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Correlates of Fatigue in Patients With Heart Failure

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Abstract

This study was conducted to determine the prevalence of fatigue and identify its demographic, clinical, and psychological correlates in 150 heart failure (HF) patients (73% men, 66% Caucasian, mean age 55 years, mean ejection fraction 26.7%±11%), from a single HF center, using the Profile of Mood States-Fatigue Subscale, the Minnesota Living With Heart Failure Questionnaire, and the Beck Depression Inventory. Sociodemographic and clinical data were obtained through self-report and chart abstraction. High levels of fatigue were reported in 50.4% of men and 51.2% of women. In a multivariate model, maximal workload, physical health, emotional health, and depression explained 51% of the variance in fatigue ($P<.001$). Fatigue in patients with HF is associated with both clinical and psychosocial variables, offering a number of targets for intervention. These findings suggest the need for multiple risk factor intervention strategies that improve physical and emotional health to decrease fatigue. Patients with depression warrant particular scrutiny.

Fatigue accompanies many illnesses and can be an incapacitating to work, activities of daily living, and social or family responsibilities.[1] Factors underlying fatigue have been examined extensively in patients with cancer[2] and multiple sclerosis,[3] and findings strongly support an association between fatigue, depression, and quality of life (QOL). Fatigue in these conditions is multifactorial and involves complex pathophysiologic and psychological processes that reflect both disease conditions. Interest in the impact of fatigue in cancer patients has led to the development of a treatment algorithm in which patients are evaluated regularly for fatigue, and treatment is targeted to their fatigue level.[2] In addition, treatment strategies including exercise programs, cooling, dietary changes, and energy conservation have also been developed to ameliorate fatigue in these patient populations.[2,3]

Fatigue is one of the 2 most common symptoms (along with dyspnea) reported by patients with heart failure (HF).[4–7] Also commonly referred to as activity intolerance, fatigue in patients with HF is defined as persistent tiredness and the perception of difficulty performing daily activities because of this persistent tiredness. Fatigue is often one of the first symptoms of HF and is commonly overlooked because it is viewed by both lay people and health care providers as a vague complaint. Indeed, as many as one-third of patients with HF view fatigue as an unimportant symptom and up to 50% report having difficulty recognizing it as a symptom of worsening HF.[8] The origins of fatigue in HF are unclear and are likely to be multifactorial.

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Probable pathophysiologic causes of fatigue in HF include low cardiac output and poor tissue perfusion, muscle metabolic abnormalities, autonomic nervous system abnormalities, deconditioning effects, and endothelial dysfunction.

Investigators have examined the relative contribution of psychological factors and physical symptoms to the variance in fatigue in older women with HF and demonstrated that fatigue was related more to physical symptoms than to psychological factors.[4] In another study, both men and women with HF were examined during hospitalization to assess relationships among physical symptoms, functional limitations, and depression.[5] Depression was strongly related to physical symptoms but not functional limitations. Ekman and Ehrenberg[9] explored sex differences in experiences of fatigue and found that there was an agreement in fatigue prevalence between men and women with HF, but the rating for fatigue severity differed by sex. When describing the character and intensity of fatigue, women described their fatigue as severe, whereas men described their fatigue as mild.[9] Despite earlier studies examining the nature of fatigue in patients with HF, this symptom continues to be poorly understood by clinicians and researchers. The purpose of the current investigation was to examine the prevalence of fatigue and identify its demographic, clinical, and psychological correlates in patients with systolic HF. Knowledge of the patterns and mechanisms of fatigue experienced by HF patients may provide information about the type and nature of interventions needed to cope with this distressing symptom and the challenges related to living with the chronic illness of HF.

STUDY DESIGN AND PATIENTS

A cross-sectional, correlational design was used. A convenience sample of 150 patients with HF was recruited from a single outpatient HF clinic located within a tertiary, university-affiliated medical center on the US West Coast. Patients were included in the study if they were aged 18 years or older; able to read, write, and speak English; had a left ventricular ejection fraction <40% documented by echocardiography or ventriculography; and had symptoms of HF for 6 months or longer.

