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The Role of Heart Failure, Daytime Sleepiness, and Disturbed Sleep on Cognition

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Abstract

Disturbed sleep and daytime sleepiness may interfere with possible direct relationships between HF and cognition, yet there is limited research investigating this relationship. We aimed to investigate possible mediating roles of disturbed sleep and daytime sleepiness on the relationship between heart failure (HF) and selected cognitive domains among individuals with and without HF. In a cross-sectional design study, we examined the data of 841 older adults with and without HF from the Aging, Demographics, and Memory Study (ADAMS). We found individuals with HF were likely to have a higher degree of disturbed sleep and daytime sleepiness. Both disturbed sleep and daytime sleepiness were significant predictors of cognition. We found that only daytime sleepiness mediated the relationship between the presence of HF and cognitive domains, such as in attention, memory, and executive function after controlling for covariates. Interventions to improve daytime sleepiness among individuals with HF may also help improving cognition.

Keywords

Cognition; sleep; aged; heart failure

Heart failure (HF) is a significant public health burden affecting more than 5.7 million adults in the U.S with an incidence of approximately 10 per 1000 people aged 65 and older. It is the most expensive diagnosis in terms of Medicare payments, with the total costs estimated at \$32 billion in 2013 (Mozaffarian et al., 2015). Among Medicare beneficiaries, HF is also the most frequent reason for re-hospitalization (Jencks, Williams, & Coleman, 2009). Findings from a cohort study involving 765 adults showed lifetime medical care costs

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following an HF diagnosis to be \$110,000 per person on average, with most of the cost being directly attributable to frequent re-hospitalizations (Dunlay et al., 2011).

Researchers have documented that cognitive impairment contributes to changes in self-care ability involving symptom monitoring and management (Dickson, Tkacs, & Riegel, 2007). For instance, HF patients with cognitive impairment might be unable to process information regarding complex medical regimens or recognize symptoms (Bauer & Pozehl, 2011). This, in turn, increases the hospitalization, re-hospitalization, and mortality rates (Pressler et al., 2010; Zuccalà et al., 2003). Among HF patients, cognitive impairment is common, occurring in about 25% to 50% of the cases, especially in domains related to attention, memory, and executive function (Pressler et al., 2010; Vogels, Scheltens, Schroeder-Tanka, & Weinstein, 2007). As people age, they may experience cognitive changes, but HF patients may experience greater cognitive problems on attention, memory, and executive function than age-matched controls without HF, suggesting that the cognitive changes present among HF patients are more severe than normal aging, but not at the level of needing to diagnose dementia (Vogels et al., 2007). It is widely recognized that HF patients experience greater comorbidities, psychological disease, sleep problems, demands for self-care, and diminished quality of life (Heo, Moser, Lennie, Zambroski, & Chung, 2007). However, less is known about the mechanisms of cognitive impairment in HF patients. Reductions in cerebral blood flow from insufficient cardiac output could contribute to cognitive impairment, but the etiology remains unclear (Bauer, Johnson, & Pozehl, 2011).

Factors contributing to cognitive impairment among HF patients may include disturbed sleep and daytime sleepiness. Up to 70% of people with HF have sleep-related problems (Broström & Johansson, 2005; Redeker & Stein, 2006). Excessive daytime sleepiness occurs in 20% - 44% of HF patients (Redeker, 2006; Riegel et al., 2012). Although disturbed sleep and daytime sleepiness are common problems among older adults in general (25% and 20%, respectively), the rate of these problems is higher among HF patients (Wolkove, Elkholy, Baltzan, & Palayew, 2007; Young, 2004). Possible reasons for these discrepancies are sleep related breathing disorders, insomnia, progression of HF, age, and comorbidities (Redeker, 2008). A conceptual framework developed by Riegel and Weaver (Riegel & Weaver, 2009) hypothesizes that cognitive impairment among HF patients arises from cerebral hypoperfusion, multiple cardiogenic emboli, and poor sleep and daytime sleepiness. Further, studies in community-dwelling older adults without HF have documented a relationship between sleep and various brain functions and cognitive domains, such as attention (Lim & Dinges, 2010), learning (Ambrosini & Giuditta, 2001), memory consolidation (Stickgold & Walker, 2007), and brain plasticity (Tononi & Cirelli, 2014).

