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Symptoms of fatigue in chronic heart failure patients: Clinical and psychological predictors ☆

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Abstract

Objective: To examine the role of clinical and psychological characteristics as predictors of fatigue in CHF.
Background: Little is known about predictors of fatigue in CHF. Next to heart failure characteristics, depressive symptoms and type-D personality may explain individual differences in fatigue.
Methods: At baseline, 136 CHF outpatients (age ≤ 80 years) completed a questionnaire to assess depressive symptoms, type-D personality and cardiac symptoms. At one-year follow-up, they completed the Dutch Exertion Fatigue Scale and the Fatigue Assessment Scale to assess symptoms of fatigue. Medical information was obtained from the patients' medical records.
Results: Exertion fatigue and general fatigue were identified as different manifestations of fatigue. We found that exertion fatigue at 12-month follow-up was predicted by decreased exercise capacity ($\beta = -.35$; $p < .001$), dyspnoea ($\beta = 24$; $p = .002$), hypertension ($\beta = .16$; $p = .03$), and depressive symptoms ($\beta = .16$; $p = .05$). In contrast, general fatigue at 12-month follow-up was predicted by dyspnoea ($\beta = .24$; $p = .003$), depressive symptoms ($\beta = .27$; $p < .001$), type-D personality ($\beta = 17$; $p = .03$), and sleep problems ($\beta = .20$; $p = .01$). Together, these variables explained 32% and 37% of the variance, respectively.
Conclusion: The present study showed that fatigue was related to both clinical and psychological characteristics. The use of this knowledge may lead to a better understanding and treatment of the clinical manifestations of fatigue in CHF.

Keywords: Symptoms of fatigue; Chronic heart failure; Type-D personality; Depressive symptoms

1. Introduction

Chronic heart failure (CHF) is accompanied by severe symptoms and poor prognosis. Recent studies have underlined the importance of symptoms in CHF, both in terms of prognosis [1,2] and quality of life [3]. One poorly understood symptom of CHF is fatigue.

Fatigue is often rated as one of the most disabling symptoms in chronic heart failure [4], however, little is known about its predictors [1,5,6]. One small study in women with CHF found that only symptoms of dyspnoea predicted fatigue [6]. Clearly, more studies are needed to give a more in-depth insight into the variables that predict fatigue. In addition, previous research has shown that different forms of fatigue are relevant to CHF patients; these are exercise-related symptoms of fatigue, and general feelings of fatigue which are not necessarily related to exercise [7]. Accordingly, it is necessary to examine the dimensionality of fatigue before relating it to other variables.

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Haemodynamically, symptoms of fatigue during exercise are thought to arise from failure of muscle perfusion due to an inadequate rise in cardiac output. However, many studies have shown that there is no relation between cardiac performance and exercise performance [8,9]. Recently, it has been suggested that chronic, low grade haemodynamic stress as seen in CHF, may lead to dominance of catabolic processes. This in turn leads to skeletal myopathy, causing the sensation of fatigue [10]. Future studies should aim to demonstrate to what extent skeletal myopathy is able to explain individual differences in fatigue.

Besides physiological explanations for symptoms of fatigue in CHF, psychological factors should also be taken into account. Depressive symptoms have previously been associated with fatigue in CHF [11,12]. However, the role of personality as a predictor of fatigue in CHF has received little attention up to now. A study in patients with ischaemic heart disease revealed that patients with a type-D personality, a joint tendency toward negative affectivity and social inhibition, were more likely to report symptoms of fatigue and exhaustion [13]. Comparable results were found in a related set of personality variables in patients with multiple sclerosis [14]. Therefore, it seems important to examine the role of personality as a predictor of fatigue in CHF patients as well.

The aim of the present prospective study was (1) to examine the nature of fatigue, and (2) to examine the role of clinical and psychological characteristics as predictors of fatigue in CHF.

2. Methods

2.1. Participants

The sample included 136 CHF patients visiting the heart failure outpatient clinic of the Twee Steden Ziekenhuis, Tilburg, the Netherlands. As displayed in Table 1, the majority of subjects were male, married, unemployed, non-smokers, and not academically educated. About half the sample was classified as NYHA-class III/IV, had a cardiac history, and ischaemic CHF. Only a minority of the sample was overweight and anaemic. Co-morbidities that were most common included hypertension, diabetes mellitus, and peripheral artery disease. Diuretics, ACE-inhibitors, and beta-blockers were the most prescribed medications.

