The Utility of Home Sleep Apnea Testing in the Advanced Heart Failure Populations

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Untreated sleep disorders form a risk of coronary artery disease, hypertension, obesity, and diabetes mellitus. Access to polysomnography is limited, especially during the COVID-19 pandemic, with home sleep apnea testing (HSAT) being a potentially viable alternative. We describe an HSAT protocol in patients with advanced heart failure (HF). In a single-center, observational analysis between 2019 and 2021 in patients with advanced HF and heart transplant (HT), 135 screened positive on the STOP-Bang sleep survey and underwent a validated HSAT (WatchPAT, ZOLL-Itamar). HSAT was successful in 123 patients (97.6%), of whom 112 (91.1%; 84 HF and 28 HT) tested positive for sleep apnea. A total of 91% of sleep apnea cases were obstructive, and 63% were moderate to severe. Multivariable linear regression showed that the apnea hypopnea index was 34% lower in the HT group than in the HF group (p = 0.046) after adjusting for gender, and that this effect persisted in White patients but not among African-Americans. Patient characteristics were similar between groups, with coronary artery disease, diabetes mellitus, and hypertension as the most prevalent co-morbidities. In conclusion, sleep apnea remains prevalent in patients with HF with a high co-morbidity burden. HSAT is a feasible and effective tool for screening and diagnosis in this population. **(Am J Cardiol 2023;191:8−13)**

Obstructive sleep apnea (OSA) is the most prevalent sleep apnea diagnosis in the general population. However, although infrequent, central sleep apnea (CSA) is common among patients with heart failure (HF).[1] In this population, CSA is strongly linked to poor outcomes, whereas both diagnosis and treatment of CSA have proved difficult. The accepted gold standard for the diagnosis of sleep apnea is polysomnography.[2] However, a device for home sleep apnea testing (HSAT) was cleared for use by the United States. The Food and Drug Administration in 2007 and[3−5] the American Academy of Sleep Medicine has since then included the peripheral artery tone, as measured by the device, for use in their HSAT guidelines.[3−5] HSAT has been reported to provide an accurate measure of the overall apnea hypopnea index (AHI), and it effectively differentiates between CSA and OSA.[1] To date, no study has described its use in patients with advanced HF or after heart transplant (HT). Herein, we describe the use of HSAT to diagnose sleep apnea in a cohort consisting of patients with HF and HT who tested positive on the STOP-Bang Sleep Disorder Survey, a validated screening method for sleep apnea.[6,7]

Methods

This was a single-center study with a retrospective pilot phase (patients tested before December 2020) and prospective observational phase (patients tested after December 2020). The protocol and written informed consent form were approved by the institutional review board of Baylor Scott and White Research Institute. Adult patients (aged ≥18 years) who were referred to our Advanced Heart Failure Clinic or who were recipients of a HT were eligible for inclusion in this study if they screened positive on the STOP-Bang Sleep Disorder Survey (defined as score ≥3). For all patients who tested positive on the STOP-Bang survey and who met all other eligibility criteria, an HSAT (WatchPAT; ZOLL-Itamar, Atlanta, Georgia) was ordered as part of their standard of care. Patients were excluded from the study if they had previously been diagnosed with sleep apnea. Patient characteristics and co-morbidities were collected from the electronic medical record at the time of the screening visit. The main objectives were to evaluate a protocol to diagnose sleep apnea and to assess the incidence and severity in patients with HF and recipients of a HT.

The HSAT measurements recorded from the sleep study report included sleep duration, the division of total number of apneic and hypopneic events (captured in the AHI), rapid eye movement percentage, and arterial O_2 saturation, and sleep apnea type (OSA, CSA, or mixed) and severity classified according to none (AHI <5), mild (AHI = 5 to 14),

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Funding: This research was funded by the Baylor Healthcare System Foundation (Dallas, Texas) through a grant from the Cardiovascular Research Review Committee.

See page 13 for disclosure information.

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0002-9149/
https://doi.org/10.1016/j.amjcard.2022.12.005

moderate (AHI = 15 to 30), or severe (AHI >30).[8] All HSAT sleep studies were scored by 1 of the several sleep physicians at our center.

