

# Cardiac Interbeat Interval Increment for the Identification of Obstructive Sleep Apnea

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**ROCHE, F., ET AL.: Cardiac Interbeat Interval Increment for the Identification of Obstructive Sleep Apnea.** *The prevalence of obstructive sleep apnea syndrome (OSAS) is high in developed countries but its diagnosis is costly. Based on physiological evidence, the frequency component of heart rate variability (HRV) was evaluated as a simple and inexpensive diagnostic tool in OSAS. The predictive accuracy of frequency-domain HRV variables obtained from 24-hour ECG Holter monitoring (the power spectral density of the interbeat interval increment of very low frequencies, "VLF<sub>Ipsd</sub>," and its percentage over the total power spectral density, "%VLF<sub>I</sub>"), and of established time-domain HRV variables were analyzed by comparison with respiratory disturbances indexes assessed by complete polysomnography in 124 consecutive patients (98 men aged  $53.8 \pm 11.2$  years) with clinically suspected OSAS. OSAS was present in 54 (43.5%) patients according to standard criteria. Using receiver operating characteristic curve analysis, two of the three most powerful predictors were frequency-domain variables: %VLF<sub>I</sub> ( $W = 0.80, P < 0.0001$ ), and VLF<sub>Ipsd</sub> ( $W = 0.79, P < 0.0001$ ). Using a multiple logistic regression analysis, %VLF<sub>I</sub> was the most strongly associated with diseased status (adjusted OR: 8.4; 95% CI: 3.4–19.5). Using an appropriate threshold, %VLF<sub>I</sub> demonstrated a diagnostic sensitivity of 87%. A 3-month continuous positive airway pressure treatment significantly improved the same parameter. Frequency-domain analysis of the interbeat interval increment appears as a powerful tool for OSAS diagnosis and follow-up. The simplicity of its analysis and of its use makes of it a well-suited variable for mass screening of OSAS patients. (PACE 2002; 25:1192–1199)*

**heart rate variability, ECG Holter monitoring, obstructive sleep apnea syndrome, autonomous nervous system**

## Introduction

Sleep related breathing disorders are not only common,<sup>1</sup> but they bear significant health consequences since they may imply severe daytime repercussions<sup>2</sup> and increased cardiac morbidity.<sup>3</sup> In spite of these complications, recent studies have reported that obstructive sleep apnea syndrome (OSAS), by far the more frequent of these disorders, was largely underdiagnosed in the middle-aged population;<sup>4</sup> its prevalence could reach 10%. Because of limited financial resources for

health care, it would be cost-effective to establish OSAS diagnosis and perform its follow-up using ambulatory techniques instead of in hospital full night monitoring.

Among the numerous parameters known to be altered by sleep related breathing disorders, those derived from the autonomic nervous system activity appear as good candidates to establish the diagnosis of OSAS and to perform its follow-up because they are profoundly modified by it and easily measurable.

Nocturnal cyclical heart rate variability (HRV) has already been described in sleep related breathing disorders,<sup>5</sup> however, without pragmatic quantification. The authors recently identified<sup>6</sup> an enhanced contrast between day and night time-domain values of HRV, that allowed identification of OSAS with a sensitivity of 89.7% and a speci-

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ficity of 98.1%. However, this method needs to select, somewhat arbitrarily, night and day periods of a long enough duration. Some data suggest that a frequency-domain analysis could provide new powerful diagnostic parameters that are easier to use. Prosthetic mandibular advancement treatment in OSAS patients was shown by Shiomi et al.<sup>7</sup> to decrease the very low frequency (VLF) power component of spectral analysis of HRV. Other studies have demonstrated marked changes in heart rate dynamics associated with periodic breathing,<sup>8</sup> including the emergence of intermittent relatively low frequency heart rate oscillations, as low as 1 to 4 cycles per minute.

The purpose of this study was to prospectively evaluate the predictive accuracy of frequency-domain parameters of the interbeat interval increment, known to accurately extract VLF, in patients referred to the sleep laboratory for suspected OSAS and to monitor the effects of its treatment.