Adequate nighttime sleep is related to human cognitive performance including brain function and memory consolidation. Sleep disruption could produce sleepiness during the daytime and result in interferences in neural pathways or neurodegeneration through increases in inflammation and oxidative stress. Researchers hypothesize that these changes in the brain commonly seen in the frontal cortex and medial temporal lobes are the result of sleep fragmentation due to sleep-related breathing disorders (Woo, Macey, Fonarow, Hamilton, & Harper, 2003; Woo et al., 2014). As a result, there may be cognitive deficits in processes associated with those brain regions (i.e., attention, memory, and executive

function; Yaffe, Falvey, & Hoang, 2014). HF patients often exhibit increased sleep fragmentation or daytime sleepiness (Redeker & Stein, 2006), and findings from studies suggest that HF patients and sleep deprived individuals share similar domains of cognition impairment, such as attention, psychomotor speed, memory, and executive function (Lim & Dinges, 2010; Pressler et al., 2010). Disturbed sleep refers to symptoms of poor sleep quality or insomnia, such as difficulty falling asleep, maintaining sleep, or early wake up frequently or too early (Okun, 2016). Daytime sleepiness is often characterized by difficulty maintaining a desired level of alertness (Young, 2004). Previous studies examining how sleep impacts cognition in HF patients indicate that nighttime sleep problems or daytime sleepiness is associated with reductions in cognitive test scores in attention and executive function (Garcia et al., 2012; Moon, Phelan, Lauver, & Bratzke, 2015).

Much uncertainty, however, still exists surrounding the relationship between disturbed sleep, daytime sleepiness, cognitive impairment, and HF because of several limitations. First, researchers have only studied the direct, main association between disturbed sleep or daytime sleepiness and cognition among individuals with HF (Garcia et al., 2012; Hjelm, Strömberg, Arestedt, & Broström, 2013; Moon et al., 2015). Second, these studies have only included HF patients without including individuals without HF, which may prevent understanding how HF influence disturbed sleep, daytime sleepiness, and cognition in older adults. Finally, there are only a limited number of studies examining how disturbed sleep is related to cognition. In particular, studies investigating the mediating effects of disturbed sleep or daytime sleepiness on cognition for individuals with HF are needed because an understanding of this relationship is important to the design of tailored interventions. If we could understand the role of daytime sleepiness and disturbed sleep on the relationship between HF and cognition, clinicians could intervene on improving sleep to improve cognition for HF patients.

The purpose of this paper is to examine the potential mediating effects of disturbed sleep and daytime sleepiness on the relationship between HF and cognitive domains, such as attention, memory, and executive function among community-dwelling older adults with and without HF. Attention, memory, and executive function are cognitive domains that have been found to be linked with HF, disturbed sleep, and daytime sleepiness (Bauer et al., 2012; Blackwell et al., 2011). We hypothesize that a) HF patients have lower cognitive scores, more disturbed sleep, and more daytime sleepiness compared to individuals without HF, and that b) lower cognitive tests scores are mediated through the relationship between disturbed sleep and daytime sleepiness among individuals with HF. The specific aims are to examine a) the relationships among HF, disturbed sleep, daytime sleepiness, and cognitive test scores, and b) the mediating effect of disturbed sleep and daytime sleepiness on the relationships between HF and cognitive test scores (i.e., attention, memory, and executive function).

Methods

Design

This secondary analysis will use across-sectional study design to examine the potential mediating effect of disturbed sleep and daytime sleepiness on the relationship between HF

and selected cognitive domains among community dwelling older adults with and without HF.