Inclusion criteria were defined as systolic heart failure, LVEF ≤40%, and sufficient understanding of spoken and written Dutch language. Exclusion criteria were defined as diastolic heart failure, age ≤80 years, myocardial infarction in the month prior to inclusion, other life-threatening diseases, clinical signs of an acute infection, use of anti-inflammatory medication.

Patients filled out questionnaires with regard to personality, dyspnoea, and depressive symptoms at baseline, and fatigue at 12-month follow-up. All patients participated voluntarily and signed informed consent. The study protocol was approved by the medical ethics committee of the St. Elisabeth Hospital, Tilburg, the Netherlands.

2.2. Measures

2.2.1. Symptoms of fatigue

Previous research has shown that general fatigue does not necessarily have a relationship with exertion [7]. Therefore, separate measures were used to assess exertion fatigue and general fatigue, respectively. Exertion fatigue may be defined as fatigue directly related to the performing of activities in daily living [7], whereas general fatigue has been defined as an overwhelming, sustained sense of exhaustion and decreased capacity for physical and mental work [15].

The Dutch Exertion Fatigue Scale (DEFS) assesses exertion fatigue by means of 9 items [10]. Items are answered with five response alternatives ranging from 0 (no) to 4 (yes). Chronbach's alpha is high (α=91). The Fatigue Assessment Scale (FAS) was used to assess symptoms of general fatigue [16]. This questionnaire consists of 10 items, which are answered on a 5-point Likert scale, ranging from 1 (never) to 5 (always). The reliability of this instrument is high (α=.90).

2.2.2. Dyspnoea, chest pain, and sleep problems

Cardiac symptoms were measured by means of the 12-item Somatic complaints subscale of the Health Complaints Scale (HCS) [17]. Items are answered on a 5-point Likert scale, ranging from 0 (not at all) to 4 (extremely). The items measuring chest pain, shortness of breath, and sleep problems

Table 1
Baseline characteristics (n=136)

Age: Mean (S.D.)	65.6 (8.5)
Male	104 (76.5%)
Having a partner	106 (77.9%)
No academic education	117 (86.0%)
Unemployed	113 (83.1%)
NYHA-class III/IV	73 (53.7%)
LVEF: Mean(S.D.)	30.0% (6.9)
Ischaemic aetiology	72 (52.9%)
Cardiac history*	76 (55.9%)
Non-smokers	102 (75.0%)
Co-morbidities	
Stroke	13 (9.6%)
COPD	13 (9.6%)
Renal insufficiency	17 (12.5%)
Liver disease	6 (4.4%)
Diabetes mellitus	34 (25%)
Hypertension	49 (36.0%)
Peripheral arterial disease	21 (15.4%)
Medication	
ACE-inhibitor	108 (79.4%)
All-antagonist	22 (16.2%)
Diuretics	109 (80.1%)
Spironolactone	29 (21.3%)
Digoxin	43 (31.6%)
Beta blocker	91 (66.9%)
Statins	67 (49.3)
Aspirin	63 (46.3%)
Anaemia (Hb≤120 g/L)	27 (19.9%)
BMI: Mean (S.D.)	28.3 (4.9)

BMI: body mass index; LVEF: left ventricular ejection fraction.
*MI, angina, PCI, or CABG.

were used as separate subscales. The items measuring fatigue were excluded.

2.2.3. Symptoms of depression

Symptoms of depression were measured by means of the Beck Depression Inventory (BDI) [18]. Each item is rated on a 0–3 scale. The BDI is a reliable and well-validated measure of depressive symptomatology [19,20], and is the most widely used self-report measure of depression. Since the somatic items of the BDI may be confounded by symptoms of fatigue, only the cognitive–affective subscale was used [21]. Because of non-normality, the subscale was dichotomized at the highest tertile.

2.2.4. Type-D personality

Type-D personality was measured by means of the DS14 [22]. This 14-item questionnaire comprises two subscales, Negative Affectivity and Social Inhibition, each consisting of 7 items. The items are answered on a 5-point Likert scale, ranging from 0 (false) to 4 (true). Negative affectivity refers to the tendency to experience negative emotions across time/situations, whereas social inhibition refers to the tendency to inhibit the expression of emotions/behaviours in social interactions to avoid disapproval by others. Previous studies in coronary patients have shown that type-Ds are at risk for a wide range of adverse health outcomes, including mortality [23], morbidity [24], and mood status [25].

