Photoplethysmographic Signal to Screen Sleep-Disordered Breathing in Hospitalized Heart Failure Patients

Feasibility of a Prospective Clinical Pathway

Sunil Sharma, MD,* Paul Mather, MD,* Jimmy T. Efird, PhD,† Daron Kahn, MD,* Mohammed Cheema, MD,‡ Sharon Rubin, MD,* Gordon Reeves, MD,* Raphael Bonita, MD,* Raymond Malloy, MS,* David J. Whellan, MD*

ABSTRACT

OBJECTIVES The purpose of this study was to evaluate the photoplethysmographic signal-derived oxygen desaturation index (ODI) as an inpatient screening strategy to identify sleep-disordered breathing (SDB) in patients with congestive heart failure (CHF).

BACKGROUND SDB is highly prevalent among patients hospitalized with CHF but is widely underdiagnosed. We evaluated overnight photoplethysmography as a possible screening strategy for hospitalized patients with CHF.

METHODS Consecutively admitted heart failure patients with high clinical suspicion of SDB and ODI $\geq 5$ were offered outpatient polysomnography (PSG), which was completed within 4 weeks of discharge. PSG was considered positive if the apnea hypoxia index (AHI) was $\geq 5$. A Bland-Altman plot was used to assess agreement between ODI and AHI. Receiver-operator characteristics were determined for ODI $\geq 5$ and AHI $\geq 5$.

RESULTS A screening questionnaire identified 246 of 282 consecutive patients with positive symptoms for SDB. Of these patients, 105 patients were offered further evaluation and 86 had ODI $\geq 5$ (mean ODI 17 ± 17). Among these 86 patients, 68 underwent outpatient PSG within 4 weeks of discharge. PSG showed that 64 (94%) had SDB, with a mean AHI of 28. Inpatient ODI correlated well with PSG-derived AHI. The area under the curve was 0.82 for AHI $\geq 5$. The Bland-Altman plot revealed no major bias. Matthew’s correlation coefficient revealed that the optimal cut-off for ODI is 5.

CONCLUSIONS Screening hospitalized patients with heart failure using targeted inpatient ODI identifies a cohort of patients with a high prevalence of SDB. Our screening strategy provides a potentially cost-effective method for early detection and treatment of SDB. (J Am Coll Cardiol HF 2015;3:725–31) © 2015 by the American College of Cardiology Foundation.
To improve on early identification of SDB in hospitalized HF patients, we undertook a study of photoplethysmography signal recording for screening SDB in hospitalized patients with HF. Photoplethysmography signal recording is a simple, low-cost tool to determine the oxygen desaturation index (ODI) (oxygen desaturations per hour), and it is readily available in the hospital. In the outpatient setting, ODI has been shown to correlate with apnea hypopnea index (AHI) (apnea hypoxia episodes per hour) derived from PSG (11,12). However, data on the usefulness of overnight inpatient ODI for early diagnosis of SDB in patients admitted for congestive heart failure is lacking. To evaluate the value of a screening strategy in patients admitted with ADHF (acute decompensated heart failure), our study combined symptom assessment, sleep evaluation, and inpatient ODI to identify SDB, using PSG-derived AHI to verify the diagnosis.

**METHODS**

This is a prospective study of a clinical pathway evaluation. The Thomas Jefferson University Institutional Review Board approved the study.

Participants were patients admitted to an academic tertiary care hospital for ADHF from April 2013 to March 2014. Patients admitted were screened by a trained respiratory therapist for SDB-related symptoms using the STOP-BANG questionnaire. The questionnaire included the following measurements: heavy snoring, tiredness, observed apneas, hypertension, body mass index $>$35 kg/m², age $>$50 years, neck circumference $>$40 cm, and male sex.

