Initiation of CPAP for Newly Diagnosed OSA in Hospitalized Heart Failure Patients

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Research Strategy:

Background: The use of portable sleep testing for the diagnosis of obstructive sleep apnea has dramatically increased in recent years. The growth of portable testing has also led to the use of these devices in the hospital setting. Current guidelines recommend the use of portable testing in ambulatory patients with high pretest probability for obstructive sleep apnea who do not have significant cardiopulmonary comorbidities (1-2). Despite these recommendations these devices are commonly utilized in the hospital setting for the diagnosis of obstructive sleep apnea in ill patients with multiple comorbidities. One patient population which has been of significant interest regarding the diagnosis and treatment of obstructive sleep apnea is those with chronic heart failure.

Chronic heart failure (CHF) is the leading cause of hospitalization and readmissions. About one-fifth of Medicare beneficiaries are readmitted to the hospital within 30 days of leaving, costing more than $15 billion annually (3). Obstructive sleep apnea is highly prevalent in the CHF population and evidence suggests treatment of obstructive sleep apnea in this population leads to improvement in outcomes (4-6). This heart failure population provides a clinically important and convenient population to test our hypotheses. The study aim is assess the efficacy of portable sleep monitoring to diagnose obstructive sleep apnea (OSA) in hospitalized heart failure patients in terms of adherence to continuous positive airway pressure (CPAP) therapy.

Hypothesis: Inpatient diagnosis of OSA in hospitalized patients with a history of heart failure using a portable level III sleep study and the immediate initiation of auto-adjusting CPAP is not inferior to the standard outpatient diagnosis and treatment pathway.

Significance: West Virginia has one of the highest obesity rates and one of the highest rates of cardiovascular disease in the country (7-8). Inpatient sleeping testing is used frequently nationally as well as locally however the effectiveness of this diagnosis and intervention has never been evaluated outside the ambulatory setting (1). This intervention is of interest in the heart failure population as more than 85% of patients with clinically significant and treatable sleep apnea are never diagnosed (9). Early recognition and therapy for sleep apnea in the heart failure population may improve quality of life, reduce hospitalization rate, improve cardiac function, and blood pressure control (10-11). However, if this shift in paradigm from an outpatient diagnosis to an inpatient diagnosis pathway leads to less long-term success with CPAP therapy these benefits will not be sustained. Thus, evaluating the efficacy of this model and identifying factors that predict success with an inpatient diagnostic pathway could have significant implication on care decisions in the heart failure population.

Specific Aims:

1. Determine the efficacy of inpatient diagnosis of OSA in hospitalized patients with a history of heart failure using a portable level III sleep study and the immediate initiation of auto-adjusting CPAP (APAP) is not inferior to the standard outpatient diagnosis and treatment pathway.

2. Identify factors that predict adherence at discharge with CPAP therapy in this population of hospitalized heart failure patients diagnosed with OSA. We will assess demographic factors including distance from the sleep center and age, socioeconomic factors including household income and age, as well as quality of life measures including the Epworth Sleeping Score and Minnesota Heart Failure Quality Life Questionnaire. We hypothesize that access to healthcare, low socioeconomic status, poorer general health will impact the success of the intervention and may lead to alternate considerations in diagnostic and treatment pathways for this population. We will also assess hospital readmission rates as potentially adversely affecting CPAP adherence.

3. Assess inpatient education on OSA and teaching by a sleep certified technician in terms of adherence to CPAP therapy versus a standard treatment pathway through a durable medical equipment company

Innovation: Portable sleep studies are used frequently in the hospital yet no research to date has assessed the efficacy of inpatient diagnosis OSA and treatment upon discharge with APAP. Locally we have seen a tremendous increase in the use of portable sleep studies both in the inpatient and outpatient diagnosis of OSA. Large randomized trials to date have shown non-inferiority of an ambulatory approach to the diagnosis and treatment of OSA (12). However, these studies were completed at academic and VA medical centers located in large metropolitan areas which do not reflect our local population (12). We are presenting data in abstract form that suggests an ambulatory pathway for the outpatient diagnosis and treatment of OSA is inferior in our local rural population (13). The unique characteristics of the West Virginia population may make the use of portable monitoring and home initiation of APAP therapy less effective. A multisite approach will allow assessment not only of the efficacy of this intervention but also assessment of factors that predict success with this pathway. We have completed a feasibility study demonstrating identifying and following these patients overtime is practical.

