Symptom Cluster Profiles Among Adults with Insomnia and Heart Failure

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Abstract

Objective/Background: Both heart failure (HF) and insomnia are associated with high symptom burden that may be manifested in clustered symptoms. To date, studies of insomnia have focused only on its association with single symptoms. The purposes of this study were to: (1) describe daytime symptom cluster profiles in adults with insomnia and chronic HF; and (2) determine the associations between demographic and clinical characteristics, insomnia and sleep characteristics and membership in symptom cluster profiles.

Participants: One hundred and ninety-five participants [M age 63.0 (SD12.8); 84 (43.1%) male; 148 (75.9%) New York Heart Association Class I/II] from the HeartSleep study (NCT0266038), a randomized controlled trial of the sustained effects of cognitive behavioral therapy for insomnia (CBT-I).

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The authors declare that there is no conflict of interest.

Methods: We analyzed baseline data, including daytime symptoms (fatigue, pain, anxiety, depression, dyspnea, sleepiness) and insomnia (Insomnia Severity Index), and sleep characteristics (Pittsburgh Sleep Quality Index, wrist actigraphy). We conducted latent class analysis to identify symptom cluster profiles, bivariate associations, and multinomial regression.

Results: We identified three daytime symptom cluster profiles, physical (N = 73 participants; 37.4%), emotional (N =12; 5.6%), and all-high symptoms (N = 111; 56.4%). Body mass index, beta blockers, and insomnia severity were independently associated with membership in the all-high symptom profile, compared with the other symptom profile groups.

Conclusions: Higher symptom burden is associated with more severe insomnia in people with stable HF. There is a need to understand whether treatment of insomnia improves symptom burden as reflected in transition from symptom cluster profiles reflecting higher to lower symptom burden.

Introduction

Approximately six million Americans and 26 million adults worldwide experience chronic heart failure (HF) (Savarese & Lund, 2017; Virani et al., 2021). Approximately 50% of people with HF have insomnia, a condition marked by either an inability to fall or stay asleep and/or awakening too early in the morning accompanied by daytime dysfunction (Redeker et al., 2010). Insomnia is well-known to be associated with daytime symptoms, including fatigue, daytime sleepiness, and depression among many groups (Buysse et al., 2007; Ustinov et al., 2010), including people with HF, among whom insomnia, but not sleep-disordered breathing, was associated with individual daytime symptoms (Redeker et al., 2010).

Previous studies of the associations between insomnia, sleep disturbance, and symptoms addressed single daytime symptoms but have not used approaches that elicit clusters of two or more co-occurring symptoms (Kim et al., 2005), which may better reflect the ways in which people with chronic medical conditions experience symptom burden. Symptom clusters can be empirically determined through person-centered (e.g., latent class analysis, hierarchical cluster analysis) or variable-centered approaches (e.g., factor analysis). In this report, we use a person-centered approach, recommended because it classifies heterogenous participants into subgroups based on similar response patterns (Ryan et al., 2019). Adults with chronic HF demonstrate heterogeneity in symptom burden as reflected in symptom cluster profiles that reflect levels of physical, psychological, and emotional symptoms, and these profiles may vary based on clinical and demographic characteristics of the participants as well as prognostic potential (Hertzog et al., 2010; Park et al., 2019; Song et al., 2010). Defining symptom cluster profiles and contributing factors is needed to target interventions to reduce symptom burden. This approach better reflects the experience of the occurrence of multiple daytime symptoms than investigations that consider isolated symptoms.

Given the close association between insomnia and single symptoms of fatigue, depressive symptoms, and excessive daytime sleepiness (Redeker et al., 2010; Redeker et al., 2014), evidence that symptoms may cluster together, and the potential for efficacious behavioral and pharmacological insomnia treatment to improve sleep-related symptom burden, the purposes of this study are to: (1) describe daytime symptom cluster profiles in adults with insomnia and chronic HF; and (2) determine the associations between demographic and clinical characteristics, insomnia and sleep characteristics and membership in symptom cluster profiles.