If requested by the admitting team, patients who screened positive underwent a comprehensive sleep evaluation by a board-certified sleep specialist with an appropriate work-up including overnight photoplethysmographic signal recording, unless contraindicated. Contraindications were the following: oxygen requirement $>$30% fraction of inspired oxygen, severe pain, significant complaints of difficulty initiating and maintaining sleep (defined as $<$2 h of continuous sleep), altered mental status, or anticipated disruption during sleep (imaging/tests or surgeries). An ODI $>5$ was considered positive for SDB. If clinical suspicion of SDB was high (defined according to the Adult OSA Task Force of the American Academy of Sleep Medicine (15) and ODI $>5$, then patients were advised to undergo a post-discharge confirmatory PSG study. All patients who agreed to a PSG had the procedure done within 4 weeks of discharge from the hospital.

The primary clinical team carried out guideline-driven acute decompensated heart failure care based on the clinical care pathway. This pathway included finding the causative triggers for the decompensation, addressing both the hemodynamic and neurohormonal milieu of the patient, and guideline-directed medical therapy. The care was coordinated with education of the patient and the caregivers, dietary modification, and social evaluation for needs-based care. Heart failure medications were titrated per guidelines-driven protocols.

PSG evaluations were conducted at the Jefferson Sleep Disorders Center, an American Academy of Sleep Medicine (AASM)-accredited facility. The evaluations included an electrocardiograph, electroencephalograph, continuous oronasal airflow recording (with a thermistor and a pressure transducer), recording of chest wall and abdomen movement (using respiratory inductive plethysmography belts), pulse oximetry, and chin electromyography (Comet AS 40 PSG, Grass Technologies, Warwick, Rhode Island). Sleep was staged manually by a registered PSG technologist, according to AASM scoring guidelines (16). A board-certified sleep physician interpreted the polysomnograms.

Photoplethysmographic signal recording was performed using a Masimo RAD-57 machine (Irvine, California) standardized to an average time of 3 s and an ODI cutoff point of 4%. Hypopnea was similarly defined by a 4% desaturation event during outpatient PSG study. These standards are consistent with the AASM recommendations (16). Signal quality and waveform analysis was performed by a board-certified sleep physician post-study. If the recording time was $<$1 h or signal quality was poor, the recordings were excluded from the study.

**STATISTICAL ANALYSIS.** Categorical variables were presented as frequency and percentage, whereas continuous variables were presented as a mean $\pm$ 1 SD or median and interquartile range.

A confusion matrix was generated to summarize standard classification measures. These included sensitivity, specificity, likelihood ratio for a $(+/-)$
test, and Matthew’s correlation coefficient (MCC) (17). The positive likelihood ratio (LR), also known as the informational odds ratio, is equal to the positive post-test odds divided by the pre-test odds (18). Similarly, the negative LR is equal to the negative post-test odds divided by the pre-test odds. The MCC, based on the geometric mean of the regression beta terms, was used to determine the optimal cut-off point for ODI. The latter represents a single “balanced measure” for positive and negative LR, respectively.

A Tukey mean-difference (Bland-Altman) plot was used to assess the agreement between ODI and AHI values. In this exploratory plot, the x-axis represents the maximum-likelihood average estimate of the true result, whereas the y-axis is the computed difference between the 2 recordings. Measures are considered to have poor agreement if greater than one-half of the plot points fall within the discordance region outside of the 95% confidence limits for the mean difference line. A receiver-operating characteristic curve was used to plot sensitivity by 1 − specificity (area under the curve) (19).

The iterative expectation-maximization (EM) method was used to account for missing values (20). Statistical significance was defined as \( p < 0.05 \). SAS version 9.3 (SAS Institute, Cary, North Carolina) was used for all analyses.

RESULTS

Figure 1 shows patient recruitment. A total of 282 patients who were admitted with decompensated CHF were screened during the time frame of this study. The mean age of this cohort was 63 ± 12 years, and 159 (56%) were male. The mean BMI was 36 ± 9.3 kg/m². All 282 patients were screened for SDB using the STOP-BANG questionnaire, and 246 tested as high risk (87%) for SDB. Table 1 shows the baseline characteristics and demographics of this group. The admitting team requested formal evaluation for 171 of 246 high-risk patients. The remaining 75 patients were not formally evaluated due to various reasons, including hemodynamic instability, high oxygen requirement, known SDB on therapy, planning same day discharge, or the patient declining further evaluation.