## Methods

### Study Group

The population under study included 124 patients (98 men, 26 women) with a mean ( $\pm$  SD) age of  $53.8 \pm 11.2$  years (range 22–78 years), who were referred for a polysomnography recording based on clinically suspected OSAS. Exclusion criteria were permanent or paroxysmal atrial fibrillation, diabetes mellitus, Shy-Drager syndrome, and permanent ventricular or atrial pacing. In all patients, 24-hour ECG Holter monitoring started 6 hours before the beginning of the polysomnogram recording and was continued so as to obtain a standard 24-hour duration. These prospective investigations at the pulmonary and at the cardiac level were performed by two complementary clinical teams, each one blinded to the results of the other; 18 OSAS patients were recorded a second time in the same conditions after 3 months of treatment with continuous positive airway pressure (CPAP).

### Sleep Study and Polysomnography Scoring

OSAS was diagnosed on the basis of clinical criteria and on the polysomnography performed following the recommendations of the American Sleep Disorders Association.<sup>9</sup> The presence and stages of sleep were monitored using two pairs of electroencephalographic leads ( $C_4-A_1$ ,  $O_2-A_1$ ), two pairs of electrooculographic leads and chin electromyographic leads. Airflow was measured by an oronasal thermocoupler. Respiratory efforts were monitored using inductive plethysmography with transducers placed around the chest and the abdomen. Arterial oxygen saturation was recorded continuously by pulse oximetry (Criticare Sys-

tems Inc., Waukesha, WI, USA), during the whole night period. The polysomnogram was scored manually according to standard criteria.<sup>10,11</sup> Apnea was defined as the absence of airflow for more than 10 seconds in the presence of persistent respiratory efforts. Hypopnea was defined as the association of a reduction of 50% or more of the amplitude of respiratory efforts during at least 10 seconds, associated to a fall in  $SaO_2$  of at least 4%. The apnea/hypopnea index (AHI) was defined as the number of episodes of apnea and hypopnea per hour of sleep and reflected the respiratory index disorder; the threshold to identify OSAS was chosen as an  $AHI \geq 10$ . Apnea duration and mean and minimal  $SaO_2$  were determined for each episode of apnea. Total sleep time (TST), number and duration of rapid eye movement (REM) periods, and number and duration of arousals were evaluated. Arterial desaturation was quantitated as the total time with  $SaO_2 < 90\%$ .

### 24-Hour Electrocardiographic (ECG) Holter Monitoring and HRV Analysis

The recordings were analyzed on a Novacor system (Rueil-Malmaison, France), model Duo-Holter, equipped with the HRV module. To perform the analysis, each QRS complex was validated and the length between each QRS (RR interval) calculated. Only normal to normal beats were considered for analysis. Mean duration of Holter recording reached  $22 \pm 2$  hours.

To identify the VLF oscillations, a power spectral analysis of the Interbeat Interval Increment (PS31) was performed as a function of the inverse of the increment on the full recording length without selecting any period. The individual spectral data obtained were then smoothed by a sliding average of over 50 consecutive values. On such plots, the occurrence of Cheyne-Stokes respiration is characterized by a spectral peak centered at about  $0.01-0.05 \text{ beat}^{-1}$ .<sup>8</sup> The repetitive occurrence of homogenous episodes of apnea and their ECG counterparts should document a similar periodic breathing pattern. Thus, on this Interbeat Interval Increment the absolute value of the power spectral density of that VLF band ( $0.01-0.05 \text{ beat}^{-1}$ , VLF<sub>Ipsd</sub>) was calculated, and the relative importance of this component (%VLF<sub>I</sub>) over the total power spectral density ( $0.01-0.5 \text{ beat}^{-1}$ , TI<sub>Ipsd</sub>). In the same manner, the power spectral density of the low frequency band ( $0.05-0.15 \text{ beat}^{-1}$ , LF<sub>Ipsd</sub>), and of the high frequency band ( $0.15-0.40 \text{ beat}^{-1}$ , HF<sub>Ipsd</sub>), and their expression in a percentage of the total power spectral density (respectively, %LFI, %HFI) were computed.