A standardized cut-off score of ≥10 on both subscales classifies subjects as a type-D personality [22]. Initially, this cut-off corresponded to a median split of both subscales which resulted in a prevalence rate between 27% and 31% of type-Ds among patients with coronary heart disease. In the present study, the prevalence rate of type-D was 26%, which is in accordance with the rates mentioned above. Both scales have good internal validity (α=.88 for Negative Affectivity and α=.86 for Social Inhibition).

In a sample of coronary patients who underwent cardiac rehabilitation, both Negative Affectivity and Social Inhibition were relatively stable over a 3-month period (test–retest r=.82 for Negative Affectivity and r=.72 for Social Inhibition), and DS14 mean scores did not change significantly over time. In contrast, measures of mood and health status did show significant changes over this 3-month period [22], suggesting that a patients' score on the DS14 is relatively independent from changes in mood and health status.

Additionally, it has been shown that type-D is different from established personality constructs like neuroticism and extraversion, even though they are related. Negative affectivity only shared 46% of its variance with neuroticism, and social inhibition only shared 35% of its variance with extraversion [22]. Although more research on its situational stability is needed, the findings support the validity of type-D as a personality construct.

2.2.5. Demographics and clinical variables

Demographics included sex, age, educational level, marital status, and employment status. Medical variables, obtained from patients' medical record included Left Ventricular Ejection Fraction (LVEF), functional class (NYHA-classification), aetiology of heart failure, co-morbidities, cardiac history, and prescribed medications. Exercise capacity was measured by means of the six-minute walking test (walking small circuits of 52 meters), which was carried out within the hospital as part of this study. Patients were instructed to walk at a normal pace, and to continue walking until they were told to stop or until they experienced

Table 2
Dimensions of fatigue at 12-month follow-up

Item	Content	F1	F2	F3
DEFS 9	It is fatiguing for me to go to a birthday party	.89		
DEFS 7	It is fatiguing for me to hoover	.89		
DEFS 8	It is fatiguing for me to visit someone	.85		
DEFS 6	It is fatiguing for me to clean up my household waste	.81		
DEFS 5	It is fatiguing for me to shop	.72		
DEFS 3	It is fatiguing for me to take a shower standing	.65		
DEFS 1	It is fatiguing for me to walk 10 min	.60		
DEFS 2*	It is fatiguing for me to walk 30 min	.50	−.35	
DEFS 4*	It is fatiguing for me to go up- and downstairs	.46	−.35	
FAS 6	I have problems starting things		−.83	
FAS 5	Physically, I feel exhausted		−.80	
FAS 8	I feel no desire to do anything		−.79	
FAS 3	I don't do much during the day		−.73	
FAS 1	I am bothered by fatigue	.30	−.67	
FAS 9	Mentally, I feel exhausted		−.66	−.46
FAS 2	I get tired very quickly	.33	−.62	
FAS 4*	I have enough energy for everyday life		−.33	
FAS 10*	When I am doing something, I can concentrate quite well			.83
FAS 7*	I have problems thinking clearly		−.54	−.56

DEFS: Dutch Exertion Fatigue Scale; FAS: Fatigue Assessment Scale.
*Excluded from further analyses.

Table 3
Univariate correlates of 12-month fatigue

Factor	12-month follow-up	
	r	*p*
Exertion fatigue		
Female sex	.23	.007
Low educational level	.24	.006
Unemployment	.23	.006
Exercise capacity	−.44	<.001
NHYA class III/IV	.30	<.001
Cardiac history	.17	.04
Stroke	.21	.013
Hypertension	.23	.008
Beta blocker	−.18	.04
Sleep problems	.29	.001
Dyspnoea	.33	<.001
Cardiac pain	.42	<.001
Depressive symptoms	.33	<.001
Type-D	.20	.02
General fatigue		
Exercise capacity	−.24	.005
NHYA class III/IV	.26	.002
COPD	.20	.02
Hypertension	.17	.05
Sleep problems	.42	<.001
Dyspnoea	.45	<.001
Cardiac pain	.44	<.001
Depressive symptoms	.42	<.001
Type-D	.36	<.001

too many adverse symptoms. Patients were not encouraged to walk as far as possible because the test was meant to reflect daily life exercise capacity.