Procedures

Institutional Review Board approval was received before study initiation. Patients who expressed an interest in participating in the study signed an informed consent during their routine clinic visit and received a battery of paper and pencil instruments to complete. Sociodemographic (ie, sex, age, race, income, education, marital status, and employment status) and clinical data (ie, etiology of HF, left ventricular ejection fraction, current medications, maximal oxygen uptake [peak VO_2], and maximal workload) were obtained from patient self-reports and verified through most current (within 3 months of study participation) diagnostic tests obtained during medical records abstraction.

Instruments

The questionnaires took 10 to 15 minutes to complete and included the following:

Profile of Mood States-Fatigue (POMS-F)—The POMS-F, used to measure fatigue, is a 7-item subscale obtained from the 65-item Profile of Mood States instrument that was developed to assess transient distinct mood states specific to fatigue-inertia.[10] Participants were asked to rate their feelings related to being “worn out,” “listless,” “fatigued,” “exhausted,” “sluggish,” “weary,” and “bushed” on a 0 (not at all) to 4 (extremely) scale. Summative scores range from 0 to 28, with a higher score denoting greater fatigue. The standardized POMS-F scores were established in a sample of adult patients (N=400) between the ages of 18 and 94 years with a mean age of 44±18.4 years. Sixty-four percent of the patients in the normative sample were married; 48% were men; and the average years of education was 14.3±2.7 years. The mean scores for men and women in the sample were 7.3±5.7 and 8.7±6.1, respectively.[11] These mean values were used in the current study to determine the presence of low (ie, below norm) and high (ie, above norm) levels of fatigue. The POMS Total Mood Disturbance score correlated highly (r=0.79) with a Visual Analog Composite score.[2] Reliability of the POMS-F was 0.91 in a sample of 428 cancer patients.[12] Internal consistency of the POMS-F was acceptable with a Cronbach's α of 0.88.

Quality of Life—Quality of life was measured using the Minnesota Living with Heart Failure Questionnaire (LHFQ), a 21-item disease-specific tool that asks participants to indicate the extent to which various symptoms they have experienced in the previous month have prevented them from living as they wanted to. The items can be combined to form an overall QOL score as well as scores for physical health (8 items) and emotional health (5 items). The physical subscale contains items associated with the fatigue and dyspnea of HF. The emotional subscale consists of items such as being worried or feeling depressed. The remaining 8 items include questions about other areas of life affected by HF and are used to compute the overall QOL score.[13] Response options are presented as 6-point ordinal scales ranging from 0 (no) to 5 (very much), with a total maximum score of 105 (40 for physical and 25 for emotional health); a lower LHFQ score indicates better QOL.

Beck Depression Inventory (BDI)—Depression was measured using the BDI, which is widely used in chronically ill populations and is well validated.[14] The BDI is a self-reported inventory designed to measure severity of depressive mood or symptoms. The 21-item inventory consists of a Likert-type scale from 0 (absence of symptom) to 3 (severe or persistent presence of the symptom). Five of the BDI items pertain to somatic symptoms of depression (eg, loss of appetite and sleep disturbance) and 16 of the items reflect nonsomatic symptoms of depression (eg, hopelessness and social withdrawal). Scores on the BDI range from 0 to 63. Patients with BDI scores 0 to 9 are considered as having minimal symptoms of depression, scores 10 to 16 mild, scores 17 to 29 moderate, and scores 30 to 63 as having severe symptoms of depression.[15]

Data Analyses

Data were analyzed using SPSS for Windows (version 11.0; SPSS, Inc, Chicago, IL).[5] Descriptive statistics were used to characterize the study population and analyze mean fatigue scores. Sex differences in fatigue scores were compared using the independent t test. Fatigue was dichotomized using validated cutoff points; a score >7.3 for men and >8.7 in women was indicative of moderate to high levels of fatigue.[11]

Univariate analyses were conducted to assess the impact of sociodemographic, clinical, and psychosocial factors on fatigue. Group comparisons of patients with low vs moderate to high fatigue levels were conducted using chi-square statistics or t test, depending on the level of measurement. Multivariate stepwise regression analyses were then used to identify which combination of variables provided the most predictive power for overall fatigue. Variables significant at an $\alpha < .10$ in the univariate analysis were included in the regression model.