Of the 171 patients formally evaluated by a board-certified sleep physician, 105 underwent overnight pulse-oximetry during their hospital stay. The remaining 66 patients had relative contraindication to overnight pulse-oximetry or were being discharged the same day. Three patients had poor recordings that were considered uninterpretable.

Of these 105 patients, 68 patients underwent full outpatient PSG within 4 weeks of the discharge.

Table 1 shows the baseline characteristics and demographics of this group. The remaining 37 of 105 patients were not included for various reasons, including PSG evaluation performed at a different sleep center, not returning for study, discharged to nursing home, or patient refusal at time of discharge.

Among the 68 patients who underwent PSG, the test showed that 64 (94%) were positive for SDB (AHI ≥5): 25 (39%) were categorized as having severe SDB (AHI ≥30), 16 (25%) as having moderate SDB (AHI 16 to 29), and 23 (36%) as having mild SDB.
As the testing of the patients in our study showed, SDB is common and underdiagnosed in CHF, and a clinical pathway for screening and evaluation of sleep apnea in hospitalized patients with decompensated CHF results in a high yield of SDB. Furthermore, our study showed that plethysmographic signal-derived ODI correlates well with outpatient PSG-derived AHI. These findings suggest that plethysmographic signal-derived ODI may be a cost-effective tool to screen for SDB in decompensated CHF in hospitalized patients.

Various factors result in poor detection of SDB in CHF. Traditional symptoms of sleep disordered breathing, such as excessive daytime sleepiness and heavy snoring, are not prominent in patients with CHF. According to prior studies, only 13% of patients with CHF reported excessive daytime sleepiness (22). Our data suggest that use of the STOP-BANG screening questionnaire might result in a higher yield (87% patients were positive). Questionnaires based on clinical symptoms only have low sensitivity and specificity in predicting SDB in heart failure patients. The addition of BMI, sex, and arterial blood gas results may improve pre-test probability (23).

Previous studies have indicated that a pre-discharge overnight pulse-oximetry derived ODI ≥5 independently predicted readmission and mortality in patients admitted to the hospital with decompensated CHF (24). Photopletysmographic signal monitoring is now widely available in most hospitals and can be easily performed by respiratory therapists. Recent advances in pulse-oximetry have also improved plethysmographic signal recording and reduced motion artifacts and false alarms (25). In particular, the ability to reduce averaging time to 2 to 3 s without compromising on signal-to-noise ratio has ensured that respiratory events can be recorded with high precision. This is also consistent with the standards established by the AASM for using an averaging time of no more than 3 s (15). Our study used stricter standards of 4% desaturations for definition of hypopnea as per the CMS criteria and may have underestimated AHI compared with more liberal AASM criteria (26).

Current data suggest that there may be a role for treating SDB in hospitalized HF patients. Early detection of SDB is important, as newly diagnosed central sleep apnea and obstructive sleep apnea in AHF are independently associated with increased post-discharge mortality (27). Treatment of SDB in hospitalized patients has been shown to improve ejection fraction in 72 h (10). A recent study showed reduced 30-day hospital readmission in patients hospitalized with cardiac conditions including HF, diagnosed with SDB, and subsequently treated with positive airway pressure therapy (28). Current studies are underway to evaluate the potential benefit of early interventions for SDB (29).

