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# Nocturnal oxyhemoglobin desaturation during sleep in congestive heart failure patients

## *Dessaturação da oxihemoglobina durante o sono em pacientes com insuficiência cardíaca congestiva*

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**Abstract**

**Introduction:** Sleep breathing disorders occur in 45% of patients with heart failure, with 36%–50% manifesting Cheyne-Stokes respiration with central sleep apnea and 12% exhibiting obstructive sleep apnea. Several studies have shown that sleep pathophysiology may negatively affect the cardiovascular system and that cardiac dysfunction alters sleep and respiration. **Objective:** The aim of this study was to examine oxyhemoglobin desaturation during sleep in patients with congestive heart failure (CHF) using overnight pulse oximetry. **Methods:** Overnight pulse oximetry was conducted in the patients' homes with wrist pulse oximeters and finger probes that were placed around the forefingers of 15 patients with CHF and ejection fractions less than 50%, who were classified as New York Heart Association functional classes II and III. **Results:** The patients were divided into two groups. The first group consisted of seven patients with oxyhemoglobin desaturation

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indices of over 5 events/h, and the second group contained eight patients with oxyhemoglobin desaturation indices of 5 or less events/h. Student's t-tests did not show any significant differences between the groups. The patients' body mass indices correlated positively with the total desaturation episodes and desaturation time less than 90% and correlated negatively with the arterial oxygen saturation nadir. **Conclusion:** Pulse oximetry monitoring during sleep can be used to detect sleep breathing disorders in stable patients with CHF.

**Keywords**: Sleep Disorders. Obstructive Sleep Apnea. Oximetry.

***Resumo***

***Introdução:*** *Os distúrbios respiratórios do sono ocorrem em 45% dos pacientes com insuficiência cardíaca, com 36%-50% manifestando respiração Cheyne-Stokes com apneia do sono central e 12% exibindo apneia obstrutiva do sono. Vários estudos têm demonstrado que a fisiopatologia do sono pode afetar negativamente o sistema cardiovascular e que a disfunção cardíaca altera o sono e a respiração. Objetivo: Examinar a dessaturação da oxihemoglobina durante o sono em pacientes com insuficiência cardíaca congestiva (ICC), utilizando a oximetria de pulso durante a noite. Métodos: A oximetria de pulso noturna foi realizada nas casas dos pacientes com oxímetros de pulso acoplados ao redor dos dedos indicadores de 15 pacientes com ICC e fração de ejeção menor que 50%, sendo classificados pelo New York Heart Association como classes funcionais II e III. Resultados: Os pacientes foram divididos em dois grupos. O primeiro grupo era composto por sete pacientes com índices de dessaturação da oxihemoglobina (IDO) maior que 5 eventos/h e o segundo grupo continha oito pacientes com IDO igual ou menos que 5 eventos/h. Testes t de Student não apresentou diferenças significativas entre os grupos. Os índices de massa corporal dos pacientes foram positivamente correlacionados com o total de episódios de dessaturação e tempo de dessaturação inferior a 90% e negativamente com a saturação de oxigênio arterial. Conclusão: O monitoramento da oximetria de pulso durante o sono pode ser usado para detectar distúrbios respiratórios do sono em pacientes estáveis com ICC.*

***Palavras-chave****: Transtornos do Sono. Apneia do Sono Tipo Obstrutiva. Oximetria.*

## Introduction

Over 180 years ago, irregular breathing patterns were observed in patients with congestive heart failure (CHF). These breathing pattern disorders have only been considered clinically significant since the 1980s, when sleep-disordered breathing (SDB) was shown to be related to worsening heart function (1). Is observed in patients with more severe SDB a higher prevalence of left atrial enlargement (LAE), suggesting that SDB may cause LAE. The SDB leads to nocturnal hypoxemia, excitement reactions and consecutive repetitive bursts of sympathetic activity (2).