Materials and Methods

In this paper, we report baseline data from the HeartSleep Study (NCT0266038), a 5-year prospective randomized control trial to evaluate the sustained effects of cognitive-behavioral therapy for insomnia (CBT-I), compared with an attention control condition, among adults with stable chronic HF and insomnia. We published the study protocol (Redeker, N. S. et al., 2017) and portions of the baseline data (Ash et al., 2020; Gaffey et al., 2020), participant recruitment strategies (Conley et al., 2020), and the results of the randomized control trial (Redeker et al., 2022). We obtained human subjects approval, and all participants provided written informed consent.

The study was conducted in the Northeastern United States with participants from a large tertiary referral academic medical center that includes participants who have HF due to various etiologies (e.g., ischemic, inherited cardiomyopathy) and the affiliated Veterans Administration. We included adults (ages 18 years) with a diagnosis of HF and at least mild insomnia (Insomnia Severity Score > 7 and symptoms for at least one month).

Exclusion criteria were the following: untreated restless legs syndrome; conditions that contraindicated sleep restriction (a component of CBT-I), including scores > 18 on the Epworth Sleepiness Scale, seizure disorders, severe depressive symptoms (> 14 on the Patient Health Questionnaire-9) (Kroenke & Spitzer, 2002), bipolar disorder, active illicit drug use, and neurological/musculoskeletal conditions affecting the motion of the non-dominant arm (due to use of wrist-worn actigraphs). We included people with mild sleep-disordered breathing (Apnea-Hypopnea Index < 15) (based on home sleep apnea screening or medical record review) and those with moderate or severe sleep-disordered breathing who by self-report were adherent to continuous positive airway pressure therapy for at least 4 hours per night (Redeker et al., 2017).

Variables and Measures

We obtained demographic and clinical data, including medications, via interviews and medical record review. We elicited age, gender, race/ethnicity, body mass index (BMI), New York Heart Association Functional Classification (NYHA), left ventricular ejection fraction (LVEF), Seattle Heart Failure Model score, which is used to caluclate projected survival (Levy et al., 2006), and comorbidity (Charlson Comorbidity Index) (Charlson et al., 2008).

We used the PROMIS 8a short form measures developed through the Patient-Reported Outcomes Measurement Information System (an NIH initiative) to elicit fatigue (Ameringer

et al., 2016), pain intensity (Amtmann et al., 2010), anxiety (Pilkonis et al., 2011), and depressive symptoms (Riley et al., 2011). PROMIS measures were developed with item-response theory and are reliable and valid (Cella et al., 2010). We converted the normalized t-scores with means of 50 and 10-point standard deviations that indicate population norms. Higher scores indicate more severe symptoms. A cut-off of 50 was used to indicate clinically significant symptoms (Cella, et al., 2014).

We measured dyspnea with the Multidimensional Assessment of Dyspnea Scale (Redeker 2006), adapted from the Multidimensional Assessment of Fatigue Scale (Belza, 1990), a 16-item scale that measures severity, distress, interference, and timing of dyspnea. We used scores greater than the median of 2 to signify the presence of dyspnea. Cronbach's alpha was 0.96 for this sample.

We used the Epworth Sleepiness Scale, a reliable and valid measure of self-reported daytime sleepiness (Johns, 1991; Johns, 1992). We used a cut of 11, indicating excess daytime sleepiness Cronbach's alpha was .83 (Gaffey et al., 2020).

We used the Insomnia Severity Index (ISI), a measure consistent with the International Classification of Sleep Disorders Criteria, to elicit insomnia (Bastien et al., 2001). Scores 15 indicate clinical insomnia. The ISI was internally consistent in this sample (Gaffey et al., 2020).