Data Source and Sample

A total of 841 participants' data was derived from the Aging, Demographics, and Memory Study (ADAMS). The ADAMS is a supplement to the Health and Retirement Study (HRS). The HRS, funded by the National Institute of Aging (UQ-QG009740), is an ongoing population-based study with a sample of more than 20,000 persons aged 50 and older interviewed biannually since 1992. The aim of the ADAMS is to estimate the prevalence of dementia at the population level in the U.S. The ADAMS data is publicly available and can be obtained from the HRS website (<http://hrsonline.isr.umich.edu/>). The ADAMS was stratified from a sample of 1,770 respondents who were aged 70 and over on the 2000 and 2002 HRS waves based on the scores of the HRS determined self- or proxy-cognitive assessment measures. To ensure an adequate number of subgroups, the respondents were stratified by cognitive measure, age, and sex. Among these subgroups, a total of 856 respondents were initially assessed from July 2001 to December 2003 after the HRS interview for ADAMS. Eight hundred and fifty-six individuals from the ADAMS were identified as potential participants. The total sample was 841 participants after excluding 15 participants who self-identified as having sleep apnea, because sleep apnea could impact daytime sleepiness and disturbed sleep (American Academy of Sleep Medicine Task, 1999). The original study received Institutional Review Boards (IRB) approval and study participants or their surrogates provided informed consents. IRB approval was exempted for the current study by the local institution. Full details regarding ADAMS are published elsewhere (Langa et al., 2005).

Variables and Measures

1) Dependent variable—The dependent variable in this study was cognitive function, which was measured using a comprehensive neuropsychological battery. We used test scores from the ADAMS to create cognitive constructs, such as memory, attention, and executive function. Tests used in the neuropsychological battery, described in Table 1, are validated measures and widely utilized in clinical settings (Lezak, Howieson, Bigler, & Tranel, 2012). First, we used the digit span test and digit symbol test to construct composite scores for attention (Wechsler, 1981). Second, to construct composite scores for memory, we used scores from the Consortium to Established Registry for Alzheimer's Disease (CERAD) Word-List Learning and word recognition, and the Wechsler Memory scale-logical memory exam, and delayed recall (Wechsler, 1987; Welsh et al., 1994). Third, we used the Controlled Oral Word Association Test (COWAT) to construct composite scores for executive function (Ruff, Light, Parker, & Levin, 1996). During the ADAMS, a nurse or a neuropsychological technician conducted extensive cognitive and physical assessments and examinations.

2) Mediating variables—The mediating variables in this study were disturbed sleep and daytime sleepiness during the previous year of the initial interview, which were measured using added questions from the Neuropsychiatric Inventory (NPI). The questions were chosen based on previous sleep literature describing disturbed sleep and daytime sleepiness (Jelicic et al., 2002; Yaffe et al., 2014). The presence of disturbed sleep was operationalized

as the composite number of symptoms (range: 0 ~ 3) participants reported based on the following three dichotomous (yes/no) questions: a) Do you have problems falling asleep? b) Do you wake frequently? and c) Do you have trouble waking too early? Similarly, the presence of daytime sleepiness was determined by the composite number of symptoms (range: 0~2) participants reported based on the following two dichotomous (yes/ no) questions: a) Do you have difficulty staying awake during the daytime? and b) Do you feel overly tired? We interpreted higher scores indicate higher degree of disturbed sleep or daytime sleepiness. In the ADAMS, researchers added questions related to disturbed sleep along with other symptoms and behaviors that are often present, such as appetite loss and weight loss.

3) Independent variable—Self-reported presence of HF was used as an independent variable for our analysis. Data regarding the presence of HF was collected in the ADAMS survey. As part of the medical history questionnaire during the initial visit, participants received a question “Have you ever had congestive heart failure?” We defined HF in people who answered “yes” to the question.

4) Covariates—Demographic variables, such as age, gender, and years of education were collected from each wave of the HRS survey. Body mass index (BMI) was calculated using weight and height data provided from the physical examinations completed during the ADAMS visits. Presence of medical conditions, such as comorbidities including hypertension, diabetes, dementia, chronic obstructive pulmonary disorders, arthritis, and psychological diseases, were collected during medical history questionnaire at the initial visit and were included as dichotomous variables in the analysis.

