Published in final edited form as:

Clin Nurs Res. 2012 August ; 21(3): 271–293. doi:10.1177/1054773811419842.

Determinants of Excessive Daytime Sleepiness and Fatigue in Adults with Heart Failure

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Abstract

Little is known about excessive daytime sleepiness (EDS) in heart failure (HF). The aim of this cross-sectional descriptive study was to describe the prevalence of EDS and factors associated with it in HF. A secondary purpose was to explore the correlates of fatigue. We enrolled a consecutive sample of 280 adults with a confirmed diagnosis of chronic HF from three outpatient settings in the northeastern US. Patients with major depressive illness were excluded. Clinical, sociodemographic, behavioral, and perceptual factors were explored as possible correlates of EDS. Using an Epworth Sleepiness Scale score >10, the prevalence of EDS was 23.6%. Significant determinants of EDS were worse sleep quality ($p=0.048$), worse functional class ($p=0.004$), not taking a diuretic ($p=0.005$), and lack of physical activity ($p=0.04$). Only sleep quality was

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associated with fatigue ($p<0.001$). Sleep disordered breathing was not significantly associated with EDS or with fatigue. These factors may be amenable to intervention.

Keywords

fatigue; physical activity; exercise; diuretics; functional class; excessive daytime sleepiness; heart failure

Determinants of Excessive Daytime Sleepiness and Fatigue in Adults with Heart Failure

Heart failure (HF) affects almost 6 million Americans (2.4% of the population) (Roger et al., 2011) and as many as 70% of these patients report poor sleep (Jaarsma et al., 1999). Adults with HF have more frequent wake bouts, poorer overall sleep quality, and more excessive daytime sleepiness (EDS) than adults without HF (Redeker & Stein, 2006). EDS can be disabling, reducing waking performance, (Philip et al., 2008) increasing psychosocial stress, (Redeker, 2006) and decreasing quality of life (Skobel et al., 2005).

What This Study is About

This study is about EDS and fatigue in adults with HF. This is an area of research that is new in HF and the correlates of EDS are unknown in these patients. Fatigue is very common in HF and patients have difficulty discriminating between EDS and fatigue. So, we also explored the prevalence and correlates of fatigue as well.

What is Known about Excessive Daytime Sleepiness

EDS refers to difficulty maintaining a desired level of wakefulness with a feeling of being drowsy during wakeful states (Ohayon, 2008; Young, 2004). The prevalence of EDS in adults with HF is unclear. In the general population EDS has been reported in 8% (Johansson et al., 2010) to 20% of samples (Whitney et al., 1998). In adults with HF, there is considerable overlap with the general population, with rates between 15% and 44% reported (Brostrom, Stromberg, Dahlstrom, & Fridlund, 2004; Javaheri et al., 1998; Johansson, Alehagen, Svanborg, Dahlstrom, & Brostrom, 2009; Johansson, et al., 2010; Redeker & Stein, 2006; Staniforth, Kinnear, Starling, & Cowley, 1998).

The factors associated with EDS in adults with HF have not been explored previously. Correlates of EDS have been explored in other populations with mixed results. For example, in the Cardiovascular Health Study of 4578 Medicare enrollees in the US, factors associated with EDS were non-white race, depression, loud snoring, awakening with dyspnea or snorting, frequent nocturnal awakenings, HF medications, non-use of sleeping pills, a sedentary lifestyle, and limitation of activities of daily living (Whitney, et al., 1998). In a population-based sample of middle-aged (mean 47 ± 8 years) adults ($n=2913$), EDS was related to gender (females), age (younger), and higher sleep debt (Kim & Young, 2005). A consistent finding across several of studies is that EDS is not associated with sleep disordered breathing (SDB) in adults with HF (Michael Arzt et al., 2006; Ferreira et al., 2010; Johansson, Alehagen, Svanborg, Dahlstrom, & Brostrom, 2009; Kaneko et al., 2003; Redeker, Muench, et al., 2010). But, in a sample of 293 older adults without HF (mean 78 years, range 65–98 years) EDS was associated with gender (males), severe sleep-disordered breathing (SDB), poor sleep quality, increased percentage of time in rapid eye movement sleep, frequent pain at night, wheezing or whistling from chest at night, and daytime medications with sleepiness as a side effect (Pack et al., 2006). Alcohol use reduced the risk

of EDS. The only consistent factor among these samples was poor sleep quality. These mixed findings highlight the need for further study of EDS in adults with HF.

Since the prevalence of EDS in adults with HF is still in question and the correlates of EDS are unknown in adults with HF, the primary purpose of this study was to describe the prevalence of EDS and the factors associated with it in this population. Specifically, we sought to identify contributors to EDS in HF patients that may be reversible and potentially amenable to intervention.