We used raw data from the Pittsburgh Sleep Quality Index (PSQI) to elicit self-reported sleep duration (time asleep), sleep efficiency (time asleep/time in bed X 100), and sleep latency (minutes to fall asleep) (Buysse et al., 1989). We did not use the PSQI global score because it includes items that elicit daytime sleepiness and distress due to the overlap with daytime symptoms in the symptom cluster profiles.

We used wrist actigraphs (Actiwatch 2, Philips Respironics, Inc.), valid measures of sleep in people with chronic conditions (Conley et al., 2019; Jeon et al., 2019). Participants were instructed to wear actigraphs on their non-dominant wrists for 14 continuous days. We used Actiware v. 6 (Philips Respironics, Inc.) to compute sleep duration (amount of time between the estimated sleep onset and final awakening), sleep efficiency [(total sleep duration/time in bed) X 100], sleep latency (number of minutes after lights off until estimated sleep onset), and wake after sleep onset (WASO; the average number of minutes awake between sleep and final awakening). Actigraph data were scored by trained research assistants and reviewed by a trained actigraph scorer. We defined the rest period as the time from lights off to lights on, determined (in order of consideration) using the actigraph light meter (lux = 0), event markers (depressed for lights on/off), and daily sleep diaries (Morin et al., 2007).

Statistical Analysis

We used REDCap, an electronic data capture system, to manage the clinical, demographic, and self-report data. We downloaded and merged the data from REDCap, and the scored actigraph data in SAS version 9.4. Instruments with missing values were imputed based on observed items using PROC MI with the EM-algorithm. We computed descriptive statistics with the demographic, clinical, sleep, and symptoms and computed bivariate associations.

We used latent class analysis (LCA), a categorical person-centered clustering approach to identify subgroups of people who experience similar clustered symptoms to determine symptom cluster profiles (Collins & Lanza, 2010). No *a priori* hypotheses are needed for LCA, a data-driven approach. Based on previous studies that found that 100 participants are required in order to obtain a well-identified model, our sample of 195 participants was adequate (Dziak et al., 2014).

We performed LCA with the categorized symptoms of fatigue, pain, anxiety, depression, dyspnea, and daytime sleepiness. We determined the relative model fit using G^2, and the relative fit statistics, Akaike information criterion (AIC), Bayesian information criteria (BIC), the calculated Akaike information criterion (CAIC), and the adjusted BIC. The final model was parsimonious and clinically logical, consistent with standard approaches to LCA (Collins & Lanza, 2010). We used the PROC LCA (Version 1.3.0) add-on for SAS from the Penn State Methodology Center (Lanza et al., 2015). PROC LCA handles missing data using a full-information maximum likelihood approach and identifies class memberships for participants with missing data on symptoms.

We examined differences in demographic and clinical characteristics, insomnia severity, and sleep characteristics across the identified symptom profiles using chi-square tests and analysis of variance (ANOVA). We also examined whether the use of HF medication, insomnia severity, and sleep variables differed across the symptom profiles after adjusting for age, gender, body mass index, ejection fraction, and Charlson comorbidity index using the generalized linear model (GLM). We checked the residuals for normality in the ANOVA and GLM and corrected the skewed distributions of residuals by log-transforming the variables.

We also used multinomial regression, an extension of logistic regression that allows for categorical outcomes that include more than two groups, to develop a model to determine how demographic and clinical characteristics differed between symptom cluster profiles. We created a parsimonious model using stepwise selection with the variables that had significant bivariate association with the symptom profiles. All continuous variables were standardized with zero means and one standard deviation in the model.

Results

The sample included 195 participants [mean age = 63.0 (SD 12.8) years]. The majority of the sample was male (n = 111, 56.9%) and White (n = 146, 74.9%). Table 1 reports the demographic and clinical characteristics of the participants. The most frequently reported symptom was fatigue (n = 142, 73.6%), and the least frequent was daytime sleepiness (n = 61, 31.3%), based on the dichotomized variables. Table 2 reports the means and standard deviations of the symptom scores, symptom prevalence (severe vs. none-mild), and bivariate correlations between the symptoms. Most symptoms were correlated with each other (r = .21 to .73 for statistically significant correlations with ps < .05). However, pain was not associated with anxiety, depression, or daytime sleepiness, and dyspnea was not associated with anxiety. Daytime sleepiness was associated with fatigue but not with the other daytime symptoms.