Patient demographics and characteristics were described according to frequency (%) for categorical variables, mean ± SD for normally distributed continuous variables, and median (interquartile range [IQR]) for non-normal continuous variables. The comparisons between HF and HT groups were made using chi-square tests or Fisher's exact test for categorical data and *t* tests or Wilcoxon rank sum tests for continuous data. The Jonckheere-Terpstra test was used to evaluate for a trend between sleep apnea severity and body mass index (BMI). Sleep apnea severity was described and compared by gender and race overall and within the HF and HT cohorts. The differences between HF and HT groups comparing the severity of sleep apnea were evaluated using multivariable linear regression on log-transformed AHI, a continuous measure of sleep apnea severity (expressed in number of events per hour). Subsequently, group effects comparing HF and HT were reported overall unadjusted and adjusted for gender. Given the exploratory and descriptive nature of this analysis to describe the potential differences in AHI, the group effects were also described within the racial groups (White and African-American). All analysis were performed in R statistical software (version 4.1.1). Statistical significance was assessed using 2-sided p values at a threshold of 0.05.

Results

A total of 135 patients who screened positive on the STOP-Bang survey underwent testing. Among them, 9 subjects with a left ventricular assist device (LVAD) screen-failed after inconclusive test results. Subjects with LVAD were subsequently not approached for HSAT and excluded from the study (Figure 1). Of 126 patients with HF and/or HT, 123 (98%) obtained a successful HSAT test result. There were 4 failed HSAT attempts (unusable sleep data for analysis) among 3 patients who did not have a subsequent successful test. Among patients who tested positive on the STOP-Bang survey with a successful HSAT, 91% (n = 84 HF and n = 28 HT) tested positive for sleep apnea and 9% (11 of 123) had no sleep apnea on HSAT. The patient characteristics of those with sleep apnea were similar between the HF and HT groups (Table 1).

The median time from HT to HSAT was 137 days (IQR 82 to 295) in the HT cohort. The results from HSAT are described in Table 2. OSA accounted for 91%, CSA for 1%, and mixed sleep apnea for 8% of the overall cohort. In the HF group, 11% had a component of CSA compared with 4% in the transplant group, which did not differ statistically (p = 0.44). Among 9 patients diagnosed with CSA or mixed sleep apnea, the median AHI was 50.3 (IQR 33.7 to 69.4) and the median central AHI was 24.5 (IQR 18.4 to 25.8) with 8 patients presenting with a moderate to severe CSA component of central AHI ≥15 events per hour. The severity of sleep apnea was associated with increasing BMI (median BMI in patients with mild sleep apnea: 27.7 kg/m^2, moderate: 29.7 kg/m^2, severe: 34.6 kg/m^2; Jonckheere-Terpstra test p <0.001; Figure 2). The median AHI of 22.0 events per hour (IQR 10.5 to 42.2) in patients with HF and 19.2 (8.7 to 38.9) in patients with HT did not differ significantly (p = 0.33). No statistical differences were noted between the 2 cohorts in rapid eye movement percentage (p = 0.82) and nocturnal O_2 saturation (p = 0.90).

The prevalence of moderate to severe sleep apnea was 69% in men and 53% in women. The median AHI was 13.6 (8.6 to 28.2) in women compared with 22.0 (11.6 to 42.6) in men, which was not statistically different overall (p = 0.14) or within groups (Figure 3). Moderate to severe sleep apnea was detected in 69% of African-American patients and in 60% of White patients. Overall, the median AHI was similar among racial groups (White vs African-American: 20.3 [9.1 to 34.5] vs 23.9 [11.6 to 47.6], p = 0.27). Considering race by group, the highest median AHI of 32.8 (13.9, 46.4) was observed in African-American patients with HT. This was not significantly different relative to the lowest median AHI of 13.2 (6.2 to 23.1) recorded in White patients with HT (Wilcoxon p = 0.07; Figure 3).

In a multivariable analysis, AHI was 34% lower in the HT group than the HF group after adjusting for gender (effect on geometric mean 0.66, 95% confidence interval [CI] 0.44 to 0.99, p = 0.046; Table 3). Unadjusted, these differences were not statistically significant (p = 0.09). An interaction term between race and group was considered in the multivariable models to evaluate for a differential effect by group but did not reach statistical significance (White race and HT group effect on geometric mean 0.45, 95% CI 0.20 to 1.03, p = 0.061). As an exploratory analysis, the differences in AHI by group were also described within White and African-American race. Similar to the overall comparison, AHI remained 49% lower comparing HF and HT among White patients (effect on geometric mean: 0.53, 95% CI 0.33 to 0.86, p = 0.011; Table 3). However, there was no significant difference comparing AHI between HF and transplant groups among African-American patients (effect on geometric mean 1.16, 95% CI 0.59 to 2.27, p = 0.67). The results were similar adjusting for gender among White patients (0.51, 95% CI 0.31 to 0.81, p = 0.006) and African-American patients (effect on geometric mean 1.12, 95% CI 0.54 to 2.31, p = 0.76).