Statistical Analysis

We computed descriptive statistics to calculate the means, standard deviations, and frequencies of the demographic and clinical variables. We used t-test and chi-square test to compare demographic, clinical, and neuropsychological test scores on people with and without HF. To explore the correlations across HF, daytime sleepiness, disturbed sleep, and cognitive test scores, we conducted Pearson's correlations. To examine two possible mediating factors, daytime sleepiness and disturbed sleep, on the relationship between HF and cognitive domains, we estimated a Structural Equation Model (SEM) with different cognitive domains (i.e., attention, memory, and executive function; Preacher & Hayes, 2008). SEM is an extension of multiple regression analysis aiming to provide estimates of the coefficients of hypothesized causal relationships, such as testing the mediating effects between the independent and dependent variables accounting for measurement errors. Baron and Kenny's approach of mediation analysis based on hierarchical linear regression has been used frequently. However, SEM has better power and a more accurate Type I error rate correction than Baron and Kenny's traditional method. SEM is a widely used method because of its computational efficiency and flexibility of use for testing a joint significant test of α and β (Krause et al., 2010; MacKinnon, 2008)

Considering the non-normality of the study variables, we used a weighted least squares mean and variance adjusted (WLSMV) estimation method. We also used bias corrected

bootstrap technique in the SEM to address unevenness of two groups (i.e., HF and non-HF group) and non-normality of the data (Kline, 2011; Preacher & Hayes, 2008). Factors known to be associated with cognitive function including medical conditions (i.e., comorbidities including hypertension, diabetes, dementia, chronic obstructive pulmonary disorders, arthritis, and psychological diseases) and demographic information (i.e., age, sex, and years of education) were selected as covariates to control for the dependent variables in the model (Pressler et al., 2010; Riegel & Weaver, 2009).

Covariates for daytime sleepiness and disturbed sleep included age, sex, HF, hypertension, psychological diseases, dementia, chronic obstructive pulmonary disorders, and arthritis, depression, and BMI because these factors are known to be associated with daytime sleepiness and disturbed sleep (Pressler et al., 2010; Redeker, 2008; Riegel & Weaver, 2009; Young, 2004). When testing the model fit, the following criteria were adopted for the fit indices: chi-square ($\chi^2 > 0.05$), comparative fit index (CFI) > 0.95 , and root mean squared error of approximation (RMSEA) < 0.08 (Browne & Cudeck, 1993). Descriptive analyses were completed using SPSS version 22 and SEM was estimated using Mplus version 7.3 software.

Results

Demographic and clinical information

The demographic, clinical and cognitive information by HF status is presented in Table 2. There were 97 people with HF and 744 people without HF. The mean age was significantly higher in the HF group (84.80 ± 7.62) than in the non-HF group (81.26 ± 6.93). The proportions of some of the clinical conditions were significantly higher in the HF group than in the non-HF group such as dementia, or diabetes. The rate of depression was also significantly higher in the HF group (28% vs 14%). The mean daytime sleepiness and disturbed sleep were higher in individuals with HF than without. All the mean neuropsychological test scores except for the word recognition test were significantly higher in individuals without HF than those with HF. The mean cognitive test scores were significantly higher in individuals without HF than in individuals with HF.

Correlation of HF, disturbed sleep, daytime sleepiness, and cognitive test scores

HF, disturbed sleep, daytime sleepiness, and cognitive test scores had significant bivariate correlations with each other. The HF status correlated with composite attention scores, $r = -0.13$, composite memory scores, $r = -0.08$, and the composite executive function scores, $r = -0.09$, indicating significant but not strong relationships. HF was significantly correlated with daytime sleepiness and disturbed sleep. Daytime sleepiness was correlated with all the composite cognitive test scores ($r = -0.24$, $r = -0.19$, $r = -0.22$). However, disturbed sleep did not show a correlation with any of the composite cognitive test scores. The bivariate correlation table across variables is shown in Table 3.