A secondary purpose was to explore the prevalence and correlates of fatigue because patients have difficulty differentiating between EDS and fatigue (Hossain et al., 2005; Singareddy, Bixler, & Vgontzas, 2010). Both symptoms are cardinal indicators of cytokine-induced sickness behavior, which is now recognized as an important contributor to the HF symptom experience (Dantzer & Kelley, 2007). In response to an infection, physiological concentrations of proinflammatory cytokines act in the brain to produce the common symptoms of sickness, such as loss of appetite, sleepiness, withdrawal from normal social activities, fever, aching joints and fatigue. Cytokines may produce these same symptoms in HF. Few investigators have studied both EDS and fatigue in HF patients and the one team that did so demonstrated that EDS and fatigue were not highly correlated (Redeker, Jeon, et al., 2010). Therefore, after identifying the factors associated with EDS we tested the same model using fatigue as the outcome to determine if the factors explaining EDS also explained fatigue.

Methods

This was a planned analysis of cross-sectional data from a study enrolling a consecutive sample of 280 adults with HF. Subjects were enrolled from three outpatient settings in Philadelphia, Pennsylvania and Newark, Delaware. One site was a university referral center, one site was a large community hospital, and one was a Veterans Affairs medical center. The local Institutional Review Board approved the study at each site. All participants provided informed consent. These data were collected between 2007 and 2009.

Patients were included if they had chronic Stage C HF confirmed based on recent echocardiographic and clinical evidence. Stage C HF patients are currently or previously symptomatic. Patients with either systolic or preserved left ventricular systolic function (diastolic HF) were included. Systolic dysfunction was defined as having a left ventricular ejection fraction $\leq 40\%$. Diastolic HF was confirmed based on clinical symptoms in addition to echocardiographic findings of an ejection fraction $>40\%$ and a reversed mitral inflow E/A ratio plus exclusion of alternative diagnoses (i.e., ischemia, valvular disease, occult arrhythmia, pericardial disease, restrictive cardiomyopathy, lung disease) (Hunt et al., 2005).

Inclusion criteria specified the ability to perform tests (e.g., vision, hearing, and English literacy). The cognitive ability to provide informed consent was screened using the Telephone Interview of Cognitive Status (Buckwalter, Crooks, & Petitti, 2002). Otherwise eligible individuals were excluded if they lived in a long term care setting or worked nights or rotating shifts, or had a major depressive illness, dementia, renal failure requiring dialysis, a life expectancy of less than 6 months, plans to move out of the area, or a history of serious drug or alcohol abuse within the past year at the time of screening (Cherpitel, 2000). Major depressive illness was screened first by a review of the medical record; patients identified as having major depressive illness were not contacted. In addition, everyone was screened with the 9-item Patient Health Questionnaire (PHQ-9) (Kroenke, Spitzer, & Williams, 2001). We excluded anyone reporting 5 or more of the 9 symptoms more than half the days in the past 2 weeks; 1 of the symptoms had to be depressed mood or anhedonia. Most of the data were

collected during home visits by trained research assistants. Clinical information was abstracted from the medical record by registered nurses.

Measurement

Using information collected at enrollment, we tested a model of sociodemographic, clinical, behavioral, and perceptual factors suggested by others to be associated with EDS in other populations. We explored sociodemographic characteristics of age (Kim & Young, 2005; Whitney, et al., 1998), race (Whitney, et al., 1998), gender (Kim & Young, 2005; Pack, et al., 2006; Teodorescu et al., 2006), education (Kim & Young, 2005; Whitney, et al., 1998), income (Ekici et al., 2008), and social support (Whitney, et al., 1998). Clinical factors tested were SDB (Pack, et al., 2006), number of comorbid illnesses (Katz & McHorney, 1998; Pack, et al., 2006; Whitney, et al., 1998), blood pressure (Drager et al., 2009), body mass index (BMI) (Guilleminault et al., 1988; Whitney, et al., 1998), HF type, severity (Staniforth, et al., 1998), and duration (Whitney, et al., 1998), number and type of medications (Whitney, et al., 1998), including drugs known to cause daytime somnolence (Pack, et al., 2006), and diuretics, which may cause nocturia (Asplund, 2004; Foley et al., 2007). Behavioral and perceptual factors included exercise (Whitney, et al., 1998), alcohol use (Pack, et al., 2006; Whitney, et al., 1998), smoking (Whitney, et al., 1998), sleep duration and quality (Redeker & Stein, 2006), and perceived health (Enright et al., 1996). Depression was not included as a potential correlate because subjects with major depression were excluded and because of the conceptual overlap between EDS, fatigue, and depression.

