.0005$) and cognitive dysfunction ($r = 0.513$, $p \leq 0.0005$). Cognitive impairment was inversely correlated with anxiety ($r = -0.567$, $p \leq 0.005$), fatigue ($r = -0.469$, $p \leq 0.0005$) and daytime sleepiness ($r = -0.432$, $p \leq 0.0005$).

Discomforts of illness. Dyspnea, edema, and pain composed the discomforts of illness cluster (mean = 16.03; *SD* = 8.69). Shortness of breath and pain ($r = 0.484$, $p \leq 0.0005$) were moderately correlated, as were shortness of breath and edema ($r = 0.426$, $p \leq 0.0005$), as well as edema and pain ($r = 0.414$, $p \leq 0.0005$).

GI Distress. GI distress was composed of appetite and hunger (mean = 9.45; *SD* = 3.75). There was a moderate correlation between appetite and hunger ($r = 0.416$, $p \leq 0.0005$).

Quality of life. Overall, participants were slightly satisfied with their QOL (mean = 149.4; *SD* = 32.8; range = 48–209). They were most satisfied with socioeconomic status (item mean = 5.32), psychological/spiritual status (item mean = 5.08), and family (item mean = 3.90); they were least satisfied with their health and functioning (item mean = 3.45).

Correlations among model variables

Table 6 includes correlations among the model variables. Because this study was guided by the TUS, all variables were included in the initial regression analysis.

Regression analysis

The initial model examining factors influencing QOL included the three symptom clusters, the 3 two-way interaction terms of the symptom clusters, and selected participant characteristics (age, co-morbidity). The backwards stepwise elimination process resulted in a trimmed model incorporating sickness behaviors as the only factor

Table 1
Variables and measures.

Conceptual model concepts	Variables	Instruments	Description	Comments/validity and reliability
Demographic and clinical characteristics:	Age (years.)	Demographic questionnaire		Retrieved from the Medical Record
	Gender	Clinical characteristics questionnaire		
	Education employment Marital status NYHA Class EF(%) Etiology of heart failure (ischemic vs. non-ischemic) Time since diagnosis (yrs.) Prescribed medications Evaluation for advanced therapy			
Influencing factors:	Co-morbidity burden	Charlson Co-morbidity Index[30]	Provides a weighted taxonomy of co-morbid conditions with prognostic implications	Retrieved from the Medical Record
Symptoms:	Anxiety and depression	Hospital Anxiety and Depression Scale (HADS)[31]	Each sub-scale is composed of 7 items on a 4-point scale (0 = absence/occasionally/very seldom; 3=occurs most of the time/very definitely/as much as I ever did). Items are summed to calculate a total score; a higher score indicates	Scores of ≥11 on a subscale suggest depression or anxiety. Internal consistency reliability for the anxiety and depression subscales have been reported as 0.73 and 0.95, respectively[11] Cronbach's α for the anxiety and depression subscales was 0.84 and 0.81, respectively.
	Dyspnea	Cardiovascular Limitations and Symptoms Profile (CLASP)[32] • Dyspnea sub-scale	5 questions assessing perception of shortness of breath over the previous 2 weeks. Items evaluate frequency, severity, and interference with activities; categorized as mild, moderate or severe (5–7 points =mild; 8–10 points=moderate; 11–14 points =severe). Items are summed to calculate a total score; a higher score indicates more severe dyspnea.	Test-retest reliability of the shortness of breath scale has been reported as 0.59 ($p = 0.001$)[33] and in individuals with coronary heart disease; internal consistency reliability has been reported as 0.70 for the CLASP and 0.82for the shortness of breath subscale.[33] In the present study, Cronbach's α was 0.85.
	Fatigue	Brief fatigue inventory[34]	Consists of 9 items assessing fatigue severity and interference with aspects of life associated with fatigue (activity, mood, work, relations with others, enjoyment of life). Items are rated as 0 (no fatigue; no interference) to 10 (fatigue as bad as you can imagine; a great deal of interference). Items are summed to calculate a total score; a higher score indicates greater fatigue.	Cronbach's α is reported to be 0.96.[34] In this study, Cronbach's α was 0.95.
	Peripheral edema	10 cm Visual Analog Scale (VAS)	Scale anchored by the descriptors "no swelling" (0) and "worst swelling I have ever had" (10); participants were asked to evaluate their edema over the previous two weeks and make a mark on the scale at the point that best represented their perception of the severity of their edema. location of edema (1=feet and ankles; 2=up to the knees; 3=above the knees).	
	Pain		Bodily Pain Scale of the Medical Outcomes Study (MOS) 36 – Item Short-Form Health Survey (SF-36) .[35] Items assess frequency of pain, discomfort, and extent of interference with normal activities in the previous two weeks. Item responses range from 1=infrequently/a few minutes/mild to 5=every day/more than two days/extremely/severe. Items are summed to calculate a total score; a higher score indicates greater severity of pain.	Previously reported a Cronbach's α of 0.77.[36]