2.3. Statistical analyses

Principal component analysis (PCA) with oblimin rotation was used to determine whether general fatigue and exertion fatigue could be distinguished from each other. Factors with an eigenvalue > 1 were retained according to Kaiser's criterion. KMO and Bartlett's test of sphericity were used as fit indices.

Prior to further statistical analyses, educational level, marital status, employment status, NYHA-class, aetiology of heart failure, co-morbidities, haemoglobin levels, and cardiac history were recoded into dichotomous variables. Associations with fatigue at 12-month follow-up were examined with Pearson's product moment correlation coefficients for continuous variables, and with point-biserial correlations for discrete variables. Factors that were significantly associated with fatigue at 12-month follow-up were entered into a stepwise regression procedure. Regression analyses were performed for each dimension of fatigue. In order to examine the generalizability of the models obtained by the stepwise procedure, the population cross-validation coefficient R_c^2 was computed using Steins formula [26]. It has been shown that the R_c^2 is a far more accurate correction for shrinkage than the adjusted R^2. In addition, R_c^2 is also preferred over empirical cross-validation [27,28].

3. Results

3.1. Nature of fatigue

Principal component analysis on the two fatigue scales at 12-month follow-up revealed a 3-factor solution (Table 2). KMO (0.89) and Bartlett's test of sphericity ($\chi^2(171, N=136)=1580.2$, $p<.001$) indicated that PCA was adequate for this data. Two specific components were found, i.e. exertion fatigue and general fatigue. The nonspecific third factor was excluded from further analysis. Items with component loadings >.40 and Δcross-loadings <.20 were used to construct subscales. Accordingly, 7-item subscales of exertion fatigue (α=.89) and general fatigue (α=.90) were formed, respectively. Exertion fatigue and general fatigue were moderately correlated ($r=.55$; $p<.001$).

3.2. Predictors of fatigue

Significant univariate correlates of exertion fatigue and general fatigue at 12-month follow-up are displayed in Table 3. Variables with a bivariate correlation ≥.30 with respect to exertion fatigue were exercise capacity, NYHA-class, dyspnoea, cardiac pain, and depressive symptoms. A correlation ≥.30 with general fatigue was found for sleep problems, dyspnoea, cardiac pain, depressive symptoms, and type-D personality.

Stepwise regression analysis revealed that exertion fatigue at 12-month follow-up was best predicted by exercise capacity, dyspnoea, hypertension, and depressive symptoms. Together, these four variables explained 32% of the variance in exertion fatigue. General fatigue at 12-month follow-up was best predicted by dyspnoea, depressive symptoms, type-D personality, and sleep problems. Together, these four variables explained 37% of the variance in general fatigue (see also Table 4).

Table 4
Determinants of 12-month fatigue in stepwise regression analyses

Factor	β	*t*-value	*p*-value
Exertion fatigue			
Exercise capacity	−.35	−4.62	<.001
Hypertension	.16	2.19	.03
Dyspnoea	.24	3.16	.002
Depressive symptoms	.16	2.01	.05
Full model information: $R^2=.32$; $F(4,131)=15.18$; $p<.001$			
General fatigue			
Sleep problems	.20	2.54	.01
Dyspnoea	.24	3.00	.003
Depressive symptoms	.27	3.67	<.001
Type-D	.17	2.23	.03
Full model information: $R^2=.37$; $F(4,131)=19.22$; $p<.001$			

As displayed in Table 5, the amount of shrinkage was relatively small. This indicates that if the prediction equations were applied to other samples of chronic heart failure patients, then on average the same proportion of variance accounted for would be found. That is, the identified predictors of fatigue are likely to be valid in CHF patients.

4. Discussion

Fatigue is one of the most prevalent and aggravating symptoms in CHF, and patients often rate fatigue as one of the most burdening consequences of CHF [4]. However, little is known about factors that explain individual differences in symptoms of fatigue [1,5,6]. Therefore, the primary aim of this prospective study was to identify predictors of fatigue in chronic heart failure patients. Exertion fatigue and general fatigue were identified as different manifestations of fatigue. We found that exertion fatigue at 12-month follow-up was predicted by decreased exercise capacity, dyspnoea, hypertension, and depressive symptoms. In contrast, general fatigue at 12-month follow-up was predicted by dyspnoea, depressive symptoms, type-D personality, and sleep problems. The finding that exertion fatigue and general fatigue were not predicted by the same variables underlined that they represented different dimensions of fatigue.