The primary measure of EDS was the Epworth Sleepiness Scale (M. W. Johns, 1992), an 8-item measure. Each item is rated on a 4-point Likert scale ranging from never dozing (0) to high chance of dozing (3) in specific soporific situations. Scores are summed, with higher scores indicating greater sleepiness (M.W. Johns, 2000). A score >10 is usually considered to indicate EDS. Previous research demonstrated a moderate level of discordance (40%) between subjective and objective sleepiness with those who were discordant found to be more likely to have only subjective sleepiness (Chugh, Weaver, & Dinges, 1996). To capture the full number of subjects experiencing EDS the decision was made to use a self-report measure of sleepiness as the primary outcome.

Items from the Kansas City Cardiomyopathy Questionnaire (KCCQ) (Green, Porter, Bresnahan, & Spertus, 2000) were used as the measure of fatigue. Two items asking how many times fatigue has limited the ability to do activities and how bothersome fatigue has been were summed. Each item is scored 1 to 7. Scores ranging from 2 to 14 were reversed so that higher scores indicated more fatigue. Although the median score was 5 in this sample, a conservative score of 8 or more was used to indicate fatigue. The alpha coefficient of the fatigue measure was 0.90 in this sample.

Sociodemographic characteristics were self-reported. Most clinical information (e.g., comorbid illnesses, HF type and duration, left ventricular ejection fraction) was gathered from the medical record immediately prior to enrollment by a registered nurse. The total number of comorbid conditions was used in analysis. Information on functional class was gathered during the data collection visit by research assistants. Scoring of the New York Heart Association (NYHA) is known to be subjective, so a standardized interview developed for use in a NIH-funded trial was used to collect information on symptoms occurring in response to activity (Kubo et al., 2004). The interview responses were provided to a single board-certified cardiologist who scored NYHA in every subject. The score provided by the cardiologist was used in analysis. Length of time with HF was calculated after a historical search of the record to identify the initial physician diagnosis. BMI was calculated using known height and body weight measured during the home visit. Research assistants recorded

all current prescriptive and over-the-counter medications, including dose and frequency of use.

A physician-judged diagnosis of SDB based on polysomnography was obtained from the medical record at the time of enrollment. If no documentation of recent sleep testing was found in the medical record, one night of sleep was assessed in the home using Embletta (Medcare, Buffalo, NY), a highly sensitive and specific screening device useful in quantifying the apnea hypopnea index (AHI) in persons with suspected SDB.(Ng et al., 2010) An AHI ≥ 5 was used to classify subjects as having SDB (Ruehland et al., 2009).

Exercise frequency, alcohol use, and smoking history were self-reported. Exercise frequency was gathered as categorical data in response to a question asking about the amount of exercise obtained in the past week (none or fewer than 30 minutes, 30–59 minutes, 1–3 hours, or >3 hours). We asked about only the past week to avoid issues with recall related to this type of behavior. To assess alcohol use participants were asked how often, on average, they drink alcoholic beverages (never, 1 or fewer drinks/week, 2–7 drinks per week, 7 or more per week, or 5 or more drinks on one occasion). Smoking history was categorized as current smoker (smoking with 1 month of the encounter), recent smoker (stopped smoking between 1 month and 1 year prior), former smoker (stopped more than one year ago), or never smoked.

Sleep quality was assessed using the 19-item Pittsburgh Sleep Quality Index (PSQI), a self-report measure of the perception of habitual sleep quality. Higher scores indicate worse global sleep quality; a PSQI score greater than 5 indicates poor sleep quality (Buysse, 1989). Perceived overall health was measured using a single item from the Medical Outcomes Study (Ware, 1993). In general, would you say your health is poor, fair, good, very good, or excellent?

Analysis

Standard descriptive statistics were used to depict the sample overall. Subjects were categorized as having EDS or not. Then, Student's t-tests were used to test for differences in continuous variables and chi-square tests were used with categorical variables. The same analyses were performed after categorizing subjects as fatigued or not. Simple linear regression with backward elimination was used to evaluate the association between the continuous Epworth Sleepiness Scale scores and the sociodemographic, clinical, behavioral, and perceptual variables. The same procedures were used with the measure of fatigue. Logistic regression was used to model the dichotomized EDS outcome, as well as the dichotomized fatigued outcome. All analyses were adjusted for site, age, race and gender. Analyses were conducted using SAS 9.2 (SAS Institute Inc., Cary, NC).

