Prevalence of Sleep Disordered Breathing in Congestive Heart Failure as Determined by ApneaLink, a Simplified Screening Device

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Abstract

Background: Sleep disordered breathing (SDB) is very common in patients with congestive heart failure (CHF), with some studies reporting an incidence of 50%. Increased sympathetic activity, caused by frequent arousals (increased Apnea-Hypopnea Index [AHI]) during the night has been implicated as a contributing factor in a four-fold increase in mortality for CHF patients. Many patients are undiagnosed for SDB due to lack of awareness of the disorder and access to an easy, reliable screening test. The purpose of this study is to evaluate the prevalence of SDB in patients with CHF in the inpatient and outpatient settings using the ApneaLink (AL) (ResMed Corp, San Diego, CA) screening device.

Methods: 86 patients with CHF from the VA San Diego Healthcare System were enrolled. Eligible patients are those with diagnosis of CHF, treatment naïve for SDB, and symptomatic for sleep apnea (SA) per an SDB questionnaire created by study personnel. The mean age was 66 years, and the mean BMI was 32 kg/m^2. SDB was defined using an AHI result of ≥5 events/hour. The prevalence of SA was determined from the Apnea-Hypopnea Index (AHI) data recorded by the AL. Patients were included in the analysis if they had a minimum of 4 hours evaluation time (ET). Determination for the presence of Cheyne-Stokes respiration (CSR) was performed by evaluation of the flow signal data.

Results: Seventy percent (61/86) of the patients met the enrollment criteria. The overall prevalence of SA was 85% (52/61 subjects). CSR was detected in 33% (20/61 subjects). For the 46 subjects who completed the study in the outpatient setting, the prevalence of SA and CSR are 83% and 26%, respectively. In the inpatient setting, 15 patients with an admission diagnosis of CHF completed the study with a prevalence of 93% and 53% for SA and CSR, respectively.

Conclusions: SDB appears to be relatively common in the CHF population, regardless of age. Preliminary results provide supportive evidence for the clinical need to identify, diagnose and treat the CHF patient with SDB. The AL is a relatively simple test to administer to patients and easy to use by patients in the home setting. A larger sample size of hospital patients using the device is required to evaluate utility in the inpatient setting.

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Introduction

Sleep disordered breathing (SDB) is a common underlying disease in patients with congestive heart failure (CHF) and left ventricular dysfunction, with some studies reporting a prevalence from 50% to as high as 70%.[1,2] However, SDB is frequently overlooked in the management of heart failure patients. SDB incorporates both central sleep apnea (CSA, including Cheyne-Stokes respiration or periodic breathing) and obstructive forms of sleep apnea. Cheyne-Stokes respiration (CSR) is described as recurring episodes of crescendo hyperventilation and decrescendo hypoventilation with periodic apnea (cessation of breathing) and hypopnea (reduction of airflow) events that can lead to excessive arousals, oxygen desaturation, and changes in intrathoracic pressure.[3–5] This can result in adverse cardiac effects such as ischemia and arrhythmias from sympathetic nervous activation, increased blood pressure, and increased myocardial oxygen demand.[3–13] The National Institutes of Health (NIH) stated in their JNC-7 High Blood Pressure Guidelines that sleep apnea was an identifiable cause of hypertension. Several studies have shown that patients with SDB have an increased morbidity and worsened prognosis.[14–16] Furthermore, the presence of SDB has been correlated with an increased risk of developing CHF.[17]

Sleep apnea, primarily CSA and CSR, is known to be prevalent in patients with CHF. Schulz et al. found that 71% of patients with CHF had an AHI > 10 events/hour.[18] However, many patients in this population remain undiagnosed because of several obstacles. First, because symptoms of SDB often mimic those of heart failure, patients with these symptoms may be thought to just be suffering from worsened heart failure, and as such, are not referred for sleep testing. Second, because traditional sleep testing is time consuming and cumbersome, many practitioners and patients may be reluctant to take this step.