Discussion

HF affects 5 to 6 million people in North America. Despite the introduction of new drugs over the last 2 decades, the mortality rate remains high, with only a slight improvement in morbidity and HF hospitalizations.[1,9] Patients with HF sleep fewer hours at night and experience interrupted sleep, and despite that, they do not have the same level of daytime sleepiness. Based on recent studies, half of the patients with HF either had OSA or CSA or a combination of both. Unfortunately, sleep apnea remains underdiagnosed, especially in this patient population. Our intent was to establish the feasibility and effective utilization of this screening and diagnostic tool in HF and HT populations.

Overall, HSAT was successful in the vast majority of subjects in both groups. Patients were generally more

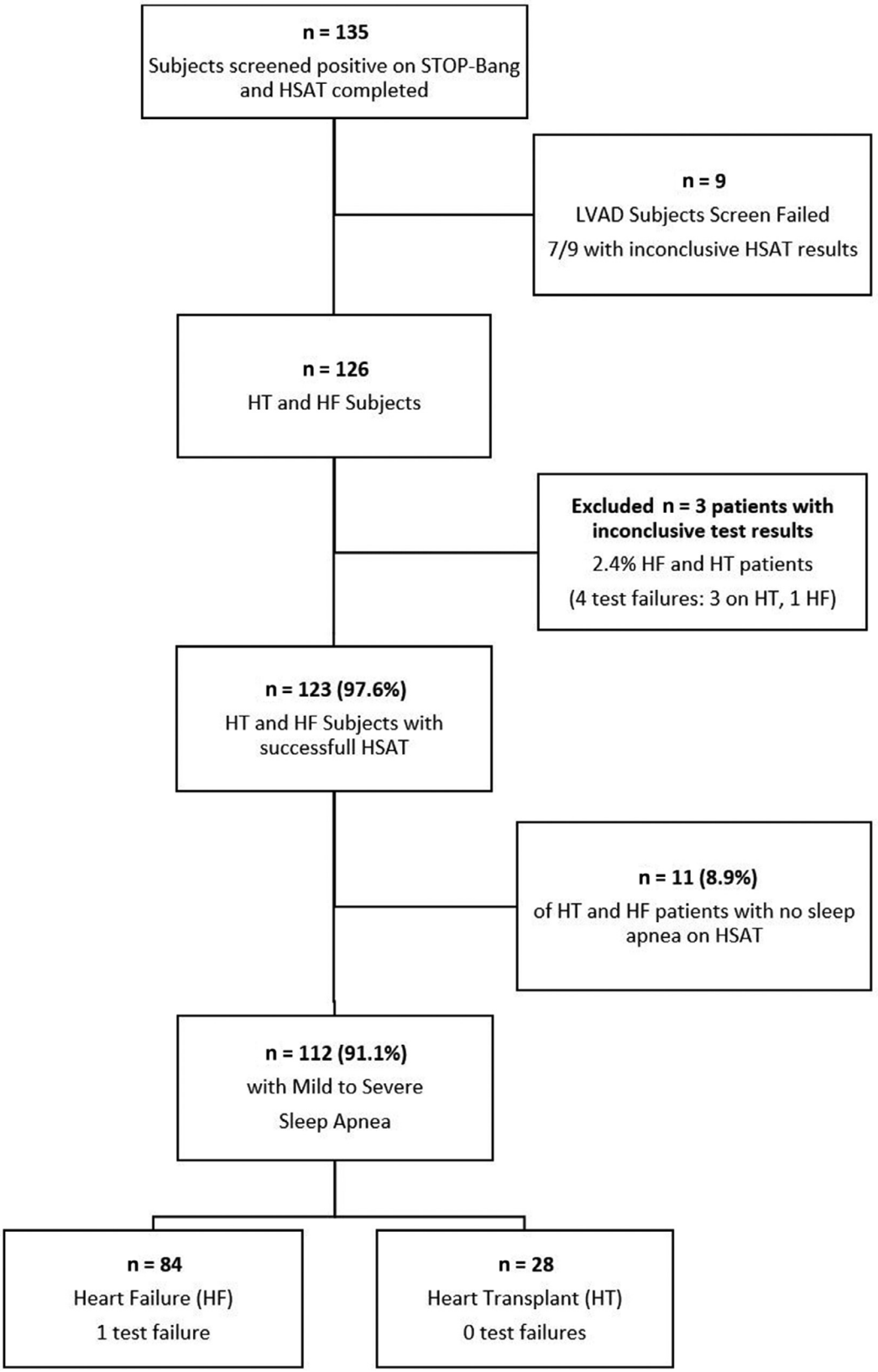

Figure 1. CONSORT patient flow diagram. CONSORT = Consolidated Standards of Reporting Trials.

Table 1
Demographics and characteristics in heart failure and heart transplant patients

Variable	Overall (n = 112)	Heart failure (n = 84)	Hear transplant (n = 28)	p Value
Age, yr	59 [51, 67]	59 [50, 67]	58 [55, 66]	0.79
Sex, female	32 (29%)	28 (33%)	4 (14%)	0.09
Race				0.24
African-American	37 (33%)	27 32%)	10 (36%)	
Native Hawaiian or other Pacific Islander	1 (1%)	0 (0%)	1 (4%)	
White	74 (66%)	57 (68%)	17 (61%)	
BMI, kg·m^2	30 [26, 36]	31 [26, 37]	30 [27, 33]	0.53
Asthma	6 (5%)	6 (7%)	0 (0%)	0.33
CAD	55 (49%)	43 (51%)	12 (43%)	0.55
COPD	5 (4%)	4 (5%)	1 (4%)	1
Diabetes mellitus	48 (43%)	36 (43%)	12 (43%)	1
Hypertension	110 (98%)	83 (100%)	27 (96%)	0.25
Heart failure etiology				0.16
ICM	54 (50%)	44 (54%)	10 (36%)	
NICM	53 (49%)	35 (43%)	18 (64%)	
Other	2 (2%)	2 (2%)	0 (0%)	

BMI = body mass index; CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; ICM = ischemic cardiomyopathy; NICM = non-ischemic cardiomyopathy.