(*continued*)

Table 1 (*Continued*)

Conceptual model concepts	Variables	Instruments	Description	Comments/validity and reliability
				In this study Cronbach's α was 0.83.
	Appetite and hunger	Food, Eating Experiences, and Diet (FEED) questionnaire[37]	Hunger and appetite were measured on 10-point scales: (1=no hunger sensations; no appetite/cravings; 10=hungriest I have ever been or my appetite was extremely good/strong cravings). Further characterized using 19 items measured on a 5-point scale (0=no effect on food eaten; 4=great effect on food eaten).	Cronbach's α was 0.90.
	Daytime functioning	General sleep disturbance scale[38] • Daytime functioning sub-scale	5 items captured using an 8-point scale (0=no days; 7=every day) Items are summed to calculate a total score; a higher score indicates greater impact on daytime functioning.	Cronbach's α of 0.88 has been reported for the instrument.[38] Cronbach's α in this study was 0.74.
	Cognitive impairment	MOS cognitive function scale[39]	Assessment day-to-day difficulties with cognitive functioning of which an individual has awareness (e.g., confusion; difficulty with reasoning/problem-solving, concentration/thinking, keeping attention on an activity). The 6-items (1=all the time; 6=none of the time) were re-coded so that higher scores reflected more difficulty with cognitive functioning.	Cronbach's α for the Cognitive Function Scale has been reported as 0.88.[39]
				In this study, Cronbach's α was 0.91.
Consequences:	Quality of life	Quality of life index (cardiac version-IV)[29,40]	Adapted 35-item questionnaire (1=very dissatisfied; 6=very satisfied). Includes 4 sub-scales: (family, health/functioning, psychosocial/spiritual, socioeconomic). Higher scores on summated scale/sub-scales indicate greater life satisfaction.	Internal consistency reliability for the total scale has been supported by Cronbach's alphas ranging from 0.73 to 0.99 across 48 studies. Cronbach's α for the 35-item scale used in this study was 0.95.

Table 2
Sample characteristics (n = 117).

Variables:	*f*(%)	Mean (*SD*)	Range
Age		56 (12.95)	20–84
Gender			
Female	44 (38%)		
Male	73 (62%)		
Race			
White	55 (47%)		
Black	59 (50%)		
American Indian/Alaska Native	2 (2%)		
Education			
Did not complete high school	20 (17%)		
High school graduate	60 (51%)		
College graduate	37 (32%)		
Marital status			
Never married	25 (21%)		
Previously married	28 (24%)		
Currently married	64 (55%)		
Employment status			
Unemployed (but looking for work)	8 (7%)		
Employed part time	2 (2%)		
Employed full time	18 (15%)		
Homemaker	1 (1%)		
Receiving disability	49 (42%)		
Retired	36 (31%)		
Student	1 (1%)		
Volunteer	2 (2%)		

Table 3
Clinical characteristics (n = 117).

Variables:	*f*(%)	Mean (*SD*)	Range
Co-morbidity		3.21 (1.93)	1–11
Diabetes mellitus	51 (44.3%)		
Renal insufficiency	34 (29.6%)		
Chronic obstructive pulmonary disease	33 (28.7%)		
Arthritis	25 (21.7%)		
Peripheral vascular disease	21 (18.4%)		
Cerebrovascular disease/hemiplegia	22 (17.4%)		
Recent myocardial infarction	7 (6.1%)		
Liver disease	5 (4.3%)		
Malignant tumor(s)	4 (3.6%)		
Leukemia/Lymphoma	2 (1.8%)		
Length of time with HF (years)		5.26 (5.27)	0.25–30
Etiology of HF			
Ischemic cardiomyopathy	56 (48.7%)		
Idiopathic/Non-ischemic 59	59 (51.3%)		
NYHA classification			
Class 2	46 (39.3%)		
Class 3	54 (46.2%)		
Class 4	15 (12.8%)		
Ejection Fraction (EF%)		0.25 (0.10)	0.05–0.35

influencing QOL, explaining 40% of the variance ($\beta = -0.603$; $F = 75.12$, $R^2 = 0.404$; $p < 0.0001$). See Table 7.