Early diagnosis of SDB and initiation of therapy may significantly improve the prognoses and reduction of symptoms in patients with heart failure. A study of nocturnal home oxygen therapy for treatment of sleep apnea showed concurrent improvements in AHI and LVEF.[19] CPAP therapy has also been shown to have a beneficial effect on LVEF in patients with SA. In a study by Egea et al., mean LVEF in patients treated with CPAP increased from 28.0% to 30.5% ($p<0.001$) after therapy, whereas patients in the sham-CPAP group did not show any improvement in LVEF.[20] In a similar study, Kaneko et al. examined the effects of CPAP on LVEF, blood pressure and heart rate in patients with dilated cardiomyopathy. They found that the CPAP group had significant increases in LVEF after one month of CPAP, as well as a mean decrease in systolic

blood pressure of 10 mmHg (p=0.02) and decrease in heart rate of 4 beats per minute (p=0.007). The control group did not show improvement in any of these variables.[21] Additionally, for patients with CHF and CSA/CSR, studies have shown that Adaptive Servo Ventilation (VPAP Adapt SV™, ResMed Inc, Poway, CA) improves not only AHI, SpO2, and sleep architecture, but also may improve VO2 max, six minute walk, quality of life, LVEF and other important cardiovascular outcomes for heart failure patients.[22–26]

With recent evidence implicating a positive impact on CHF symptoms with treatment of SDB, there may be an increasing need to screen for SDB.[18] Primary care providers as well as Cardiologists have been frustrated by the lack of a simple-to-use, yet sensitive and specific device to detect SDB in their patients. The major aim of the present study was to determine if assessing for SDB was feasible in a population of stable outpatient CHF patients using a portable apnea detector, the ApneaLink™ (AL) device. The secondary aims of the study were to determine prevalence of SDB in this population, clinician and patient ease of use, as well as the cost-effectiveness of the portable device in a real-world setting.

Methods

Patient Enrollment

From September 2005 through January 2007, 86 patients with a known diagnosis of left ventricular dysfunction with CHF and who were being followed in the outpatient specialized cardiology clinic or being treated for decompensation in the hospital at the Veterans Affairs Medical Center, La Jolla, California, were enrolled. The inclusion criteria were age >18 years, diagnosis of CHF, symptomatic for possible SDB (as measured by using a questionnaire created for the study which asked about specific symptoms of SDB including snoring, daytime sleepiness, waking up at night feeling short of breath and others, or by clinical suspicion of an examining physician), treatment naïve for SDB, and ability to provide informed consent. The study was approved by an Institutional Review Board. Patients were excluded from the study if they were asymptomatic for SDB, had a history of treatment for SDB or were currently receiving positive airway pressure therapy. Other exclusion criteria were outpatients requiring home oxygen therapy, or inpatients requiring >4 L/minute of oxygen or receiving oxygen via face mask.

Of the 120 patients screened for this study, 86 were eligible for enrollment. Of the 86 patients consented, approximately 75% were outpatients and 25% inpatients. Seventy one of these 86 subjects completed the study and 15 withdrew, stating that the primary reason for withdrawal was lack of interest in continuing their participation. Sixty one patients met the criteria of 4 or more hours of study time and are included in the analyses. See Figure 1.

ApneaLink Screening Device

The ApneaLink™ (ResMed Inc, Poway, CA) is a portable, battery-powered, respiratory pressure sensor-based sleep apnea testing system and provides detailed recordings of respiratory flow during sleep (Figure 2). Patients were instructed on the proper use of the device and nasal cannula at the time of consent and were provided with an instruction sheet that included both diagrams and written instructions. The recorder was fastened with a belt onto the patient's chest.