Results

Demographic and clinical characteristics of the sample of 280 are shown in Table 1. The average subject tended to be a white (63%) male (64%) aged 62 ± 12 years. The average Epworth Sleepiness Scale total score was 6.95 ± 4.56 (median = 6.0, mode 3.0) with a range of 0 to 23 out of a possible score of 24. Many subjects were former smokers (55%) who rated themselves to be in fair or poor health (54%). Almost all of these HF patients were taking a beta-blocker (92%), 58% were taking an angiotensin-converting enzyme (ACE) inhibitor, 30% were on an angiotensin II receptor blocker (ARB), and 81% were on a diuretic. Of those on a diuretic, 84.5% were taking furosemide. Many subjects ($n=132$, 47.1%) had a recent polysomnography (PSG) and did not need further sleep testing. Embletta was performed on 90 subjects (32.1%), but 4 studies were unsuccessful and 2 subjects removed the device during the night. In another 52 (18.6%) subjects, the presence

or absence of SDB had been judged by a physician and noted in the medical record, but PSG was not recent so we wanted to retest the patient. However, these 52 subjects either refused the Embletta or delayed scheduling until it was too late to perform. In these patients, SDB was judged based on the medical history in the record. A total of 151 (53.9%) subjects were judged to have SDB based on the information in the medical record or Embletta testing. Of these 151 patients with SDB, only 75 (49.7%) had been treated with CPAP and of these, only 35 of the 151 (23.2%) reported using it 6 hours per night in the past week.

Characteristics of the sample separated by EDS and by fatigue are shown in Table 1. Compared to subjects without EDS, subjects with EDS were younger ($p=0.040$), less likely to have atrial fibrillation ($p=0.033$), less likely to be taking a diuretic ($p=0.010$), more likely to be in NYHA functional class IV ($p=0.002$), and more likely to be classified as poor sleepers on the PSQI ($p=0.009$). The prevalence of SDB did not differ between the groups (Table 1).

Compared to subjects without fatigue, subjects with high levels of fatigue were younger ($p<0.001$) and more likely to be non-white race ($p<0.001$), to report an income that was inadequate to meet their needs ($p<0.001$), and to perceive their health to be only fair or poor ($p<0.001$). Fatigued subjects were more likely to be poor sleepers ($p<0.001$), to have slept less the night before data collection ($p<0.001$), to be taking a higher number of prescription drugs ($p=.03$) and more drugs causing daytime somnolence ($p=.03$) compared to subjects who were not fatigued. Fatigued subjects were more likely to be in NYHA functional class IV ($p=0.001$), more likely to be anemic ($p=0.03$), less likely to have atrial fibrillation ($p=0.01$), and more likely to have diastolic HF ($p=0.03$) (Table 1).

Because sleep quality was anticipated to be a major contributor to both EDS and fatigue, we tested bivariate associations between subjective sleep quality subscale scores, EDS, and fatigue (Table 2). In unadjusted analyses, subjects with worse sleep quality, worse sleep duration, more sleep disturbances, worse daytime dysfunction, or worse PSQI total sleep quality scores tended to be more likely to have EDS and fatigue. The major sleep disturbance was nocturia, reported by 74% of the sample.

Prevalence

Prevalence is defined as the proportion of individuals in a population having a particular disease or diagnosis at a given time. In this case, the diagnosis of interest was EDS. Using a score >10 on the Epworth Sleepiness Scale to define sleepiness, 23.6% of the participants had EDS. Even more (28.2%) subjects were fatigued. The correlation between the Epworth Sleepiness Scale and the fatigue score was $r = .38$ ($p<0.001$).

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Linear regression was used to evaluate the relative importance of the sociodemographic, clinical, behavioral, and perceptual characteristics in predicting Epworth Sleepiness Scale scores. The variables significantly associated with a higher score in the final adjusted model were younger age ($p=0.03$), worse functional class (NYHA IV; $p=.01$), worse sleep quality ($p=0.01$), fewer comorbid illnesses ($p=0.03$), and diuretic use ($p=0.03$). These variables explained 21% of the variance in EDS.

The final adjusted models for the categorized EDS group are shown in Table 3. The odds of having EDS increased by 9% for each unit increase in the total PSQI sleep score ($p=0.048$). Those with NYHA functional class IV were more than four times as likely to have EDS ($p=0.004$) compared to subjects in NYHA class I or II. Subjects taking a diuretic were 68% less likely to have EDS ($p=0.005$). Those who were physically active between 1–3 hours each week were 61% less likely to have EDS ($p=0.04$).

Determinants of Fatigue—The final linear regression model developed for fatigue scores found that the significant determinants of higher fatigue levels were worse sleep quality score ($p<.001$) and worse NYHA functional class ($p<.001$). These variables explained 31% of the variance in fatigue. For the logistic regression of fatigue, only sleep quality was a significant determinant; fatigue increased by 24% for each unit of worsening in the total PSQI sleep quality score ($AOR=1.24$, $p<.001$).