**DISCUSSION**

<table>
<thead>
<tr>
<th>TABLE 1 Characteristics of Patients Positive for STOP-BANG (n = 246) and Those Who Underwent PSG (n = 68)*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>STOP-BANG</strong></td>
</tr>
<tr>
<td>Age, yrs</td>
</tr>
<tr>
<td>Median (IQR)</td>
</tr>
<tr>
<td>Body mass index†</td>
</tr>
<tr>
<td>Median (IQR)</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>African-American</td>
</tr>
<tr>
<td>Coronary artery disease</td>
</tr>
<tr>
<td>Diastolic heart failure</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
</tr>
<tr>
<td>COPD/asthma</td>
</tr>
<tr>
<td>Diabetes</td>
</tr>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>Beta-blocker</td>
</tr>
<tr>
<td>Calcium-channel blocker</td>
</tr>
<tr>
<td>Loop diuretic</td>
</tr>
<tr>
<td>Ejection fraction</td>
</tr>
<tr>
<td>Median (IQR)</td>
</tr>
<tr>
<td>ODI</td>
</tr>
<tr>
<td>Median (IQR)</td>
</tr>
<tr>
<td>AHI</td>
</tr>
<tr>
<td>Median (IQR)</td>
</tr>
</tbody>
</table>

Values are n (%). †Missing values imputed using the expectation-maximization algorithm (10 simulations; average imputational efficacy ≥98%). ‡Body mass index (BMI) was computed as mass in kilograms divided by height in meters squared. Values are n (%). *Missing values imputed using the expectation-maximization algorithm (10 simulations; average imputational efficacy ≥98%). †Body mass index (BMI) was computed as mass in kilograms divided by height in meters squared. AHI = apnea-hypopnea index; COPD = chronic obstructive pulmonary disease; IQR = interquartile range; NA = not applicable; ODI = oxygen desaturation index; PSG = polysomnography; STOP-BANG = questionnaire of heavy snoring, tiredness, observed apneas, hypertension, body mass index ≥35 kg/m², age ≥50 years, neck circumference ≥40 cm, and male sex.

(AHI <16). Among the 64 patients with SDB, 10 (15.5%) had predominantly central sleep apnea. The Bland-Altman plot revealed that there was no major bias when using ODI versus AHI (PSG-derived) to define SDB (Figure 2). The MCC suggested an optimal cut-off of ODI ≥5 (Table 2). This was the value with nearest distance to the MCC zenith point at 26 (not shown in table). ODI correlated well with AHI with AUC of 0.82 on the receiver-operator curve for AHI ≥5 for confirmatory diagnosis of SDB (Figure 3).
Another possibility for screening SDB in hospitalized HF patients is the portable sleep device. However, it requires much more logistical support and in-house expertise, which may not be available in very many hospitals. Current practices for performing sleep studies in hospitalized patients are cumbersome and financially unviable. Our study, by showing a close association with PSG-derived AHI, opens up a possible cost-effective strategy for early detection of SDB in ADHF patients. Photo-plethysmographic signal monitoring is readily available in most hospitals. In addition recent data suggests that time spent below 90% saturations during sleep may be a better variable than AHI in predicting cardiovascular events (30).

A strategy including the STOP-BANG questionnaire, demographic data, arterial blood gas, and overnight plethysmography could provide a cost-effective strategy for early recognition and intervention of SDB in CHF patients. Our study made an immediate clear difference in improving awareness among house staff: by the end of the study, the primary teams had placed more than 50% of consults for sleep evaluation directly, without being prompted by the screen results.

**STUDY LIMITATIONS.** This was a single-center clinical pathway study, conducted in a tertiary care hospital with an advanced heart failure service. These findings may not apply to other settings. Although the protocols were established and the data was prospectively collected, some bias may have been introduced by the standard of care within the hospital. Patients were not screened during weekends; however, we do not believe that the demographics of these patients would be significantly different. The high positivity of STOP-BANG (87%) in the current study may be a result of the clinical population seen at the center and suggests that it may not be very discriminatory in this setting. But, although the STOP-BANG questionnaire may have low specificity, in our model it served as an effective awareness tool among house staff and admitting physicians. In addition, it can be self-administered (14). Also, the screening pathway is obstructive sleep apnea specific, and central sleep apnea might be under-represented. Our novel pathway appears to have a high yield in terms of finding patients with significant sleep

**FIGURE 2** Bland-Altman Plot Illustrating the Agreement Between AHI and ODI

![Bland-Altman Plot](image)

Solid line denotes the mean of the differences between AHI and ODI ($\mu_d$). Dashed lines indicate the upper and lower limits of the agreement region ($\mu_d \pm 2 \times SD$), where $SD$ is the standard deviation of the differences. The x-axis represents maximum likelihood, harmonic mean estimate of the true result (assuming a lognormal distribution), and the y-axis is the computed difference between the 2 readings. Approximately 94% of values (shown as dots in the plot) were within the agreement region, indicating strong agreement between AHI and ODI measurements. AHI = apnea-hypopnea index; ODI = oxygen desaturation index.

