

# **Fatigue in patients with chronic heart failure**

**Patient experiences and consequences  
of fatigue in daily life**

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*To my family with love*



## ABSTRACT

Although fatigue is a prevalent and distressing symptom in patients with chronic heart failure (CHF), it is an underestimated problem in the care of patients, and consequently, insufficiently investigated. The primary aim of this thesis was, therefore, to advance the knowledge from the patients' perspective by describing characteristics of the fatigue experience and its consequences in daily life in patients with CHF. A secondary aim was to investigate the relationships between fatigue and selected physiological and psychological factors associated with fatigue. Both quantitative and qualitative methods have been used and three samples of patients have been interviewed on different occasions. In two of the quantitative studies 93 patients, and in another study 112 patients, consecutively included, were interviewed at the hospital. Fifteen patients were included in the qualitative study. These 15 participants were enrolled when they visited an outpatient clinic and most of them were interviewed in their homes. These interviews were supplemented with the content of an Internet discussion with persons living with CHF.

The results of the studies indicated that fatigue embraces the individual's body, emotions and cognitive abilities, forcing the person to physical restrictions that, in turn, perpetuate emotional discomfort. However, the physical sensation of fatigue followed by functional limitations seemed to be the most prevalent and distressing experience in patients with CHF. The patients described fatigue as lacking strength, which was associated in connection with physical efforts and lacking energy, viewed as an annoying sensation after both mental and physical strain. Another dimension of fatigue was described as being sleepy, often with a rapid and unforeseen onset. Consequences of fatigue, such as refraining from daily chores, denying oneself opportunities for rejoice and social isolation, further exaggerated the experience of fatigue. Restorative activities that engaged, absorbed or distracted the patients counteracted these negative consequences. Depressed mood was related to those fatigue dimensions that compromised functional ability and motivation to start any activities, whereas anxiety was associated with cognitive impairment. Feelings of uncertainty were related to physical tiredness, possibly inflicted by limitations in performing activities. Symptom distress that was caused by a number of reported symptoms other than fatigue had a diminutive influence on fatigue and separate symptoms that were associated with fatigue were, with the exception of breathlessness, not the first and most pressing symptom reported by the patients. Anemic patients reported more fatigue compared with non-anemic patients and functional status, according to the New York Heart Association (NYHA) functional classification criteria, was associated with those fatigue dimensions that encompassed physical tiredness and reduced functioning.

The findings provide new insights on the characteristics of fatigue and its consequences on the daily life of the patients. This work also expands existing knowledge regarding patients with CHF by showing that a number of selected physical and psychological factors are related to the fatigue experience. Altogether, this should lead to a better understanding of the patients' situation and improve patient care. The present findings challenge us to come closer to our patients and participate through supportive interventions that help the patients to deal with their experience.

Key words: fatigue, chronic heart failure, uncertainty, sense of coherence, anxiety, depression, symptom distress, hemoglobin, functional status

## ORIGINAL PAPERS

The thesis is based on the following papers, referenced in the text by Roman numerals I - IV

- I. Falk, K., Swedberg, K., Gaston-Johansson, F., Ekman, I. (2006). Fatigue and anemia in patients with chronic heart failure. *European Journal of Heart Failure* 8(7), 744-749.
- II. Falk, K., Swedberg, K., Gaston-Johansson, F., Ekman, I. (2006). Fatigue is a prevalent and severe symptom associated with uncertainty and sense of coherence in patients with chronic heart failure. *European Journal of Cardiovascular Nursing, Epub ahead of print.*
- III. Falk, K., Granger, B., Swedberg, K., Ekman, I. (2007). Breaking the vicious circle of fatigue in patients with chronic heart failure. *Qualitative Health Research, Accepted.*
- IV. Falk, K., Patel, H., Swedberg, K., Ekman, I. (2007). Fatigue in patients with chronic heart failure – a burden associated with emotional distress. *In manuscript*

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## CONTENTS

<b>ABBREVIATIONS</b>	8
<b>INTRODUCTION</b>	9
Illness	10
Symptom	11
Fatigue	14
<b>STATE OF KNOWLEDGE</b>	18
Chronic heart failure	18
Symptoms in patients with chronic heart failure	19
Fatigue in patients with chronic heart failure	21
<b>PURPOSE</b>	25
Specific aims	25
<b>RATIONALE</b>	26
<b>METHODS</b>	30
Designs	30
Setting	30
Participants	30
Inclusion and exclusion criteria	33
Procedure	34
Measurements and instruments	37
Statistical analyses	39
Constant comparative analysis	40
Ethics	42
<b>RESULTS</b>	43
Paper I	43
Paper II	44
Paper III	45
Paper IV	47
Summarize of the main findings	48
<b>DISCUSSION</b>	52
<b>CONCLUSIONS</b>	58
<b>METHODOLOGICAL CONSIDERATIONS</b>	59
<b>CLINICAL CONSIDERATIONS</b>	61
<b>FURTHER RESEARCH</b>	63
<b>ACKNOWLEDGEMENTS</b>	64
<b>REFERENCES</b>	65
<b>PAPER I-IV</b>	

## **ABBREVIATIONS**

BMI	Body Mass Index
BNP	Brain Natriuretic Protein
CHF	Chronic Heart Failure
CPS	Cardiovascular Population Scale
CVI	Cerebrovascular Incidence
DUFS	Dutch fatigue Scale
ED	Emergency Department
FAI	Fatigue Assessment Instrument
FIS	Fatigue Impact Scale
HAD	Hospital Anxiety and Depression
HPA	Hypothalamic-Pituitary-Adrenal axis
HRQOL	Health-Related Quality of Life
LVEF	Left Ventricular Ejection Fraction
MFI	Multidimensional Fatigue Inventory
MUIS	Mishel Uncertainty in Illness Scale
NANDA	North America Nursing Diagnosis Association
NYHA	New York Heart Association Functional Classification
PFS	Piper Fatigue Scale
QOL	Quality of Life
SDS	Symptom Distress Scale
SPSS	Statistical Package for the Social Sciences
SOC	Sense of Coherence
TNF- $\alpha$	Tumor Necrosis Factor-alpha
VAS	Visual Analog Scale
WMA	World Medical Association

## INTRODUCTION

Chronic heart failure (CHF) is a complex clinical syndrome resulting in disturbed and inefficient periphery circulation because of myocardial insufficiency (Swedberg et al., 2005). Despite improvement in pharmacological treatment, the curative effects are limited. Patients with heart failure have to bear a chronic and life-threatening illness trajectory, characterized by severe fatigue, dyspnea, deteriorating functional status, episodic cardiac adverse and repeated hospital readmissions with little hope that the heart disability will entirely disappear. CHF tends to oscillate between periods of exacerbation, when symptoms worsen, to periods of quiescence, when the disability is less disruptive. Nevertheless, even during the calm periods, illness problems arise from the patient's life situation, organized around the threat to vital functions, feelings of vulnerability and loss of control and the menace of untimely death.

The patients' subjective symptomatic presentation is often the first diagnostic clue because of the slow insidious onset of the syndrome. Symptoms reported by patients include breathlessness, fatigue, and concomitant to these symptoms, reduced ability to perform normal activities in daily living. The symptoms exaggerate and become more disturbing as the heart failure progresses and have been shown to predict worsening of heart disability and mortality (Ekman et al., 2005a).

The experience of fatigue is individual, complex, vague and sometimes difficult to articulate, all of which makes it difficult to assess, interpret and define. Although fatigue is a frequently occurring health problem among chronically ill persons, it is still insufficiently investigated. However, there is growing interest in the experience of fatigue and thus it is not surprising that an increasing number of studies have dealt with the health problem in different settings and samples. A view of fatigue as a multidimensional and multi-factorial continuous construct has emerged in which various dimensions of fatigue is related to different influencing factors (Tiesinga, 1999).

Fatigue is still an undervalued problem in the care of patients with CHF. Nurses are unable to assess the patients' fatigue in an accurate manner (Tiesinga et al., 2002). Some reasons for this could be the

vague and relative nature of the experience, making the symptom difficult to identify and manage and the absence of guiding working definitions of fatigue. The documentation about symptoms is remarkably poor and there is a lack of agreement between the patients' description of fatigue and the content in the patients' records (Nordgren & Sörensen, 2003, Ekman & Ehrenberg, 2002a).

### **Illness**

Illness is an experience of changes in bodily processes and the appraisal of those processes as serious or requiring treatment, whereas disease is what the practitioner creates in recasting the illness in terms of theories of disorder (Kleinman, 1988). Thus, a distinction is made between illness and disease, where illness is defined as “experiences of disvalued changes in states of being and in social function”, contrasting with diseases, which is defined as “abnormalities in the structure and function of the body organs and systems” (Eisenberg, 1977, p.11). That is, illness is laden with an individual meaning and social and cultural values, whereas disease is the scientific paradigm of modern medicine. Experiencing illness leads to disruption in our everyday lives. The reality of the world of everyday lives is characterized by common sense (i.e. a naïve and natural attitude where we take everyday for granted and behave as life lasts for ever). We live in the same world as persons around us and the world we experience and inhabit is shared by others. We also share a common apprehension of time related to everyday routines and events organized as past, present and future (Good, 1994).

The illness is present and experienced in the body, which is an essential part of the self and also the subjective entity through which we experience, comprehend and act. Many persons describe their illness experience as if they have lost faith in their body and that the “taken-for-granted world” has been stolen from them (Good, 1994).

All aspects of our every day lives are afflicted by illness and suffering and the common sense reality can no longer be taken for granted. The persons with an intrusive illness may feel alienated from others and separated from everyday life. They do not only put there lives on hold but also their identities. The illness threatens control over self and the situation, resulting in uncertainty (Charmaz, 1997). Medical activities and suffering often dominate there lives, replacing their normal ac-

tivities and interactions. They must abandon their hope and plans and relinquish their former activities. “Intrusive illness demands continue attention, allotted time and forced accommodation” (Charmaz, 1997, p. 42). Life can be abruptly changed and the awareness of disability and death gives everyday life a different meaning. Living one day at a time pulls the person’s attention to the present and forces the person to relinquish the indefinite and uncertain future. The present is compelling and gives a sense of control over self and situation and moments become longer and more substantial (Charmaz, 1997).

### **Symptom**

A symptom is a subjective indication of illness that is perceptible to the patients. A sign is the objective indication of disease, detectable by the individual and by others (Oxford English Dictionary, 1989). The word symptom can be traced from the Greek “*symptoma*”, which means “anything that has befallen one”; the Greek verb is *piptein* “to fall” (The Concise Oxford Dictionary of English Etymology, 1996). The meaning of the word has changed over the past 200 years. Consistent with medieval thinking, the word was used as a “sign” of something evil that had befallen one (Rhodes & Watson, 1987) and illness experience was considered as an integrated part of nature, the human world and cosmos, with no distinction between body and mind (Johannisson, 2005). In 1869, Fenwick proclaimed that “diseases are distinguished from each other either by such alterations in the organs themselves or their secretions, as can be ascertain by the senses of the observer (signs); or by changes in the function of the parts affected (symptom)”. Symptom was defined in a context of medical efforts to scientifically distinguish specific diseases from each other, and in the spirit of that time, symptoms were to play an increasingly subordinate role to signs (Aronowitz, 2001). Limited attention has been given to subjective symptoms ever since.

Symptoms are a regular part of the human experience. Severe symptoms manifest as illness, which refers to how the sick person and the members of the family or the wider social network perceive, live with and respond to the symptoms and disability (Kleinman, 1988). Furthermore, symptoms have agency, i.e. they are a part of the subject in the same time as the person experiences the symptom as a “thing” in the body, which becomes personified as an aversive agent. Symptoms are a matter of communication and construction of meaning. When a

symptom is articulated and communicated verbally, it becomes a part of a social and cultural context in which the meaning of the patient's illness and caring needs can be elucidated. The study of symptom within the caring sciences implies an understanding of the patient's experience and not to explain the disease.

Symptoms are the most common reason why people seek health care and they are of vital importance in the treatment and care of the patients (Ekman et al., 2005b). Symptoms are the "perceived indicators of change in normal functioning as experienced by patients.... they are the red flags of threats to health" (Hegyvary, 1993, p. 146). In the context of health care the symptom experience is communicated and interpreted, systematized and conceptualized by the professional caregivers. The subjective dimension of a symptom raises the question of whether someone other than the person experiencing the symptom is able to accurately assess or measure the sensation. There are impediments to encompass another person's experience, including situational circumstances that play a role for this experience, but symptoms can only become known and interpreted through the report of the person assessed. Hence, an inevitable principle for the study of symptoms is the individual experience, regardless of the research method.