Time-domain measurements<sup>12</sup> were performed over three different periods: the full

recording duration, and on a day and a night period, separately, to obtain the derived parameters which, as described in the authors' previous study,<sup>6</sup> represent the contrast between day and night values. The r-MSSD (root mean square of successive differences between adjacent normal RR intervals), pNN50 (percent of adjacent normal RR intervals > 50 ms), SDNN (standard deviation of all normal RR intervals), SDANN (standard deviation of the mean of all consecutive 5-minute segments of normal RR intervals), and SDNN index (mean of the standard deviations of the consecutive 5-minute segments) were computed; the derived day/night differences in these parameters was then calculated:  $\Delta$ [D/N] r-MSSD,  $\Delta$ [D/N] SDANN,  $\Delta$ [D/N] SDNN,  $\Delta$ [D/N] SDNN index.

**Statistical Analysis**

Data were analyzed using Statview and JMP (SAS Institute, Cary, NC, USA) software. Differences were considered as significant when P was < 0.05. Values were expressed as mean and 95% SD (mean  $\pm$  SD). Statistical analyses were performed to evaluate the ability of the variables to discriminate between diseased and nondiseased status. Thus, the dependent variable was diseased status (OSAS +). The independent variables analyzed were age, sex, body mass index (BMI), frequency-domain parameters of the PS3I (VLF, LFI, and HFI components), their expression as a percentage of the total power spectral density (%VLF, %LFI, %HFI, respectively), and the three time-domain parameters that were significantly associated with diseased status in the authors' previous report.<sup>6</sup> Receiver operating characteristic (ROC) curve analysis was used<sup>13</sup> with the areas under the curves represented by the letter W. A W value of 0.5 means that the distributions of the variables are similar in both populations; conversely, a W value of 1.0 means that the distributions of the variables of two populations do not overlap at all. Logistic regression models were used to further analyze the data via simple logistic regression of diseased status versus each of the covariates to confirm the previously performed ROC curve analysis. Multiple logistic regression analysis was then used to evaluate the strength of the association of each variable with diseased status after adjustment for the other variables. Odds ratios (OR) were calculated individually for the significant independent variables. The highest separation power was established for the most powerful variables to obtain a threshold value with an optimized sensitivity or specificity. A linear correlation was established between the AHI and the variables significantly and independently associated with diseased status. Finally, a paired t-test was performed to compare the evolution of the

identified variables before and 3 months after CPAP treatment in the 18 consecutive OSAS patients and was recorded twice using the standard in hospital polysomnography and HRV analysis.

**Results**

The diagnosis of OSAS was established in 54 (43.5%) of the 124 patients using polysomnography recording. The clinical variables of all patients are summarized in Table I. There were no differences in clinical characteristics between patients with and without OSAS, in particular neither age nor BMI were helpful in separating the two populations.

Frequency-domain parameters were significantly different between patients with and without OSAS: mean  $\pm$  SD VLFpsd was higher in patients with OSAS (0.18  $\pm$  0.19 vs 0.06  $\pm$  0.06 ms<sup>2</sup>.beat<sup>-1</sup>; P < 0.0001), and the mean  $\pm$  SD %VLF (5.84  $\pm$  3.60 vs 2.81  $\pm$  2.16 ms<sup>2</sup>.beat<sup>-1</sup>; P < 0.0001). Standard time-domain parameters of HRV calculated over the 24-hour recordings did not show any significant alteration in OSAS patients. However, mean  $\pm$  SD  $\Delta$ [D/N] SDNN Index,  $\Delta$ [D/N] r-MSSD, and  $\Delta$ [D/N] SDNN were found significantly higher in OSAS patients (Table II).