Mediating effect of disturbed sleep and daytime sleepiness on the relationship between HF and attention, memory, and executive function

The model fit examining the mediating effect of disturbed sleep and daytime sleepiness on the relationship between HF and attention, memory, and executive function was $X^2(148) = 1552.76$, $p < .0001$, CFI=0.611, RMSEA=0.109. According to the model fit indices, CFI was low and RMSEA was high. Figure 1 and Table 4 demonstrate the direct and indirect relationships across HF, disturbed sleep, daytime sleepiness, and cognitive domains. HF had direct significant effects on attention ($\beta = -0.073$, $p = 0.031$), disturbed sleep ($\beta = 0.100$, $p < 0.001$), and daytime sleepiness ($\beta = 0.160$, $p < 0.001$). As in Figure 1 and Table 4, HF was indirectly associated with lower levels of attention ($\beta = -0.027$, $p = 0.005$), memory ($\beta = -0.021$, $p = 0.017$), and executive function ($\beta = -0.039$, $p = 0.005$) through daytime sleepiness. Daytime sleepiness partially mediated the relationship between HF and attention ($\beta = -0.025$, $p = 0.022$). SEM revealed HF was not directly related to memory ($\beta = -0.009$, $p = 0.782$) or executive function ($\beta = -0.004$, $p = 0.937$). Daytime sleepiness fully mediated the relationships between HF and memory and HF and executive function. However, we did not find a mediating effect of disturbed sleep on the relationship between HF and the three cognitive domains. The total effect of HF, disturbed sleep, and daytime sleepiness on attention was significant ($\beta = -0.098$, $p = 0.002$), but was not significant on memory and executive function.

Discussion

This is one of the few studies that has examined the mediating effects of disturbed sleep and daytime sleepiness on the relationship between HF and cognition among individuals with and without HF from a large population based study. Previous studies examining the relationship between disturbed sleep or daytime sleepiness and cognition have mostly focused on the bivariate relationships of sleep variables and cognition and have only examined HF samples excluding people without HF (Garcia et al., 2012; Moon et al., 2015). While our study validates earlier findings on how HF is associated with cognition, disturbed sleep, and daytime sleepiness, it adds to the current literature by exploring whether disturbed sleep and daytime sleepiness mediate the relationship between HF and cognition using a representative community population including people both with and without HF. The findings of this study suggest that the relationship between HF and cognitive impairments related to attention, memory, and executive function might be mediated by the degree of daytime sleepiness.

Daytime sleepiness was the most significant mediating factor for the relationship between HF and cognitive function. Specifically, daytime sleepiness partially mediated the relationship between HF and attention. It fully mediated the relationship between HF and memory, and the relationship between HF and executive function. It is common for nighttime disturbed sleep to induce daytime sleepiness but our finding emphasize the possible importance of daytime symptoms on cognitive function. In a previous cross-sectional study of 68 HF patients, the researchers found that daytime dysfunction, which is another daytime symptom, is related to prefrontal lobe functions, such as attention and executive function; whereas, self-reported sleep quality was not associated with any of the

cognitive function scores (Moon et al., 2015). Furthermore, a population study conducted by Ohayon and colleagues (2002) found that community dwelling adults without HF also showed similar results. They demonstrated that daytime sleepiness was a risk factor for reduced memory and attention among 1,026 general older adults (Ohayon & Vecchierini, 2002).

The explanation for why daytime sleepiness mediates the relationship between HF and cognition in this study could have two possible reasons. First, individuals who exhibit daytime sleepiness might have undiagnosed sleep-related breathing disorders because daytime sleepiness is one of the key symptoms of sleep-related breathing disorders. Hypoxemia and sleep fragmentation from sleep-related breathing disorders can cause cognitive impairment in domains related to the prefrontal cortex, such as attention and executive function (Beebe & Gozal, 2002; Kerner & Roose, 2016). Because over 80% of individuals with moderate to severe sleep-related breathing disorders have not been diagnosed, there is a chance that undiagnosed underlying sleep-related breathing disorders might result in cognition changes (Finkel et al., 2009; Woo et al., 2003). Second, daytime sleepiness from sleep fragmentation due to age, sleep disorders, sleep deprivation, illnesses, or medications could result in wake state instability, where individuals can have lapses or false starts on the neuropsychological tests. Wake state instability could affect attention and processing speed, which may result in changes to other cognitive domains such as memory and executive function (Dinges et al., 1997).