A present definition of symptoms is expressed as an experience reflecting changes in the biopsychosocial functioning, sensations or cognition of an individual. In contrast, a sign is defined as any abnormality, indicative of disease that is detectable by the individual or by others (Dodd et al., 2001). There is often an interrelatedness of signs and symptoms and both can bring health problems to the attention. However, sometimes the symptoms occur in the absence of signs or they are poorly related to the severity of the disease (Swain, 2000). Nimnuan and co-workers (2001) reported a prevalence of more than 50% of unexplained symptoms in different medical specialties, such as cardiology, gastroenterology, neurology and gynecology.

A symptom can occur alone but more often multiple symptoms are experienced simultaneously. Multiple symptoms seem to affect each other and are disproportionately more severe (Lenz et al., 1997). When three or more concurrent multiplicative symptoms are related to each other, they are called symptom cluster. The symptoms in a cluster are not required to have the same etiology in that they can have a physical

as well as psychological or cognitive origin. The symptom cluster may contribute to increased symptom distress or inclusion of emotional responses, worsening the functional status and interfering with daily life and relationships with others (Kim et al., 2005).

Symptom distress can be defined as the degree of discomfort, physical and mental upset, anguish or suffering experienced from a specific symptom or from a cluster of symptoms (Rhodes & Watson, 1987; McCorke et al., 1998). Frequency or intensity is not necessarily equivalent to distress. Other dimensions of symptoms experience, such as perceived importance, existential and spiritual aspects may also be significant for suffering or distress (Tishelman et al., 2005). That is, the experience of symptom distress is composed of both cultural and personal meanings and varies from person to person and from situation to situation (Tishelman et al., 2000).

The symptom experience includes perception of the occurrence of a symptom and an additional evaluation of the characteristics of the symptom, such as timing (frequencies/duration), severity/intensity but also quality attributes, portraying the symptoms uniqueness and essential nature. People make judgments about the cause and meaning and the effect the symptom will have on their lives. Response to the symptoms includes physiological, emotional, social and behavioral components (Dodd et al., 2001, Lenz et al., 1997). The need to restrain or produce actions in response to the symptom, psychological distress and mental adjustment to illness as well as alteration in role identification and social behavior may accompany the experience.

There are many specific factors that influence the experience of symptoms and their relationships are often reciprocal or additional to one another. Influencing factors may be of a physical character, such as the existence of any pathology or decreased health status. Situational antecedents affecting the symptoms experienced include demographic variables, including age, gender, marital status, family unit and ethnicity, education, employment and financial status. Personality traits, cognitive capacity and motivation, social support network and lifestyle are conditions of the circumstances within which the symptom is perceived. Knowledge, previous experiences, expectations, beliefs and values are other aspects that may comprise the symptom experience (Larsson et al., 1994).

Patients with life-threatening or chronic disease must learn to accommodate to their illness. The patients' evaluation of their symptom experience and accompanying distress may decrease over time despite unchanged or even worsening physical disability. Additional to the possibility that the symptoms have been relieved by appropriate care or treatment, emotional adaptation related to value changes has been suggested as one reason for this accommodating process. This reorientation has been referred to as a response shift, which means that the patients deemphasize the importance of lost life values because of the chronic illness and replace unattainable values with new values that are attainable (Sprangers & Schwartz, 1999; Persson et al., 2005).

Patients suffering from symptoms need care. Identification and a holistic assessment of burdensome symptoms should alert nurses and other healthcare professionals that the goal of care may not be the complete alleviation but rather to decrease the burden of those symptoms (Zambroski et al., 2005). The interventions should be focused on the symptom experience as well as influencing factors and the consequences the symptom experience may have on the individual's daily life. The effect or outcome criterion of the interventions is often assessed as changes in performance, health-related quality of life (HRQOL), disease progression and survival (Lenz et al., 1997; Armstrong, 2003).

A comprehensive assessment of the symptoms experienced from the patient's perspective, followed by identification of strategies for interventions and evaluation of the outcomes is the most common way to plan and accomplish care for the patients (Larson et al., 1994). Improvement may be in symptom frequency, severity and distress or in other dimensions related to the symptom experience that the patient considers important (Chang & Ingham, 2003). The care of patients with a troublesome symptom requires a patient-family perspective. Symptoms are often a major problem for the individuals and their families because the efforts to interpret and relieve the symptom often become their own responsibility (Dodd et al., 2001).

### **Fatigue**

In healthy individuals fatigue is defined as a non-specific state indicative of a decreased level of vitality. This state has a protective function of forcing the body to avoid further stress, with exhaustion being the end of the fatigue continuum (ranging from tiredness to exhaustion),

eventually forcing the body to stop functioning (Grandjean, 1970). This temporary form of fatigue is identified as acute fatigue and characterized as protective and identifiably linked to a single and obvious cause. It is perceived as normal, has a rapid onset and a short duration, is usually alleviated by rest, diet, exercise and stress management and has a minor or minimal effect on activities of daily living and quality of life (QOL) (Piper, 1993).

Fatigue accompanied with diseases is referred to as chronic fatigue. It is a complex multicausal and multidimensional symptom that is difficult to characterize and define (Piper, 1993). It is one of the most frequently reported symptoms in many chronic illnesses, including cancer (Ahlberg et al., 2003), renal failure (Ossareh et al., 2003), chronic pulmonary disease (Kapella et al., 2006), multiple sclerosis (Flensner et al., 2003) and rheumatoid arthritis (Belza, 1995).

The experience of fatigue is individual, complex, vague and sometimes difficult to articulate, making it particularly difficult to characterize, interpret and measure. Fatigue encompasses a complex interaction between biological, psychosocial and behavioral processes (Swain, 2000). It is induced by the disease process or treatment regime and is characterized by having an unknown function or purpose, as having multiple additives or unknown causes and is often experienced with no relation to activity or exertion (Piper et al., 1987). Fatigue is usually perceived as abnormal, unusual or excessive, has an insidious onset, persists over time, is not generally relieved by usual restorative techniques and has a major effect on the individual's activities of daily living and QOL (Piper et al., 1989a). In fact, fatigue is reported as a key factor leading to a decreased QOL in patients with chronic diseases (Swain, 2000).

The indistinctiveness of fatigue as a theoretical concept is revealed in the broad variety of definitions in nursing. Besides the general definitions of fatigue with a broad and holistic approach, there are several related or synonymous concepts. The multiplicities have resulted in the lack of a clear and widely accepted definition of the symptom. Tiredness, weakness and exhaustion are some of the more frequently used concepts that are being used interchangeably with fatigue (Piper et al., 1987). Tiredness is distinguished from fatigue by intensity and duration and can, according to Piper (1993), not be used synonymous-

ly with fatigue. Weakness is defined as impaired physical strength or energy affecting an individual's ability to perform activities. It results from neurological or muscle disorders and it cannot be abated by will power alone (Gordon, 1986). Glaus (1998) defines weakness as an anticipatory, subjective sensation of difficulty to initiate a certain activity in the context of tiredness. Exhaustion or vital exhaustion is defined as an extreme state of fatigue. It is characterized by exhausted feelings after awakening, loss of energy, increased irritability and feelings of demoralizations (van Diest & Appels., 1991).

The definitions of fatigue in nursing science describe the subjective dimension of fatigue without consideration of the underlying disease or symptom origin. The definitions stipulate that the experience of fatigue is subjective and generalized, suggesting that the whole person is encompassed by the sensation, where the ability to perform activities is subsequently compromised. Some of these definitions reflect the current discourse and describe fatigue as "unusual abnormal or excessive whole-body tiredness disproportionate to or unrelated to activity or exertion" (Piper, 1993, p. 279) or as "the self recognized state in which an individual experiences an overwhelming sustained sense of exhaustion and decreased capacity for physical and mental work that is not relieved by rest" (Carpenito, 1992, p. 362). The authors differentiate fatigue from the concept of tiredness by stating that tiredness is a universal sensation that is expected to occur normally at certain times of the day or after certain types of activity but fatigue is an unusual, pervasive, draining feeling not possible to relieve by rest (Carpenito, 1992; Piper, 1993).

Aaronson and co-workers (1999) define chronic fatigue as "the awareness of a decreased capacity for physical and/or mental activity due to imbalance in the availability, utilization, and/or restoration of resources needed to perform activity" (p. 46). This definition is consistent with a multidimensional framework where physiological, psychological and situational factors can be apprehended as integrative resources or limitations affecting the experience, responses and outcomes of fatigue. The definition also includes idea of the subjective nature of fatigue and the self-regulation framework. Fatigue occurs when there are insufficient resources either because the demands or needs are too high or because mechanisms of utilization and restoration are disturbed.

The basic mechanisms in fatigue are generally divided into two major components: peripheral fatigue from neuromuscular dysfunction and mechanisms leading to energy imbalance and central fatigue that implies alteration in neurotransmitters in serotonergic and noradrenalin pathways and changes in the function of the hypothalamic-pituitary-adrenal axis (HPA), often coexistent with such psychological complaints as anxiety and depression (Swain, 2000, Gutstein, 2001). Other suggested mechanisms of fatigue include alteration in biochemistry with elevated levels of cytokines in plasma, resulting in immune activation. Tumor necrosis factor alpha (TNF- $\alpha$ ) is associated to a number of non-specific symptoms, including impaired skeletal muscle strength with weakness and poor functional status in patients with CHF (Cicoira et al., 2001). Impaired peripheral perfusion with reduced oxygen delivery and impaired muscle strength are some factors that may help explain the experience of fatigue in CHF (Drexler & Coats, 1996).

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## STATE OF KNOWLEDGE

### **Chronic heart failure**

Heart failure is a clinical syndrome resulting from structural or functional damage that impairs the heart's ability to fill or eject blood, resulting in dyspnea, fatigue, fluid retention and limited exercise capacity (Swedberg et al., 2005; Hunt et al., 2005). The condition is a major health problem in industrialized countries with aging populations. The prevalence of heart failure has increased over the past few decades (Mc Murray & Stewart, 2000), and is estimated to 1-2 % of the population. Further, CHF is a major cause for hospitalization in men and women above 65 years. In Sweden, heart failure is the most frequent discharge diagnosis within internal medicine (Mejhert et al., 2001). Because of the high rates of hospitalizations, the care of patients with CHF accounts for 1-2% of the total health expenditure in Sweden (Ryden-Bergsten & Andersson, 1999).

Heart failure is a lethal condition with a mortality rate of approximately 60% within five years after diagnosis (McMurray and Stewart, 2000). Data from the Framingham study showed that only 25% of the men and 38% of the women survived after 5 years (Kannel, 1999). However, the incidence of CHF seems to be decreasing or plateauing out and the prognosis has improved particularly among patients < 60 years during the past decade (Stewart et al., 2001; Schaufelberger et al., 2004). Improved treatment of coronary heart diseases and hypertension, the major causes of CHF in industrial developed countries, may be the reason for reduced incidence while improved pharmacological treatment of heart failure within the past 15 years has improved prognosis (Stewart et al., 2001; Schaufelberger et al., 2004).

Heart failure is diagnosed when there are symptoms and documented cardiac dysfunction at rest (Swedberg et al., 2005). The etiology of CHF may be due to myocardial dysfunction, arrhythmias, valve abnormalities or pericardial disease (Swedberg et al., 2005).

Dominating symptoms and signs associated with heart failure are progressively increasing dyspnea, reduced exercise capacity, fatigue and weakness and edema due to an increased level of systemic venous pressure or expanded extracellular fluid volume. Cerebral symptoms, such as mood changes and intellectual impairment are also common in

advanced stages of heart failure (Braunwald et al., 2001; Swedberg et al., 2005). The symptoms may be used to classify the severity of heart failure but often there is a poor relationship between the symptoms and the severity of cardiac dysfunction (Cleland et al., 2003). Recent research shows that left ventricular ejection fraction (LVEF), an important and widely used prognostic variable, is of less importance for predicting outcome in comparison with patients' self-reported symptoms (Ekman et al., 2007).

The goals of treatment are to improve the patients' QOL, prevent progression of the syndrome and improve survival (Swedberg et al., 2005). The management of heart failure depends on its cause and clinical manifestation. The general pharmacological treatment regime is aimed at reducing fluid retention, reduce periphery vasoconstriction and decrease the neurohormonal activation (primarily sympathetic activation). Pharmacological treatment for selected patients could also include anti-arrhythmics and anticoagulants (Swedberg et al., 2005).

Non-pharmacological treatment includes recommendation to patients concerning salt and fluid restriction, weight control, immunization with influenza vaccines, good eating habits, dietary supplements and a sound relation between exercise, activity and rest. The patients are also recommended to reduce alcohol consumption, and obese patients should lose weight and smokers should stop smoking (Swedberg et al., 2005; Hunt et al., 2005).