ROC curves (continuous data) were built separately for each HRV variable (Table III). Two of the frequency-domain variables (VLFpsd and %VLF), calculated over the full recording length, were able to separate OSAS+ from OSAS- status with statistical significance (P < 0.0001). Three variables appeared as the most powerful separators, two PS3I variables, %VLF (W = 0.796, P < 0.0001; Fig.1) and VLF (W = 0.788, P < 0.0001), and one time-domain variable,  $\Delta$ [D/N] SDNN index (W = 0.813, P < 0.0001). In accordance with the authors' previous findings,<sup>6</sup>  $\Delta$ [D/N] SDNN index,  $\Delta$ [D/N] SDNN and  $\Delta$ [D/N] r-MSSD were also significant predictors of OSAS (W = 0.676, P <

**Table I.**  
Clinical Characteristics

Clinical Characteristics	OSAS+ (n = 54)	OSAS- (n = 70)	P
Age, years (mean $\pm$ SD)	55.8 $\pm$ 11.2	54.9 $\pm$ 10.7	NS
Male, n (%)	42 (78)	55 (79)	NS
BMI, kg/m <sup>2</sup> (mean $\pm$ SD)	28.9 $\pm$ 9.2	29.9 $\pm$ 9.9	NS
Hypertension, n (%)	20 (37)	15 (21)	NS

BMI = body mass index; OSAS+ = patients with obstructive sleep apnea syndrome; OSAS- = patients without obstructive sleep apnea syndrome.

INTERBEAT INTERVAL INCREMENT IN OSAS

**Table II.**

Time-Domain and Frequency-Domain (PS3I) Characteristics of the Heart Rate Variability (HRV)

Time-Domain Analysis	OSAS+ (n = 54)	OSAS- (n = 70)	P
	Mean ± SD	Mean ± SD	
HR (beats/min)	73.19 ± 9.37	73.39 ± 11.73	NS
pNN50 (%)	10.79 ± 8. ± 88	9.70 ± 9.41	NS
r-MSSD (ms)	32.60 ± 12.38	31.88 ± 14.48	NS
SDNN index (ms)	56.86 ± 20.57	47.11 ± 18.63	NS
SDNN (ms)	117.59 ± 40.81	108.13 ± 39.49	NS
SDANN (ms)	98.69 ± 36.29	91.55 ± 36.06	NS
Δ[D/N] r-MSSD	-18.59 ± 15.02	-10.38 ± 13.1	< 0.001
Δ[D/N] SDNN index	-37.69 ± 25.94	-12.80 ± 14.33	< 0.0001
Δ[D/N] SDNN	-18.34 ± 34.49	2.50 ± 20.72	< 0.0001
<b>Frequency-Domain Analysis (PS31)</b>			
Tlpsd (ms <sup>2</sup> ·beat <sup>-1</sup> )	3.52 ± 2.91	2.97 ± 2.73	NS
VLFpsd (ms <sup>2</sup> ·beat <sup>-1</sup> )	0.18 ± 0.19	0.06 ± 0.06	< 0.0001
LFpsd (ms <sup>2</sup> ·beat <sup>-1</sup> )	0.35 ± 0.29	0.28 ± 0.33	NS
HFpsd (ms <sup>2</sup> ·beat <sup>-1</sup> )	2.20 ± 2.15	1.91 ± 2.09	NS
%VLF1	5.84 ± 3.60	2.81 ± 2.16	< 0.0001
%LFI	10.27 ± 4.93	10.06 ± 7.74	NS
%HFI	58.88 ± 13.03	59.76 ± 12.01	NS

OSAS+ = patients with obstructive sleep apnea syndrome; OSAS- = patients without obstructive sleep apnea syndrome; HR = heart rate; pNN50 = percent of adjacent normal RR intervals > 50 ms; r-MSSD = square root of the mean of the sum of the squares of differences between adjacent normal RR intervals; SDNN Index = mean of the standard deviations of all intervals for all the consecutive 5-minute segments; SDNN = standard deviation of RR intervals; SDANN = standard deviation of the mean of the consecutive 5-minute segments of RR intervals; Δ[D/N] = differences between day-time and night-time values for the same variables (r-MSSD, SDNN Index, SDNN); Tlpsd = total power spectral density; VLFpsd = power spectral density of the very low frequency components; LFpsd = power spectral density of the low frequency components; HFpsd = power spectral density of the high frequency components; % = ratio of the power spectral density (Interbeat Interval Increment) of the frequency band on the total power spectral density.