SDB occurs in approximately 60% of patients with heart failure (HF), with 36% exhibiting Cheyne-Stokes respiration (CSR), 12% demonstrating obstructive sleep apnea (OSA), and the rest having a mixed form (3). CSR is more common in male patients with HF than in females patients with HF, and its pathophysiology is not yet understood.

OSA and CSR with central sleep apnea are the two main types of SDB in patients with CHF (4). OSA, which is characterized by repetitive episodes of complete or partial closure of the upper airway during sleep, produces sleep fragmentation and oxygen desaturation (5). In contrast, central apnea is associated with no respiratory efforts for at least 10s (4).

Currently, HF is a major public health problem that has an increasing incidence and prevalence due to the increased average life spans and improved therapies of ischemic coronary artery disease and hypertension, which are the most common risk factors for HF. It is estimated that 1.5% - 2% of the population of the United States has some form of HF and that its prevalence increases to approximately 6% - 10% in individuals over 65 years of age. Of the patients with HF from ventricular systolic dysfunction, at least 45% have an apnea-hypopnea index (AHI) of 10 or more events/h (6).

A study has shown that identification and treatment of OSA may improve heart function and on the other hand, central sleep apnea identification may be indicative of heart failure with pulmonary edema, with a need to increase the targeted therapy or with drugs or devices (CPAP) (7).

OSA has several pathophysiologic effects on the afterload, hypoxia, and activation of the sympathetic nervous system. These effects can be presumed to result from the cumulative influence of hundreds of obstructive apneas that occur each night over a period of months to years and that contribute to the development and/or aggravation of left ventricular dysfunction in patients with HF (8).

Oxygen desaturation from SDB contributes to the worsening of CHF (9) and is associated with poor prognoses (10). Nakano et al. examined oxyhemoglobin desaturation by monitoring nocturnal pulse oximetry (NPO) during sleep in patients with suspected sleep apnea, and they then proposed that NPO can be used as a low-cost screening test of SDB (11).

A study on the use of the WristOx™ 3100 wrist pulse oximeter has shown that monitoring the NPO of patients with OSA is extremely important, especially in regions where polysomnography (PSG) is difficult to access. In patients with suspected sleep apnea/hypopnea syndrome (SAHS), a negative oximetry result is defined as an adjusted $O_2$ desaturation index 2 (which is the mean number of $O_2$ desaturations of 2% or less/h of total recording time) of 12.2 or less, with the exclusion of SAHS, which is defined by an AHI of 5 or more, with a sensitivity of 100%. A positive oximetry result is defined as an adjusted $O_2$ desaturation index 3 (which is the mean number of $O_2$ desaturations of 3% or less/h of total recording time) of over 32 (SAHS is defined by an AHI of 15 or more), with a specificity of 100%. The results of that study suggested that the WristOx™ 3100 might be a valuable tool for the diagnosis or exclusion of SAHS. However, additional studies are necessary to determine if the results found in their study are applicable to the use of the WristOx™ 3100 at home (12).

Few studies have examined the use of NPO to screen for OSA in patients with CHF. Thus, the aim of this study was to examine oxyhemoglobin saturation with NPO in patients with CHF who were classified as functional classes II or III according to the New York Heart Association during sleep. Our secondary objectives were to examine the relationships of the values obtained with the NPO with the anthropometrics data and Epworth Sleepiness Scale scores and to verify the possibility of using NPO as a screening test of the presence of a sleep breathing disorder (SBD).

## Methods

The present cross-sectional study was conducted at the Sleep Laboratory of Nove de Julho University. The protocol was approved by the Research Ethics Committee of Nove de Julho University (protocol number 214896), and informed consent was obtained from each patient. Data collection started after the approval of the ethics committee and was finalized in November/2015. The subjects consisted of 15 patients with CHF (eight men and seven women) from the Cardiology Service from Sao Paulo. Figure 1 shows the study design.