### **Symptoms in patients with chronic heart failure**

Symptoms are an important aspect of CHF and therefore they are used to classify the severity of heart failure and monitor the effect of the therapy (Swedberg et al., 2005). The New York Heart Association (NYHA) functional classification system (1994) has been widely used in clinical practice and research for categorizing the patients' symptoms (e.g., breathlessness and fatigue) in relation to physical activities. Evaluations of the functional status, achieved from the care providers' perspective, are often influenced by knowledge of the severity of the cardiac dysfunction, prior medical history and judgment regarding prognosis (Ekman et al., 2005b). However, symptom experience is inherently subjective and the ability to perform activities may not only be limited by physical symptoms but also by a variety of personal, environmental and social factors (Bennett et al. 2002a). This may be

one reason for the discrepancies between patients' self-assessments and the clinicians' evaluations of functional status consistently shown in recent studies (Ekman et al., 2005a; Ekman et al., 2007).

Patients with CHF experience a wide variety of symptoms. Recent studies reveal that patients with CHF reported, on average, between three and eight symptoms (Nordgren & Sørensen, 2003; Patel, et al., 2006). The most prevalent symptoms reported by the patients were, in addition to dyspnea and fatigue, dry mouth, difficult sleeping, bodily pain and loss of balance. Commonly reported psychological symptoms were difficulty concentrating, anxiety and depressed mood (Bennett et al., 2000; Zambroski et al., 2005; Patel et al., 2006). Patients with end-stage heart failure had symptoms similar to those of cancer and frequently reported nausea, loss of appetite and constipation (Nordgren & Sørensen, 2003).

The most prevalent symptoms may not be the most distressing ones from the patients' perspective. Patients described a number of relatively rare symptoms (e.g., numbness/tingling of the hands or feet, itching, problems with sexual interest and activity and change in food taste) as particularly distressing or burdensome. On the other hand, dry mouth, chest pain and feeling drowsy were highly prevalent but not ranked as particularly distressing (Zambroski et al., 2005). Patel and co-workers (2006) found that symptoms, especially shortness of breath, were the dominant reason for seeking care, even though only a few patients related their symptoms to worsening of CHF.

HRQOL is impaired in patients with CHF and it is strongly related to symptoms of heart failure, especially fatigue and dyspnea (Ekman et al., 2002b; Bennett et al., 2002b; Rector et al., 2006). Other findings suggest that depressive symptoms have an important impact on HRQOL (Dracup et al., 1992; Hawthorne & Hixon, 1994; Carels, 2004). Women reported significantly lower HRQOL because of physical symptoms, whereas depression affected HRQOL in men (Riedinger et al., 2001; Heo et al., 2006). The association between functional status, as measured with NYHA and HRQOL has been reported in several studies but other signs of cardiac dysfunction, such as LVEF, peripheral edema and natriuretic peptide (BNP) have limited influence on HRQOL (Bennett et al., 2002b; Juenger et al., 2002; Rector et al., 2006).

### **Fatigue in patients with chronic heart failure**

Fatigue is a highly severe, prevalent and distressing symptom in patients with CHF. Moreover, it is one of the most important factors affecting the patients' HRQOL (Drexler & Coats, 1996; Bennett et al., 2003a; Zambroski et al., 2005; Barnes et al., 2006). Self-reported fatigue has been shown to independently predict the worsening of CHF and rehospitalization and therefore should be considered a far greater burden for the patients than is currently realized (Ekman et al., 2005a). Stanek and co-workers (2000) found that when patients with CHF were asked to weigh the importance of relief of fatigue to a longer life, significantly more patients chose relief of fatigue.

Schaefer & Schober (1993) reported that fatigue in CHF was associated with overwhelming tiredness, which interfered with functional ability. The patients' own descriptions of the fatigue experience have been summarized by Schaefer (1990):

“Fatigue means my whole being is tired. This tiredness penetrates the whole bone structure; you feel it in the very marrow of your bones. It's total physical tiredness, and on top of that is mental tiredness. It's like an undercurrent that undermines your thinking. Your body is wearing out. The weight of fatigue is in the shadows. If I rest, the fatigue will overwhelm me” (p. 227).

Fatigue in patients with CHF has been found to be associated with other physical symptoms, such as breathlessness, chest pain and palpitations (Friedman & King, 1995; Tiesinga et al., 1998; Schaefer, 1990; Mayou et al., 1991), sleep difficulties (Friedman & King, 1995; Thiesinga et al., 1998), nausea, loss of appetite and headache (Schaefer, 1990). Fatigue has also been reported to be associated with LVEF (Schaefer, 1990) and oxygen saturation (Schaefer & Schober, 1993) but no other relationships between physical signs and experience of fatigue have been found in the literature.

Fatigue and dyspnea are highly correlated (Friedman & King, 1995). Whereas fatigue prevents the patients from pursuing activities, dyspnea generally commences before fatigue once activity is initiated.

However, it is important to distinguish fatigue from dyspnea because the presence of dyspnea associated with fatigue is an argument in favor of an organic cause of these symptoms (Casillas et al., 2006).

Fatigue is negatively associated with physical activity, regardless of gender (Mayou et al., 1991). It is just as probable for physical inactivity to cause fatigue as it is for fatigue to cause physical inactivity. The cross-sectional nature of fatigue and physical activity does not permit an unequivocal statement about the cause-effect relationship (Chen, 1986). Fatigue can be one effect of muscle atrophy depending on physical inactivity, but the loss of muscle tissue may as well be a result of physical inactivity that is caused by fatigue. Fatigue and breathlessness limit the daily physical activities and they have to be planned carefully and performed slowly with frequent stops to rest. The impaired ability to perform daily chores is associated with worry and discomfort and also has consequences for social functioning such as social leisure and work (Mayou et al., 1991; Murberg et al., 1998).

Cachectic patients report high levels of fatigue. Many patients suffering from CHF are too tired to eat or have lost their appetite because of drug treatments or other medical interventions (Friedman & King, 1995; Jacobsson et al., 2001). The pathophysiological causes of body wasting remain unclear but have been suggested to be linked to increased levels of TNF- $\alpha$ . A relation between the state of cachexia and plasma level of pro-inflammatory cytokines has been reported (Anker & Rauchhaus, 1999).

Sleep disturbances in combination with fatigue are common in patients with CHF. Sleeping problems were attributed to use of diuretics, fear about dying during sleep and shortness of breath (Bennett et al., 2000). Tiesinga and co-workers (1998) found that the quality of sleep was negatively correlated to fatigue but the quantity of sleep was not. Polysomnographic studies have shown that the total duration of sleep was shorter and that sleep was disturbed because of frequent arousals (Yamashiro & Kryger, 1993). Reported effects of sleep disturbances included fatigue, listlessness, loss of temper and difficulties with concentration (Broström et al., 2001).

Several studies of persons with heart failure have reported cognitive impairment, including forgetfulness, decreased attention and dimin-

ished concentration (Bennett et al., 1997; Bennett et al., 2000; Ekman et al., 2001). Having minor accidents, such as dropping things or tripping, difficulty in problem solving, making decisions and difficulty doing activities that require concentration or thinking, have also been reported (Bennett et al., 1998).

It has been suggested that conditions that cause significant functional limitations are associated with cognitive dysfunction in patients with CHF (Turvey et al., 2006). In a cancer population Glaus (1998) identified problems in thinking and lack of concentration as cognitive manifestations of tiredness. The involvement of fatigue in the development of cognitive impairment in patients with CHF is not yet understood. An investigation in elderly patients with CHF indicates that cognitive impairment may be partly a consequence of decreased LVEF and low systolic blood pressure (Cacciatore et al., 1998; Zucculà et al., 2005). These findings support the suggestion that decreases in cerebral blood flow affect cognitive functions (Bennett & Sauvé, 2003b).

There are conflicting views regarding the relationship between fatigue and age and gender. Tiesinga and co-workers (1998) reported that women were significantly more fatigued than men. In contrast, Ekman & Ehrenberg (2002c) did not find any significant gender difference in the degree of fatigue, but more women than men associated fatigue with old age. Younger women seemed to be more distressed from fatigue and reported more intrusive consequences in their daily life than older women. (Plach et al., 2006). Older persons seem to accept fatigue and perceive it as less bothersome because they accept it as an inevitable effect of the aging process (Schaefer, 1990; Friedman, 1997). The response to fatigue differed between men and women. Whereas men became restless, angry and depressed, women felt guilt for not having the strength to manage expected duties in the domestic domain (Ekman & Ehrenberg, 2002c). Lack of energy, leading to limited working capacity and social activities, resulted in resignation in men, whereas feelings of anxiety and worthlessness were reported in women (Mårtensson et al., 1997; Mårtensson et al., 1998).

Although fatigue is one symptom that constitutes clinical manifestation of heart failure, few patients reported fatigue as the primary cause for seeking health care. (Friedman, 1997). Many patients do not recognize exaggerating symptoms to worsening of CHF (Patel et al., 2006).

However, higher levels of distress because of fatigue were associated with higher levels of health care utilization (Plach et al., 2006).

There are a number of multidimensional questionnaires available that combine fatigue and the manifestations of the symptom, including the Piper Fatigue Scale (PFS) (Piper et al., 1989b), the Multidimensional Fatigue Inventory (MFI) (Smets et al., 1995), the Fatigue Assessment Instrument (FAI) (Schwartz et al., 1993), the Fatigue Impact Scale (FIS) (Fisk et al., 1993) and the Dutch Fatigue Scale (DUFSS) (Tiesinga et al., 1998). With the exception of the DUFSS, none of these instruments was recognized to be used in measuring fatigue in patients with CHF. A modified version of Fatigue Interview Schedule (Schaefer & Shober, 1993), containing ten characteristics of fatigue from the North American Nursing Diagnosis Association (NANDA), has been used in several studies, supplemented with a 10-point visual analog scale (VAS) to measure the severity of fatigue (Schaefer & Shober, 1993; Ekman & Ehrenberg, 2002a; Ekman & Ehrenberg, 2002c).

## PURPOSE

The primary aim of this thesis was to explore fatigue from the patients' perspective by describing the characteristics of the fatigue experience and its consequences in daily life in patients with CHF. A secondary aim was to investigate the relationships between fatigue and selected physiological and psychological factors associated with fatigue.

### Specific aims

#### *Paper I*

The aims of this study were threefold: 1) to describe the fatigue experience and explore differences between men and women; 2) to investigate the relationship between fatigue and hemoglobin concentration; and 3) to evaluate the effect of fatigue on HRQOL in an unselected hospitalized CHF population.

#### *Paper II*

The aim of this study was to examine the prevalence and severity of fatigue as a multidimensional symptom and to determine the influence of sense of coherence (SOC) and uncertainty on the fatigue experience in patients with CHF.

#### *Paper III*

The aim of this study was to provide a theoretical understanding of the fatigue experience and its consequences in everyday life. A secondary aim was to identify and conceptualize alleviating aspects of fatigue in patients with CHF.

#### *Paper IV*

The aim of this study was 1) to examine the association between fatigue and anxiety, depression and symptom distress and 2) to explore the relationships between selected symptoms and fatigue as a multidimensional concept in patients with CHF.

## RATIONALE

Fatigue is a prominent and devastating symptom in patients with CHF and has a negative impact on the patients' everyday life. Despite this, research on fatigue is a neglected field. Although there are advances in the conceptual understanding of fatigue, the mechanisms of fatigue are still poorly understood. For example, the extent to which fatigue experience and consequences because of fatigue differ based on the etiology of fatigue remains unclear. There is, with one exception, no validated domain-specific instrument used to measure fatigue in patients with CHF and the different characteristics of fatigue are rarely described. The absence of systematic and structured measurements hampers the possibility to make any comparisons between groups of patients and to evaluate the effects of interventions.

The rationale for this study is to describe the characteristic of the fatigue experience and its consequences in daily life in patients with CHF. The general definitions of fatigue embrace an overall experience of fatigue; however, we still do not know if there may be specific characteristics, such as intensity, duration or pattern of recurrence, that are specific for this group of patients. Personal expressions of fatigue (such as responses to the experience, consequences in everyday life because of fatigue and strategies for recovering) may be unique in patients with CHF. In addition to using a validated domain-specific instrument for self-assessment of fatigue, there is a need to expand the current opinion of the fatigue experience, as defined in the instrument dimensions, and deepen our understanding on the character of the fatigue experience.

A second rationale is to investigate the relationship between fatigue and some selected factors that we know is occurring frequently in patients with CHF. There is currently no specific therapy for treating fatigue in CHF (Swain, 2000). However, some of the hypothesized relating factors may be possible to influence either by pharmacological treatment or with care interventions in order to indirectly relieve fatigue or diminish the consequences of fatigue in the patient's daily life.