0.002 and W = 0.667, P < 0.002, respectively; Table III).

A separate simple logistic regression analysis of diseased versus nondiseased status was per-

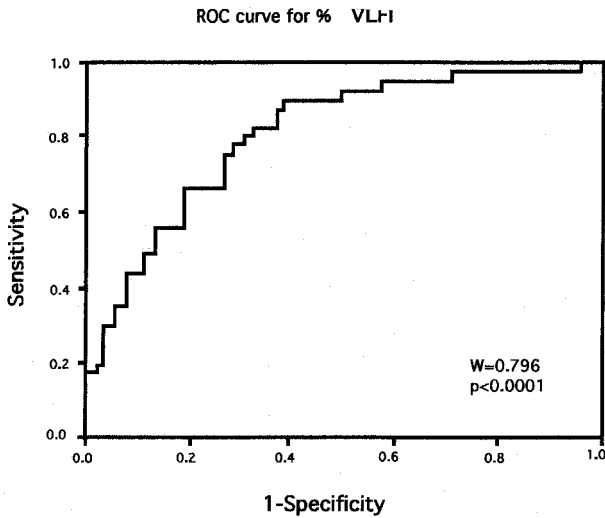
formed for each of the covariate to verify the ROC curve analysis. Maximum likelihood estimates were obtained for each of the important explanatory covariates (Table IV). Using multiple logistic regression analysis, after adjustment for the other variables, one frequency-domain and two time-domain HRV variables appeared to be independently and significantly associated with diseased status (Table IV): %VLF1, Δ[D/N] SDNN index and Δ[D/N] r-MSSD (adjusted OR: 8.4, 8.2, and 2.9, respectively; 95% confidence interval (CI): 3.36–19.5, 3.0–21.5; and 1.21–6.7, respectively). The highest separation power was obtained for the most powerful variable to derive a threshold value with an optimized sensitivity or specificity. For the variable presenting the highest OR, %VLF1, sensitivity reached 94% and specificity 42% with a threshold value of 2%. Using the same variable, threshold of 2.4% applied to our population yielded a sensitivity of 87% and a specificity of 52% (Fig. 1). The diagnostic accuracy of the two

**Table III.**

HRV Variables Significantly Associated with OSAS by Receiver Operating Characteristic (ROC) Curve Analysis, in Decreasing Order

Variable	W	P
Δ[D/N] SDNN index	0.813	< 0.0001
% VLF1	0.796	< 0.0001
VLFpsd	0.788	< 0.0001
Δ[D/N] SDNN	0.676	< 0.002
Δ[D/N] r-MSSD	0.667	< 0.002

Refer to Table II for definitions.



**Figure 1.** Receiver operating characteristic (ROC) curve analysis for identification of obstructive sleep apnea syndrome (OSAS) of the very low frequency (VLF) component of the interbeat interval increment expressed as the ratio (% VLFI) of the VLF<sub>Ipsd</sub> on the total spectral density, T<sub>Ipsd</sub>.

time-domain HRV variables significantly associated with OSAS are summarized in Table V.

Furthermore, the repeatability of a particular interbeat interval increment associated with the

presence of a sleep related breathing disorder determined, for each patient with OSAS, the occurrence of a characteristic VLFI peak (mean ± SD frequency:  $0.03257 \pm 0.009 \text{ beat}^{-1}$ , range  $0.01709\text{--}0.04954 \text{ beat}^{-1}$ ). Such a peak, corresponding to the breathing pattern disorder, was visually identifiable in 51 of the 54 OSAS patients (Fig. 2)

A significant, although weak, positive correlation was found between two frequency-domain variables of the PS3I (% VLFI,  $r = 0.56$ ,  $P < 0.001$ ; VLFI,  $r = 0.50$ ,  $P < 0.01$ ) and AHI. In addition, a significant negative correlation was found between the RDI and the three time-domain HRV variables significantly predictive of OSAS,  $\Delta[D/N]$  SDNN index,  $\Delta[D/N]$  r-MSSD, and  $\Delta[D/N]$  SDNN ( $r = 0.73$ ,  $P < 0.0001$ ;  $r = 0.52$ ,  $P < 0.001$ ; and  $r = 0.47$ ,  $P < 0.0001$ , respectively).