Approach:

As primary investigators Dr. Stansbury and Dr. Khawaja are highly qualified individuals and will ensure the success of this study. They are both board certified in pulmonary, critical care, and sleep medicine and are extremely comfortable assessing patients with obstructive sleep apnea. Dr. Khawaja is section chief of Pulmonary, Critical care, and Sleep Medicine at Marshall University. Dr. Stansbury has been named interim chief of Pulmonary, Critical, and Sleep Medicine at WVU. Dr. Stansbury has significant research experience and is currently site PI for a multicenter study evaluating outcomes in patients with diabetes newly diagnosed with OSA (NIH RO1 DK096023 The Effect of Treatment of OSA on Diabetes Self-Management and Glycemic Control). His current pilot grant demonstrates his ability to identify and recruit the target population (NIH/NIGMS U54GM104942 Initiation of CPAP for Newly Diagnosed OSA in Hospitalized Heart Failure Patients: A Randomized Clinical Trial). Dr. Khawaja has recently completed a study assessing CPAP compliance in a dedicated sleep center population (https://wvmj.scholasticahq.com/api/v1/attachments/2426/download).

Overall, the investigators' extensive training and expertise in pulmonary, critical care, and sleep medicine as well as ongoing success in sleep medicine research make them the perfect candidates to lead and conduct a study assessing the efficacy of portable monitoring for the diagnosis of and treatment of sleep apnea in the heart failure population.

Overall study design:

This is a randomized double center, open-label, parallel-group controlled trial evaluating the inpatient diagnosis of OSA using a portable sleep study. We will also compare initiation of APAP by providing a machine and education at discharge compared to a standard treatment pathway involving insurance approval and DME availability. It is planned to randomize a total of 100 patients at West Virginia University Hospital and Marshall University Medical Center (MUMC). Each site will enroll fifty patients. This total of 100 subjects is based on our power analysis as outlined in the statistics section. During the screening phase informed consent to participate will be obtained and the eligibility of the patient for enrollment will be assessed and documented. Before randomization, all patients will receive standard heart failure therapy while hospitalized. Overall duration of the study is planned to be one year. The study data will be evaluated and reported as soon as the study data of all randomized patients are entered and validated in the database, and the database is locked.

Study population:

The candidates for inclusion in the study will be all patients admitted to West Virginia University Hospital or Marshall University Medical Center with a historical diagnosis of heart failure. Patients do not necessarily have to be admitted with decompensated heart failure for inclusion, but must have a confirmed history of heart failure.

Exclusion/inclusion criteria:

Inclusion criteria: To be eligible for the study, patients must meet the following criteria:

1. Aged > 18 year-old.

2. Subject is able to provide written informed consent, including agreement to privacy language within the informed consent or in ancillary documents compliant with HIPPA before the initiation of any study-related procedure.

3. Hospitalized having a documented history of heart failure in agreement with the 2013 ACCF/AHA heart failure definition.[14]

4. Anticipated hospitalization of more than 24 hours

5. Subject is willing to comply with the protocol and attend all study visits.

Exclusion criteria: Patients with any of the following will not be included in the study:

1. A preexistent diagnosis of OSA and are on CPAP prior to the hospital admission.

2. The presence of any conditions that the investigator feels interferes with the use of CPAP (such as; pneumothorax, respiratory arrest, agonal respirations, unconsciousness, shock associated with cardiac insufficiency, penetrating chest trauma, persistent nausea/vomiting, facial anomalies/facial trauma, has active upper GI bleeding or history of recent gastric surgery).

3. Has a clinically significant illness, medical condition or medical history, that in the investigator's opinion, would prohibit the subject from participating in the study at screening or at the time of randomization if in the investigator's opinion patient would not benefit or be harmed using CPAP.

4. Is on respiratory support that in the opinion of the investigator should not be enrolled in the study

5. Declines CPAP

6. Planned transfer from hospital to a Skilled Nursing Facility (SNF), nursing home or hospice.

Screening

Following consent adult patients hospitalized at WVUH or the MUSC with a medical history of heart failure and meeting study eligibility criteria will be screened for obstructive sleep apnea using the Sleep Apnea Clinical Score (Ohio Sleep Medicine Institute Preoperative questionnaire which includes eligibility criteria [appendix 1]). If the probability of sleep apnea is high (Sleep apnea clinical Score >15) then participants will complete the Epworth Daytime Sleepiness scale and the Minnesota Living with heart Failure questionnaire. The patient will then undergo a portable sleep test which has been FDA approved for the diagnosis of obstructive sleep apnea. All participants with apnea-hypopnea index (AHI) ≥ 5 events/h in whom sleep disordered breathing is confirmed by sleep medicine physician will be eligible for randomization.