**TABLE 2** Confusion Matrix

<table>
<thead>
<tr>
<th></th>
<th>AHI = $5$</th>
<th></th>
<th>AHI = $10$</th>
<th></th>
<th>AHI = $15$</th>
</tr>
</thead>
<tbody>
<tr>
<td>ODI</td>
<td>Sensitivity (95% CI)*</td>
<td>Specificity (95% CI)*</td>
<td>LR$^+$ (95% CI)$^+$</td>
<td>LR$^-$ (95% CI)$^+$</td>
<td>MCC (95% CI)$^+$</td>
</tr>
<tr>
<td>≥5</td>
<td>0.84 (0.77–0.89)</td>
<td>0.56 (0.21–0.86)</td>
<td>1.9 (0.91–3.9)</td>
<td>0.29 (0.15–0.58)</td>
<td>0.24 (0.08–0.38)</td>
</tr>
<tr>
<td></td>
<td>p = 0.090</td>
<td></td>
<td>p = 0.0004</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥10</td>
<td>0.62 (0.53–0.70)</td>
<td>0.89 (0.52–1.0)</td>
<td>5.6 (0.87–35)</td>
<td>0.43 (0.32–0.59)</td>
<td>0.24 (0.09–0.38)</td>
</tr>
<tr>
<td></td>
<td>p = 0.070</td>
<td></td>
<td>p = 0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥15</td>
<td>0.50 (0.41–0.58)</td>
<td>0.89 (0.52–1.0)</td>
<td>4.5 (0.70–29)</td>
<td>0.57 (0.43–0.75)</td>
<td>0.18 (0.02–0.33)</td>
</tr>
<tr>
<td></td>
<td>p = 0.11</td>
<td></td>
<td>p = 0.0001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Exact CI. †Asymptotic (normal theory) CI.
CI = confidence interval; LR$^+$ = likelihood ratio of a positive test; LR$^-$ = likelihood ratio of a negative test; MCC = Matthew’s correlation coefficient; other abbreviations as in Table 1.
disordered breathing, but this study cannot evaluate the overall effectiveness of this approach in all admitted patients with AHF.

Our study was also limited by the number of patients who subsequently obtained a PSG that was available for analysis. It is worth noting, however, that the baseline characteristics of the patients for which a PSG result was available were not significantly different than the overall population with a positive STOP-BANG (Table 1). Finally, due to the nature of the study design, the investigators were unable to evaluate potential false negatives in ODI <5. As the study was conducted at a tertiary care hospital with a committed heart failure program, the diagnosis was provided by a heart failure specialist, and we did not collect detailed HF parameters.

CONCLUSIONS

SDB is common in hospitalized HF patients. An effective screening method that utilizes a simple instrument such as STOP-BANG, clinical sleep evaluation, and overnight ODI monitoring can lead to early detection of SDB. Early detection and intervention of SDB could be valuable in reducing the rate of readmission for patients with CHF.

REFERENCES

11. Whitelaw WA, Brant RF, Flemmons WW. Clinical usefulness of home oximetry compared with

PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: SDB is a common but under-recognized comorbidity in patients with ADHF. This study tests the feasibility of a cost-effective strategy for early detection of SDB in hospitalized patients. The study suggests the utility of plethysmography as an effective and economical screening tool for SDB in ADHF.

TRANSLATIONAL OUTLOOK: Additional studies are required to determine the effect of early screening and intervention of SDB strategy on readmissions, morbidity, and mortality in heart failure patients.


**KEY WORDS** acute decompensated heart failure, hospitalized patients, oxygen desaturation index, plethysmography, sleep-disordered breathing