The inclusion criteria were BMI < 35 kg/m$^2$, and the patients had been clinically stable for at least one month. Exclusion criteria were renal insufficiency, unstable angina, myocardial infarction, cardiac surgery or acute heart failure decompensation within the previous 3 months. Patients were instructed about the details of the study, including the benefits and risks. All patients signed and received a copy of the informed consent.

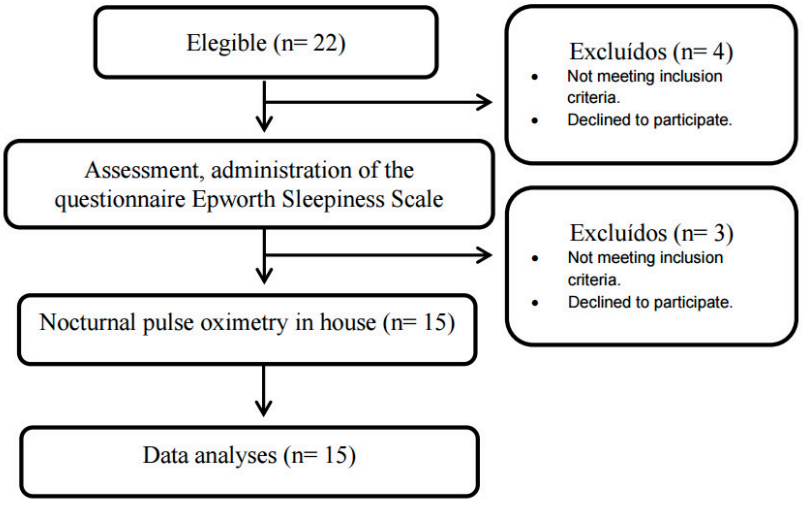


**Figure 1 -** Design of the study.

### Clinical Evaluation

The patients with CHF provided information on their medical and surgical histories, including their concomitant medications, demographic data, anthropometric measures, and physical examinations. The measurements included body weight (kg), height (cm), body mass index (BMI), heart and respiratory rates, and peripheral blood pressure.

### Epworth Sleepiness Scale

The patients completed the Epworth Sleepiness Scale, which is a simple and self-administered questionnaire that is used to assess recent daytime sleepiness with eight questions that refer to eight situations that are based on their usual way of life. They were asked to rate each situation on a scale of 0 - 3 (0, no chance of napping; 1, small chance of napping; 2, moderate chance of napping; and 3, strong chance of napping) according to their felt or estimated degree of sleepiness. Total scores of 10 or more were used to identify clinically relevant levels of sleep-related daytime dysfunction (13).

### Nocturnal pulse oximetry

NPO was monitored with a WristOx™ 3100 (Nonin Medical, Inc., Plymouth, MN, USA) and a finger probe that was placed around the patient's forefinger. The equipment was set at 1 s/sample, which was the shortest measurement time interval. Each desaturation episode was defined as a decline of the baseline oxygen saturation ($SaO_2$) of 4% during a period of at least 10s.

In addition to the $SaO_2$ data, the oximeter simultaneously recorded heart rate (HR). An HR variation episode was defined as an HR alteration of at least 6 beats/min during a period of 10 s or more. For the data analysis, the patients were divided into two groups. Patients with an oxyhemoglobin desaturation index (ODI) of 5 or more events/h, which is considered abnormal, were assigned to Group 1, while Group 2 consisted of patients with an ODI of less than 5 events/h, which is considered normal. The readings will be performed manually by a specialized technician. A report of the results will be prepared by a doctor specializing in sleep medicine at the Sleep Laboratory of Nove de Julho University.

In general, abnormal ODI values have three levels that appear to mirror the definition of abnormal AHI (apnea/hypopnea events/sleep h) values. The levels for abnormal ODI values are 5 or more desaturation events/h, 10 or more desaturation events/h, and 15 or more desaturation events/h (14). For AHI, an index of 5 or more events/h has been used to define a significant number of SBD events in OSA in population studies of subjects who do not have HF (6).