A further intention was to illuminate some specific clinical and demographic characteristics in those patients who reported fatigue as

troublesome in order to be able to identify those patients that may be at risk for severe fatigue.

All together, this knowledge is important to improve existing strategies in relieving the symptom and to develop methods that give support and help to CHF patients with fatigue. The foremost rationale for this thesis is to create a solid fundament of knowledge from the patients' perspective that will be useful in the care of patients with CHF and also serve as a basis for future longitudinal and interventional studies.

### **Paper I**

The mechanisms underlying the fatigue in patients with CHF are not well understood. There are several physiological alterations that could explain the development of fatigue. Reduced oxygen delivery to metabolizing tissues could be one factor that plays an important role. Anemia is common in patients with CHF. Depending on population and the definition of anemia used, moderate anemia has been reported in 15-55% of patients (Paul & Paul, 2004). The symptoms of anemia (e.g., fatigue, mild dyspnea and occasionally palpitations) overlap those of CHF and if reduced hemoglobin level is an additive factor that further exaggerates the fatigue experience in CHF is unknown. If so, the adjustment of low hemoglobin level may reduce the fatigue experience.

### **Paper II**

Uncertainty in illness has been identified as a major source of mood disturbances in patients with CHF (Hawthorne & Hixon, 1994). For example, patients experience uncertainty when symptoms first occur or when they lack information about the symptoms or when they contemplate deterioration of their symptoms (Winters, 1999; Patel et al., 2006). Because fatigue is a dominating illness experience in patients with CHF, it may contribute to feelings of uncertainty. An inverse relation between the variables (e.g., feelings of uncertainty increase fatigue) may also be considered.

Fatigue in patients with CHF is significantly associated with stress, both as cause and consequences (Friedman & King, 1995; Schaefer & Shober, 1993). Researchers have also reported a strong relationship between high uncertainty and stress (Mishel, 1988). Patients who

reported greater use of an active behavioral coping style (e.g., support from family and friends) demonstrated less fatigue, whereas avoidance coping was associated with less vigor and more fatigue (Doering et al., 2004).

Sense of coherence (SOC), which is distinct from coping strategies, is defined as a global personal disposition that expresses the ability to manage demanding situations. Strong SOC has been found to be associated with higher HRQOL in patients with CHF (Ekman et al., 2002b). Because the life situation in patients with CHF is afflicted by numerous symptoms, particularly fatigue, it emphasizes the need to investigate the relationship between different characteristics of fatigue and the patients' ability to manage their illness experience. It is unknown whether the patients' level of SOC influences the experience of fatigue or the feeling of uncertainty.

### **Paper III**

There are few qualitative studies describing fatigue and its consequences in the daily life of patients with CHF (Schaefer, 1990; Schaefer & Shober, 1993; Ekman & Ehrenberg, 2002c). The few numbers make it difficult to know to what extent the findings can comprise all dimensions of fatigue in patients with CHF. Therefore, there is a need for more inductive studies in order to develop knowledge about the fatigue experience from the patients' perspective. Because fatigue is a highly personal experience, there may be information about the perception and evaluation of fatigue that will not be captured by structured questionnaires. Moreover, the lack of distinctiveness of fatigue has resulted in no clear and widely accepted definition of fatigue. The purpose of this study is to contribute to the further development of the current mainstream opinion of the fatigue experience in patients with CHF.

### **Paper IV**

Depression is common in patients with CHF (30-36%) and has been found to predict mortality and be associated with fatigue and breathlessness (Rumsfield et al., 2003; Jünger et al., 2005; Friedmann et al., 2006). Furthermore, negative mood is associated with exacerbated physical symptoms, such as fatigue and breathlessness (Yu et al., 2000; Turvey et al., 2002; Sullivan et al., 2004). Fatigue and depression seem to be inherently associated with one another. Most depressed patients

are fatigued though not all fatigued patients are depressed (Tiesinga et al., 1996). Anxiety is associated with the severity of CHF and chest pain (Friedmann et al., 2006; Haworth et al., 2005) but to what extent anxiety is related to fatigue has not been investigated. However, because fatigue is a substantially complex phenomenon a more detailed exploration of the relationship between emotional distress and fatigue experiences and its manifestations is needed.

The most distressing symptoms in CHF patients are fatigue/lack of energy, breathlessness and sleeping difficulties. In addition to these characteristic symptoms associated with CHF, patients have reported a wide range of other symptoms (Zambroski et al., 2005; Barnes et al., 2006). Altogether, these symptoms may cause a general degree of distress, all of which influence the patients' well-being as well as compromising their functional status. High symptom distress in patients awaiting heart transplant is significantly associated with higher stress, lowered life satisfaction and greater functional disability (Grady et al., 1992). At present, we know almost nothing about the relationships between individual symptoms and how the inclusive experience of symptom distress affects a specific symptom (e.g., fatigue). Efforts to relieve discomfort created from symptoms that are more manageable than fatigue may be one possibility to indirectly reduce fatigue and therefore it is important to explore the relationships between reported symptoms.

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## METHODS

### Designs

The designs of the cross-sectional descriptive studies were comparative, correlational or explorative. Further, inductive and deductive research methods were used, comprising both quantitative and qualitative analysis. The quantitative approach was used to gain knowledge that can be compared and generalized between different groups of patients. The qualitative study was carried out with a constant comparative method in order to obtain knowledge about fatigue that may be specific in patients with CHF.

The research designs for the studies were as follows:

Study I:	descriptive, correlational, comparative design
Study II:	descriptive, correlational design
Study III:	explorative and descriptive design
Study IV:	descriptive, correlational design

The methodologies included in this thesis are presented in Table 1.

### Setting

The study was conducted at the Department of Medicine, Sahlgrenska University Hospital/Östra Hospital, a large university hospital serving 250 000 inhabitants in Göteborg.

### Participants

#### *Paper I and II*

Ninety-nine consecutive patients hospitalized with a diagnosis of CHF who fulfilled the criteria for inclusion were enrolled in the studies. The patients were identified at the hospital ward within the third day after hospital admission. The final study population consisted of 93 patients (48 men and 45 women). The mean age was 74 years (range 33 to 95 years) and women were significantly older than men (mean age 78 *versus* 71 years). Patients declined or did not complete the study for a variety of reasons, including morbidity or felt too ill to participate in interviews. This is a common problem in studies of patients with CHF and not unique to this study (Bennett et al., 2001).

Table 1. An overview of variables, instruments and methods

	Subjects	Demographics	Clinical variables	Instruments	Method	Analysis
Study I	93	Age Gender Marital status Living arrangements Educational level	NYHA-class Hemoglobin Comorbidity	MFI-20	Regression Correlation Comparison	Descriptive analysis Multiple regression analysis Pearson's correlation coefficient Independent t-test
Study II	93	Age Gender Marital status Living arrangements Educational level	NYHA-class Comorbidity	MFI-20 CPS SOC scale	Regression Correlation Comparison	Descriptive analysis Multiple regression analysis Pearson's correlation coefficient Independent t-test
Study III	15	Age Gender Employment status	Comorbidity		Focused interviews with open-ended questions	Constant comparison
Study IV	112	Age Gender Marital status Country of origin Living arrangements Educational level	NYHA-class LVEF BMI Systolic blood pressure Comorbidity Pharmacological treatment	MFI-20 SDS HAD scale	Regression Correlation Comparison	Descriptive analysis Multiple regression analysis Pearson's correlation coefficient Independent t-test

### *Paper III*

The 15 eligible patients in the qualitative study were identified by the nurses when the patients visited an outpatient clinic at the hospital for routine control and adjustment of their pharmacological treatment. The patients who expressed that they felt tired or exhausted were asked if they would like to participate in interviews concerning their fatigue experience and its consequences for their daily lives. Additional to the diagnosis of CHF and the experience of being fatigued, no other inclusion criteria were obtained, except for willingness to give informed consent and speak and understand Swedish. The proportion of men and women were accomplished in the selection of informants (eight men and seven women). The mean age was 76 years (range 31 to 95 years). The age and proportion of men and women were concomitant with the two other samples in this thesis.

Internet discussions from The American Heart Association Forum for patients and care givers were used as a supplementary source of data. The online discussion group worked on a “read only, free-access” basis and thus come under the public domain.

From 841 messages posted during 12-month period, 28 dealt with the fatigue experience and were thus included in the data analysis. The dispatchers were anonymous and it was not possible to identify the persons age or gender for many of those posted. One can assume that they were younger than the patients interviewed because people who use the Internet for health information are reported to be younger than those who do not (Cotten & Gupta, 2004). The diagnosis of CHF was assured from the participants’ description of their heart condition in terms of the NYHA classification or LVEF.

### *Paper IV*

Patients with exacerbation of CHF symptoms and with a primary diagnosis of CHF were screened for eligibility to participate in the study. The patients were identified either at the emergency department (ED) or at the hospital ward within the first 72 hours after hospital admission. Initially, 128 consecutive patients hospitalized for worsening CHF were eligible for the study, but 16 patients were excluded from data analysis (eight because of the extent of incomplete data from the interviews and eight because of a discharge diagnosis other than CHF). Thus, the final study sample consisted of 112 patients (67 men and 45

women). The mean age was 77 years (range 44 to 94 years), with the women being slightly older than the men (79 years versus 76 years).

The diagnosis of CHF was validated according to ESC guidelines (Swedberg et al., 2005) and verified from electronic medical records (Table 2). Doubtful cases were reviewed and resolved by a senior cardiologist.

**Table 2.** Definition of heart failure

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- I. Symptoms of heart failure (at rest or during exercise)
  - II. Objective evidence (preferably by echocardiography) of cardiac dysfunction (systolic and/or diastolic)
  - III. Response to treatment directed towards heart failure
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### **Inclusion and exclusion criteria**

Inclusion criteria were:

- a clinical diagnosis of heart failure presenting with symptoms of heart failure (e.g., breathlessness or fatigue at rest or during exercise)
- hospitalization because of exacerbation of symptoms of heart failure (Paper IV)
- willingness to give informed consent

Exclusion criteria were:

- cognitive disorientation and communicative limitations (e.g., loss of hearing and speech)
- inability to understand and speak Swedish

## **Procedure**

### *Paper I and II*

Patients were recruited from the EuroHeart Failure Survey, a prospective survey aimed at describing the quality of care in patients hospitalized with heart failure in 24 countries within the European Society of Cardiology (Cleland et al., 2000). All patients admitted to the Department of Medicine, Sahlgrenska University Hospital/Östra were continuously screened during 12 weeks and patients that fulfilled the inclusion criteria were enrolled. For the prospective survey, only data from the patients' records were collected at baseline, concerning among other things, reason for admission, etiology of the heart failure, concomitant diseases and treatment. The patients enrolled in the Euroheart Survey were asked if they were willing to attend an interview; those who accepted were included in the descriptive studies of the fatigue experience. The participants gave their informed consent in accordance with the ethic committee before data collection.

The structured interviews, based on the questionnaires (Multidimensional Fatigue Inventory (MFI-20), Sense of Coherence (SOC) scale and Cardiovascular Population Scale (CPS), were performed at the hospital ward, with the interviews lasting between 30 to 60 minutes. To standardize the data collection method and minimize missing data, the questionnaires were read to the patients by the first author and the project coordinator. Inter-observer reliability was assessed by comparing the extent to which the interviewers agreed in their understanding of the questions and the patients' answers to the questions (Polit & Hungler, 1999). The patients' hemoglobin levels and data about etiology of heart failure and concomitant diseases were extracted from the medical records. Demographics (age, gender, marital status, accommodation, employment status and educational level) and NYHA functional class were assessed in conjunction with the interviews. Data were collected during Mars and June 2000.

### *Paper III*

Data were gathering using face-to-face interviews, aimed at illuminating the informants experience or situation as expressed in their own way. Twelve of the interviews took place in the patients' homes and three interviews occurred in the hospital in conjunction with a visit to the open heart reception. The participants received verbal and written information about the purpose and procedure of the study and gave

verbal consent to participate. The interviews which lasted from 45 to 90 minutes were taped and then transcribed verbatim by the first author.

Gathering of data was following the principles for grounded theory method (Charmaz, 2006). The interviews focused on three priorities: the experience of fatigue, the behavioral response related to fatigue and the consequences of fatigue in daily life. A few broad open-ended questions were initially asked where the participants described and reflected upon his or her experiences followed by requests for more detailed explanations or questions focusing on significant statements later in the interview. An interview guide with open-ended questions of interest was established: Could you describe what it is like to be fatigued? Tell me what is happening when you get tired? How does fatigue influence your daily activity? Tell me about your thoughts and feelings about fatigue? Could you describe a typical day for you when you are fatigued? What helps you to manage fatigue? After having these experiences, what advice would you give to someone who is in the same situation as you? The interviews were informal and conversational and sometimes there was no need in asking all questions because the informant talked freely about his or her experience.