One interesting finding from this study is that disturbed sleep is not a significant mediator or predictor of attention, memory, and executive function among individuals with HF. There are conflicting results of previous studies examining associations between disturbed sleep symptoms and cognition not only in an HF sample (Garcia et al., 2012; Moon et al., 2015), but also in the general population (Blackwell et al., 2011; Nebes, Buysse, Halligan, Houck, & Monk, 2009). This inconsistent relationship between disturbed sleep and cognition in individuals with and without HF could be from the use of subjective measures to report disturbed sleep. Subjective measures could give us a general perspective on disturbed sleep, but objective measures on particular indicators of sleep quality might better estimate the true relationships. Because older adults and HF individuals are often unaware of disturbed sleep and report being satisfied with sleep, they may not report problems with sleep even though objective measures would reveal poor sleep quality (Wang, Hung, & Tsai, 2011). To confirm the relationship between disturbed sleep and cognition in individuals with and without HF, there needs to be further research using actigraphy or polysomnography to estimate indicators that are known to impact cognition, such as total sleep time, sleep fragmentation, sleep efficiencies, and wake after sleep onsets (Yaffe et al., 2014).

In spite of the significance of the findings, this study has several limitations that might affect generalizability. First, we relied on self-report measures of disease status (i.e., HF or sleep related breathing disorders), disturbed sleep, and daytime sleepiness, which could be unreliable. Although self-reporting may give an estimation of the clinical status (Kehoe, Wu, Leske, & Chylack, 1994; Lampe, Walker, Lennon, Whincup, & Ebrahim, 1999; Szklo-Coxe, Young, Peppard, Finn, & Benca, 2010), additional objective measures could help researchers understand individuals' conditions more accurately. Future studies should screen for sleep-

related breathing disorders, and examine circadian rhythm and sleep architecture using an in-lab and/or in-home overnight sleep study. An in-lab overnight sleep study, would allow researchers to also evaluate the use of positive airway therapy to examine the actual rate and types of sleep-related breathing disorders in the sample. Circadian rhythm, sleep architecture, and the presence of sleep-related breathing disorders may influence daytime sleepiness, so examining these factors would help our understanding of the biological mechanisms. Second, there is limited information regarding clinical characteristics, such as the severity of HF, ejection fraction, presence of HF symptoms, actual use of medication (i.e., HF medications, anti-depressants, anxiolytics, sleep agents, or pain medications), and hypotension. These could be important factors that influence cognition and sleep. However, we used secondary analysis from existing data that were designed with different primary aims, which was completed in 2003. Future studies may identify the severity of HF using the New York Heart Association functional class, the American College of Cardiology/American Heart Association stage, ejection fraction data, more precise symptom evaluation, and accurate medication assessment. Given the changes in the health care field, the results also might be different in more contemporary samples. Finally, our study design is cross-sectional. Thus, the design of this study is limited in its ability to make causal inferences. Future prospective studies could help highlight the causal relationships.

In conclusion, the results of this study support our hypotheses that daytime sleepiness worsens cognitive domains including attention, memory, and executive function especially for individuals who self-reported HF. Thus, the findings from this study suggest that the mechanism of cognitive impairment in HF patients present through daytime sleepiness. If we provide interventions such as management of the underlying cause of daytime sleepiness (e.g., continuous positive airway therapy), management of fragmented sleep with cognitive behavioral therapy for insomnia, or chronobiologic interventions including light therapy to improve daytime sleepiness among individuals with HF, their cognitive status may also improve. Researchers need to use longitudinal designs and objective measures of sleep and HF to better understand the relationships. Investigating the influence of circadian rhythm and/or sleep architecture such as rapid eye movement (REM) and non-REM sleep on daytime sleepiness could help researchers to unfold the actual mechanism of daytime sleepiness and nighttime sleep. In addition, future studies investigating what determines daytime sleepiness and how to decrease it could help improve cognition among HF patients. Clinicians should be aware of the relationships between disturbed sleep, daytime sleepiness, and cognitive function among individuals with and without HF.