Discussion

The purpose of this study was to describe the prevalence of EDS and the factors associated it in adults with HF. Although correlates of EDS have been tested in other populations, this is the first study of this kind in adults with HF. Almost one quarter of our sample reported EDS and even more reported fatigue. Interestingly, there was a moderately low correlation between EDS and fatigue in this sample. Our EDS prevalence rate was lower than that found in other HF studies. Redeker and Stein (2006) found EDS in 44% of their HF sample and Staniforth et al (1998) identified EDS in 35% of their HF sample. EDS prevalence differences may reflect medical management of the populations studied. We are unable to make further comparisons between our study and these studies as Redeker and Stein did not report the pharmacologic treatment of their sample. Staniforth et al reported on ACE inhibitor and diuretic use, but beta-blockers were not in wide use at the time their study was conducted.

The factors associated with EDS in these HF patients were poorer sleep quality, worse functional class, lack of physical activity, and not taking a diuretic. These factors explained more of the variance in fatigue than in EDS, although physical activity and diuretic use were not significantly associated with fatigue. SDB was not associated with either EDS or fatigue in this sample.

Poor sleep quality was a significant determinant of both EDS and fatigue, a finding similar to that of prior investigators studying other patient groups (Kim & Young, 2005; Pack, et al., 2006; Whitney, et al., 1998). The relationship between sleep quality and EDS and/or fatigue may be explained by results from Redeker and Stein (2006) who reported that adults with HF had more difficulty falling asleep, poor sleep efficiency, and more sleep disturbances, early awakenings, and frequent napping than adults without HF.

Others have found a relationship between worse NYHA functional class and EDS in adults with HF (Redeker & Stein, 2006; Staniforth, et al., 1998). A similar relationship was found in the Cardiovascular Health Study (Whitney, et al., 1998) and in community-dwelling older Americans enrolled in the National Sleep Foundation's *Sleep in America Poll* (Chasens, Sereika, Weaver, & Umlauf, 2007). One explanation for this finding is that subjects with NYHA class IV HF have difficulty staying asleep in the supine position because of fluid shifts from the peripheral to the central circulation (Yumino et al., 2010). It is also possible that the direction of causation is reversed with EDS impairing functional abilities. The direction of the effect cannot be determined from these cross-sectional data.

Subjects reporting engaging in physical activity between 1–3 hours each week experienced significantly less EDS compared to those doing less activity. Others have previously noted a relationship between physical activity and EDS (Chasens, et al., 2007; Whitney, et al., 1998). Physical activity is thought to improve sleep quality (Driver & Taylor, 2000; Youngstedt, 2005) and, in population studies, elders who are physically active report better sleep than sedentary individuals (de Castro Toledo Guimaraes, de Carvalho, Yanaguibashi, & do Prado, 2008; Paparrigopoulos, Tzavara, Theleritis, Soldatos, & Tountas, 2010; Sherrill, Kotchou, & Quan, 1998). Studies testing the effects of various forms of physical

activity on sleep parameters in older subjects have noted that sleep quality and duration are improved in subjects who engage in endurance, weight, stretching, and/or balance training (King, Oman, Brassington, Bliwise, & Haskell, 1997; King et al., 2008; Richards et al., in press; Singh, Clements, & Fiatarone, 1997). Notably, however, these studies were not performed in adults with HF.

Not taking a diuretic was associated with significantly more EDS in our sample. This was a surprising finding, as diuretic use has been implicated as a factor interrupting sleep and causing EDS (Asplund, 2004; Foley, et al., 2007). Reviewing the side effect profiles of the major diuretic classes provided little insight into this finding but three possible scenarios may explain the results. One plausible explanation is that subjects who were not taking a diuretic were more likely to experience nocturnal dyspnea while in the supine position, which would interrupt sleep. However, no interaction was found between NYHA functional class and diuretic use. And, those taking a diuretic were no more likely to report sleep disturbances than those not taking a diuretic (analysis not shown). Another possibility is that not taking a diuretic is a surrogate marker of diastolic HF because some patients with diastolic heart failure are sensitive to the preload reduction associated with diuretic use and may develop hypotension or severe prerenal azotemia (Satpathy, Mishra, Satpathy, Satpathy, & Barone, 2006). But, in this study diuretic use did not differ by HF type. The most likely explanation for the association between a lack of diuretic use and EDS might be linked to the reticular activating system (RAS), that area of the brainstem that regulates wakefulness. Neurons in the RAS that play a role in wakefulness are dopaminergic, noradrenergic, serotonergic, histaminic, and orexinic. The counterbalance to this arousal system is the inhibitory influence of the GABAergic system, activation of which overrides the wakefulness network and allows sleep (Jones & Jones, 2005). Sleep occurs when an area of the anterior hypothalamus uses GABA and galanin to initiate sleep by inhibiting the arousal regions of the brain (Foldvary-Schaefer et al., 2002). Prior investigators have demonstrated that furosemide competitively blocks GABA from binding at the receptor sites on the chloride inward channel, thus rendering them inadequately polarized to be effective (Pond et al., 2006; Wall, 2003). Given this well established neurochemistry, it is plausible that furosemide given during the day inhibits the GABAergic system, leaving the arousal/wakefulness system relatively unopposed and inhibiting EDS.