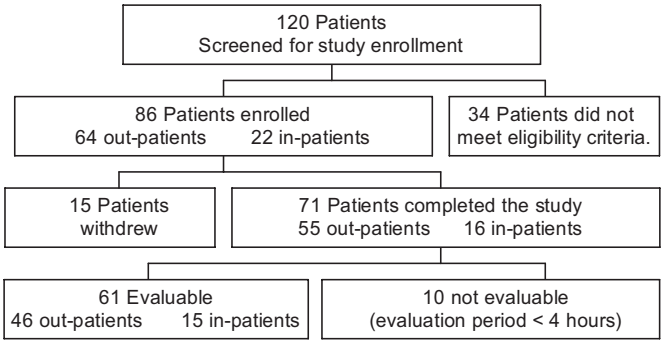

Figure 1. Consort Diagram

All relevant respiratory information, including breaths per minute, frequency of apneas and hypopneas and snoring events, during sleep was collected via nasal pressure cannula. Study personnel suggested fitting the ApneaLink device 30 minutes prior to going to sleep to get comfortable with the sensation of the cannula, and turning the ApneaLink on just before going to sleep. Patients were asked to wear the ApneaLink device overnight and return the device to study personnel for download of the data. Using ApneaLink review software installed on a computer, study personnel downloaded stored data from the ApneaLink device and generated a report which included apnea-hypopnea index (AHI) scores. If the evaluation period was less than 4 hours, patients were contacted and asked to repeat the study. An example of a standard report is illustrated in Figure 3.

Statistical Analyses

The prevalence of SA was determined from the ApneaLink results at AHI levels of ≥5 events/hour, ≥10, ≥15, and 5–14 (dependent on qualifying co-morbidities) with the use of confidence interval testing. The analyses included patients who had an evaluation period of 4 or more hours of study time on the ApneaLink device. The ApneaLink report was evaluated for the presence of Cheyne-Stokes respiration (CSR) and the prevalence of CSR. Prevalence rates along with 95% confidence intervals are reported. The analyses presents the cohort combined, as well as split out by inpatients/outpatients.

In addition, ease-of-use of the ApneaLink device and acceptability were evaluated using a 5-point Likert scale with '5' representing Excellent and '1' representing Poor. Time and