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Figure 1. Estimated model of the relationships across heart failure (HF), daytime sleepiness, disturbed sleep, and cognition

Notes. Solid lines indicate significant relationships. Bold solid lines indicate significant mediating roles on the relationship between heart failure (HF) and cognitive domains. Covariates for attention, memory, and executive function included age, sex, years of education, hypertension, diabetes, chronic obstructive pulmonary disease, arthritis, psychological disease, depression, and dementia. Covariates for daytime sleepiness and disturbed sleep included age, sex, HF, hypertension, chronic obstructive pulmonary disease, arthritis, psychological diseases, dementia, depression, and BMI. Model fit indices: $\chi^2 (148) = 1552.76$, $p < .000$, CFI=0.611, RMSEA=0.109. There were 58 missing observations. $n = 794$. Table 4 shows β coefficients and p -values for direct, indirect, and total effects of the relationships.

Table 1
Neuropsychological tests

Cognitive Domains	Neuropsychological tests	Description
Attention	Digit span test	This test is to recall series of numbers forward and backward to assess working memory. For digit span forward test, the participants are asked to repeat the series of numbers in the same order. For digit span backward, the participants are asked to recall numbers in backwards (Wechsler, 1981).
	Digit symbol test	This test is to assess complex scanning and visual tracking, participants are asked to match series of numbers with symbols using a key that shows corresponding digits and symbols to measure psychomotor speed (Wechsler, 1981).
Memory	Consortium to Established Registry for Alzheimer's Disease Word-List Learning	This is a 10-item list learning test to evaluate learning and memory. There are three trials with immediate recall; an administrator visually present 10 high imaginary words in each trial, then participants are asked to remember as many words as possible. The words are the same in each trial (Welsh et al., 1994).
	Consortium to Established Registry for Alzheimer's Disease word list learning word recognition	This is an extension of the 10-item list learning test, participants are given 20 words and asked to recall the original 10 list words and distinguish them from 10 non-target foils (Welsh et al., 1994).
	Wechsler Memory scale-logical memory exam and delayed recall	This test is to assess auditory retention and learning. An administrator reads two brief stories and asks participants to recall as much of the stories as possible immediately after the readings. Delayed recall test is when participants are asked to recall as much of the stories from the Wechsler Memory scale logical memory test as possible after a certain period of time after they were first read (Wechsler, 1987).
Executive function	Controlled Oral Word Association Test (COWAT)	This test is to assess subjects' basic language capacity and executive aspect of verbal behavior. Participants are asked to list words beginning with a designated letter in 60 seconds (Ruff, Light, Parker, & Levin, 1996).

Table 2
Comparison of demographic and clinical information by heart failure status (n=841)