The interviews and the analysis were conducted simultaneously, which mean that consecutive interviews continually became more specific as the initial codes and categories were developed. By focusing on statements, expressions or events in data that illuminated the initial categories, those could gradually be theoretical developed. Data collection continued until no further insights into fatigue were yielded in relation to the theoretical categories.

After the interviews were completed, Internet discussions were used as a supplementary source of data. Data were collected through focused online observations of the content discussed in an Internet patient discussion group concerning CHF. The reason for collecting this data was to get sufficient amount of data and to enrich the data with a combination of different sources.

#### *Paper IV*

Patients that consecutively sought hospital care for exacerbation of symptoms (e.g., breathlessness and fatigue) that might be caused by

heart failure were screened at the ED or hospital wards. After the primary diagnosis of heart failure was established, the patients who fulfilled the inclusion criteria were asked if they were willing to participate in the study. Structured interviews were performed using the following questionnaires: the Multidimensional Fatigue Inventory (MFI-20), the Hospital Depression and Anxiety (HAD) scale and the Symptom Distress Scale (SDS). The items were read to the patients to standardize the data collection and minimize missing data. Inter-observer reliability was assessed by comparing the extent to which the interviewers agreed in their understanding of the questions and the patients' answers to the questions.

All patients were informed orally and received written information about the study; data collection was conducted after obtaining written consent. The interviews lasted approximately 30 to 60 minutes and took place either at the ED or in the hospital wards. In conjunction with the interviews NYHA class, height and weight were assessed and information about demographics (age, gender, and marital status, country of origin, living arrangements and educational level) and current concomitant diseases was reported by the patients. Clinical data such as LVEF, blood pressure and pharmacological treatment were collected from the patients' medical records. Data were collected between April 2004 and June 2006.

**Table 3.** New York Heart Association classification of heart failure

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Class I	No limitation: ordinary physical exercise does not cause undue fatigue, dyspnea or palpitations
Class II	Slight limitation of physical activity: comfortable at rest but ordinary activity results in fatigue, palpitations or dyspnea
Class III	Marked limitation of physical activity: comfortable at rest but less than ordinary activity results in symptoms
Class IV	Unable to carry out any physical activity without discomfort: symptoms of heart failure are present even at rest with increased discomfort with any physical activity

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## Measurements and instruments

In conjunction with the interviews demographic and clinical data were assessed or extracted from the medical records. The patients were classified according to the NYHA functional classification system (1994) in order to categorize the severity of the heart disability based on symptoms and impaired functional status (Table 3).

Plasma hemoglobin concentration (g/L), measured closest to admission, was analyzed in the hospital central laboratory. The most recent measurement of LVEF was extracted from the hospital record and body mass index (BMI) was calculated from weight and height ( $BMI = \text{weight}/\text{height}^2$ ). Additional questions concerning overall health and QOL were obtained from the EuroHeart Failure Survey. When interviewed, the patients were asked to rate two additional items concerning their perceptions of overall health and QOL on a 7-point scale, ranging from 1 = very poor to 7 = very good.

The following instruments were used in this thesis:

### *Multidimensional Fatigue Inventory*

Multidimensional Fatigue Inventory (MFI-20) is a domain-specific 20-item self-report instrument designed to measure five dimensions of fatigue (General Fatigue, Physical Fatigue, Reduced Activity, Reduced Motivation and Mental Fatigue) (Smets et al., 1995). The instrument was used in all the quantitative studies of this thesis. The standpoint of using the Swedish version of MFI-20 (Fürst & Åhsberg, 2001) is based on the following aspects. The experience of fatigue is rated on a Lickert scale. There have been reported difficulties for older patients to assess their fatigue with visual analogue scales (VAS) (Small & Lamb, 2000). The instrument consisted of few items. It is important to reduce the number of questions as much as possible because patients with CHF are sometimes highly affected by their symptoms. The instrument assesses the individual's experiences over the past few days, which corresponds with the other instruments' windows of self-assessments and with the assessed clinical data.

General Fatigue, which includes general statements about fatigue, such as "I am tired" and decreased functioning is an overall indicator of fatigue and the dimension is sensitive to changes. Physical Fatigue concerns physical sensations related to feelings of tiredness. Reduced Activity refers to a possible consequence of fatigue, namely a decreased

level of activity. Reduced Motivation relates to lack of motivation and starting any activity. Mental Fatigue pertains to cognitive functions, including difficulties to focus and concentrate. The experiences are rated on a 5-point Likert scale, summed for each dimension to yield a range between 4 and 20, where higher scores indicate a higher level of fatigue. The instrument has demonstrated good reliability in different patient populations undergoing radiotherapy (Smets et al., 1995). The Swedish version of the MFI-20 scale demonstrated good internal consistency (Cronbach's coefficient alpha from 0.75 - 0.94) in measuring fatigue in radiotherapy patients (Fürst & Åhsberg, 2001).

#### *Cardiovascular Population Scale*

Uncertainty in illness was measured by the CPS, a disease-specific questionnaire developed by Mishel (1983) from the original Mishel Uncertainty in Illness Scale (MUIS) (Mishel, 1981). The two-factor scale consists of 16 items covering the ambiguity (ten items) the patients with heart disease perceive for that day about the severity of their illness and the complexity (six items) surrounding the treatment. Statements are rated on a 5-point Likert scale (ranging from "strongly agree" to "strongly disagree"). Ratings are summed and range from 16 to 80, where higher scores indicate a higher degree of uncertainty. Previous studies using the Swedish version of the CPS have yielded Cronbach's alphas of 0.71 - 0.74 (Hallberg & Erlandsson, 1991).

#### *Sense of Coherence Scale*

The SOC scale, developed by Antonovsky (1987, 1993), was used to measure the overall personal disposition to manage demanding life situations. The scale measures three dimensions of sense of coherence: comprehensibility (five items), manageability (four items) and meaningfulness (four items). Although the three dimensions are visually separable, the SOC questionnaire was developed to measure the SOC as a global disposition.

In this study, a 13-item version of the scale was used, which is a widely accepted short form of the original SOC scale. Statements are rated on a scale from 1 to 7 and ratings are summed to give total scores ranging from 13 to 91, where higher scores indicate a stronger sense of coherence. The Swedish version of the SOC-13 has been used in several studies in patients with different diagnoses, alphas reported between 0.76 - 0.87 (Eriksson & Lindström, 2005).

### *Hospital Anxiety and Depression Scale*

The Swedish version of the HAD scale is a 14-item scale measuring depression (seven items) and anxiety (seven items) (Zigmond & Snait, 1983). The scale provides information about the patients' emotional state during general hospital admission and can also be used to assess the presence of clinical significant degrees of anxiety and depression. The statements are rated on a 4-point scale and the summed scores on each subscale range from 0 to 7 (non-cases), 8 to 10 (doubtful cases) and 11 to 21 (definite cases). The item-to-subscale reliability correlations are reported as ranging from 0.41 to 0.76 for the anxiety items and 0.30 to 0.60 for the depression items (Bowling, 1998).

### *Symptom Distress Scale*

The Swedish version of the SDS (Tishelman et al., 1991) is a 15-item Likert scale developed from the original SDS of McCorke & Young (1978) and McCorke and co-workers (1998). The scale indexes the subjective distress experienced by patients for the day by measuring the intensity of fatigue, insomnia, appetite, mobility, concentration, mood, outlook, appearance, bowel function, cough, breathing, pain and nausea, with the frequency of pain and nausea also assessed. The statements are rated on a 5-point scale, ranging from absence of symptom to symptom being at its worst. The sum ranges from 15 to 75, with higher scores indicating a higher degree of symptom distress.

The instrument was primarily developed for patients diagnosed with cancer and the selection of symptoms is made among the most distressing physical symptoms associated with cancer and its treatment. It has been used within many clinical populations and in various settings. Cronbach alpha scores are reported between 0.70 and 0.92 in 47 studies, mainly in cancer populations using the English Likert version of 13-items (McCorke et al., 1998), and 0.81 has been reported in a Swedish study with cancer patients (Tishelman, 1993).

### **Statistical analyses**

SPSS statistical software version 11.5 (SPSS, Inc., Chicago, IL) was used for all data analyses. Missing items were extrapolated as the mean of the completed items in the scales or subscales when at least 50% of the items were completed (half-scale criterion). Otherwise, the total scale score was set to missing and excluded from analysis. Descriptive statistics were used to characterize the sample. Frequencies and per-

cents were calculated for categorical variables and means and standard deviations (SDs) for continuous variables.

Chi-square test was performed to compare proportions between nominal and dichotomous variables. Ordinal and continuous variables were compared using independent sample t-tests and ANOVAs. Post hoc comparisons were performed using Tukey's HSD procedure.

Partial correlation was used to explore relationships between fatigue and the perception of health and QOL, adjusting for NYHA. Pearson's correlation coefficient was used to determine potential correlates and to indicate possible multicollinearity before employing the multiple regression analysis (Pallant, 2001). Multicollinearity was also checked by tolerance diagnosis performed by the SPSS. The distribution was plotted to check normality. Hierarchical multiple regression analyses were run to examine the contribution of selected independent variables to the variance in the five fatigue dimensions as measured with the MFI-20. A stepwise forward multiple regression analysis was done to identify distressing symptoms associated with fatigue. All tests were two-tailed and statistical significance was set to  $p < 0.05$ .

### **Constant comparative analysis**

The inductive method of grounded theory was used to guide the analysis of the qualitative data as well as to construct the abstract theoretical categories of the fatigue experience. Grounded theory was originated by Glaser and Strauss in the late 1960s (1967). Both shared the interest in studying social psychological processes within social settings or a particular experience such as having chronic illness (Charmaz, 2006).

The method reflects the two originators epistemological assumptions; logic empiricism and a systematic approach emphasizing the emergent discovery of explaining categories, contrasting with a pragmatic philosophical tradition with symbolic interactionism as theoretical underpinning. This perspective assumes that human beings are active agents that create their own reality through engaging in interactive processes. The social and subjective meanings are relied on our use of language and emerge thought actions. In concordance with the reformulated version of grounded theory by Charmaz (2006), the present study builds on the assumption that data provide an interpretative portrayal of the studied world and the analytical categories are constructed through the

researcher's perspectives, pre-understanding and interaction with the participants. The grounded theory method was chosen because of its emphasis on processes, indicating changes in experiences and behavioral responses and because the study of action is a central focus of the method (Glaser & Strauss, 1967; Morse, 2001; Charmaz, 2006). The inductive method aims to generate analytic categories that culminate in a theoretical framework, grounded in empiric data. The analytical process is accomplished through building levels of abstraction directly from the data that are guided by basic principles including constant comparisons, theoretical sampling and saturation.

In the first step of the data analysis the transcribed interviews were coded and segments of the data were selected, sorted and labeled in order to move beyond concrete statements in the data and begin an analytic account. The transcribed interviews were read several times to obtain a holistic view and understanding about the participants' situation and condition. The transcribed data was then read line-by line and segments of data that included statements about experiences, actions, thoughts, feelings and events related to fatigue was distinguished and labeled.

The initial codes adhered closely to the data without any specific theoretical directions. For example the interviewed persons could describe the features of lacking strengths as (codes in parentheses): "When I walk in stairs, vacuum clean or wash up the dishes I feel that I am too tired to go on. It is too heavy (not capable managing daily chores) I must stay because it feels like I don't get any air (experiencing breathlessness) and I have to rest for a couple of minutes and then it feels okay again (relieving by rest). You can not overcome the tiredness by will (not overcoming by will power). It takes over and the only way to mangle the sensation is by time (reliving by time). When the body moves, then the tiredness appear. It is just to go on until the body says stop. (relating to bodily activity). In my mind I feel I can do things but I can't (discrepancy between imagining and ability)".

The focused coding continued with the development of tentative categories to construction of analytical categories. The internet discussions were analyzed concomitantly, with the intention of seeking specific data to sharpen and refine the categories. Careful attention was given to specific expressions used by the participants that capture the

fatigue experience. (e.g., “the experience is dragging me down, just listen to your body, I have no strength or energy, or I have good days and bad days”).