### Statistical Analysis

The Shapiro-Wilk test was used to test the normality of the data, which are described as mean ± standard deviation. Student's *t*-tests were used to compare the means and identify significant differences between the groups. Pearson correlation coefficients were used to assess the relationships among the measures. P values less than 0.05 were considered statistically significant in all of the analyses.

## Results

Table 1 lists the anthropometric data of the patients, their medications, and their ejection fractions that were verified with echocardiography.

Of all of the patients, seven (46.7%) had ODI values of 5 or more events/h, and these patients were assigned to Group 1 (figure 2). Student's *t*-tests did not find statistically significant differences between the groups, except for the left atria systolic diameter (LASD; Group 1: 41.50 ± 4.20; Group 2: 50.57 ± 6.95), which was significantly decreased in Group 1. Some of the echocardiographic values were collected from the patient's medical records with authorization of the responsible doctor because of the lack of echocardiography results. Thus, the LASD values were missing for two patients, and the left ventricular end-diastolic diameter (LVEDD) values were missing for two patients.

The Pearson correlation coefficients showed that BMI was positively correlated with the total episodes of oxyhemoglobin desaturation (TOD) (figure 3A) and $SaO_2$ times less than 90% (figure 3B) and negatively correlated with the minimum $SaO_2$ (figure 3C). Age correlated positively with TOD (figure 3D) and negatively with $SaO_2$, as shown in figure 3E.

**Table 1** - Anthropometric variables, type of neurological damage and classification of foot deformities in children with chronic non-progressive encephalopathy, Jequié, Bahia, Brazil, 2014

| VARIABLES | (n = 15) | ODI > 5/h (n = 7) | ODI ≤ 5/h (n = 8) |
|---|---|---|---|
| Age (years) | | 67.71 ± 11.44 | 58.88 ± 10.13 |
| Weight (Kg) | | 79.29 ± 20.32 | 67.63 ± 12.33 |
| Height (cm) | | 167.29 ± 6.24 | 164.13 ± 8.87 |
| BMI (Kg/m²) | | 28.20 ± 6.54 | 24.90 ± 2.34 |
| EF (%) | | 40.07 ± 9.40 | 38.75 ± 5.89 |
| Functional class (NYHA) | II – n = 4<br>III – n = 7<br>II-III – n = 4 | - | - |
| Schemic myocardiopathy | 7 | - | - |
| Dilated myocardiopathy | 4 | - | - |
| Idyopathic myocardiopathy | 3 | - | - |
| Schemic dilated myocardiopathy | 1 | - | - |
| Medications in use | | - | - |
| Digitalis (%) | 66.7 | - | - |
| Diuretics (%) | 66.7 | - | - |
| Anti-hypertensives (%) | 40 | - | - |
| Vasodilators (%) | 13.3 | - | - |
| ACE inhibitors (%) | 6.7 | - | - |
| Angiotensin-1 receptor antagonist (%) | 13.3 | - | - |
| Beta blockers (%) | 13.3 | - | - |

Note: NYHA = New York Heart Association; Kg = kilogram; cm = centimeters; Kg/m² = kilograms per meters squared; EF = ejection fraction; ACE = Angiotensin conversor enzyme.