Randomization

Participants will be randomized into an auto-adjusting Continuous Positive Airway Pressure (CPAP) group or standard of care (control) group. Each participant for whom informed consent is obtained will be assigned a unique patient number that is computer generated. Participants will be assigned into two groups by using blocked randomization with randomly selected block sizes used to ensure balanced allocation between 2 arms. The randomization schedule will link sequential numbers to treatment codes allocated at random with a 1:1 (CPAP vs. Standard of care) randomization ratio. Assignments will be concealed in sequentially-numbered, sealed, opaque envelopes to eliminate any risk of randomization/recruitment bias.

Intervention and comparator groups

Intervention: Patients will receive standard education by a sleep medicine technician as is commonly completed with the outpatient model of care and provided with an APAP upon discharge in addition to usual

standards of clinical care for heart failure. The patient will be called at two weeks to assess their progress, identify adverse events, hospitalizations and assess whether an unscheduled visit is necessary. They will follow-up in sleep medicine clinic at 1 month (+ 2 weeks), at 6 months (+ 2 weeks) to assess their progress on APAP and completed quality of life questionnaires.

Comparator: Patients will follow the standard pathway of APAP initiation through insurance approval and identification of a durable medical equipment company. All education and teaching will be from the company providing the APAP as per usual care. They will receive management as per usual standards of clinical care for heart failure. The patient will be called at two weeks to assess their progress, identify adverse events, hospitalizations and assess whether an unscheduled visit is necessary They will follow-up in sleep medicine clinic at 1 month (+ 2 weeks), at 6 months (+ 2 weeks) to assess their progress on APAP and completed quality of life questionnaires.

All participants will then monitored for APAP adherence using modem and data card tracking technology.

Assessment/data collection procedure

Screening/ Baseline data (Hospitalization period)

The following data will be obtained at baseline during patient's hospitalization: Demographic data, admission diagnoses, NYHA class, comorbid illnesses (diabetes, hypertension, hyperlipidemia, coronary artery disease, atrial fibrillation, depression and stroke), echocardiogram results, hospital length of stay, sleep study results. We will also use the Minnesota Heart Failure Quality Life Questionnaire and Epworth Sleepiness Scale to monitor subjective response to therapy. Eligibility criteria will be re assessed upon patient discharge from hospital. If found ineligible, patients will be considered screen failures.

Follow Up Phone Calls: (2-3 weeks after hospital discharge)

A member of the study team will contact the patient to remind them of their 1-month visit. They will collect the following data: AEs, readmission data to include length of stay, any doctor or ED visits, CPAP problems and troubleshooting.

1 Month, 6 Month and Unscheduled Visits

The following data will be obtained at follow up and unscheduled visits: CPAP compliance, CPAP problems and troubleshooting, AEs, any doctor or ED visits, and readmission data will be collected. We will also use the Minnesota heart Failure Quality of Life Questionnaire and the Epworth Sleepiness Scale to monitor subjective response to therapy.

Main Outcome Measures

The primary outcome is CPAP adherence at six months. Studies evaluating adherence to positive airway pressure therapy, which is defined by use of the device > 4 hours per night 70% of nights, report the percent of individuals not adherent to therapy at six months to year range from 46-80% (10). We will accept this intervention as non-inferior if patient adherence is 60%. We will also evaluate factors that predict adherence at discharge with APAP therapy in this population of hospitalized heart failure patients identified with OSA as outlined above. Finally, all-cause hospital readmission within 30 days of hospital discharge will be another secondary endpoint evaluated by the research team.

Sleep Studies

Recent comparative effectiveness research studies have shown that clinical outcomes of patients with a high pretest probability for obstructive sleep apnea who receive ambulatory management using portable-monitor testing have similar functional outcomes and adherence to continuous positive airway pressure treatment, compared to patients managed with in laboratory polysomnography (15) Guidelines from the American Academy of Sleep Medicine (AASM) in 2017 states that unattended portable sleep testing is an option for patients with a high pretest probability of moderate to severe sleep apnea. The guideline further states, for patients with a high pretest probability of OSA, unattended portable recording for the assessment of obstructive sleep apnea is an acceptable alternative to standard polysomnogram(1). All participants with apnea-hypopnea

index (AHI) ≥ 5 events/h in whom sleep disordered breathing is confirmed by sleep medicine physician will be eligible for randomization. Apnea is defined as an as a ≥ 90% cessation of airflow detected through the nasal pressure sensor. Hypopnea is defined a ≥ 30% reduction in airflow with an associated ≥ 3% oxyhemoglobin desaturation. Apnea-hypopnea index (AHI) is defined as the number of apneas plus hypopneas per hour of recording. We will use an FDA approved level III portable sleep study as is currently used for inpatient testing at our institution (Resmed Apnea-Link©). Stopping point.