The three-class LCA model was selected to describe the symptom cluster profiles. This model had the lowest BIC and CAIC and was more parsimonious and clinically logical than the 4-class model (see Table 3). As reported in Table 4, Class 1 (N = 73, 37.4% of the sample) was comprised of "physical" symptoms. Participants had a high probability of experiencing fatigue, pain, dyspnea, and daytime sleepiness. Participants in Class 2 (N = 12, 16.6%) (emotional symptom profile) had a high probability of experiencing anxiety and depression but not physical symptoms. Class 3 (N = 110, 57.1%) (all-high symptoms) was the largest class. People in this class had a high probability of experiencing both physical and emotional symptoms. The probability of experiencing symptoms in the physical symptom profile ranged from .000 (anxiety and depression) to .484 (fatigue). The probability of experiencing symptoms in the emotional profile ranged from .000 (fatigue, pain, dyspnea, and sleepiness) to .6417 (anxiety). The probability of experiencing symptoms in the all-high symptom profile ranged from .3522 (pain) to 1.00 (fatigue).

We examined differences in participants' demographic and clinical characteristics across the three symptom profiles (Table 3). There were no statistically significant differences across the groups in the proportion of participants with preserved [left ventricular ejection fraction (LVEF)　50%], midrange (LVEF = 41 to 49%) or reduced ejection fraction (LVEF　40%), proportion of each group who had New York Heart Association Class I-II or Class III-IV HF, or by Seattle Heart Failure Model score. However, almost one-quarter of people with HF in the all-high symptom group were classified with NYHA Class III-IV HF, compared to 18% in the physical symptom group and 8% in the emotional symptoms group. Body mass index (BMI), the Charlson Comorbidity Index, and use of beta blockers were highest in participants in the all-high symptom profile. Insomnia severity, but not actigraph-recorded or self-reported specific sleep characteristics (i.e., sleep duration, sleep efficiency, sleep onset latency), was highest among participants in the all-high symptom profile. Participants taking beta blocker medications [n = 128, Mean LVEF = 47.4% (SD=15.1)] had significantly lower LVEF than those not taking beta blockers [n = 63, Mean LVEF = 53.6% (SD = 14.3)] based on two sample T-tests (T(df=189) = 2.72, p = .0071).

Table 6 presents the results of the multinominal regression. People in the all-high symptom cluster profile, compared to those in the physical symptom cluster profile, had higher odds of having a higher BMI, using beta blockers, and more severe insomnia. Compared to the emotional symptom cluster profile, people in the all-high symptom cluster profile had higher odds of having more comorbidity and using beta blockers.

Discussion

To our knowledge, this was the first study to evaluate the associations between insomnia severity, sleep characteristics, and daytime symptom cluster profiles among adults with stable chronic HF and comorbid insomnia and extends previous insomnia research that focused on single daytime symptoms. Notably, the majority (56.4%) of the participants belonged to the all-high symptom cluster profile, and there were no symptom cluster profiles that reflected all low symptoms as in previous studies of people with HF (Lee et al., 2014; Moser et al., 2014; Park et al., 2019). This may reflect the higher symptom burden among

people who have insomnia in addition to HF and suggests the need to develop and test interventions to improve clustered symptoms.