It ended up in a few conceptual concepts, which comprised the meaning of the initial categories and indirectly the participants’ statements. For example the initial codes that comprehended feelings related to the discrepancy between expectations and ability were defined as demoralizing, which constituted one of the analytical categories that comprised the mental aspects of fatigue experience. There was a high correspondence between the theoretical concepts and the initial codes, reflecting the content in the interviews, which may be regarded as strong evidence of trustworthiness.

Finally, the relationships between the developed theoretical concepts were established and their properties described. Trustworthiness of data and the process of analysis were also ensured by investing sufficient time for the interviews (to build a sense of trust and mutual understanding of the fatigue experience), using data from different sources and audit of the constructed categories by the co-workers, who were all senior researcher in the field of cardiology. Moreover, the findings were compared with research where we found some conceptual congruencies that confirmed our findings.

### **Ethics**

The ethical principles in this thesis follow The World Medical Association Declaration of Helsinki (WMA, 2004) regulations regarding research involving human research subjects. Autonomy, informed consent and the risk of causing emotional discomfort through the questions are ethical issues that have been taken into consideration.

All personal identifications have been removed to ensure anonymity. The data will be saved in discs and kept in a locked file cabinet and will only be used for research purposes. The participants were informed about their rights to withdraw from the study without any particular reason and the possibility to take part of the registered data. The Research Ethic Committee at Göteborg University approved the proposal for Paper I, II and III 2002-08-26 (Ö 307-02) and the Regional Ethical Review Board in Göteborg for Paper IV 2003-05-19 (Ö 253-03).

## RESULTS

The results of the original papers are presented in chronological order. No tables or figures are presented in the presentation and the readers' are referred to the original papers. A summary of the findings will be presented in the end of the result section.

### Paper I

The final study population consisted of 93 patients (48 men and 45 women). The mean age was  $74 \pm 12$  years. Women were significantly older than men: mean  $78 \pm 11$  years versus mean  $71 \pm 11$  years. ( $p = 0.001$ ). Eighty-eight patients (95%) lived at home. Thirty-one (69%) of the women lived alone compared with 20 (42%) of the men. Most of the patients (88%) were retired and 54 (61%) had a relatively low level of education (compulsory school): only 8 patients (9%) had college or university as the highest educational level. NYHA functional class I, II, III and IV were 5, 37, 46 and 5, respectively. No significant differences between gender and age were observed regarding NYHA class.

The etiology of heart failure was ischemic heart disease in 56 patients (63%); of these, 46 (82%) were reported to have had myocardial infarction. Other causes of heart failure were dilated cardiomyopathy (7%) and valve disease (6%). Reported concomitant diseases were diabetes ( $n = 46$ , 50%), disabling stroke ( $n = 2$ , 2%), renal failure ( $n = 7$ , 8%) and respiratory disease ( $n = 16$ , 17%). No correlation was found between these conditions and fatigue experience. Nor did we find any statistical significant differences between the proportion of concomitant diseases in the anemic and non-anemic groups of patients.

No differences in reported fatigue experience were found between men and women. When the patients were divided into three age groups:  $\leq 64$  years ( $n = 19$ ), 65 - 79 years ( $n = 39$ ) and  $\geq 80$  years ( $n = 35$ ), the mean scores for the dimension Reduced Motivation for the group aged  $< 64$  years ( $7.8 \pm 4.0$ ) and the group aged 65 - 79 years ( $9.3 \pm 3.7$ ) were significantly ( $p = < 0.01$ ) lower than for group aged  $> 80$  years ( $12.0 \pm 4.0$ ). No other statistically significant difference was found between age and the other fatigue dimensions.

The mean hemoglobin level was  $133 \pm 21$  g/L. No significant difference was found between men ( $135 \pm 19$  g/L) and women ( $132 \pm 23$  g/L). There was no interaction with age and no significant difference between NYHA class and hemoglobin levels. Anemia, defined as a hemoglobin level  $\leq 125$  g/L, was found in 31 (33%) patients. The mean hemoglobin level in patients with anemia was  $110 \pm 14$ g/L ( $114 \pm 11$  g/L for men ( $n = 15$ ) and  $107 \pm 17$ g/L for women ( $n = 16$ ). No statistical differences were found between anemic and non-anemic patients on gender, age and NYHA class, or between anemic and non-anemic patients because of etiology of heart failure.

Anemic patients reported significantly more fatigue compared with non-anemic patients on all MFI-20 dimensions, except for Reduced Motivation. Severe anemia ( $\leq 109$  g/L) was found in ten patients (three men and seven women) and moderate anemia ( $110$  g/L –  $125$  g/L) in 21 patients (twelve men and nine women). No significant difference in reported fatigue was found between patients with moderate and severe anemia.

Multiple regression analysis was used to explore the relationship between the five dimensions of fatigue and NYHA class and hemoglobin levels, controlling for age and gender. The analysis indicated that 30% of the variance in General Fatigue were explained by decreased hemoglobin level ( $\beta = -0.23$ ) and higher NYHA classes ( $\beta = 0.47$ ), whereas 21% of the variance in Physical Fatigue and 8% of the variance in Reduced Activity were accounted for by a poorer (higher) NYHA class. There were no significant associations between Reduced Motivation, Mental Fatigue, and NYHA class and hemoglobin values. The variance in Reduced Motivation was significantly explained only by age ( $r^2 = 0.16$ ).

The relationships between the fatigue experience and perceived global health and QOL were explored. After controlling for NYHA class, significant negative correlations were found. Age and gender were unrelated to either perceived global health or QOL.

## **Paper II**

The previous presentation of the patients' demographics and clinical status in is consistent with the studied sample in this paper. The highest mean scores of fatigue were found in General Fatigue ( $14.5 \pm 4.6$ ),

Physical Fatigue ( $16.1 \pm 4.2$ ) and Reduced Activity ( $14.0 \pm 4.5$ ), closely followed by Reduced Motivation ( $10.0 \pm 4.2$ ) and Mental Fatigue ( $9.8 \pm 4.5$ ). The scores in each fatigue dimension were categorized as none (score 1 – 4), mild (score 5 – 8), moderate (score 9 – 12), severe (score 13 – 16) and very severe (score 17 – 20). This categorization was applied in order to explore the prevalence distribution in relation to fatigue severity across the fatigue dimensions, as measured with MFI-20. Only one patient reported no fatigue experience at all. The highest prevalence of very severe/severe fatigue was noted in the Physical Fatigue dimension ( $n = 77, 83\%$ ), followed by General Fatigue ( $n = 66, 71\%$ ) and Reduced Activity ( $n = 59, 63\%$ ). The prevalence rates of very severe/severe fatigue were less prominent in Reduced Motivation and Mental Fatigue. NYHA class was significantly associated with General Fatigue, Physical Fatigue and Reduced Activity. Significant differences ( $p < 0.05$ ) were found between General Fatigue and all four NYHA classes (I,  $7.0 \pm 2$ ; II,  $13.0 \pm 5.0$ ; III,  $16.2 \pm 3.2$ ; and IV,  $17.4 \pm 2.6$ ).

A series of regression analyses were performed to determine the relative contribution of SOC and uncertainty to the variance in the fatigue dimensions, controlling for possible effects of correlating demographic and clinical variables. NYHA (correlating with General Fatigue, Physical Fatigue and Reduced Activity) and age (correlating with Reduced Motivation), were entered in the first step, followed by SOC and uncertainty, which were entered one at a time. The contribution of SOC on the variance of General Fatigue (6%) was significant after controlling for NYHA. Uncertainty accounted for a small portion (4%) of the variance in Physical Fatigue, whereas neither uncertainty nor sense of coherence had any influence on Reduced Activity. Age explained 18% of the variance in Reduced Motivation and 20% of the variance in Mental Fatigue was explained by SOC.

### **Paper III**

Based on our findings, fatigue can be described as a circular process between the experience and the consequences of being fatigued (i.e. the vicious circle of fatigue). The process of being fatigued indicates that the consequences of fatigue further exaggerate the experience of the symptom. Such exaggeration could be alleviated by identified and employed restorative activities. The description of the bodily experience of fatigue was defined as lacking strength, feeling sleepy and

lacking energy. The mental aspects included feelings of demoralization and experiencing intellectual deficiency. Fatigue led to sacrificing, which the patients described as refraining, denying oneself and being isolated. The restoring aspects were defined as being involuntarily attentive, being socially interactive and being mentally absorbed.

The patients described the physical experience of tiredness as a decrease or lack in strength. The feeling of tiredness was related to physical activity and could be alleviated through resting or slowing down their activity level. The sensation was not possible to overcome by will power. Another dimension of fatigue was described as being sleepy, often with a rapid and unforeseen onset. The sleepiness could be interrupted with external stimuli and relived by voluntary efforts and sleep. Lacking energy was described as an overwhelming and unknown experience that interfered with the whole person. The sensation was described as “dragging the person down” and impossible to overcome by will power alone. The experience fluctuated with good and bad days, normally occurring with regularity. The sensation affected the patients emotionally, making them sad, angry or irritated. The loss of energy could be regained by resting periods throughout the day.

The fatigue experience also had other mental implications. Patients expressed guilt feelings because they could not manage what they or persons closest to them expected. They blamed themselves because their own incapacities restricted not only themselves but also influenced the life of all members of the family. They felt humiliated that others could see how bad their condition really was and fear of not being able to manage and control unknown situations. They also experienced memory loss and difficulties with mobilizing intellectual energy and many patients reported lack of creativity.

The fatigue experience had notable consequences for all patients and was reported to result as patients making sacrifices. A consequence of fatigue was that fatigue forced the patients into inactivity by refraining from daily chores and to participate in recreational activities. The fatigue experience forced the patients to relinquish opportunities for rejoicing and prohibited them from doing things they valued in life and to plan for the future. Their socially integrated life was negatively affected because of an ever-decreasing social life and many patients felt as though they were prisoners in their own homes.

Besides purposeful strategies (e.g., reducing or slowing down activity, resting or sleeping) some restorative efforts were identified. Restoration of fatigue was reported to result when patients engaged in activity that distracted them and/or repressed the experience of fatigue. These activities were characterized by not having a specific purpose or that required conscious effort, such as appreciation of phenomenon in nature or mental experiences that stimulated sensations of happiness, curiosity and satisfaction. Commitment to preferred activities reduced the likelihood of fatigue and diminished the severity of the fatigue experience. Leisure activities and meeting other people preoccupied their mind made them simply forget how tired they were.

#### **Paper IV**

The final study sample consisted of 112 hospitalized patients with CHF. The mean age was 77 years  $\pm 10$ , with a range from 44 to 99 years: men; 76 years  $\pm 10$ , women; 79  $\pm 10$  years. Men were more likely to be married (79% vs. 21%,  $p = 0.001$ ) and more likely to have a higher educational level ( $> 9$  years) (85% vs. 15%,  $p = 0.01$ ). No gender or age differences were noted in functional status (NYHA), BMI, systolic blood pressure and pitting edema. No patient was identified as NYHA class I, 20 (18%) patients were classified as NYHA II, 82 (73%) as NYHA III and 7 (6%) as NYHA IV. LVEF was significantly lower ( $\leq 20\%$ ) in men (76% vs. 24%,  $p = 0.01$ ) and coronary artery disease (69% vs. 31%,  $p = 0.02$ ) and myocardial infarction were more prevalent in men. There were no gender or age differences in pharmacological treatment of CHF though antidepressants were more common in women (61% vs. 39%,  $p = 0.04$ ). Reported concomitant diseases were hypertension,  $n = 56$  (50%), diabetes mellitus  $n = 45$  (40%), cerebrovascular incidence (CVI),  $n = 25$  (22%), respiratory disease,  $n = 24$  (21%) and renal diseases,  $n = 10$  (9%).

The highest mean scores of fatigue were noted in General Fatigue ( $15.6 \pm 4.5$ ), Physical fatigue ( $16.8 \pm 3.9$ ) and Reduced Activity ( $15.4 \pm 4.6$ ), followed by Reduced Motivation ( $10.0 \pm 4.2$ ) and Mental Fatigue ( $8.8 \pm 4.4$ ). No differences in gender and age were found. CVI was significantly associated with General Fatigue ( $r = 0.310$ ,  $p = 0.01$ ) and with Physical Fatigue ( $r = 0.203$ ,  $p = 0.05$ ).

The mean score for anxiety was  $4.9 \pm 3.9$ , for depression  $6.4 \pm 4.5$  and for symptom distress  $36.2 \pm 9.3$ . There were no differences between

men and women in reported levels of fatigue, anxiety or depression but women reported significantly more symptom distress ( $p = 0.02$ ) than men.