Figure 2. ApneaLink

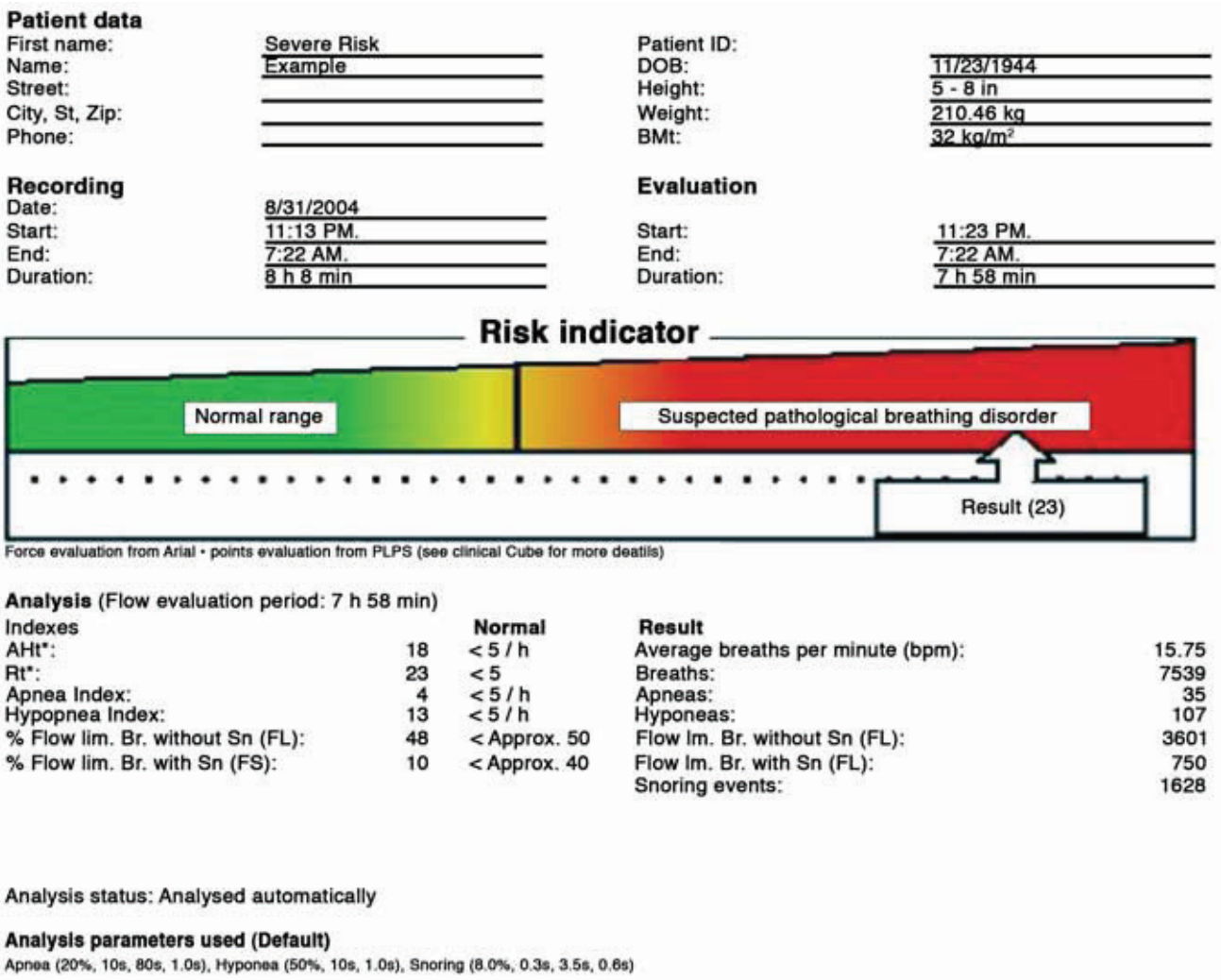

Figure 3. Standard Report

cost analyses related to use of the device were completed by an outside economic and health outcomes consultant. The variables were assessed by evaluating the set-up time and report generation features of the ApneaLink device.

Results

Of the 86 patients who consented to participate in the study, 61 (46 outpatients and 15 inpatients) had 4 or more hours of recorded evaluable data for assessment of the prevalence of SA. Demographic information is presented in Table 1. The mean age of the 61 evaluable patients was 65 years (range 38–84) and the mean BMI was 32.0 kg/m^2 (range 21.4–51.1). 98% of the cohort were male and 70% were white.

Medical history information is presented in Table 2. Most patients were classified as having moderate CHF, with 46% (28/61) of patients in NYHA Class II and 33% (20/61) in Class III. Diagnosis of CHF was made an average of 7.1 years prior to enrollment in this study (range <1–26 years). A history of systolic heart failure was present in 95%, (52/61) of the patients, and 80% (49/61) had a history of hypertension. The most common etiology of CHF was ischemia (56%, 34/61). With respect to sleep history, the most frequently reported sleep characteristics were excessive sleepiness (74%), feeling un-refreshed after sleeping (74%), and frequent snoring (62%).

Prevalence rates of SA based on AHI along with 95% confidence intervals are presented in Table 3. Prevalence of obstructive sleep apnea was 85% (SA defined as an AHI of 5 events/hour or greater as recorded by the ApneaLink). Prevalence in inpatients was found to be slightly higher (93%) than for outpatients (83%). Forty-nine percent of patients had an AHI of 15 events/hour or greater, and 36% had an AHI between 5–14 events/hour with qualifying co-morbidities: documented symptoms of excessive daytime sleepiness, impaired cognition, mood disorders or insomnia, or documented hypertension, ischemic heart disease, or history of stroke, per CMS criteria. This sample size (N=61) was able to estimate the assumed SDB rate of 50% with a precision of 12.5%. No significant difference was seen in prevalence of SDB between obese and non-obese patients.