In the 18 patients with OSAS who underwent a second Holter monitoring during a control polysomnogram after 3 months of treatment with CPAP, the apnea/hypopnea index decreased from  $50.6 \pm 13$  to  $2.2 \pm 2.5$  events per hour. CPAP treatment determined a significant decrease (Fig. 3) in the % VLFI component ( $2.1 \pm 1.3$  vs  $4.8 \pm 3.1\%$ ;  $P < 0.03$ ) and a reduction in the  $\Delta[D/N]$  SDNN index ( $-22.8 \pm 21.7$  vs  $-48.3 \pm 31.2$ ;  $P < 0.03$ ) and in the  $\Delta[D/N]$  r-MSSD ( $-15.8 \pm 10.6$  vs  $-23.5 \pm 12.3$ ;  $P < 0.05$ ). The polysomnograms of all the patients improved significantly after CPAP treat-

**Table IV.**

Simple and Multiple Logistic Regression Analyses

**Simple Logistic Regression Analysis**

Variables	-Log Likelihood	Chi-Square	Prob > Chi-Square
Individual maximum likelihood estimates computed for each variable			
$\Delta[D/N]$ r-MSSD	5.21	10.43	< 0.001
$\Delta[D/N]$ SDNN index	20.55	41.11	< 0.0001
$\Delta[D/N]$ SDNN	8.15	16.31	< 0.0001
VLF <sub>Ipsd</sub>	16.87	33.75	< 0.0001
%VLFI	15.48	30.97	< 0.0001

**Multiple logistic regression analysis**

Term	Estimate	SE	Chi-Square	Prob > Chi-Square
Likelihood ratio test computed for the whole model (converged by gradient)				
Intercept	-2.650	0.531	24.92	< 0.0001
$\Delta[D/N]$ r-MSSD	0.066	0.033	3.85	0.0497
$\Delta[D/N]$ SDNN index	-0.082	0.028	8.67	0.0032
$\Delta[D/N]$ SDNN	0.020	0.013	2.49	0.1054
VLF <sub>Ipsd</sub>	6.057	4.901	1.53	0.2166
%VLFI	0.211	0.103	4.13	0.0421

Refer to Table II for definitions.

**Table V.**  
Optimized Threshold Values of Heart Rate Variables Significantly Associated with Obstructive Sleep Apnea Syndrome

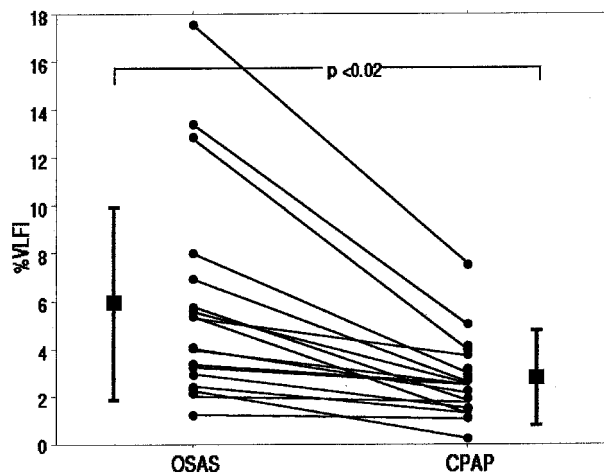
Variable	Threshold Value	Sensitivity %	Specificity %
%VLFI	2.4	86.5	52
$\Delta[D/N]$ SDNN index	-11.1	86.5	55
$\Delta[D/N]$ r-MSSD	-2.5	90.5	48

Refer to Table II for definitions.

ment (AHI 0–10). Moreover, the two patients with no total disappearance of apnea/hypopnea events during the polygraphic control performed after this standard 3-month CPAP treatment (mean level + 10 cm H<sub>2</sub>O), presented AHI and %VLFI abnormal values, above 5 and 3, respectively.