receptive to HSAT as a testing modality versus going to a polysomnography testing center. Strikingly, 91% of those with a successful HSAT tested positive for sleep apnea, supporting the need to screen and test all patients with HF and HT as part of routine care. At a success rate of 97.6%, we were able to confidently establish that HSAT can be utilized as a tool for screening and diagnostics in the patient populations with advanced HF and HT. However, based on our previous study, WatchPAT HSAT was unable to provide conclusive data for patients with LVAD, potentially because of the lack of native pulsatility.[4]

The cohort was 29% women, which possibly reflects a lower prevalence of sleep apnea in women. This finding is consistent with the gender distribution in patients with advanced HF and HT.[10–12] The prevalence of moderate to severe sleep apnea in our study was higher in men than in women, with no significant gender difference in AHI. This supports the SchlaHF registry results identifying male gender, age, obesity, severe impairment of systolic cardiac function, New York Heart Association functional classes III and IV, and atrial fibrillation as independent predictors of sleep-related breathing disorders.[12] However, there were no differences between male or female participants that had these significant predictors. Thus, although the overall prevalence of sleep-related breathing disorders has been reported higher in men than women, gender differences may not exist if significant risk factors that predict sleep disorders, such as HF, are present.

Roughly 2/3 of the cohort had moderate to severe sleep apnea, consistent with previous studies.[13] Interestingly, only a small portion of our patient sample had CSA or mixed sleep apnea, a finding that was especially pronounced in the transplant group. Previous studies on small samples have shown that CSA is generally eliminated after HT.[14] In the present study, a lower prevalence of CSA and mixed sleep apnea was noted in the HT cohort and mainly