We did not find EDS to be associated with SDB. SDB is exceedingly common in adults with HF (MacDonald, Fang, Pittman, White, & Malhotra, 2008) and often assumed to be associated with the high rates of EDS (Brostrom & Johansson, 2005; Redeker, 2006). However, our results are consistent with those of recent studies of adults with HF in which no association was found between SDB and EDS (Johansson et al., 2009; Redeker, Muench, et al., 2010; Roure et al., 2008). The explanation for this lack of association remains unclear, although Artz and colleagues (2006) note the HF patients appear to have a reduced propensity to fall asleep, which may be explained by the increased sympathetic nervous system activity in HF. The sympathetic stimulation is further accentuated by SDB. This finding is important because it focuses our attention on issues such as functional class, sleep quality, the medication regimen, and physical activity, which may be even more amenable to treatment.

To our knowledge, this is the first study to simultaneously explore both EDS and fatigue in the same sample. Several variables with univariate differences may help to explain the differences between EDS and fatigue. Both those with EDS and with fatigue were significantly younger than those without either symptom. Sensitivity of younger individuals to symptoms could reflect age-related differences in interoception or the ability to receive and process stimuli that originate inside the body (Cameron, 2001). Fatigued HF patients were more likely to report an inadequate income and fair or poor health compared to patients

without fatigue. This picture suggests that fatigue may reflect depression better than EDS. However, fatigued HF patients were also more likely to be anemic and to be taking more medicines—including those known to cause daytime somnolence—than patients who are not fatigued. These characteristics suggest that patients who report fatigue should have their medication regimen reevaluated and be checked for anemia.

A strength of this study is the relatively large sample size for a study of this nature. In addition, the sample was older and more obese than prior studies of EDS, which makes these results unique. Another strength was the inclusion of both EDS and fatigue. A limitation was that a significant proportion of the sample refused Embletta testing so we had to depend on historical data obtained from the medical record. Another limitation was the cross-sectional nature of the data, which limits our ability to identify whether EDS is a cause or an effect. Another limitation was the subjective nature of the symptom measures. However, symptoms are defined as sensations or changes in bodily function experienced by a patient, so self-report may be considered the gold standard for assessment. The sample itself was another limitation; these subjects were fairly well-educated and overweight or obese. They were also well-managed medically and had had HF longer than many published samples. Thus, these results may not reflect the general population of HF patients elsewhere.

Application

In this sample, the major factors associated with EDS were poor sleep quality, worse NYHA functional class, lack of physical activity, and not taking a diuretic. These results suggest that medications that improve functional class, including diuretics, may decrease daytime sleepiness in these patients. Sleep quality should be explored even in HF patients without SDB; even mild decrements in sleep quality warrant concern and treatment.

These results are important because although SDB is widely studied in adults with HF, EDS is not routinely addressed. Almost one-quarter of this sample experienced a high and bothersome level of excessive daytime sleepiness, which illustrates the importance of screening for this symptom in patients with HF. Patients with HF and risks for SDB should be referred for testing, even if they do not have EDS.

Acknowledgments

This work was funded by a grant from the National Heart, Lung & Blood Institute (RO1 HL084394-01A1) and by the Philadelphia Veterans Affairs Medical Center, VISN 4 Mental Illness Research, Education, and Clinical Center (MIREC).

The authors gratefully acknowledge Thomas A. Gillespie, MD, FACC for scoring the New York Heart Association (NYHA) interviews.

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Table 1

Characteristics of the sample overall and by EDS (ESS >10 vs. ESS 10) and by Fatigue (6 vs. >6). Mean $\pm$ standard deviation or n (%) is reported.