CPAP Compliance Data

APAP adherence tracking systems (implemented by APAP manufacturers) will be used to assess APAP adherence and efficacy. Such systems monitor APAP efficacy (residual sleep-disordered breathing), hours of APAP use, mask leak, and several different flow signals. Most systems use wireless modems or smart cards (smart cards or SD cards) to track CPAP adherence and efficacy. Adherence data derived from CPAP tracking systems will be monitored.

Based on the data available, patients will be classified adherent or non-adherent. Adherent users are classified based on Centers of Medicare and Medicaid Services (CMS) guidelines defined as use of PAP ≥ 4 h/night on 70% of nights during 30 consecutive days in the first 90 days of PAP treatment. This definition is also used in research studies and will be taken at six months. All other users will be considered non-adherent users. (Centers for Medicare & Medicaid Services, PAP Devices for the Treatment of OSA (L11528, L11528, L11518, L171), U.S. Department of Health and Human Services)

Data handling and record keeping

All study information will be maintained in a password-protected database. All paper copies will be stored in a locked file cabinet. The participants will be identified by a unique trial specific number and/or code in any database. Study records that identify participants will be kept separate from data records, and kept confidential as required by law, and as prescribed by HIPAA guidelines. Protected Health Information (PHI) will be obtained through proper authorization by participants.

Data and Safety Monitoring

CPAP is a non-invasive procedure, however, as it does come in contact with the skin and therefore can cause local irritation to the skin where it is applied. CPAP common adverse effects will be recorded during the study period which may include dry mouth, nasal symptoms, eye problems, claustrophobia, noise problems, soreness or skin irritation, mask fit or leak problems

Design/Sample size estimation

This is a randomized double center, open-label, parallel-group controlled trial evaluating the inpatient diagnosis of OSA using a portable sleep study. The primary outcome is CPAP adherence at six months. For the secondary endpoints, we will evaluate factors that predict adherence at discharge with APAP therapy in this population of hospitalized heart failure patients identified with OSA as outlined above. Finally, all-cause hospital readmission within 30 days of hospital discharge. One hundred patients will be randomized equally to the two treatment arms. The sample size justification is based on CPAP adherence at six months in 100 patients. Studies evaluating adherence to positive airway pressure therapy report the percent of individuals not adherent to therapy at six month to year ranging from 46-80% (16). We will accept this intervention as promising if patient adherence is 60% at 6 months. Given a sample size of 50 patients per group, a 95% confidence interval (CI) of CPAP adherence will be (46%, 73%) for CPAP adherence of 60%. In the final analysis, the intervention will be considered promising if the adherence at 6 month is 46% (lower boundary of the 95% CI) or higher. We will have 96.5% chance to declare that the intervention is promising if the true adherence is 60%, while this chance is only 16.1% if the true adherence is 40%.

Statistics

Descriptive statistics analysis will be performed first. Categorical data will be described using contingency tables. Continuously scaled measures will be summarized with mean (± s.d.) and median (range). Histograms and box plots will be applied. The adherence rate and its 95% confidence interval will be estimated based on a binomial distribution. Chi-square test will be applied to test the association between adherence (yes/no) and categorical variables. A two-sample t-test will be used to assess the association between adherence (yes/no) and a continuous variable. The data will be examined to ensure that the underlying assumptions (i.e., normality and homogeneity of variance) are met. If not, standard transformations (e.g., log-transformation) will be performed, or nonparametric alternatives (Wilcoxon's rank test) will be used. In the multivariate analysis, a logistic model will be used, with the adherence taken as the outcome variable. Multiple covariates include treatments, patient medical demographical variables and other potential factors that predict adherence at discharge as outlined above. A generalized estimating equation (GEE) and a mixed model will be used to analyze the longitudinal data on adherence over time. All statistical tests will be two sided and $p < 0.05$ will be considered statistically significant. SPSS and SAS will be used for data entry and analysis.