Discussion

The purpose of this study was to examine prevalent symptoms experienced by individuals with HF, identify those forming clusters, and evaluate their impact on QOL. Symptom clusters have not been extensively examined in the HF population; however, single symptoms and their relationships with other symptoms have been widely studied. In fact, a recent systematic review of 34 studies reported relationships between depression and fatigue, depression and anxiety, depression and sleep, depression and pain, anxiety and fatigue, and dyspnea and fatigue.[43] These findings support the presence of symptom clusters in the HF population.

Influencing factors. The mean age of participants was 56 years. Although the incidence of HF is higher in individuals over 65 as compared to other adult age groups,[44] many of our participants were younger individuals referred for advanced therapy. The majority had a markedly reduced EF and over half required an ICD. While the

Table 4
Symptom prevalence and descriptive statistics ($n = 117$).

Symptom	*f* (%)	Mean (*SD*)	Range
Shortness of breath/dyspnea	117 (100%)	9.23 (3.61)	1–15
Cognitive impairment	107 (91.2%)	14.12 (6.96)	6–36
Fatigue	86 (73%)	30.04 (17.59)	0–60
• Interfered with walking	55 (64%)		
• Interfered with normal work	54 (63%)		
• Interfered with general activity	47 (55%)		
Edema	84 (71.8%)	3.91 (3.63)	0–10
• Feet & ankles	56 (47.9%)		
• Up to the knees	19 (16.2%)		
• Above the knees	9 (10.7%)		
Pain	73 (62%)	8.08 (6.98)	0–20
• Moderate to severe	47 (78%)		
• Interfered with normal work	57 (63%)		
• Location:	30 (41%)		
lower extremities	27 (37%)		
chest	12 (16%)		
back	9 (12%)		
upper extremities	7 (10%)		
abdomen	73 (62%)		
Daytime sleepiness	63 (54%)	17.75 (7.29)	3–32
• Alert/energetic most days	41 (35%)		
• Sleepy during the day most days	79 (68%)		
• Struggling to stay awake most days	52(45%)		
Anxiety	≥ 11 = 37 (32.5%)	8.28 (4.64)	0–19
Depressive symptoms	≥ 11 = 25 (21%)	7.67 (4.27)	0–21
Appetite:		6.46 (2.74)	0–10
• No appetite	7 (6%)		
• Extremely good	17 (14.5%)		
Hunger		5.01 (2.66)	0–10
• No hunger sensations	16 (13.3%)		
• Extremely hungry	6 (5.1%)		
Factors influencing eating behavior:		1.59 (1.56)	0–4
• Diet restrictions		1.48 (1.51)	0–4
• Feeling full after eating small amount		1.38 (1.51)	0–4
• Being short of breath		1.33 (1.50)	0–4
• Not enough energy to prepare meals		1.27 (1.57)	0–4
• Lack of energy to shop		1.26 (1.40)	0–5
• Not feeling hungry		1.19 (1.41)	0–4
• Limited variety of foods in my diet		1.02 (1.50)	0–4
• Number of pills taken		0.94 (1.32)	0–4
• Feeling nauseated		0.91 (1.48)	0–4
• Limited money to buy food		0.88 (1.23)	0–4
• Feeling nervous		0.84 (1.26)	0–4
• Feeling sad		0.79 (1.21)	0–4
• Decreased sense of taste		0.74 (1.32)	0–4
• Family members eating different food than I do		0.72 (1.15)	0–4
• Feeling lonely		0.72 (1.09)	0–4
• Not enough energy to eat		0.57 (1.11)	0–4
• Eating alone		0.59 (1.21)	0–4
• Decreased sense of smell		0.57 (1.11)	0–4
• Lack of transportation to buy food		0.46 (1.15)	0–4

majority were NYHA Class 2 or 3, 13% ($n = 15$) were class 4. Patients who have NYHA Class 4 HF are symptomatic at rest and may be difficult to enroll in outpatient settings. In our participants, these patients were either listed for transplantation or were being evaluated for transplantation and/or mechanical circulatory support.

On average, participants experienced 3 co-morbidities. These co-morbidities may contribute to symptoms associated with HF; however, there are additional conditions that are not incorporated in the Charlson Comorbidity Index that need to be accounted for to best capture the associated burden. For example, atrial fibrillation and other arrhythmias,[45] sleep-disordered breathing, anemia, and obesity[46] may precipitate symptoms we examined.