	Entire Sample (n=280)	Sleepy (n=66)	Not Sleepy (n=214)	p-value ¹	Fatigued (n=79)	Not Fatigued (n=201)	p-value ¹
Age (years)	62.0 $\pm$ 12.5	59.2 $\pm$ 13.5	62.8 $\pm$ 12.02	0.040	57.9 $\pm$ 13.6	63.6 $\pm$ 11.6	0.002
Male	180 (64.3)	41 (62.1)	139 (65.0)	0.675	47 (59.5)	133 (66.2)	0.18
Race/Ethnicity							
White	175 (62.5)	41 (62.1)	134 (62.6)	0.991	35 (44.3)	140 (69.7)	<0.001
Black	96 (34.3)	23 (34.9)	73 (34.1)		40 (50.6)	56 (27.9)	
Other	9 (3.2)	2 (3.0)	7 (3.3)		4 (5.1)	5 (2.5)	
Education							
Less than high school	27 (9.7)	5 (7.6)	22 (10.3)	0.74	6 (7.6)	21 (10.4)	0.76
High school	101 (36.2)	26 (39.4)	76 (35.6)		29 (36.7)	7336.3)	
At least some college	78 (28.0)	35 (53.0)	116 (54.2)		44 (55.7)	107 (53.2)	
Household income insufficient to make ends meet	45 (16.1)	14 (21.2)	31 (14.5)	0.37	24 (30.4)	21 (10.4)	<0.001
Smoking							
Current	30 (10.7)	9 (13.6)	21 (9.8)	0.40	10 (12.7)	20(10.0)	0.65
Former	155 (55.4)	32 (48.5)	123 (57.5)		45 (57.0)	110 (54.7)	
Never	95 (33.9)	25 (37.9)	70 (32.7)		24 (30.4)	71 (35.3)	
Body mass index (BMI)	31.0 $\pm$ 8.0	32.7 $\pm$ 8.4	30.5 $\pm$ 7.8	0.051	32.3 $\pm$ 9.2	30.4 $\pm$ 7.3	0.104
Exercise							
None or <30 minutes/week	109 (38.9)	32 (48.5)	77 (36.0)	0.079	36 (33.0)	73 (67.0)	0.475
30–59 minutes/week	52 (18.6)	15 (22.7)	37 (17.3)		14 (26.9)	38 (73.1)	
1–3 hours/week	68 (24.3)	10 (15.2)	58 (27.1)		18 (26.5)	50 (75.3)	
>3 hours/week	51 (18.2)	9 (13.6)	42 (19.6)		11 (21.6)	40 (78.4)	
Perceived overall health							
Excellent/Very Good	34 (12.1)	7 (10.6)	27 (12.6)	0.67	2 (2.5)	32 (15.9)	<0.001
Good	94 (33.6)	20 (30.3)	74 (34.6)		18 (22.8)	76 (37.8)	
Fair/Poor	152 (54.3)	39 (59.1)	113 (52.8)		59 (74.7)	93 (46.3)	
Systolic blood pressure	116.1 $\pm$ 18.4	113.8 $\pm$ 18.9	116.9 $\pm$ 18.2	0.24	115.7 $\pm$ 17.6	116.3 $\pm$ 18.7	0.82
Diastolic blood pressure	69.0 $\pm$ 11.2	69.4 $\pm$ 11.4	68.8 $\pm$ 11.1	0.70	70.0 $\pm$ 11.3	68.5 $\pm$ 11.1	0.32
Months with HF	73.4 $\pm$ 71.1	61.0 $\pm$ 53.7	77.2 $\pm$ 75.3	0.06	64.0 $\pm$ 52.8	76.8 $\pm$ 76.7	0.19
Ejection fraction	35.4 $\pm$ 17.0	36.7 $\pm$ 17.6	35.0 $\pm$ 16.8	0.49	36.3 $\pm$ 18.1	35.0 $\pm$ 16.5	0.57
Atrial fibrillation	94 (33.6)	15 (22.7)	79 (36.9)	0.03	18 (22.8)	75 (37.5)	0.01
Diabetic	108 (38.6)	25 (37.9)	83 (38.8)	0.92	29 (36.7)	70 (34.8)	0.43
Cerebrovascular disease	42 (15.0)	7 (10.6)	35 (16.4)	0.25	13 (16.5)	29 (14.4)	0.39
Renal disease	74 (26.4)	12 (18.2)	62 (29.0)	0.08	20 (25.3)	49 (25.0)	0.53