The prevalence of Cheyne-Stokes Respiration (CSR) is presented in Table 4. Thirty-three percent (20/61) of patients were diagnosed with CSR, with inpatients having a much higher prevalence than outpatients (53% vs. 26%, p=0.051) 80%

Table 1. Demographic Information For 61 Study Participants, Based on 4 or More Hours of Study Time For Assessment of Prevalence of Sleep Apnea

Factor	*Patients % (no.)**
Age (years)	
Mean ± SF	65.2 ± 11.6
Range	38 – 84
Age (yr): frequency grouping	
<45	3 (2)
45-54	18 (11)
55-64	26 (16)
>65	52 (32)
Ethnicity	
Asian	2 (1)
Black	10 (6)
Pacific Islander/Native Hawaiian	2 (1)
White	70 (43)
Hispanic	15 (9)
American Indian	2 (1)
Body mass index (kg/m^2)	
Mean ± SD	32.0 ± 7.4
Range	21.4 – 51.1
Gender	
Male	98 (60)
Female	2 (1)
In-/Outpatient	
Inpatients	25 (15)
Outpatients	75 (46)

* Except where indicated otherwise.

Table 2. Medical History Information for Study Participants (N=61)

History	*Patients % (no.)**
Characterization of Cardiovascular disease	
NYHA Class	
Class I	7 (4)
Class II	46 (28)
Class III	33 (20)
Class IV	15 (9)
CHF etiology	
Myocarditis	2 (1)
Alcohol abuse	3 (2)
Drug Abuse	3 (2)
Hypertension	20 (12)
Hypertrophy	2 (1)
Idiopathic	23 (14)
Ischemia	56 (34)
Valvular	3 (2)
Angina	56 (34)
Myocardial infarction	52 (32)
Heart failure type	
Diastolic	79 (48)
Systolic	95 (52)
Valvular disease	21 (13)
Hypertension	80 (49)
Sleep Characteristics	
Frequent snoring	62 (38)
Excessive sleepiness	74 (45)
Breathless at night	34 (21)
Stop breathing at night	38 (23)
Unrefreshed after sleeping	74 (45)
Years since CHF diagnosis	
Mean ± SD	7.1 ± 6.1
Range	<1–25.8

* Except where indicated

Table 3. Prevalence Rates and 95% Confidence Intervals for Obstructive Sleep Apnea, Based on 4 or More Hours of Study Time (N=61)

Apnea-hypopnea index (events/h)	*All (N = 61) % (no.) 95% CI*	*Inpatient (N = 15) % (no.) 95% CI*	*Outpatient (N = 46) % (no.) 95% CI*
≥5	85.3 (52)	93.3 (14)	82.6 (38)
	73.8 – 93.0	68.1 – 99.8	68.6 – 92.2
≥10	68.9 (42)	80.0 (12)	65.2 (30)
	55.7 – 80.1	51.9 – 95.7	49.8 – 78.7
5–14	36.1 (22)	26.7 (4)	39.1 (18)
	24.2 – 49.4	7.8 – 55.1	25.1 – 54.6
≥15	49.2 (30)	66.7 (10)	43.5 (20)
	36.1 – 62.3	38.4 – 88.2	28.9 – 58.9

Table 4. Prevalence Rates and 95% Confidence Intervals for Cheyne-Stokes Respiration, Based on 4 or More Hours of Study Time (N=61)

	All (N = 61) % (no.) 95% CI	*Inpatient (N = 15) % (no.) 95% CI*	*Outpatient (N = 46) % (no.) 95% CI*
Positive for CSR	32.8 (20)	53.3 (8)	26.1 (12)
	21.3 – 46.0	26.6 – 78.7	14.3 – 41.1