To reflect the context variables, age and sex of patients were the first variables added to the model. Next, to depict the impact of clinical variables (peak VO_2, maximal workload, use of lipid-lowering medications [statins]) were added as a second set. Psychological factors including QOL, physical and emotional health, and depression were added last. Criteria for entry and removal of variables were based on the likelihood ratio test with enter and remove limits set at $P \leq .05$ and $P \leq .10$, respectively.

RESULTS

Mean age of the patients in the sample was 55.0±12.1 years (range, 20–72 years). No significant differences were found in the sociodemographic characteristics and most clinical characteristics between patients who reported low vs high levels of fatigue (Table I). Ejection fraction was similar in both groups; however, peak VO_2 and maximal workload were significantly lower in patients who reported high levels of fatigue compared with those reporting lower levels of fatigue. This finding validates the measure of fatigue used in this study.

Fatigue scores for men and women were higher than the category scores for moderate-severe fatigue in a healthy adult population; men scored 9.5 (SD±7.5) and women scored 10.4 (SD ±7.0). These scores reflect high levels of fatigue reported in 55 (50.4%) men and 21 (51.2%) women. The QOL, physical and emotional health, and depression scores are listed in Table II. No differences were found between men and women in the variables studied. Depression was detected in >28% of the sample by the BDI questionnaire; 29 (19%) had mild depressive symptoms and 14 (9%) had moderate to severe depressive symptoms.

In a univariate analysis, age and sex were not correlated with fatigue; however, a strong correlation existed between fatigue, total QOL, physical and emotional health, and depression (Table III). Clinical and physiological variables associated with higher levels of fatigue were use of statins, lower peak VO_2, and lower maximal workload. Cardiac factors including HF etiology, New York Heart Association (NYHA) functional class, and left ventricular ejection fraction were not related to fatigue.

In a multiple regression model, lower maximal workload, physical and emotional health scores, and depression were found to be independent predictors of fatigue (Table IV). These 4 predictors accounted for 51% of variance in the fatigue scores of patients. There was evidence of a linear fit for each variable in the final model. Post hoc analysis, done to test for multicollinearity among variables, demonstrated that each of the predictors had unique effects on fatigue.

DISCUSSION

Despite the pervasiveness of fatigue in patients with HF, little research has concentrated on this phenomenon. Given the importance of symptom status to patients and the value of symptom status as an indicator of the effectiveness of clinical therapies to clinicians, it is vital that research efforts are directed toward understanding fatigue. The current study is novel in that we used a multivariate model to determine correlates of fatigue and demonstrated the multifactorial nature of fatigue in this population. Both clinical and psychological variables were important correlates of fatigue: maximal workload, physical and emotional health scores, and depression were independent correlates of fatigue. In addition, we found that approximately one-half the the study participants experienced fatigue when compared with a healthy adult population utilizing the same measure.[11] Similar prevalence was also reported in a cohort of older women with HF in the United States[4] and in an elderly cohort of men and women with HF in Sweden.[16,17]

Lower peak VO_2 and maximal workload both correlated with higher fatigue; however, only lower maximal workload was found to independently predict higher fatigue in this sample. Peak VO_2 is traditionally used for risk stratification in HF; the impact it has on mortality is well supported in the literature.[18] Peak VO_2 has also been used to predict limitations (VO_2 ≤14 mL/kg/min) in daily activities as a result of poor exercise tolerance.[19] Intuitively, patients with high levels of fatigue are less tolerant to increasing maximum workloads and experience decreased levels of peak VO_2. Although the mechanisms for these physiological responses are not well understood, our findings indicate that HF patients with lower maximal workload thresholds and peak VO_2 indices are at high risk for fatigue.

Higher fatigue correlated with poorer physical health. Our findings are consistent with previous study results that showed an association between fatigue and restrictions in physical activity and limitations in self-care.[7,16,17] Additionally, fatigue in older women with HF was related more to other concurrent physical symptoms than to psychological factors.[4] Investigators examined plausible explanations that link fatigue with higher functional limitations and identified impaired peripheral circulatory perfusion with reduced oxygen delivery and impaired muscle strength as potential confounders.[20] Fatigue and physical health warrant further investigation including what comes first, fatigue or physical health limitations. Our findings support the need to assess for ongoing physical symptoms (ie, dyspnea, edema) that may increase susceptibility to increased fatigue. At the current time, the best method of assessing for fatigue may be the most direct and simple, ie, asking patients about the presence of the symptom and helping patients to identify fatigue by specific questioning directed at uncovering fatigue in the context of daily activities. Patients who report a chronic physical symptom pattern should be screened for concomitant fatigue that may merit intervention. Finally, the need to consider interventions that focus on physical symptoms as a first step to managing fatigue in HF patients is vital.