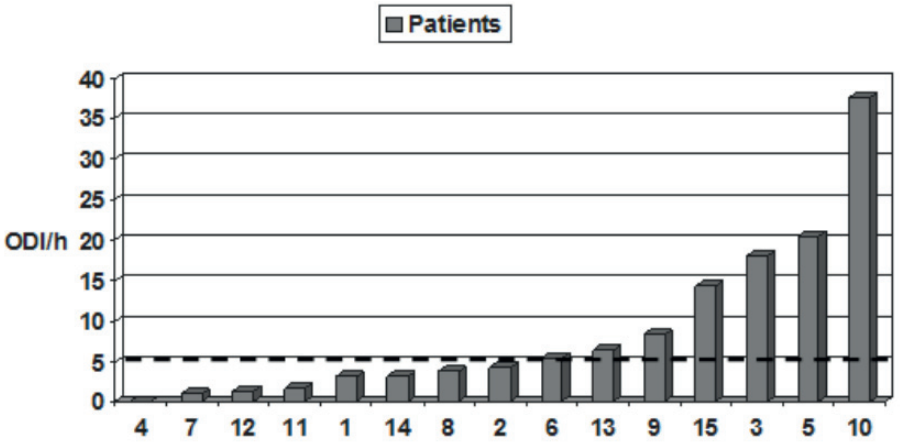


**Figure 2** - Oxyhemoglobin desaturation index per hour during sleep of the 15 patients.

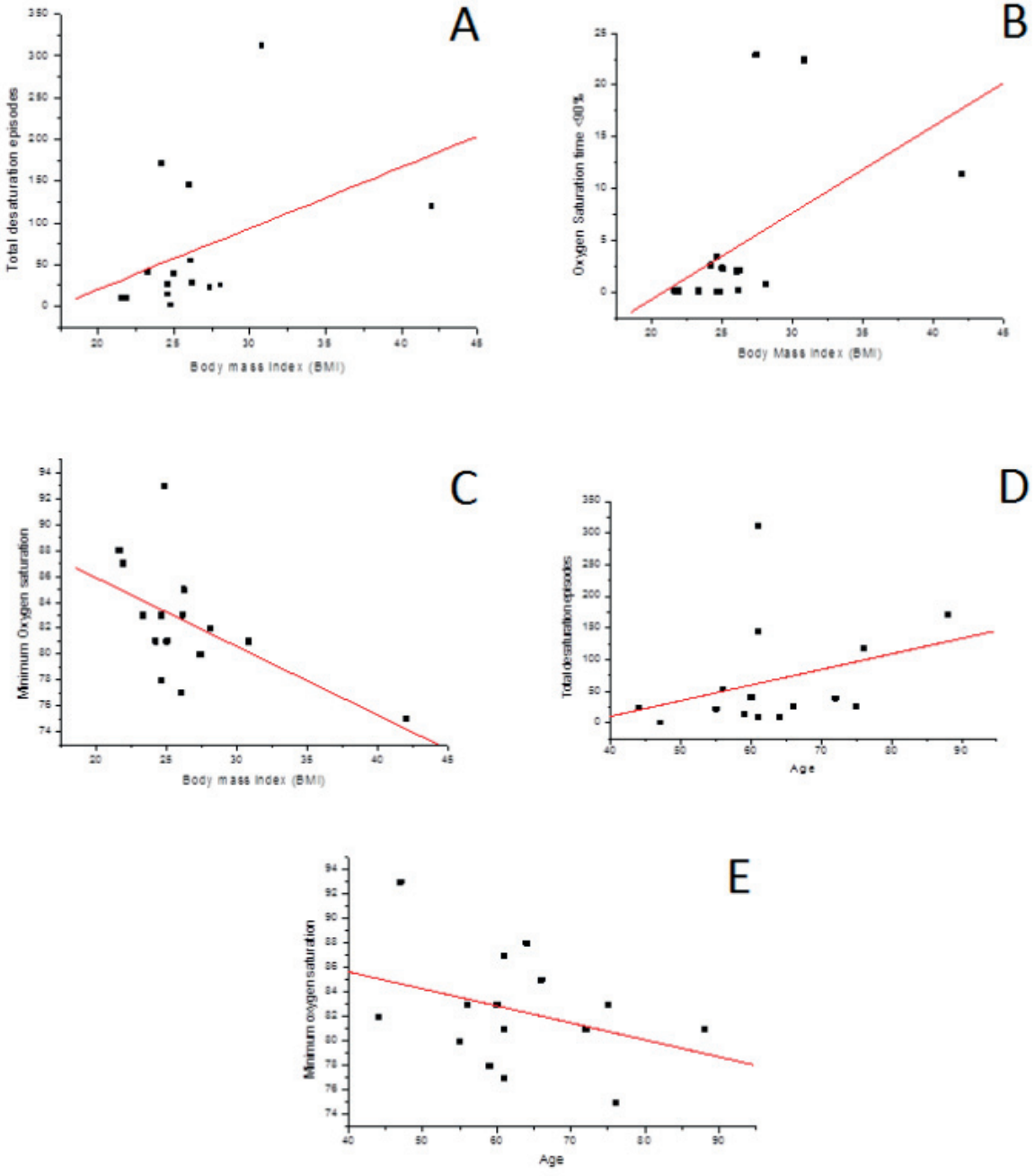


**Figure 3** - A = Correlation coefficient between BMI and total desaturation episodes (r = 0.419); B = Correlation coefficient between BMI and SaO2 time < 90% (r = 0.522); C = Correlation coefficient between BMI and SaO2 minimum (r = -0.522); D = Correlation coefficient between the age and total desaturation episodes (r = 0.327); E = Correlation coefficient between the age and SaO2 minimum (r = -0.347).

## Discussion

The incidence and prevalence of HF, which has become one of the main cardiovascular disorders, have been increasing, which has resulted in excessive morbidity and mortality. HF is therefore one of the major risk factors for SDB, and it adversely affects cardiovascular function and contributes to morbidity and mortality. The different prevalence rates of SBDs that have been reported in patients with systolic HF can be attributed to differences in the studies, the various thresholds used to define the disorders, and the several definitions of hypopnea (6).

In our study, we observed that 46.7% of the patients with CHF had ODI values of 5 or more events/h, which is considered abnormal. Thus, the ODI mirrored the presence of SBD. Our results were in accordance with the majority of studies that have been performed on patients with CHF (15 - 18).

The ODI values of the seven patients that exhibited a number of important desaturation episodes varied from 6.4 to 37.7 events/h, with a mean of 15.8 events/h. These results for a sample of patients with a severe number and degree of oxyhemoglobin desaturation episodes were similar to the results of a number of previous studies, as described above.