	Entire Sample (n=280)	Sleepy (n=66)	Not Sleepy (n=214)	p-value ¹	Fatigued (n=79)	Not Fatigued (n=201)	p-value ¹
Anemia	47 (17.0)	12 (18.8)	35 (16.5)	0.40	19 (24.4)	28 (14.1)	0.03
Number of comorbid illnesses	3.1±2.1	2.8±2.0	3.2±2.1	0.19	3.3±2.3	3.1±2.0	0.36
Heart failure type	226 (80.7)	54 (81.8)	172 (80.4)	0.85	57 (72.2)	169 (84.1)	0.03
• systolic / mixed	53 (18.9)	12 (18.2)	41 (19.2)		21 (26.6)	32 (15.9)	
• diastolic	1 (0.4)	0 (0.0)	1 (0.5)		1 (1.3)	0	
• unspecified ²							
NYHA functional class	66 (23.6)	8 (12.1)	58 (27.1)	0.002	10 (15.1)	56 (84.8)	0.001
• Class I & II	164 (58.6)	38 (57.6)	126 (58.9)		46 (28.0)	118 (72.0)	
• Class III	50 (17.9)	20 (30.3)	30 (14.0)		23 (46.0)	27 (54.0)	
• Class IV							
Angiotensin-Converting Enzyme (ACE) inhibitor	162 (57.9)	38 (57.6)	124 (57.9)	0.96	42 (53.2)	120 (59.7)	0.19
Angiotensin II Receptor Blocker (ARB)	83 (29.6)	20 (30.3)	63 (29.4)	0.89	22 (27.8)	61 (30.3)	0.40
Diuretic	226 (80.7)	46 (69.7)	180 (84.1)	0.01	65 (82.3)	161 (80.1)	0.41
Beta-Blocker	259 (92.5)	62 (93.9)	197 (92.1)	0.61	72 (91.1)	187 (93.0)	0.37
Number of prescription medicines	9.8±4.0	10.1±4.1	9.8±3.9	0.57	10.6±4.6	9.5±3.6	0.03
Number of drugs commonly causing daytime somnolence	1.6±1.0	1.7±1.1	1.5±0.9	0.31	1.8±1.3	1.5±0.8	0.03
Poor sleeper on the PSQI	162 (58.1)	47 (71.2)	115 (54.0)	0.009	73 (92.4)	1:30 (64.7)	<0.001
Hours slept night prior to testing	6.41±2.3	6.34±3.7	6.44±1.6	0.83	5.5±1.8	6.5±1.6	<0.001
Sleep Disordered Breathing	153 (54.6)	40 (60.6)	113 (52.8)	0.27	49 (62.0)	104 (51.7)	0.08

¹ Comparison of sleepy/not sleepy, fatigued/not fatigued groups via Student's t- or Chi-square tests.

² Category not included in analyses.

HF= heart failure; ESS = Epworth Sleepiness Scale; NYHA = New York Heart Association; PSQI = Pittsburgh Sleep Quality Index

Table 2
Summary of PSQI sleep variables overall and by sleepiness (ESS 11) and fatigue (8) groups.

	Entire Sample (n=280)	Sleepy (n=66)	Not Sleepy (n=214)	p-value	Fatigued	Not Fatigued	p-value
Sleep Quality	1.16± 0.82	1.39± 0.91	1.09± 0.78	0.009	1.6± 0.8	1.0± 0.8	<0.001
Sleep Latency	1.10± 1.05	1.28± 1.16	1.05± 1.02	0.10	1.5± 1.1	0.9± 1.0	<0.001
Sleep Duration	1.23± 0.98	1.44± 0.98	1.16± 0.98	0.04	1.5± 1.1	1.1± 0.9	0.001
Sleep Efficiency	0.98± 1.16	1.20± 1.17	0.92± 1.16	0.09	1.5± 1.2	0.8± 1.1	<0.001
Sleep Disturbance	1.26± 0.63	1.42± 0.68	1.21± 0.60	0.01	1.6± 0.6	1.1± 0.6	<0.001
Sleep Medications	0.62± 1.15	0.71± 1.20	0.59± 1.13	0.46	0.7± 1.2	0.6± 1.1	0.42
Daytime Dysfunction	0.85± 0.77	1.30± 0.78	0.71± 0.71	<.001	1.3± 0.9	0.6± 0.6	<0.001
Total Sleep Score	7.20± 4.06	8.76± 4.25	6.72± 3.88	<.001	9.8± 3.9	6.1± 3.6	<0.001

Mean ± STD is reported.

¹Unadjusted Odds Ratio for the odds of being sleepy/fatigued for each unit increase in the PSQI variable.

ESS = Epworth Sleepiness Scale; OR = odds ratio

Table 3

Final logistic regression model for Sleepy (ESS 11) and Fatigued (8).

Variable	Excessive Daytime Sleepiness			Fatigued		
	AOR [/]	95% CI	p-value	AOR [/]	95% CI	p-value
PSQI Total Sleep Score	1.09	1.001–1.17	0.048	1.24	1.13–1.35	<0.001
NYHA functional class	(ref)	0.80–4.81	0.141	(ref)	0.29–4.79	0.73
NYHA class I or II	1.96	1.40–12.10	0.010	.82	.51–2.67	0.72
NYHA class III	4.11			1.16		
NYHA class IV						
Diuretic use	0.32	0.14–0.70	0.005			
Exercise	0.39	0.16–0.95	0.037			

[/] Adjusted Odds Ratio for the odds of being sleepy/fatigued. Model also adjusted for site, age, gender, and race. (ref=reference group for AOR).

ESS = Epworth Sleepiness Scale