Symptom clusters. The sickness behavior symptom cluster includes cognitive impairment, anxiety, depression, daytime sleepiness and fatigue. Cognitive impairment is an important concomitant of HF;

Table 5
Principle components analysis ($n = 117$).

Symptom:	Component 1 loadings (Sickness Behavior)	Component 2 loadings (GI Disturbance)	Component 3 loadings (Discomforts of Illness)
Shortness of breath	0.584	−0.269	**0.758**
Edema	0.234	0.067	**0.824**
Pain	0.512	−0.001	**0.737**
Anxiety	**0.832**	0.067	0.381
Depressive symptoms	**0.822**	−0.201	0.472
Daytime sleepiness	**0.741**	−0.079	−0.066
Cognitive function	**0.761**	0.043	0.312
Fatigue	**0.757**	−0.240	0.544
Appetite	−0.246	**0.829**	−0.066
Hunger	0.264	**0.819**	0.098
Eigenvalues:	4.309	1.082	1.494

Note: Bolded loadings indicate symptoms that loaded on the component.

however, it is unclear whether or not it is due to poor cardiac output or is a result of neurological or other co-existing conditions. Although structural brain changes, functional capacity, and biochemical parameters have all been associated with poor cognitive performance in HF patients, their contribution appears modest.[47] Regardless of the cause, cognitive impairment may influence performance of everyday activities that impact ability to manage a chronic illness.

The prevalence of anxiety and depression was low when compared to other symptoms; it was, however, consistent with rates reported in the HF population. Approximately 20–40% have depressive symptoms, and 15–20% suffer from a major depressive disorder.[48] A recent meta-analysis suggests that over 50% of HF patients have anxiety, and 13% meet criteria for an anxiety disorder.[49] These rates are higher than in the general population and highlight the high-risk status of HF patients for these disorders.

The sickness behavior cluster also includes symptoms identified by both Dantzler[50] and Kelly et al.[51] Dantzler suggests these symptoms represent a response to activation of the immune system or to non-immune stimuli. Fatigue, depression and changes in cognitive processes are features of the construct. Kelly and colleagues reported that hypersomnia, listlessness, and loss of interest in social activities are features of sickness behavior. The components of this cluster are also consistent with those identified by other investigators who have studied HF symptom clusters.[15,17] For example, Johansson et al. identified a cluster with depression, fatigue, non-restorative sleep and daytime sleepiness. Similarly, Smith and colleagues[17] described manifest vital exhaustion, cognitive affective depressive symptoms, and sleep difficulties as a cluster. Investigators have also identified some attributes of cognitive impairment in symptom clusters. For example, Hertzog and colleagues[6] observed that forgetfulness, fatigue, and difficulty sleeping were included in a cluster with shortness of breath, whereas Jurgens et al.[26] identified a cluster including depression and worry along with difficulty concentrating and remembering things. The cluster we identified incorporates several symptoms addressed in these studies.

Discomforts of illness was composed of dyspnea, peripheral edema, and pain. One symptom occurred in 100% of participants: dyspnea. Edema was reported by 72% and was most prevalent in the feet and ankles (48.7%). Co-morbidities such as arthritis and peripheral vascular disease could contribute to both edema and pain in the feet and ankles and was relatively prevalent in participants (21.7% and 18.4%, respectively). When co-morbidities were examined (e.g., diabetes mellitus, peripheral vascular disease, arthritis), we considered neuropathic, ischemic, or musculoskeletal etiologies. Although pain is not often associated with heart failure, a systematic review of nine descriptive studies found that 23–75% of patients reported pain.[52] As well, in the Pain in Heart Failure study,[53] the most common site of pain was below the knee; the strongest predictors of pain were

Table 6
Correlations among model variables ($n = 117$).

Variables	Age $r(p)$	Co-morbidity burden $r(p)$	Discomforts of Illness $r(p)$	GI Disturbances $r(p)$	Sickness Behavior $r(p)$	Quality of Life $r(p)$
Age		0.231 (0.01)	−0.007 (0.94)	−0.220 (0.02)	−0.206 (0.03)	0.273 (0.003)
Co-morbidity burden			0.302 (0.001)	0.095 (0.31)	0.230 (0.01)	−0.136 (0.15)
Discomforts of Illness				−0.019 (0.84)	0.662 (0.0001)	−0.482 (0.0001)
GI Disturbances					−0.053 (0.58)	−0.015 (0.87)
Sickness Behavior						−0.635 (0.0001)

Table 7
Factors influencing quality of life ($n = 117$).