These results do not dismiss the need for studies of SDB in patients with CHF because the repetitive oxyhemoglobin desaturations that accompany apnea episodes contribute to the progression of myocardial failure due to increased left ventricular afterload. The arousals and increased sympathetic nervous system activity, with the consequent increases in HR and blood pressure, contribute to a greater need for cardiac $O_2$ supply, which is not available (19).

Chung et al. examined ODI in surgical patients who were monitored with NPO and demonstrated strong correlations with PSG parameters. The ODI levels of over 5, over 15, and over 30 were good predictors of AHI values of over 5, over 15, and over 30, respectively, and ODI effectively identified surgical patients with moderate and severe OSA (20).

Tkacova et al. (21) showed that patients with CHF that is associated with CSR have greater left ventricular volumes than patients with CHF without CSR, which is consistent with a higher filling pressure. In addition, Lanfranchi et al. (22) found an association of the area of the left atria (LA) with greater mortality in patients with CHF and CSR. The authors of that study verified that the risk of cardiac death increased gradually with increases in the AHI values and LA areas. Patients who were at a very high risk for a fatal outcome were identified by AHI values of 30 or more events/h and LAs of 25 or more $cm^2$. Nevertheless, in patients with isolated findings of enlarged LAs without SBDs and vice versa, the risk was low for patients with AHI values of 30 or more events/h and small LAs.