Table 5. Frequency of Cheyne-Stokes Respiration by AHI Group

	N = 20 (Patients with CSR = Yes)		
AHI (e/hr)	*All Percent % (n/N)*	*Inpatient Percent % (n/N)*	*Outpatient Percent % (n/N)*
< 5	0% (0/20)	0% (0/8)	0% (0/12)
5 –14	20% (4/20)	12% (1/8)	25% (3/12)
≥15	80% (16/20)	88% (7/8)	75% (9/12)

of subjects with CSR had an AHI of 15 events/hour or greater (Table 5).

One of the objectives of the study was to perform a time/cost analysis related to the use of the device. Overall, the user (study coordinator) required 3.1 minutes to set up the ApneaLink device and 2.1 minutes to generate the report. A simple model was constructed to compare the labor cost for performing the ApneaLink with the labor cost for performing a similar test - an ECG. The model applies estimated times to perform each component of the two procedures to national hourly wage and benefit rates. Hourly rates ranged from a low of $10.00/hour (nurse's aide) to a high of $25.96/hour (registered nurse, US Bureau of Labor Statistics (BLS) National Compensation Survey), while the average fringe benefit rate was 28%. Based on model results, the labor cost is roughly equivalent for the two procedures, with the ApneaLink costing slightly less. For example, using the national hourly wage and including fringe benefits for a RN ($33.23) the cost to perform an ApneaLink test is $2.77 (5 minutes to perform complete test) vs. $3.88 (7 minutes to perform an ECG test).

A further objective was to determine the ease of use and acceptability of ApneaLink as a screening tool in CHF patients using the 5-point Likert scale mentioned in the methods section. Both patients and clinicians showed a very high rate of acceptance, with overall patient acceptance rated above average or excellent by 95% of the subjects and overall performance rated above average or excellent by 100% of respondents. All questions relating to the clinician's experience were rated above average or excellent by 100% of respondents.

For questions relating to the patient's experience (unobtrusiveness and ease of use), most items were rated above average or excellent by more than 90% of respondents, with the lowest response at 87%. Little difference was found between inpatients and outpatients in the rate of positive responses. All criteria were rated above average or excellent by at least 83% of inpatients, and by at least 87% of outpatients. In the category Patient Ease of Use, outpatients were especially positive in their ratings: 100% of outpatients and 86% of inpatients rated usefulness of supplied patient instructions as above average or excellent; operations of controls and buttons was rated above average or excellent by 96% of outpatients and 85% of inpatients. The higher level of positive ratings may reflect a greater reliance on instructions and controls in the outpatient group.

Discussion

The results of this study indicate that when CHF patients in a Veterans population are prescreened for symptoms that might represent SDB, the prevalence of SA is high (85%), with a slightly higher prevalence in inpatients versus outpatients. CSR was present in approximately one third of the patients. There was a high level of satisfaction expressed by both patients and clinicians in terms of ease of use of the ApneaLink. Additionally, the cost analysis proved ApneaLink to be cost-effective for screening use in the inpatient and outpatient settings.

Our results bring into focus the degree to which SBD may exist in a Veteran CHF population. The high prevalence of SDB in this population and the physiological insults experienced by patients with SDB (ischemia and arrhythmias from sympathetic nervous activation, increased blood pressure, and increased myocardial oxygen demand) suggest that on both an individual and epidemiological level, SDB may significantly impact the progression of CHF and the prognosis of these patients.[3–5]

As such, the benefits of a convenient and readily available sleep-screening tool are several-fold. The device used in this study, the ApneaLink, has been shown to have strong clinical utility for providers to screen their patients suspected of having SDB. The accuracy of the ApneaLink was validated in a study comparing ApneaLink recordings with simultaneously collected data from polysomnography recordings. The ApneaLink was shown to be highly sensitive and specific (91% and 95%) when AHI data from the two measurements were compared. Additionally, ApneaLink results from screening in patients homes showed high sensitivity and specificity when compared with the polysomnography laboratory results.[27]