Specific interventions to combat fatigue have not yet been tested in patients with HF, but data to date on the impact of exercise suggest that fatigue may be managed best by assisting patients to increase their activity levels. Given the relationship between depression and fatigue found in this and other studies, interventions to treat depression will likely have a beneficial impact on fatigue also. Exercise has a positive influence on depression. Assisting patients to increase their activity levels, which has been shown to be safe in the management of HF, can be recommended for the management of fatigue in patients with HF. It is also appropriate to teach HF patients energy conservation techniques for the management of fatigue, so their activity efforts are efficient and not exhausting.

The study supports previous reports that poor QOL and emotional health are common in patients with HF and that higher fatigue was related to poorer QOL.[17] Women who scored high on fatigue also scored high on stress related to illness and were less satisfied with life.[4] Our findings were similar and also showed that more than a fourth of the participants reported depressive symptoms, which is higher than depression rates reported among patients hospitalized with HF.[5] Both studies, however, consistently showed that higher depressive symptoms were associated with higher fatigue. The relationship between fatigue and depression has also been reported in women with breast cancer. Women reporting high levels of fatigue also reported greater symptom distress, lower activity, and poorer physical and social health status.[2] Hence, treatment strategies that help patients manage symptoms, relax, and obtain adequate sleep, especially patients experiencing greater emotional distress and depressive symptoms, may modify fatigue. Complementary therapies (eg, yoga, meditation, massage) and self-care strategies that promote sleep and exercise may also help patients cope with the emotional impact of fatigue.[5]

It may seem counterintuitive that we failed to find an association between fatigue and NYHA functional class or ejection fraction. However, given the nature of measurement of fatigue and the aspects of HF pathophysiology captured by NYHA functional class or ejection fraction, these findings are not unexpected. Given its subjective nature, fatigue is difficult to measure with precision. The NYHA classification also suffers from lack of precision in its measurement; at each of the 3 indicators at which symptoms are present (ie, classes II, III, and IV), the assessment seeks only whether any symptom is present, not specifically whether fatigue is present. Ejection fraction is likely not associated with fatigue because all patients with HF, regardless of ejection fraction, are expected to have symptoms such as fatigue, and symptom status has never correlated well with ejection fraction. This lack of correlation is one reason HF guidelines do not recommend using ejection fraction to reflect effectiveness of drug therapy, but they do recommend that symptom improvement be a major indicator.

Of interest, fatigue in HF was associated with the use of statins, which has been shown to increase the risk of myopathy, resulting in symptoms of fatigue, weakness, and pain. Although statin-related side effects were originally identified as affecting only 1% to 5% of patients,[21] some investigators have indicated that these effects may be common and often go unreported.[22] The risk of these adverse effects with statin use can be exacerbated by several factors, including compromised hepatic and renal function, hypothyroidism, diabetes, and use of concomitant medications, but the mechanisms causing statin-induced myopathy have not been elucidated and warrant further study.[23] Our finding, however, that statin use was not independently associated with fatigue suggests that discontinuation of statins to treat fatigue in patients with HF may not be warranted.

Some limitations must be considered when interpreting the results from our study. First, causation cannot be inferred; thus, we cannot say that low QOL, poor physical and emotional health, or depression leads to high levels of fatigue, nor can we comment on the direction of the hypothesized causality. The experience of severe fatigue may lead to low QOL, poor physical and emotional health, or depression. Our findings merely support the association between fatigue and several clinical and psychosocial variables. Next, the sample that was used for the study was fairly homogeneous; patients were all being seen at a single transplant referral center and their mean age was lower than the typical mean age for HF in the general community, thus limiting our ability to generalize to all patients with HF. Finally, the use of a convenience sample from a single center limits the utility of any estimate of prevalence of fatigue and could also introduce a bias in the ascertainment of correlates of fatigue.