In the present study, the means ± standard deviations of the LASD and LVEDD were 46.39 ± 7.3 mm and 66.92 ± 8.22 mm respectively, which are both considered abnormal, and that of ODI was 8.64 ± 10.20, which suggested the existence of a group of patients with a low to moderate risk of cardiac death, except for one patient who presented an ODI of 37 events/h, an LASD of 44 mm, and an LVEDD of 79 mm (19). However, in order to confirm these results, more long-term studies on the prognostic value of SBD and cardiac dysfunction, sleep architecture, and arousals with PSG are needed.

The significantly greater LASD mean in Group 2 can be explained by the observations that two patients in Group 1 (one had a pacemaker) had normal LASD values, even though they had more disturbed sleep, as shown by their exhibiting more than 5 desaturation episodes during sleep, and one patient in this group did not have a LASD value.

Javaheri et al. studied 42 ambulatory patients with stable CHF who had ejection fractions of 45% of less. The patients underwent basic tests, pulmonary function tests, blood gas analyses, PSG, and Holter heart monitoring. They found that 45% of the patients with stable CHF who were subjected to the optimized treatment conditions presented mean AHIs of approximately 44 events/h, and that the prevalence of severe occult respiratory disorder was high in these patients with stable CHF. In addition, they reported that the respiratory disorder was associated with excessive awakenings and severe arterial oxyhemoglobin desaturation (23).

In a prospective study of 81 stable male patients with HF due to systolic dysfunction and left ventricular ejection fractions of 45% or less, Javaheri et al. found that 51% of the patients had moderate to severe respiratory disorder. In addition, the patients with HF and sleep apnea had a high prevalence of atrial fibrillation, ventricular tachycardia, and low ejection fractions compared with patients with no SBD (24). Javaheri observed that an interaction between SDB and left ventricular dysfunction can result in a vicious circle that increases the morbidity and mortality of patients with HF (25).

In contrast, in Group 2, all of the patients presented with abnormal LASD values, even though they did not have desaturation episodes and one patient in this group did not have a LASD value. These results suggested that cardiac remodeling might be unaffected by the number of oxyhemoglobin desaturation episodes during sleep and that it is therefore affected by other factors. In addition, the degree of desaturation in the patients in Group 2 could not have been severe enough to cause greater overload in the heart.

Being overweight and obese are well-established major risk factors for HF. The probable mechanisms by which obesity increases the risk of HF include the promotion of atherogenic risk traits, alterations in cardiac loading conditions, the potentiation of structural and functional changes, neurohormonal activation, natriuretic handicaps, and predisposition to SBD (26).

We observed that BMI was positively correlated with the TOD and $SaO_2$ time less than 90% and negatively correlated with the minimum $SaO_2$. Therefore, our study found that the greater the BMI, the greater was the damage from the $SaO_2$ during sleep.

The most important risk factors for OSA in patients with HF are obesity and age over 60 in women (27). The degree of desaturation in an apnea event is correlated with the degree of obesity expressed by the BMI. Nakano et al. have hypothesized that the diagnostic sensitivity of oximetry for OSA is lower in nonobese patients (9). Those authors classified 424 patients with OSA so that the OSA was the dominant type and then divided them into three groups according to BMI: normal-weight (BMI < 25), overweight (25 ≤ BMI < 30), and obese (BMI ≥ 30). The AHI values did not differ among the groups, but the parameters related to $SaO_2$ were worse in the overweight and obese groups, which suggested a high sensitivity of oximetry in the obese group.

This might have been related to the observation that the ODI and AHI values were significantly greater in the overweight and obese groups. The higher sensitivity of the oximetry might be because the rate of oxygen desaturation in an apnea event is exaggerated by a number of factors, such as low baseline oxygen saturation, low lung volume, and high oxygen expenditure, all of which are expected to be present in obese subjects.

Javaheri et al. observed a positive correlation between BMI and obstructive AHI, but not with central AHI, and age did not correlate with any episodes of SBD, including the AHI (16). Of the seven patients (46.7%) with ODI values of 5 or more events/h in our study, five had BMIs of 25 or less. Nevertheless, it is necessary to emphasize that these patients had CHF, and this characteristic differs from the patients with OSA who were examined in the previous study (11). In order to clarify if the patients with CHF having ODI values of 5 or more events/h and BMIs of 25 or more were desaturated more because of the higher sensitivity of oximetry, PSG is required to confirm the AHI data.