The results from ApneaLink testing can be used to stratify patients according to need for further testing in a polysomnography lab in the case of SDB with CSR, with subsequent Adaptive Servo-Ventilation (ADV) therapy and also to identify patients who would benefit from immediate titration and/or initiation of CPAP therapy for SDB without CSR. Inpatients being treated for decompensated heart failure that undergo ApneaLink testing during the hospital stay could potentially be started on CPAP, or ASV depending on the level of CSR detected, as an adjunct to their CHF management.

Further studies examining the clinical utility of ApneaLink should encourage more widespread screening in different populations. The new model of the ApneaLink device includes a pulse oximeter, and studies testing this device will be helpful to determine how the presence of pulse rate and pulse oximetry data improve the quality of assessments. Additional studies comparing results from ApneaLink and polysomnography are likely to be helpful in determining the accuracy of the ApneaLink in measuring severity of SDB.

Study Limitations

The number of patients enrolled in the study was relatively small due to a limited patient population from which to recruit, as well as a small number of patients admitted to the hospital who fit the inclusion/exclusion criteria. Additionally, seven patients were included in the study that did not answer yes to at least two screening questions. The investigator made the decisions to enroll these patients based on clinical suspicion of possible SDB and the potential benefit of sleep screening to the patient.

Inability to obtain a full 4-hour recording was a common problem encountered during the study. The reasons most often cited for less than 4 hours of evaluation time were difficulty with the on/off switch and some difficulty keeping the nasal cannula in place. This feedback was passed on to the manufacturer and was added to improvements in their ApneaLink with Oximetry product that is now released to the market but was unavailable during this trial. The ApneaLink with Oximetry meets the CMS definitions of a Type IV Home Diagnostic Device with the following measurement signals: respiratory flow, heart rate and oximetry. Several subjects withdrew from the study because they were not interested in repeating the screening. Reasons cited by these patients included lack of a return appointment at VA hospital, trouble sleeping through the night, and no recording after two attempts.

Conclusion

The ApneaLink is an easy-to-use, portable, cost-effective way to assess SDB in patients with heart failure. It provides a useful way to differentiate SDB into a group with CSR and a group without CSR, which has important treatment implications for the heart failure patient population. The high prevalence of SDB in this population suggests that heart failure patients should be routinely screened for SDB.

References

1. Javaheri, S., et al., *Sleep apnea in 81 ambulatory male patients with stable heart failure. Types and their prevalences, consequences, and presentations.* Circulation, 1998. 97(21): p. 2154–2159.
2. Ferrier, K., et al., *Sleep-disordered breathing occurs frequently in stable outpatients with congestive heart failure.* Chest, 2005. 128(4): p. 2116–2122.
3. Bradley, T.D. and J.S. Floras, *Sleep apnea and heart failure: Part I: obstructive sleep apnea.* Circulation, 2003. 107(12): p. 1671–1678.
4. Bradley, T.D. and J.S. Floras, *Sleep apnea and heart failure: Part II: central sleep apnea.* Circulation, 2003. 107(13): p. 1822–1826.