Table 2
Sleep study results

Variable	Overall (n = 112)	Heart failure (n = 84)	Heart transplant (n = 28)	p Value
AHI (events/hr)	21.7 [9.3, 41.1]	22.0 [10.5, 42.2]	19.2 [8.7, 38.9]	0.33
REM (%)	18.4±8.2	18.5±8.3	18.1±8.2	0.82
Nocturnal arterial O_2 saturation	83 [79, 87]	83 [80, 87]	83 [78, 89]	0.90
Sleep (hr)	7.0±1.8	7.0±1.9	6.9±1.3	0.80
Sleep apnea type				0.76
Obstructive	94 (91%)	68 (90%)	26 (96%)	
Central	1 (1%)	1 (1%)	0 (0%)	
Mixed	8 (8%)	7 (9%)	1 (4%)	
Central or mixed sleep apnea	9 (9%)	8 (11%)	1 (4%)	0.44
Sleep apnea severity				0.58
Mild	41 (37%)	29 (35%)	12 (44%)	
Moderate	32 (29%)	26 (31%)	6 (22%)	
Severe	38 (34%)	29 (35%)	9 (33%)	
Moderate to severe sleep apnea	70 (63%)	55 (65%)	15 (56%)	0.48

AHI = apnea hypopnea index; REM = rapid eye movements.

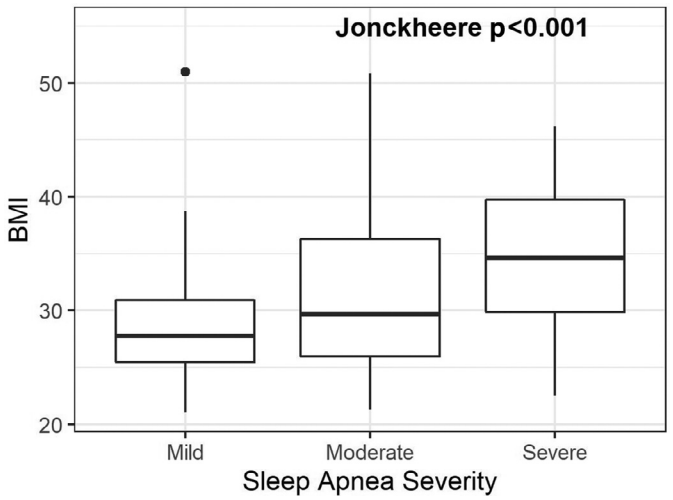

Figure 2. BMI by sleep apnea severity, sex, and race. The median BMI increased with increasing sleep apnea severity (JT test p <0.001). There were no significant differences comparing the median BMI by sex or race within each group (heart failure or heart transplant) (Wilcoxon p >0.05). JT = Jonckheere-Terpstra.

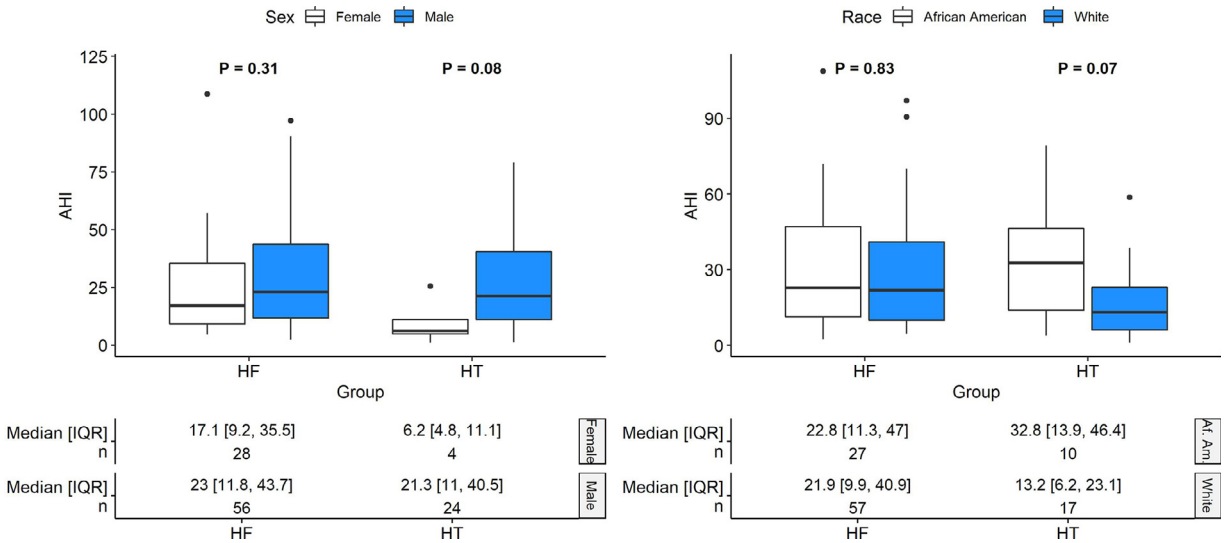

Figure 3. AHI by sex and race within groups (heart failure and heart transplant).