While all participants had insomnia symptoms in our study, the moderate to severe levels of insomnia in the group in the all-high symptom burden suggests the particular importance of insomnia to co-occurring physical and psychological symptoms. Habitual sleep quality, likely reflecting insomnia, was poor overall, while sleep latency, sleep efficiency and sleep duration were consistently lower than recommended values in all three symptom cluster profile groups (Hirshkowitz et al., 2015; Ohayon et al., 2017). Although there were not statistically significant differences between groups in these sleep characteristics, sleep duration was almost an hour longer in the emotional symptoms group compared to the all symptoms group, and mean sleep latency was 50 minutes in the emotional symptoms groups, considerably longer than in either of the other symptom cluster profile groups. Therefore, the lack of statistically significant differences in sleep variables may be due to overall poor sleep quality, but in the case of self-reported sleep duration and latency, the lack of difference may be due to the small sample sizes in the emotional symptom cluster profile that were underpowered for these comparisons. On the other hand, lack of an association between sleep duration and other sleep characteristics and symptoms is consistent with our previous study of people with stable HF and insomnia, in which insomnia, but not sleep duration, was associated with individual symptoms of fatigue, depression, and excessive daytime sleepiness (Redeker et al., 2010). Additional research is needed in a sample with and without insomnia to confirm if actigraph- measured sleep and other sleep characteristics are associated with daytime symptom burden in people with HF.

As in our past study, in which we found that sleep-disordered breathing did not explain insomnia or individual symptoms (Redeker et al. 2010), the presence of continuous positive airway pressure (CPAP)-treated sleep-disordered breathing was not associated with membership in daytime symptom cluster profiles. This finding is consistent with previous research in Veterans with obstructive sleep apnea that found that only 14% of the sample experienced moderate or severe daytime symptoms (Wallace & Wohlgemuth, 2019). It is possible that objective measures of adherence to CPAP might be more sensitive to differences in symptom profiles.

We found that beta blocker medication use was more common among members of the all-high symptom profile. Consistent with the equivocal evidence of the efficacy of beta blockers for people with HF with preserved ejection fraction (Xu & Wang, 2019), beta blocker medication was more common among people with reduced ejection fraction. Yet, reduced ejection fraction was not associated with higher symptom burden. Thus, the reasons for these apparently contradictory findings are not clear, and it is possible that they may be explained by difference in the presentation or pathogenesis of HF, a heterogeneous condition. Our findings may also be explained by differences in the types, timing, or dosages of beta blocker medications that may differ in their effects on sleep and daytime symptoms (Cojocariu et al., 2021; Stoschitzky et al., 1999). However, data on the specific types and timing of beta blockers used or detail on the pathogenesis of HF were not available in the current study. Given that some beta blocker medications suppress the endogenous release of nocturnal melatonin, which may produce symptoms of insomnia, and in turn, contribute

to daytime symptoms (Arendt et al., 1985; Nathan et al., 1997), future research in a larger study is needed to evaluate the role of these medications in sleep and circadian timing among people with HF.

Although our data are cross-sectional, the associations between insomnia and symptom cluster profiles it is possible that interventions to improve insomnia, such as cognitive behavioral therapy for insomnia (CBT-I), may improve daytime symptom burden as indicated by symptom cluster profiles. CBT-I had a small to moderate effect on individual daytime symptoms of fatigue, depressive symptoms, and daytime sleepiness as reported in a recent systematic review and meta-analysis (Benz et al., 2020) and our previous preliminary efficacy study and the study from which the current data were drawn (Redeker et al., 2015; Redeker et al., 2022).

Future studies are needed to evaluate the biological mechanisms that may explain the relationships between insomnia and symptom burden, as indicated by symptom cluster profiles. Insomnia and HF are both characterized by sympathetic hyperarousal, a phenomena that may explain the relationships between insomnia and HF or HF severity. As in our previous study, activation and diurnal variations in the HPA axis may also play a role, as suggested by our previous research in which anxiety, depression, and fatigue were negatively associated with the ratio between daytime and nocturnal cortisol, a measure of hypothalamic pituitary adrenal (HPA) axis function (Redeker et al., 2020).