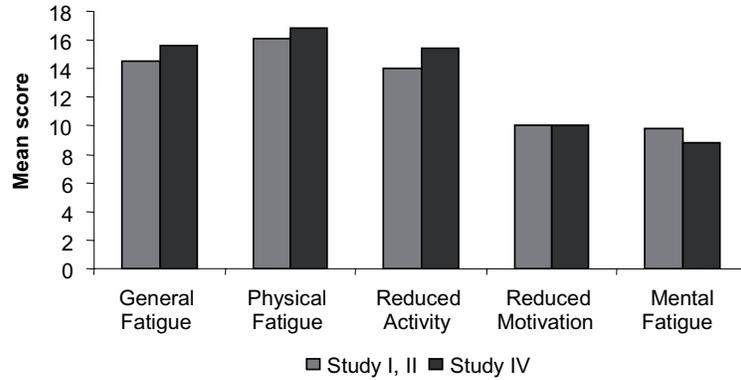
For the purpose of evaluating the independent contribution of anxiety, depression and symptom distress on the variance of fatigue, a hierarchical multiple regression analysis was performed, adjusting for the confounding variables. The analysis showed that anxiety explained 25% of the variance in Mental Fatigue and depression explained 15% of the variance of General fatigue, 18% of reduced Activity and 11% of Reduced Motivation. Symptom distress explained only a small portion of the variance in General fatigue (4%), Physical Fatigue (5%) and Mental Fatigue (3%).

The most distressing symptoms, measured as intensity according to SDS, were fatigue, difficulties with breathing and insomnia. The symptoms that made the strongest contribution of the variance in fatigue were nausea, bad appetite, pain, difficulties with breathing, bad mood and difficulties with concentration. With the exception of difficulties in breathing, it was not the most dominating reported symptoms that were associated with the different fatigue dimensions. Difficulties in breathing ( $\beta = 0.3$ ,  $p = 0.001$ ), bad mood ( $\beta = 0.24$ ,  $p = 0.01$ ), bodily pain ( $\beta = 0.22$ ,  $p = 0.05$ ) and nausea ( $\beta = 0.18$ ,  $p = 0.05$ ) explained together 31% of the variance in General Fatigue ( $p = 0.001$ ). Bad appetite ( $\beta = 0.26$ ,  $p = 0.01$ ) and bodily pain ( $\beta = 0.22$ ,  $p = 0.05$ ) accounted for increased Physical fatigue ( $r^2 = 0.13$ ,  $p = 0.001$ ). Bad mood ( $\beta = 0.23$ ) and nausea ( $\beta = 0.23$ ) were related to Reduced Activity ( $r^2 = 0.12$ ,  $p = 0.01$ ). Bad mood was also associated with Reduced Motivation ( $r^2 = 0.07$ ,  $p = 0.01$ ) and difficulties in concentrating explained 28% ( $p = 0.001$ ) of the variance in Mental Fatigue.

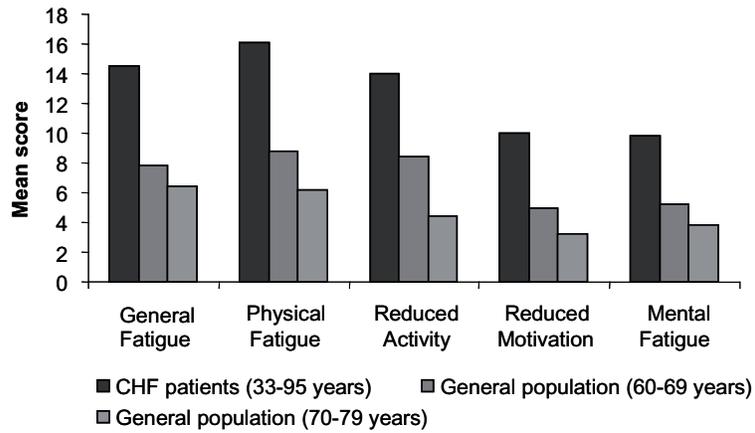
### **Summarize of the main findings**

Studies I, II and IV were carried out with two different samples of patients. A comparison between the two quantitatively studied samples showed no significant differences in reported fatigue scores more than in the Reduced Activity (Figure 1). An explanation why the patients in the last study experienced more reduced ability to accomplish activities is their significantly poorer functional status (higher NYHA class) ( $p \leq 0.001$ ). The patients in Study I and II reported significantly higher fatigue scores in all MFI-20 fatigue dimensions as compared with a

general Nordic population ( $p = \leq 0.001$ ) (Watt et al., 2000). This finding verifies that patients with CHF experience fatigue to greater extent compared with persons of the same age. The reported fatigue scores are shown in Figure 2.



**Figure 1.** Comparison between the two samples in Study I, II and IV.



**Figure 2.** Comparison of fatigue scores as measured with MFI-20 between a general Nordic population with CHF in Study I and II.

The main findings in this thesis were:

- Fatigue experience involves the whole person. It embraces the body, emotions and cognitive abilities and must be considered within the context of the patients' daily life.
- The physical sensation of fatigue followed by functional limitations seems to be the most prevalent and distressing experience in patients with CHF.
- Fatigue was described by the patients as lacking strength in direct connection with physical efforts. Fatigue was also described in terms of lack of energy. This lack of energy was experienced as an annoying sensation occurring with delay after both mental and physical strain. Another dimension of fatigue was described as being sleepy, often with a rapid and unforeseen onset.
- One third of the patients were anemic and reported more fatigue compared with those who were not. Decreased hemoglobin level may be an additive factor that further exaggerates the general experience of fatigue.
- Depressed mood was related to those dimensions of fatigue that compromised functional ability and motivation to start any activities, suggesting that the relationship increased the patients' state of inactivity.
- Mental fatigue was affected by low SOC and associated with anxiety, which suggest that the decreased ability to manage problems in every day life was associated with difficulties in focusing thought and concentration.
- Physical tiredness was related to feelings of uncertainty that might be imposed by limitations in performing activities, reminding the patients about their chronic heart disabilities.

- Symptom distress that is caused by a number of reported symptoms had a diminutive influence on fatigue. Separate symptoms that were associated with fatigue were, with the exception of breathlessness, not the most dominant symptoms reported by the patients.
- Men and women did not report fatigue differently, but high age was associated with reduced motivation. No relationships were found between demographics, clinical variables and diagnostic signs, except for NYHA class, which was associated with those fatigue dimensions that encompassed physical tiredness and reduced functioning.
- Consequences of fatigue, such as refraining from daily chores, denying oneself opportunities for rejoice and social isolation, further exaggerated the experience of fatigue. Restorative activities that engaged, absorbed or distracted the patients counteracted these consequences.
- Fatigue affected the patients' perception of health and QOL.

## DISCUSSION

Fatigue is a symptom that is difficult to articulate and interpret, which makes the assessment and measurement challenging. Although there are several more or less identified organic mechanisms that may be responsible for the cause of fatigue, it is difficult to identify the relationships between biological markers for changes in bodily composition or signs for pathological processes and the subjective experience of fatigue. There are also obstacles in demonstrating linear relationships between the subjective expressed fatigue and the presence of signs that establish the severity and progress of the heart disability. Sometimes patients with very severe heart failure can exhibit less fatigue than patients with more moderate heart disability. The reason for this may be that the subjective experiences of a symptom always interfere with a variety of influencing factors, more or less communicative and possible to identify.

The main findings in this thesis emphasize a comprehensive understanding of the subjective interpretation and communication of fatigue. This knowledge emanates from the patients everyday life and includes their thoughts, acts and those components of life that give a unique meaning to the symptom experience.

Our findings indicate that fatigue in patients with CHF is an experience that embraces the body, emotions and cognitive abilities, forcing the person to physical restrictions, which, in turn, perpetuates feelings of limitations and emotional discomfort. General and physical fatigue was reported as the most prevalent and severe dimensions of fatigue along with reduced ability to perform activity. Uncertainty was associated with physical tiredness and limitation in the functional ability.

The sensation of tiredness is disabling and may contribute to feelings of uncertainty by reminding the patients about their ongoing heart disability and the unstable and unpredictable future. One conclusion may be that uncertainty is primarily related to the symptom distress and consequences of the symptom and not exclusively to symptom severity. Mishel (1999) calls attention to the fact that management of uncertainty should not only be focused on relieving symptom experience but also on helping the patients to accept uncertainty as a reality of life.

Not surprisingly, we found a strong relationship between NYHA functional classification and those dimensions of fatigue that encompassed physical tiredness and reduced functioning because fatigue in exertion is one of the variables that is included in the NYHA functional classification system. Previous research on fatigue in patients with CHF has often equated the experience of fatigue with limitations to functional ability. However, our present studies expand the existing literature by showing that fatigue in CHF is greater than decreased functional status.

Functional status assessed by care providers and scored using the NYHA classification is the most common way in clinical work to assess fatigue in patients with CHF. Bennett and co-workers (2002a) have shown that the NYHA classification system is a valid measurement instrument but suggested that patients' self-report may be a more appropriate way for measuring functional status related to symptoms of CHF. The ability to perform activities may not only be limited by symptoms of heart failure (fatigue and breathlessness) but also by a variety of personal, environmental and social factors. Recently, research has also shown discrepancies between the patients' self-assessment of their symptoms and the assessment of NYHA performed by health providers (Ekman et al., 2005a).

Moreover, functional status, as measured with NYHA class, is used as a prognostic marker as well as to categorize the severity of the heart disability. After adjusting for NYHA class, we found that most of the fatigue dimensions, as measured with MFI-20, were negatively associated with the perception of global health and QOL. This observation means that physical fatigue has an independently strong impact on the perception of health and that both physical and mental aspects of fatigue influenced the QOL. The finding is consistent with a study showing that the general sensation of fatigue (measured with MFI-20) was significantly related to lower HRQOL (Hägglund et al., 2006).

HRQOL is considered an outcome criterion for symptom experience and its consequences in daily life and a tool for evaluating interventions aimed at alleviating the symptom. Patients' self appraisals of their HRQOL seem to be a better indicator of symptom experience and its consequences than objective indicators of heart severity. The

presumption is supported by Lewis and co-workers (2007) who found that greater symptom burden and worse functional status were associated with worse HRQOL, regardless of the heart condition measured with LVEF.

Objective indicators of severity of heart failure (LVEF), perfusion (systolic blood pressure) and oxygen delivery (hemoglobin concentration), together with assessment of under or overweight (BMI), were analyzed in relation to fatigue. We found that anemic patients were more physically and mentally fatigued than non-anemic patients and that decreased hemoglobin level predicted the sensation of general fatigue. Because anemia is common in patients with CHF, it is important to recognize the hemoglobin concentration in fatigued patients and, if possible, correct decreased levels in order to reduce fatigue and improve functional status and HRQOL (Silverberg et al., 2000).

Even though LVEF is related to worsening of CHF and death, it is of less importance in comparison with symptoms (Ekman et al., 2007). With one exception (Scheafer, 1990), no relationships have been observed between fatigue and LVEF, which is consistent with our findings.

Both cachetic and obese patients are at risk to be fatigued but we could not establish any associations even though 61% of the patients were judged overweight or obese (only 4% were underweight).

Peripheral hypoperfusion is regarded as one factor contributing to fatigue (Swedberg et al., 2005). Low systolic blood pressure has been detected in patients with cognitive impairment, which may be a result of reduced cerebral perfusion (Zuccalá et al., 2005); however, no association was found between systolic blood pressure and mental fatigue in our study.

No relationships with concomitant diseases were found besides the association of CVI and general and physical fatigue. This does not mean that patients suffering from these diseases are not experiencing fatigue (fatigue is a common complaint in patients with chronic diseases) but the rare number of reported comorbidity in our studies did not contribute to any statistic interference.

We did not find any differences between men and women regarding self-reported experiences of fatigue. This finding contrasts to a recent study in which women reported higher degrees of general fatigue and reduced activity (Hägglund et al., 2006). Women were slightly older than men and older age was associated with reduced motivation. Women were overrepresented in the group aged > 80 years where the highest mean score in the Reduced Motivation was reported.

Moreover, it has been noted that older patients explain their fatigue as a natural part of the aging process and therefore did not relate the experience to their heart disability (Friedman, 1997; Ekman & Ehrenberg, 2002c). Jurgens (2006) found that 71% of the patients with acute heart failure complained of fatigue but fatigue was not the motivating force in seeking hospital care. Rather than a normal aging process, one explanation could be that even if the patients are aware of their symptoms, they delay care until the symptom interferes with their daily activities. Fatigue has an insidious and slow development and the patients may get used to the sensation and accept it as a part of their lives or they do not know that exaggerating fatigue may be a “sign” of a worsening heart condition. Our findings support another possible reason for delay. The fatigue experience itself, with reduced motivation and demoralization, may explain why patients refrain from seeking health care.