5. Leung, R.S., et al., *Provocation of ventricular ectopy by cheyne-stokes respiration in patients with heart failure.* Sleep, 2004. 27(7): p. 1337–1343.
6. Andreas, S., et al., *Cheyne-Stokes respiration and prognosis in congestive heart failure.* Am J Cardiol, 1996. 78(11): p. 1260–1264.
7. Hanly, P.J. and N.S. Zuberi-Khokhar, *Increased mortality associated with Cheyne-Stokes respiration in patients with congestive heart failure.* Am J Respir Crit Care Med, 1996. 153(1): p. 272–276.
8. Sin, D.D., et al., *Risk factors for central and obstructive sleep apnea in 450 men and women with congestive heart failure.* Am J Respir Crit Care Med, 1999. 160(4): p. 1101–1106.
9. Bradley, T.D. and J.S. Floras, *Pathophysiologic and therapeutic implications of sleep apnea in congestive heart failure.* J Card Fail, 1996. 2(3): p. 223–240.
10. Javaheri, S., *Central sleep apnea-hypopnea syndrome in heart failure: prevalence, impact, and treatment.* Sleep, 1996. 19(10 Suppl): p. S229–S231.
11. Yamashiro, Y. and M.H. Kryger, *Review: sleep in heart failure.* Sleep, 1993. 16(6): p. 513–523.
12. Franklin, K.A., et al., *Sleep apnea and nocturnal angina.* Lancet, 1995. 345(8957): p. 1085–1087.
13. Javaheri, S., *Sleep disorders in systolic heart failure: a prospective study of 100 male patients. The final report.* Int J Cardiol, 2006. 106(1): p. 21–28.
14. Ancoli-Israel, S., et al., *Comparison of patients with central sleep apnea. With and without Cheyne-Stokes respiration.* Chest, 1994. 106(3): p. 780–786.
15. Javaheri, S., et al., *Central sleep apnea, right ventricular dysfunction, and low diastolic blood pressure are predictors of mortality in systolic heart failure.* J Am Coll Cardiol, 2007. 49(20): p. 2028–2034.
16. Wang, H., et al., *Influence of obstructive sleep apnea on mortality in patients with heart failure.* J Am Coll Cardiol, 2007. 49(15): p. 1625–1631.
17. Shahar, E., et al., *Sleep-disordered breathing and cardiovascular disease: cross-sectional results of the Sleep Heart Health Study.* Am J Respir Crit Care Med, 2001. 163(1): p. 19–25.
18. Schulz, R., et al., *Sleep apnea in heart failure.* Eur Respir J, 2007. 29(6): p. 1201–1205.
19. Seino, Y., et al., *Clinical efficacy and cost-benefit analysis of nocturnal home oxygen therapy in patients with central sleep apnea caused by chronic heart failure.* Circ J, 2007. 71(11): p. 1738–1743.
20. Egea, C.J., et al., *Cardiac function after CPAP therapy in patients with chronic heart failure and sleep apnea: A multicenter study.* Sleep Med, 2007.
21. Kaneko, Y., et al., *Cardiovascular effects of continuous positive airway pressure in patients with heart failure and obstructive sleep apnea.* N Engl J Med, 2003. 348(13): p. 1233–1241.
22. Zhang, X.L., et al., *Efficacy of adaptive servoventilation in patients with congestive heart failure and Cheyne-Stokes respiration.* Chin Med J (Engl), 2006. 119(8): p. 622–627.
23. Philippe, C., et al., *Compliance with and effectiveness of adaptive servoventilation versus continuous positive airway pressure in the treatment of Cheyne-Stokes respiration in heart failure over a six month period.* Heart, 2006. 92(3): p. 337–342.
24. Morgenthaler, T.I., et al., *Adaptive servoventilation versus non-invasive positive pressure ventilation for central, mixed, and complex sleep apnea syndromes.* Sleep, 2007. 30(4): p. 468–475.
25. Pepperell, J.C., et al., *A randomized controlled trial of adaptive ventilation for Cheyne-Stokes breathing in heart failure.* Am J Respir Crit Care Med, 2003. 168(9): p. 1109–1114.
26. Teschler, H., et al., *Adaptive pressure support servo-ventilation: a novel treatment for Cheyne-Stokes respiration in heart failure.* Am J Respir Crit Care Med, 2001. 164(4): p. 614–619.
27. Erman, M.K., et al., *Validation of the ApneaLink for the screening of sleep apnea: a novel and simple single-channel recording device.* J Clin Sleep Med, 2007. 3(4): p. 387–392.