The cross-sectional nature of this study precludes evaluation of causality among the primary study variables. Although the sample size was appropriate for the LCA approach to identify symptom cluster profiles, there may not have been adequate statistical power to detect statistically significant differences across symptom cluster profiles on all of the clinical, demographic, and sleep-related correlates of the symptom cluster profiles. However, a power analysis to address these differences would not have been possible conduct *a priori*, given the fact that the size or number of symptom cluster profiles could not have been known in advance.

The parent study was designed as a clinical trial to treat insomnia and included people with even mild insomnia due to the lack of information on the role of any level of insomnia in HF and the effects of CBT-I. Due to this design characteristic, we do not have available data on people who did not have insomnia symptoms. Therefore, we cannot infer from our findings to this group. Nevertheless, it is notable that the all-high symptom cluster profile group met the threshold for clinical insomnia (ISI   14) (Gagnon et al., 2013), while the other groups had sub-threshold levels of insomnia. Additionally, our sample was younger and had less severe HF than some previous HF studies, which may limit the generalizability of our findings. However, only two previous studies have used CBT-I to treat insomnia in people with insomnia and HF, both of which primarily included participants with NYHA HF stages I and II, similar to the study participants characteristics in this study (Harris, Schiele & Emery, 2019; Redeker et al., 2015). Additional study is needed to include more participants with advanced HF and also to determine the extent to which treatment of insomnia may prevent advancement of symptoms and even progression of HF (Javaheri & Redline, 2017).

HF and sleep clinicians should carefully evaluate people with HF for the presence of insomnia and multiple co-occurring daytime symptoms. This seems especially important among people with clinical levels of insomnia who had higher symptom burden. Interventions for insomnia such as CBT-I should be offered as they may improve both insomnia severity and reduce daytime symptom burden.

People with HF and insomnia experience a high burden of daytime symptoms, and insomnia severity is a meaningful correlation of these symptoms. Future research is needed to determine the effects of treating insomnia on the transition between symptom cluster profiles reflecting higher to lower symptom burden and the biological mechanisms that may explain these relationships.

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Table 1.

Demographic, Clinical, and Sleep Characteristics (N=195)

Variables	Mean (SD) / N (%)
Age	63.0 (12.8)
Gender: Female	84 (43.1%)
Race	
White	146 (74.9%)
African American	35 (17.9%)
Native American	1 (0.5%)
Asian	1 (0.5%)
Other	12 (6.2%)
Ethnicity	
Hispanic	9 (4.6%)
Non-Hispanic	185 (95.4%)
Veterans	24 (12.3%)
Body Mass Index (BMI)	31.9 (8.4)
<18.5	3 (1.6%)
18.5 - <25	37 (20.0%)
25 - <30	44 (23.8%)
30+	101 (54.6%)
New York Heart Association (NYHA) Classification	
I	60 (31.1%)
II	88 (45.6%)
III	40 (20.7%)
IV	5 (2.6%)
Ejection Fraction (EF) %	49.5 (15.1)
HFpEF (LVEF 50%)	104 (54.4%)
HFmEF (LVEF 41–49%)	29 (15.2%)
HFrEF (LVEF 40%)	58 (30.4%)
Seattle Heart Failure Model	11.6 (5.0)
Charlson Comorbidity Index (CCI)	2.8 (1.9)
Sleep Apnea / CPAP Use	104 (53.3%)
Heart Failure Medications	
ACE or ARB	96 (49.2%)
Beta-blocker	129 (66.2%)
Statin	118 (60.5%)
HCTZ	8 (5.7%)
Loop diuretic[*]	124 (71.3%)
Insomnia Severity Index (ISI)	15.0 (4.6)

Note. HFpEF = heart failure persevered ejection fraction, HFmEF = heart failure midrange ejection fraction, HFrER = heart failure reduced ejection fraction, LVEF = left ventricular ejection fraction.

Loop diuretic* counts any loop diuretic among Bumex, Demadex, and Lasix.