The positive correlation between age and minimum $SaO_2$ that was found in this study was not in accordance with the results of the study of Javaheri et al. (16). However, Quan et al. (27) have suggested that age is a risk factor for OSA and CSR in patients with HF, and Kenchaiah et al. (26) have shown that age and being male have consistently been identified as risk factors for HF. The increased incidence of HF in men is due in part to the greater prevalence and incidence of coronary heart disease in men.

Of the 15 patients examined in this study, seven were women, and eight were men. Of the seven patients (46.7%) with ODI values of 5 or more events/h, five were men. However, the anthropometrics values and ejection fractions did not differ significantly between the groups. The TOD and the total episodes of HR variations did not correlate. Moreover, four patients had pacemakers for at least 5 years. Thus, a lower average number of total episodes of HR variation was found in these patients compared to those patients who did not have pacemakers. This did not change the observation that the TOD average (116.25 ± 138.54) of the patients with pacemakers was greater than the TOD (49.82 ± 55.86) of the patients who did not have pacemakers, which suggested that the oxyhemoglobin desaturation episodes did not depend on HR variations during sleep.

HR variability correlated positively and directly proportionally with ODI and AHI in a study by Tateishi, but they did not find any correlations with either desaturation time or mean $SaO_2$, which indicated that HR variability can be regarded as a predictor of oxyhemoglobin desaturation but that it does not reflect its degree (28).

The Epworth Sleepiness Scale scores did not correlate significantly with any of the analyzed parameters. This might have been because the treating of a work group with desaturation degree minus severe and due to the small number of patients examined compared with other studies (16, 29). Pulse oximetry is conducted as a component of PSA for OSA

diagnostics. Recently, the utility of NPO as a screening tool for OSA has been newly recognized due to its economic benefits, easy applicability, and automated analysis, and because it could potentially satisfy the great demand for home diagnostic testing. NPO can be easily performed at home and repeated if necessary, which is unlike PSG (11, 30 - 32).

Sériès et al. evaluated the diagnostic value of nocturnal home oximetry in identifying SBD in patients with CHF and in distinguishing central events from obstructive events in 50 consecutive patients. The patients underwent two oximetry recordings: one at home and one during a PSG study. Home oximetry had 85% sensitivity and 93% specificity ($p < 0.001$) for detecting an SBD. The authors used the criteria for an SBD as the presence of more than 15 apneas and hypopneas/sleep h during PSG and an ODI of 10 events/h during oximetry, and a 2% fall in the pulse oximetry saturation was used as the criterion for oxyhemoglobin desaturation and a signal-averaging time of 8s (32).

However, studies that used NPO as an initial test in the assessment of SBDs have verified that the oxyhemoglobin desaturation during sleep is worse in a greater number of patients with CHF. Studies that are done in conjunction with PSG are necessary to determine the best analysis parameters to use as the criterion for oxyhemoglobin desaturation, signal-averaging time, and BMI if more studies confirm its influence on oximetry sensitivity and specificity.

## Conclusion

In conclusion, 46.7% of the patients with CHF exhibited ODI values of 5 or more events/h. In addition, the results showed that the greater the age and BMI of the patient, the greater the change in $SaO_2$ during sleep, which suggested that NPO can be used at home as a screening test for the presence of SBD in patients with CHF.

NPO was useful as a tool for the prompt identification of the presence of a SBD, which is essential for early diagnosis and intervention. It is important that health professionals, especially physiotherapists, understand when SBDs are detected with NPO in patients with CHF because they can offer guidance after the diagnosis of interventions with noninvasive ventilation that improve the patients' quality of life and reduce morbidity and mortality.

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