References

1. Kapur VK, Auckley DH, Chowdhuri S, etl al. Clinical Practice Parameter for Diagnostic Testing for Adult Obstructive Sleep Apnea: An American Academy of Sleep Medicine Clinical Practice Guideline. J Clinic Sleep Med. 2017;13(3):479-504.

2. Epstein LJ, Kristo D, Strollo PJ, et al. Clinical guidelines for the evaluation, management, and long-term care of obstructive sleep apnea in adults. J Clinic Sleep Med. 2009;5(3):263-276.

3. Jencks SF, Willaims MV, Coleman EA. Rehospitalizations among patients in the Medicare fee-for-service program. N Engl J Med 2009, 360(14):1418-1428.

4. Shahar E, Whitney CW, Redline S, et al. Sleep-disordered breathing cardiovascular disease: cross-sectional results of the Sleep Heart Health Study. Am J Respir Crit Car Med 2001, 163(1):19-25.

5. Rick Schwab study

6. Stansbury RC and Strollo PJ. Clinical manifestations of sleep apnea. J Thorac Dis 2015 Sep; 7(9): 298–310.

7. Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Division of Population Health. BRFSS Prevalence & Trends Data [online]. 2015. [accessed Apr 30, 2017]. URL https://www.cdc.gov/obesity/data/prevalence-maps.html

8. Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Division of Population Health. BRFSS Prevalence & Trends Data [online]. 2015. [accessed Apr 30, 2017]. URL: http://wwwdev.cdc.gov/brfss/brfssprevalence/.

9. Kapur V, Strohl KP, Redline S, Iber C, O'Connor G, Nieto J: Underdiagnosis of sleep apnea syndrome in U.S. communities. Sleep Breath. 2002, 6(2):49-54.

10. Khayat RN, Abraham WT, Patt B, Pu M, Jarjoura D: In-hospital treatment of obstructive sleep apnea during decompensation of heart failure. Chest 2009, 136(4):991-997.

11. Kauta SR, Keenan BT, Goldberg L, Schwab RJ: Diagnosis and treatment of sleep disordered breathing in hospitalized cardiac patients: a reduction in 30-day hospital readmission rates. J Clin Sleep Med 2014, 10(10):1051-1059.

12. Cooksey JA and Balachandran JS. Portable monitoring for the diagnosis of OSA. Chest 2016 Apr; 149(4):107481.

13. Allhaddad A, Stansbury RC, Weaver B. Adherence to positive airway pressure therapy for obstructive sleep apnea in patients undergoing home versus in lab testing: Results from a rural tertiary care academic medical center. Am J Respir Crit Car Med (Abstract accepted for publication).

14. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE, et al: 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2013, 62(16):e147-239.

15. Kuna ST, Gurubhagavatula I, Maislin G, Hin S, Hartwig KC, McCloskey S, Hachadoorian R, Hurley S, Gupta R, Staley B et al: Noninferiority of functional outcome in ambulatory management of obstructive sleep apnea. Am J Respir Crit Care Med 2011, 183(9):1238-1244.

16. Weaver TE and Grunstein RR. Adherence to continuous positive airway pressure therapy. Proc Am Thorac Soc 2008 Feb 15;5(2):173-8.

Efficacy of Inpatient Diagnosis of Obstructive Sleep Apnea in Hospitalized Heart Failure Patients: A Randomized Clinical Trial

Schema

	Visit 1 Screening/Enrollment/ Hospital Stay	**Visit 2 Follow-Up Phone Call (2-3 weeks after DC)**	**Visit 3 Follow-Up (1 month)**	**Visit 4 Follow-Up (6 months)**	**Unscheduled visit**
Eligibility	X				
Reconfirm eligibility					
Consent	X				
Ohio State Sleep Medicine Pre-Op Questionnaire/Sleep Evaluation.	X				
Epworth Sleepiness Scale	X		X	X	
Minnesota Living with Heart Failure Questionnaire	X		X	X	
Demographics	X				
Admission Diagnosis	X				
NYHA class	X				
Comorbid illness	X				
ECG results	X				
Portable polysomnography monitor for (qualifying patients)	X				
Sleep Medicine evaluation	X				
Randomization for patients with obstructive sleep disorder	X				
AEs		X	X	X	X
Auto-CPAP adherence tracking			X	X	X
Control Group CPAP adherence tracking				X	X
Hospital length of stay		X	X	X	X
Re-admission data		X	X	X	X
ED visits		X	X	X	X
CPAP machine troubleshooting (mask fitting, machine settings, humidity settings, etc)		X	X	X	X