Table 2.

Descriptive Statistics and Correlations among Daytime Symptoms (N=195)

Symptom Variables	Mean (SD)	Cut-off for Severe N (%)	Correlation				
			Pain	Anxiety	Depression	Dyspnea	Sleepiness
Fatigue – PROMIS	55.0 (8.9)	50 142 (73.6%)	**0.31	**0.44	**0.53	**0.51	*0.21
Pain – PROMIS	44.9 (10.5)	50 63 (32.8%)	-	0.16	0.18	**0.34	0.11
Anxiety – PROMIS	51.5 (8.8)	50 109 (56.2%)		-	**0.75	0.19	0.14
Depression – PROMIS	50.3 (8.7)	50 101 (52.9%)			-	*0.23	0.13
Dyspnea – MADS	19.7 (13.9)	20 92 (47.9%)				-	0.02
Sleepiness – ESS	8.1 (4.8)	11 61 (31.3%)					-

Note. Correlation was calculated with continuous variables using the Pearson coefficient.

*, ** indicate significance at 0.05 and 0.01, respectively, after Bonferroni correction for 15 multiple tests.

Table 3.

Latent Analysis Fit Statistics

Number of statuses	Likelihood Ratio G^2	Degree of freedom	AIC	BIC	cAIC	Adj. BIC
2	77.33	50	103.33	145.88	158.88	104.7
3	**46.42**	**43**	**86.42**	**151.88**	**171.88**	**88.52**
4	28.42	36	82.49	170.86	197.86	85.33
5	22.45	29	90.45	201.74	235.74	94.03

Note: Bold indicated the selected latent class model

Table 4.

Response Probabilities of Severe Symptoms in Each Class-membership from Latent Class Model (N=195)

Symptoms	Class I N=73 (37.4%)	Class II N=12 (6.2%)	Class III N=110 (56.4%)
Fatigue	0.4840	0.0000	1.0000
Pain	0.3522	0.0000	0.3522
Anxiety	0.0781	0.6417	0.8652
Depression	0.0000	0.5496	0.8651
Dyspnea	0.4126	0.0000	0.5864
Sleepiness	0.2359	0.0000	0.4042

Table 5.

Comparison of the Three Symptom Class Profiles on Demographic and Clinical Characteristics, Adjusting for Age, Gender, Body Mass Index, Ejection Fraction, and Charlson Comorbidity Index. (N=195)