CONCLUSIONS

Our data demonstrate that fatigue levels were moderately intense and highly prevalent in our sample of patients with systolic HF. We found that fatigue has predictable clinical dimensions and psychosocial correlates and is an important symptom to consider. Fatigue may influence patients' adherence to the medical regimen, their social relationships, and general QOL. Early identification of fatigue could facilitate the initiation of interventions to reduce the cost of associated health care.

Evaluation and treatment of fatigue in HF patients requires a multidisciplinary approach because the fatigue has many possible etiologies and several contributing factors. A comprehensive approach is required, especially for patients with moderate to severe fatigue, so that all possible contributing factors can be determined and an appropriate treatment plan created. The short- and long-term effects of various treatment strategies on the fatigue in HF patients should be assessed in future studies.

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Table I

Demographic and clinical characteristics of HF patients with low or high fatigue levels

	Total N= 150	Low Fatigue N= 74	High Fatigue N= 76
Age, y	55.0±12.1	56.8± 2.2	54.7±13.0
Years with HF	5.9±6.1	5.8±5.0	6.2±7.1
Ejection fraction, %	26.7±11.5	26.1±11.7	27.3±11.6
Maximal oxygen uptake (peak VO_2), ml/kg/min	15.8±5.3	16.4±5.3	13.2±4.3[a]
Maximal workload, watts	96±53	102±52	72±46[b]
Men, %	72.7	73.0	72.4
Race, %			
White	65.6	62.5	68.8
Black	26.9	28.8	25.0
Asians	7.5	8.7	6.2
Married, %	65.6	68.8	62.5
Education, %			
Some high school	12.5	12.5	12.5
High school graduate	21.9	25.0	18.8
Some college	37.5	25.0	50.0
College graduate	28.1	37.5	18.7
Not employed, %	78.0	72.0	75.0
Heart failure etiology, %			
Idiopathic	57.5	58.8	56.3
Ischemic	42.5	41.2	43.7
NYHA class, %			
II	44.8	46.3	43.3
III	42.7	41.2	44.2
IV	12.5	12.5	12.5
Medications, %			
ACE inhibitors	78.7	75.7	78.9
β-Blockers	73.3	68.9	68.4
Diuretics	96.0	93.2	93.4
Digoxin	57.3	58.1	48.7
Statins	64.0	63.5	68.4[a]

Abbreviations: ACE, angiotensin-converting enzyme; HF, heart failure; NYHA, New York Heart Association. Values are expressed as mean±SD, unless otherwise indicated.

[a] $p<.05$.

[b] $p<.001$.

Table II

Quality of Life, Physical and Emotional Health, and Depression Scores (N=150)

Characteristic	Mean	SD	Range[a]
Quality of life-total, sum score	42.2	26.7	0–100
Quality of life-physical health, sum score	18.0	12.0	0–40
Quality of life-emotional health, sum score	8.4	7.1	0–25
Depression, sum score	9.9	8.2	0–50

[a]These values reflect the actual range of scores for the sample.

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Table III

Correlational Matrix for the Key Variables (N=150)

	1	2	3	4	5	6	7	8	9
1. Fatigue									
2. Age	−.067								
3. EF%	.095	.032							
4. Peak VO_2	−.227[a]	−.116	−.155						
5. Maximal workload	−.354[b]	−.178	.103	.203[a]					
6. Use of statins	.204[a]	−.230[b]	.010	.100	−.065				
7. QOL (total)	.596[b]	−.071	−.056	−.177[a]	−.318[b]	.182[a]			
8. Physical health	.595[b]	.002	−.039	−.167[a]	−.419[b]	.077	.945[b]		
9. Emotional health	.627[b]	−.069	−.056	−.172[a]	−.402[b]	.134	.807[b]	.638[b]	
10. Depression	.576[b]	−.166[a]	−.042	−.226[a]	−.249[b]	.239[b]	.511[b]	.367[b]	.684[b]

Abbreviations: EF, ejection fraction; QOL, quality of life.

[a] $p<.05$.

[b] $p<.001$.

Table IV

Predictors of Fatigue (N=150)

Variable	**Adjusted r^2**	**F**	***P* Value**
Maximal workload, watts	.114	14.66	<.0001
Emotional health	.415	38.53	<.0001
Physical health	.466	31.8	<.0001
Depression	.506	28.13	<.0001