	Heart failure group (n = 97)		Non-Heart failure group (n = 744)		p-values
	Mean ± SD	N (%)	Mean ± SD	N (%)	
Age	84.80 ± 7.62		81.26 ± 6.93		< 0.001
Male		40 (41%)		305 (41%)	0.524
Race (White)		74 (76%)		571 (77%)	0.944
Education (years)	9.49 ± 4.29		10.11 ± 4.33		0.186
Body Mass Index (kg/m ²)	26.19 ± 6.61		25.97 ± 4.78		0.683
Dementia		5 (5%)		81 (11%)	0.050
Hypertension		64 (66%)		445 (60%)	0.145
Diabetes		26 (27%)		140 (19%)	0.046
Chronic obstructive pulmonary disorder		5 (5%)		17 (2%)	0.098
Arthritis		42 (43%)		290 (39%)	0.239
Psychological diseases		2 (2%)		21 (3%)	0.493
Depression		27 (28%)		106 (14%)	0.001
Sleep problems					
Disturbed sleep [range: 0 – 3]	0.96 ± 1.09		0.63 ± 0.93		0.002
Daytime sleepiness [range: 0 – 2]	0.89 ± 0.80		0.46 ± 0.66		< 0.001
Neuropsychological Test					
Word list learning 1 ~ 3 [range: 0-30]	11.44 ± 5.86		13.24 ± 6.01		0.008
Word recognition delayed recall [range: 0-30]	8.15 ± 2.00		8.25 ± 2.33		0.718
Logical memory [range: 0-37]	11.73 ± 8.21		14.12 ± 9.23		0.026
Logical memory delayed recall [range: 0-37]	7.77 ± 7.84		10.04 ± 8.85		0.031
Digit span forward [range: 0-14]	6.89 ± 2.12		7.63 ± 2.37		0.010
Digit span backward [range: 0-14]	3.31 ± 2.25		4.22 ± 2.37		0.002
Digit Symbol [range: 0-63]	19.50 ± 9.10		25.00 ± 12.50		0.004
Controlled Oral Word Association Test [range: 0-66]	19.92 ± 11.44		23.84 ± 12.57		0.016

Note. Bold numbers indicate *p* 0.05

Table 3
Correlation of heart failure, disturbed sleep, daytime sleepiness, and cognitive test scores (n = 841)

	Heart Failure	Daytime Sleepiness	Disturbed Sleep	Attention Score	Memory Score	Executive function Score
Heart Failure	1.00					
Daytime Sleepiness	0.19	1.00				
Disturbed Sleep	0.11	0.28	1.00			
Attention Score	-0.13	-0.24	-0.07	1.00		
Memory Score	-0.08	-0.19	-0.05	0.60	1.00	
Executive function Score	-0.09	-0.22	-0.05	0.65	0.55	1.00

Note. Bold numbers indicate $p < 0.05$

Table 4
Direct, indirect, and total effects across heart failure, daytime sleepiness, disturbed sleep, and cognition

	β (SE)	P-Value
Direct effect		
Heart failure → Attention	-0.073 (0.033)	0.031
Heart failure → Memory	-0.009 (0.028)	0.782
Heart failure → Executive function	-0.004 (0.013)	0.937
Heart failure → Daytime sleepiness	0.160 (0.038)	< 0.001
Heart failure → Disturbed sleep	0.100 (0.043)	0.020
Daytime sleepiness → Attention	-0.169 (0.038)	< 0.001
Daytime sleepiness → Memory	-0.132 (0.036)	< 0.001
Daytime sleepiness → Executive function	-0.166 (0.041)	< 0.001
Disturbed sleep → Attention	0.014 (0.035)	0.687
Disturbed sleep → Memory	-0.006 (0.036)	0.866
Disturbed sleep → Executive function	0.019 (0.041)	0.625
Indirect effect		
Heart failure → Daytime sleepiness → Attention	-0.027 (0.010)	0.005
Heart failure → Disturbed sleep → Attention	0.002 (0.004)	0.748
Heart failure → Daytime sleepiness → Memory	-0.021 (0.009)	0.017
Heart failure → Disturbed sleep → Memory	-0.001 (0.004)	0.877
Heart failure → Daytime sleepiness → Executive function	-0.039 (0.015)	0.005
Heart failure → Disturbed sleep → Executive function	0.003 (0.007)	0.672
Total indirect effect		
Heart failure to Attention	-0.025 (0.011)	0.022
Heart failure to Memory	-0.022 (0.010)	0.038
Heart failure to Executive function	-0.036 (0.017)	0.028
Total effect		
Heart failure to Attention	-0.098 (0.032)	0.002
Heart failure to Memory	-0.031 (0.032)	0.331
Heart failure to Executive function	-0.041 (0.052)	0.439

Note. Direct effect illustrates the strength of the relationship between variables A and B ($A \rightarrow B$); Indirect effect illustrates the strength of the relationship between variables A and B through C ($A \rightarrow C \rightarrow B$); β is standardized coefficients; There were 58 missing observations. $n = 794$; Bold numbers indicate $p < 0.05$.