Table 3
Linear regression results on log-transformed AHI

Term	Effect on log AHI (95%CI)	Effect on geometric mean (95%CI)	p Value
Overall			
HT vs HF: unadjusted	−0.35 (−0.75, 0.05)	0.70 (0.48, 1.05)	0.090
Adjusted (sex)	−0.41 (−0.81, −0.01)	0.66 (0.44, 0.99)	0.046
Comparison among White patients			
HT vs HF: unadjusted	−0.64 (−1.13, −0.16)	0.53 (0.33, 0.86)	0.011
Adjusted (sex)	−0.68 (−1.16, −0.21)	0.51 (0.31, 0.81)	0.005
Comparison among African-American patients			
HT vs HF: unadjusted	0.15 (−0.52, 0.82)	1.16 (0.59, 2.27)	0.67
Adjusted (sex)	0.11 (−0.61, 0.84)	1.12 (0.54, 2.31)	0.76

Results are reported as the estimated group effect (*HT vs. HF*) on log-transformed AHI and the exponentiated effect that estimates the effect on the geometric mean of AHI.

AHI = apnea hypopnea index; CI = confidence interval; HF = heart failure; HT = heart transplant.

attributed to lower rates of mixed sleep apnea, although these differences were not statistically significant. In the HT group, higher AHI index values were observed in African-American than White patients, despite no racial differences in obesity or co-morbidity burden. Adjusted for gender, AHI was 34% lower comparing HF and HT groups. This finding was consistent among White patients, with significantly lower AHI in the HT group than in the HF group. However, among the African-American patients, no differences in AHI were observed between groups. The etiology of these observations is not clear, and larger studies are needed to determine if this trend persists.

This is the largest study to date using the HSAT in HF and HT and evaluating the burden of sleep apnea in these populations. Our study highlights the important role that advanced HF centers across the country can play in establishing a pathway to sleep apnea diagnosis and its management. This pathway is very much integrated within the advanced HF clinic. To ensure adequate follow-through on the diagnosis and test results, a provider champion should be identified at each HF clinic, and screening with every new patient consultation. This was also seen in the only Medicare study that reported improving survival, less hospitalization, and lower cost of treated than untreated patients with HF, again after adjusting for confounders.[9]

Since the COVID-19 pandemic era, significant challenges exist, limiting the therapies for those patients, specifically with OSA or mixed sleep apnea. Fortunately, newer technologies, such as upper airway stimulation for OSA[15] and phrenic nerve stimulation for CSA[16] offer hope and can be used within the confines of the HF treatment pathway. The emergence of effective treatments will reinforce the call for more accurate sleep apnea screening and monitoring.[17]

The limitations to this study are inherent to any single-center, observational study. The patient characteristics may only be a regional representation and thus may not be extrapolated nationally. Patients with LVAD were excluded after the failure of WatchPAT HSAT, potentially because of the lack of native pulsatility. HSAT was performed only on patients who screened positive in the STOP-Bang screening survey, and thus, patients may have been ruled out incorrectly. We do not have follow-up results on the efficacy of therapy on patients who tested positive and were subsequently treated. However, future initiatives will examine sleep device therapies and clinical outcomes in this patient population. Finally, we had more than 1 sleep physician interpreting the HSAT results; therefore, variances in the interpretations could exist.

In conclusion, the prevalence of sleep apnea remains high in patients with HF and adds a significant and ominous high-risk co-morbidity that can persist in the post-HT populations. This will continue to facilitate poor short- and long-term clinical outcomes in both cohorts. HSAT is a feasible and effective tool for screening and diagnosis of sleep apnea in advanced HF. Continued work on the short- and long-term outcomes of screening and management of sleep apnea in this patient population is warranted.

Disclosures

Dr. Germany is a paid employee of ZOLL Medical Corporation. The remaining authors have no conflicts of interest to declare.

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