Depression and feelings of demoralization were associated with fatigue. Depression seems to be associated with those fatigue dimensions that comprised reduction of activity, low motivation and decreased functioning. Depressed mood leads the patients into an inactive state, with not only a physical lack of energy to take part in daily activities but also a mental lack of energy to initiate intended physical work. In contrast, feelings of helplessness and hopelessness were associated with the complex experience of fatigue, i.e. lacking strength, feeling sleepy and lacking energy.

There is a strong association between depressive symptoms and adverse outcome of CHF, but the reason is unknown (Rumsfeldt et al., 2003). Behavioural responses that are due to depressed mood and fatigue could be one explanation in the sense that the patients may be at risk for non-adherence to prescribed treatment and inability to manage symptoms properly. However, it may sometimes be difficult to extract

the response from one symptom from the total experience of being ill. The fatigue experience may be an emotionally charged negative accelerator of a larger illness complex and therefore the relation between mood changes and fatigue must be interpreted with caution.

Mental fatigue (e.g., difficulties to concentrate and focus, affecting thoughts and cognitive ability) was associated with both anxiety and low SOC. Anxiety is a future-oriented negative affect state resulting from perceptions of threat and typified by an inability to predict, control or obtain desired results in upcoming situations (e.g., difficulties to adopt adequate coping strategies) (Jiang et al., 2004). SOC comprises the overall personal disposition to manage stressors in daily life. The strong association found between anxiety and mental fatigue may have been mediated through an impaired ability to manage problems in daily life. Our findings can be interpreted to mean that when persons with low SOC or anxiety are exposed to stressful situations, their ability to concentrate and solve problems is decreased and experienced as mental fatigue.

The patients' experience of total symptom distress was not related to fatigue to the extent that we expected. Women reported higher symptom distress than men in our study even though we did not find any differences in fatigue experience or severity of CHF. Why women experience more distress relating to fatigue is not clear. The meanings ascribed to symptoms are relative to one's life situation and symptom distress increases when the symptoms entail alteration (restrain or produce) of actions in response to the experiences (Rhodes & Watson, 1987). Perhaps the burden of symptoms and lack of strength afflicts women more than men because of their endless work in the domestic domain, afflicting the traditional female role identity. Moreover, it may be easier for women to communicate and express their emotional response to the symptoms according to social conventions about feminine and masculine characteristics.

A noteworthy finding in our study was the poor agreement between fatigue and the most prevalent reported distressing symptoms. With exception of breathlessness, less intense symptoms, such as nausea, bad appetite and bodily pain were significantly associated with the general and physical dimensions of fatigue. These findings motivate the need to recognise the patients' appraisal of all experienced symptoms, ei-

ther typical or atypical of heart failure (Patel et al., 2006) Symptoms that the caregivers do not expect to find in patients with CHF may be those that reinforce the experience of fatigue.

In addition to the quantitative measurements of fatigue and relating manifestations, in the qualitative study we identified some different categories of fatigue that comprised a deeper understanding of the meaning of fatigue and its relation to everyday life for the patients. Unique for our data was the clear distinction between lacking energy and lacking strength and its relationship to activity. Whereas lacking strength seemed to appear in direct connection to physical efforts, lacking energy mainly occurred with delay after both mental and physical strain. The two categories were, to a certain extent, congruent with previous use of the terms tiredness and exhaustion (Glaus, 1998; van Diest & Apple, 1991), which confirms the independent properties of the dimensions we identified.

It is difficult to see the correspondence between the patients' description of fatigue as lacking strength and lacking energy and the fatigue dimensions Physical Fatigue and General Fatigue in the MFI-20. However, there are some similarities. The Physical Fatigue dimension concerns the physical sensation of fatigue as related to tiredness while General Fatigue embraces the whole person concerning his or her functioning. However, none of the MFI dimensions clarifies the fatigue experiences in relationship to activity, which is one crucial point in the patients' own descriptions.

A third patient experience of fatigue identified in this study was described as being sleepy, with a rapid and unforeseen onset, followed by embarrassment. We have not found any studies that define "feeling sleepy" as a dimension of fatigue in patients with CHF. The different characters of fatigue described by the patients required different strategies to be managed and, taken together, they resulted in notable consequences, which further exaggerated the experience of fatigue. The findings made us aware of the need to break the viscous circle of fatigue. In addition to self-care strategies such as rest and exercise in well-balanced proportions, restorative activities must be individually adopted as they seem to counteract the negative consequences of fatigue.

## CONCLUSIONS

This thesis provides increased knowledge concerning fatigue in patients with CHF. It provides new insights about the characteristics and manifestations of fatigue and what consequences the experience has for the patients' everyday life. The present study also expands existing knowledge about patients with CHF by showing that a number of selected physical and psychological factors are related to the fatigue experience. One of the most intriguing findings was the distinction between lacking strength and lacking energy and its relationship to activity. The experience of feeling sleepy was reported as a significant problem, irrespective of sleep patterns. The different dimensions of fatigue emphasize the need for thorough and exhaustive assessment of fatigue and recognition of what eases or worsens the problem.

Some of the studied variables, such as low hemoglobin level, depressed mood, anxiety and uncertainty, were associated with different dimensions of fatigue. All of these afflicting conditions may be possible to influence by appropriate interventions and thus indirectly relieve the fatigue experience. Nausea, poor appetite and bodily pain were not the most dominating symptoms reported, yet they were associated with fatigue. This finding emphasizes the importance of comprehensive assessment and a broad approach to interventions because reduction of fatigue may get through alleviation of more manageable influencing symptoms.

The importance of restorative activities in order to comfort and relieve suffering is sorely underestimated in the care of patients with CHF. Our findings reveal the necessity to support patients in their effort to adopt and create such activities. Altogether, these findings should lead to a better understanding of the patients' situation and improve patient care. The present findings challenge us to be accountable to our patients and participate with compassion and commitment in supportive interventions that help them with their experience of fatigue.

## METHODOLOGICAL CONSIDERATIONS

There are several issues related to the statistical procedure that need to be addressed. First, no power analysis is presented. It is relevant in studies with hypothesis testing designs, but less relevant in descriptive studies. The risk of a Type II ( $\beta$ ) error is obvious in small samples. A Type II error here refers to the risk of drawing the conclusion that no association exists when in fact one does (Altman, 1999). Because the two samples in studies I, II and IV only showed significant differences in Reduced Activity dimension, we can exclude the probability of a Type II error. Type I ( $\alpha$ ) error refers to the risk of making the conclusion that relationships exist when they do not. This type of error occurs when a number of statistical calculations are performed and that anyone of these is caused at random (Altman, 1999). Even though the statistical significance was set at  $p < 0.05$ , many of the calculations showed significance at  $p < 0.01$ , which reduces the possibility of a Type I error.

Multiple regression analysis was used to explore the relationships between fatigue and a number of influencing variables. According to Stevens (1996), approximately 15 subjects per predictor are needed for a reliable equation. Because fatigue is a multidimensional phenomenon that is influenced by many factors, we had to select and consider the choice of independent variables cautiously so that the available sample size was not exceeded. However, one should consider that the study was conducted among a relatively small sample, but representative when comparing with other studies in CHF patients. Information on all factors that could possibly influence the fatigue experience is unavailable and the possibility that the sample does not represent the entire population of patients with CHF must always be taken into consideration.

Second, there are disadvantages in measuring categorical variables (such as fatigue) with the scales used in this study. The MFI-20 has no defined cut-off scores, which precludes any judgments of the presence or absence of clinical significant levels of fatigue. To make any assumptions about the fatigue severity on a group level, comparisons must be made with results from other studied groups. On an individual level, it is important to notice any changes, irrespective of the magnitude of the change. The MFI-20 fatigue scale has not been validated in

heart failure patients. In the physical dimensions in fatigue (General fatigue, Physical fatigue) there was a ceiling effect, indicating that the scales do not discriminate properly at the higher levels of fatigue. This is a limitation that needs to be considered when the results are analyzed.

We chose to describe and analyze the fatigue scores as continuous variables, which enabled us to compare and evaluate our results with those from other studies where mean (SD) was calculated. However, only small differences were found when the data were analyzed using nonparametric methods (Spearman's Rank Order Correlation, Kruskal Wallis test and the Mann-Whitney U Test). We wanted to calculate the associations between the main variables, adjusting for the effect of influencing factors with multiple regressions. Such an analysis implies continuous data. To be consequent in the assumptions drawn from the data and in the choice of statistical methods, we used parametric methods throughout all studies.

Third, the cross-sectional nature of our data inhibited the possibility to make causal interference on the effect of the categorical independent variables on fatigue. The relationships between the independent and dependent variables may be bidirectional or it may be fatigue that determines the levels of some of the independent variables. Consequently, directionality and revealed connections cannot be ascertained, and the influence of the studied variables on fatigue is therefore expressed as associative rather than predicative.

## CLINICAL CONSIDERATIONS

Casillas (2006) proclaims that the ambition to reduce fatigue in patients with CHF is threefold: improve independence, improve quality of life and limit morbidity and mortality. Although medical treatment and self-care strategies aimed at improving heart condition and reducing systemic affects of heart failure are important, the goal of care may not be the total alleviation of fatigue but to decrease the burden and consequences of fatigue.

The patients with CHF are suffering from fatigue. According to Morse (2002), nurses are the “caretakers of suffering” because they are close to the patients and their families and therefore in a position to ease and relieve the suffering and to provide comfort when it is needed. To accomplish comfort and support to patients that suffer is an integral part of the caring process. We must start with exploring the nature of the illness experience in order to develop strategies that support patients who are trying to cope with their suffering or to decrease the patients’ burden from a specific symptom.

Several authors propose pedagogical strategies for patients with CHF as a means of helping them to live with and manage their symptoms (Ekman et al., 2000; Jaarsma et al., 2000). Based on our findings, we suggest that interventions address different aspects of the fatigue experience, such as recognition, evaluation and monitoring the severity and changes of fatigue. By giving the patients the time and opportunity to describe the fatigue experience, we could better target and refine the care and treatment for those most in need. It is sometimes difficult to find adequate strategies in the alleviation of fatigue; however, more manageable influencing symptoms and treatable physiological factors may be one way to decrease the severity of fatigue.

Psychological responses to fatigue (such as uncertainty, distress and mood disturbances) may be affected by attitudes, expectations and knowledge. Pedagogical strategies aimed at clarifying the meaning of fatigue and to confront the situation may help patients in reappraising the situation positively. We suggest the use of a narrative approach as a means of facilitating comprehensibility, manageability and meaningfulness. By recounting the experience of a symptom or illness, the patients may be aware of the nature of their problem and how to deal

with the situation (Ekman et al., 2005b). Acceptance of the illness as a reality of life may lead to new values and perspectives, which in turn may help to expand the patient's options and choices.

Attention must be given to the consequences of fatigue in daily life. Isolation and inactivity exaggerate fatigue, which undoubtedly leads to more inactivity and isolation. One way to help patients relieve the fatigue burden would be to provide them the necessary support in interrupting the vicious circle of fatigue by identifying restorative activities. These restorative activities are individually adopted and created from each person's ability and prerequisites. By giving the patient support with the necessary life-sustaining efforts and practicing how to set their own priorities and concentrate on what is important for them, they can preserve their energy supplies for relevant and meaningful activities.

## FURTHER RESEARCH

The issues regarding fatigue could not be solved within this thesis. There is much left to be done. First, more research must be carried out to clarify the origin and pathology of fatigue. The bridge between subjective experience and objective physiological processes must be explored and selected biological markers measured and analyzed in relation to fatigue (e.g., corticosteroids, catecholamines, cytokines and oxytocin). The credibility of the knowledge involving symptom experience may be enhanced when objective parameters or phenomena relating to the symptom are identified.

Second, comprehensive understanding about influencing variables must be endeavored. Treatment and care regimes, clinical variables, illness history and personal attitudes and expectations must be further analyzed in relation to fatigue. Longitudinal or interventional studies, employing causal modeling techniques, are needed to elucidate the relationships between fatigue and other categorical trait variables (e.g., identify predictors of fatigue). Inductive studies exploring the fatigue experience in different patient samples aimed at developing formative theories of fatigue and further clarify theoretical and operational definitions of fatigue are needed.

Third, there is a need for the development of theoretically driven domain- and disease-specific measurement instruments, conceptually mapping the various dimensions of fatigue. Symptom measurements with validated instruments are important because it gives us the opportunity to compare findings from different settings and patient samples. Although valid instruments are used in the interpretation of the significant level or changes in the subjective ratings of the symptom, levels of cut-off limits of severity or distress remain a challenge. However, patient self-reports must be the primary source of information and be considered as the gold standard for all measurements of symptom experience.

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