Variables	Class I: Severe in physical symptoms only N=73	Class II: Severe in emotional symptoms only N=12	Class III: All-high symptoms N=110	Difference P-value
Age	64.1 (12.4)	67.3 (19.1)	61.8 (12.1)	.2407
Gender: Male				
Male	45 (61.6%)	8 (66.7%)	58 (52.7%)	.4009
Female	28 (38.4%)	4 (33.3%)	52 (47.3%)	
Race				
White	50 (68.5%)	8 (66.7%)	88 (80.0%)	.1539
Others	23 (31.5%)	4 (33.3%)	22 (20.0%)	
Ethnicity				
Hispanic	4 (5.5%)	1 (8.3%)	4 (3.7%)	.6983
Non-Hispanic	69 (94.5%)	11 (91.7%)	105 (96.3%)	
Body Mass Index (BMI)	29.5 (6.5)	29.9 (6.8)	33.7 (9.2)	.0028
New York Heart Association (NYHA) Classification				
I & II	59 (81.9%)	11 (91.7%)	78 (71.6%)	.1490
III & IV	13 (18.1%)	1 (8.3%)	31 (24.4%)	
Ejection Fraction (EF) %	50.6 (14.9)	42.6 (14.7)	48.0 (15.8)	.2417
HFpEF (LVEF 50%)	39 (54.9%)	4 (33.3%)	61 (56.5%)	.6462
HFmEF (LVEF 41–49%)	11 (15.5%)	3 (25.0%)	15 (13.9%)	
HFrEF (LVEF 40%)	21 (29.6%)	5 (41.7%)	32 (29.6%)	
Seattle Heart Failure Model	11.7 (5.5)	11.0 (3.9)	11.7 (5.0)	.9052
Charlson Comorbidity Index (CCI)	2.6 (1.9)	1.5 (1.0)	3.0 (1.9)	.0163
Sleep Apnea / CPAP Use	33 (45.2%)	7 (58.3%)	64 (58.2%)	.2074
Heart Failure Medications				
ACE or ARB	40 (54.8%)	5 (41.7%)	51 (46.4%)	.4629
Beta blocker	42 (57.5%)	4 (33.3%)	83 (75.4%)	*.0018
Statin	45 (61.6%)	5 (41.7%)	68 (61.8%)	.3865
HCTZ	1 (2.0%)	2 (20.0%)	5 (6.2%)	.0927
Loop diuretic	51 (78.5%)	6 (60.0%)	67 (67.7%)	.2362
Insomnia Severity Index (ISI)	13.5 (4.5)	13.6 (3.9)	16.4 (4.4)	**<.0001
Self-reported sleep characteristics (PSQI)				
Sleep Duration	6.1 (2.1)	6.7 (1.6)	5.8 (1.4)	.1469
Sleep Efficiency	80.2 (15.3)	80.1 (12.6)	76.5 (14.7)	.2508
Sleep Latency	28.5 (27.6)	50.0 (54.1)	36.9 (39.1)	.1221
Nocturia (3 or more times per week)	47 (66.2%)	6 (50.0%)	79 (75.1%)	.2060
Actigraph sleep characteristics				
Sleep Duration (h)	7.9 (1.8)	7.9 (1.2)	7.6 (1.6)	.4690
Sleep Efficiency (%)	80.3 (7.5)	82.0 (7.1)	79.7 (10.3)	7066

Variables	Class I: Severe in physical symptoms only N=73	Class II: Severe in emotional symptoms only N=12	Class III: All-high symptoms N=110	Difference P-value
Sleep Latency (min)	19.4 (16.4)	20.2 (10.9)	20.2 (22.8)	.9711
Wake After Sleep Onset (min)	62.0 (26.4)	57.3 (26.2)	62.8 (36.2)	.8658

Note.

*, ** indicates that p-value is still <.05 and <.01 respectively after adjusting for age, gender, body mass index, ejection fraction, and Charlson Comorbidity Index.

The p-value for sleep latency was obtained using log-transformed sleep latency. HFpEF = heart failure persevered ejection fraction, HFmEF = heart failure midrange ejection fraction, HFrER = heart failure reduced ejection fraction, LVEF = left ventricular ejection fraction.

Table 6.

Demographic, Clinical, and Sleep Correlates of Symptom Profile Membership: Multinomial Model

	All High (Class III) vs. Physical Only (Class I)		All High (Class III) vs. Emotion only (Class II)		
	Coefficient ± SE (p-value)	Odds Ratio [95% CI]	Coefficient ± SE (p-value)	Odds Ratio [95% CI]	P-value
Charlson Comorbidity Index (CCI)	0.07±0.18 (.6819)	1.08 [0.76, 1.52]	1.37±0.66 (.0381)	3.93 [1.08, 14.30]	.1156
Body Mass Index	0.51±0.20 (.0115)	1.66 [1.12, 2.46]	0.26±0.37 (.4881)	1.29 [0.62, 2.68]	.0407
Beta blocker	0.79±0.36 (.0291)	2.21 [1.08, 4.52]	1.64±0.68 (.0160)	5.14 [1.36, 19.46]	.0162
Insomnia Severity	0.58±0.18 (.0018)	1.79 [1.24, 2.57]	0.63±0.39 (.1090)	1.87 [0.87, 4.01]	.0051

Note. Continuous variables including CCI, body mass index, and insomnia severity index were standardized with zero mean and one standard deviation