Full Model:	Beta	Standard Error	p-value
• Age	0.164	0.224	0.056
• Co-morbidity	−0.009	1.429	0.908
• Discomforts of illness	−0.383	1.059	0.194
• GI Distress	0.164	1.280	0.891
• Sickness behavior	−0.646	0.230	<0.001
• Sickness behavior [a] Discomforts of illness	0.310	0.012	0.322
• Sickness behavior [a] GI distress	0.208	0.036	0.568
• Discomforts of illness [a] GI distress	−0.091	0.101	0.776
$F = 9.68$, $p < 0.0001$, $R^2 = 0.439$			
Trimmed model:			
• Age	0.145	0.197	0.055
• Sickness behavior	−0.603	0.098	<0.0001
$F = 75.12$, $p < 0.0001$, $R^2 = 0.404$			

[a] Denotes interaction term.

degenerative joint disease and other arthritis, dyspnea, and chest pain. These findings are consistent with our findings and the reported co-morbidities.

Factors influencing adequate nutrition in HF patients include social-emotional factors, illness-related factors, and appetite and hunger.[37] Gastrointestinal symptoms, such as decreased appetite and hunger, are prevalent and may contribute to under-nutrition and protein-calorie malnutrition. Few investigators have observed symptom clusters that include appetite or hunger. One such study, conducted by Song et al. ,[19] isolated a cluster that included lack of appetite, lack of energy and difficulty sleeping. In our study, GI disturbances were not highly prevalent (Table 4). The factor that had the most impact on eating behavior was diet restrictions. Several factors were similar to symptoms included in the other two symptom clusters (e.g., dyspnea, feeling nervous, feeling sad, feeling lonely, lack of energy). Since diet is a crucial component of effective HF management, the association of appetite and hunger with other symptoms in HF symptom clusters needs further investigation.

Consequences. QOL was negatively influenced by the sickness behavior symptom cluster, but was not influenced by discomforts of illness or GI disturbances. Since two of the three symptoms composing the discomforts of illness cluster are dyspnea and peripheral edema, this was unexpected. However, since HF patients expect to have these symptoms, they may have had less impact than unanticipated symptoms—such as those in the sickness behavior cluster.

Limitations

Our findings provide insight into symptom clusters in patients with HF; however, we recognize some limitations. The study was cross-sectional; therefore, we were unable to establish causality and examine stability of the clusters over time. The findings may not be generalizable because the sample was a convenience sample of patients followed at one institution. Although we examined 10 frequently reported symptoms, these symptoms may not be inclusive of symptom experiences of all HF patients. In addition, the sample was composed of symptomatic outpatients followed in a tertiary care setting and the symptom profile may not be representative of profiles observed in settings without capability to deliver advanced therapies. Data were obtained from self-reported symptom experiences; therefore, participants could have magnified or minimized their symptom experiences. By definition, however, symptoms reflect individual perceptions—which can only be recognized and confirmed by the individual.[54,55]

Implications

This study provides information about the relationship of three symptom clusters to QOL and adds to evidence validating the composition of HF symptom clusters. Based on our findings, symptom assessment and management are essential to improving QOL; however, symptoms usually associated with HF did not influence QOL. Therefore, clinicians need to expand symptom assessment to include symptoms included in the sickness behavior cluster, educate patients and family members about these unanticipated symptoms, and treat these symptoms to improve QOL.

Summary and conclusions

This study adds to the evidence on symptom science in HF through identification of clinically significant symptom clusters. The TUS is an adequate model to guide the study of HF symptom clusters. Three groups of HF symptoms that met the definition of a symptom cluster were identified. We were able to demonstrate that one symptom cluster influenced perceptions of QOL. Incorporating an evaluation of these symptoms may facilitate identification and treatment of symptoms having an additive and detrimental influence on QOL. It is early in the evaluation of clusters of HF symptoms and the stability of these symptom clusters across samples and over time has not been established. However, this study supports the existence of a cluster of HF symptoms similar to those symptoms associated with sickness behaviors as described by Dantzler[50] and Kelly et al. .[51] The identification of a cluster composed of symptoms associated with discomforts highlights the significance of illness discomforts such as pain, edema and dyspnea in patients living with HF. The relationship of appetite and hunger with other HF symptoms has received limited attention by investigators and provides an opportunity for future research.

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