In accordance with the study of Friedman and King [6], feelings of fatigue were often accompanied by symptoms of dyspnoea. This was in line with expectations since dyspnoea and fatigue are core symptoms of CHF [29]. Depressive symptoms were also associated with symptoms of fatigue, which has previously been reported in studies of CHF [11,12], coronary [30], and stroke patients [31]. Apart from dyspnoea and depressive symptoms, exercise capacity and hypertension were important predictors of exertion fatigue. A intervention study by Mayou et al. [32] also found an association between fatigue and exercise capacity. Moreover, they found that increased exercise capacity after the intervention was associated with decreased fatigue. From previous studies, it is known that hypertension is often accompanied by fatigue, especially in combination with certain kinds of medication [33,34].

Next to dyspnoea and depressive symptoms, sleep problems and type-D personality emerged as predictors of general fatigue. Sleep problems and fatigue were found to be associated in previous studies in CHF [35] and cancer [36]. The effect of type-D on general fatigue might be explained by chronic exposure to distress. Over time, the chronic nature of type-D may elicit a discrepancy between resources and demands, which in turn may lead to greater feelings of general fatigue as compared to non-type-Ds. Moreover, the association is in line with studies in coronary artery disease [13] and multiple sclerosis [14]. The study by Friedman and King [6] did not find a relationship between fatigue and personality in CHF. However, they examined the effect of optimism and pessimism, instead of type-D personality. Although optimism/pessimism has been linked to negative affectivity [37], type-D personality does not only comprise negative affectivity, but also social inhibition. This different finding could also be explained by the fact that the present study used different questionnaires to assess fatigue, and by the fact that the sample characteristics were not similar. Their subjects were more likely to be female, to be older, to be unmarried, and to have a better left ventricular ejection fraction as compared to our sample.

To our knowledge, this was the first study in *chronic* heart failure patients that tried to identify predictors of both exertion and general fatigue. Exertion fatigue was primarily predicted by physical characteristics, whereas general fatigue was predicted by both physical and psychological characteristics. This distinction might be important with respect to future interventions aimed at the reduction of fatigue in CHF patients. After all, it is unclear if and to what extent interventions should focus on either physical symptoms, psychological symptoms, or both. Future studies should also aim to reduce the effect of personality on general fatigue. Although changing personality characteristics is very difficult, previous research has shown that type-Ds benefit from behavioural interventions in terms of mood and health status [22]. Hence, targets of counselling could be improvement of self-management abilities, consolidation of the social network, and improving coping abilities. The results of this study are important, because use of this knowledge by doctors and nurses may lead to a better understanding of the clinical manifestations of fatigue in CHF, which in turn may lead to a more effective treatment.

This study had a number of limitations. First, there may have been a bias in the selection of patients. The cardiologist or heart failure nurses asked patients to participate in the study, and this interaction pattern might have influenced selection. Secondly, some variables were assessed by means of self-report. In summary, the present study showed that fatigue was predicted by both clinical and psychological characteristics. Exertion fatigue at the 12-month follow-up was predicted by dyspnoea, exercise capacity, hypertension, and depressive symptoms, whereas general fatigue was predicted by dyspnoea, depressive symptoms, type-D personality, and sleep problems.

Although the present study revealed a number of predictors of fatigue in CHF, a large portion of variance remained unexplained. Therefore, future studies should focus on identifying these predictors. We suggest that more physiological measures, which are known to be abnormal in CHF patients and which are relevant with respect to symptoms of fatigue, for example measures of abnormal muscle metabolism

Table 5
Cross-validity of regression models

Dependent variable	R^2	R_c^2	Shrinkage (%)
Exertion fatigue at follow-up	.32	.27	14.9
General fatigue at follow-up	.37	.33	11.9

and enhanced ergo reflex response, should be used [10]. Furthermore, future studies should examine the specific role of exertion fatigue and general fatigue as predictors of poor prognosis in CHF. Since some studies have already identified the importance of fatigue in terms of CHF prognosis [1,2], it is also necessary to identify potential mechanisms through which fatigue exerts its toxic effect. In this regard, it would be interesting to investigate whether fatigue is related to poor self-management. After all, it is well documented that poor self-management is associated with adverse clinical outcome [38].

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