**Discussion**

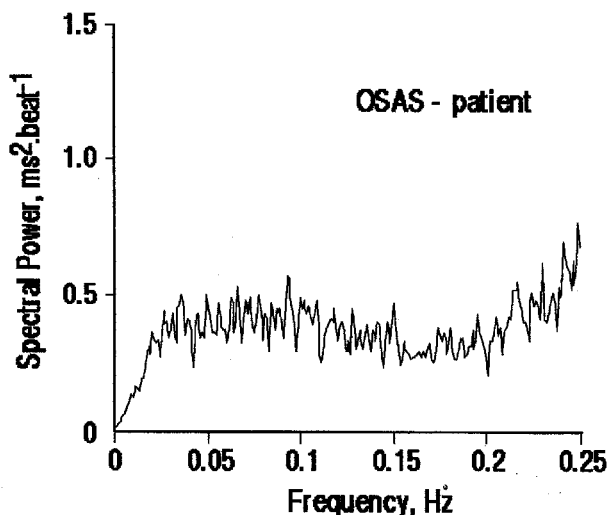
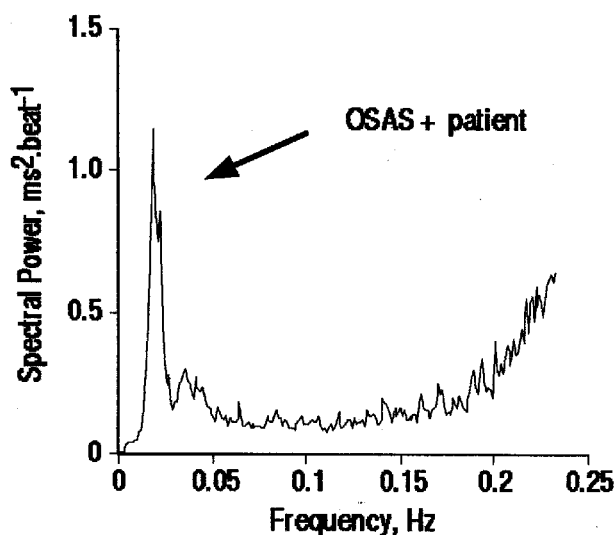
Repeated episodes of sleep apnea determined a significant increase in the VLF component of the interbeat interval increment of HRV, which was also visually identifiable. In the study population, such an increased VLF spectral power density was highly predictive of a sleep related breathing disorder. Its sensitivity was similar to the one of the time-domain variables previously reported<sup>6</sup> but



**Figure 3.** Evolution of the interbeat interval increment expressed as the ratio (%VLFI) of the VLFIpsd on the total spectral density, TIpsd, observed after a 3-month treatment for continuous positive airway pressure in a group of 18 patients. %VLFI = percent of very low frequency power spectral density on the total power spectral density; VLFIpsd = absolute value of the power spectral density of the very low frequency band; TIpsd = total power spectral density.

with the advantage of being easier to analyze and to use. Its power as an independent predictor of that disease, makes of it a potential ambulatory screening test for patients with clinically suspected OSAS on a widespread basis.<sup>12</sup>

The approach in the current study was to use



**Figure 2.** Power spectral analysis of the interbeat interval increment in obstructive sleep apnea syndrome OSAS+ (left) and OSAS- (right) patients. OSAS determines the appearance of a clear visually identifiable peak in the very low frequency band in 51 of the 54 OSAS patients.

the opportunity of a physiological signal directly reflecting the abnormal respiration pattern (i.e. the swing in heart rate that occurs with each apnea or hypopnea event). As a matter of fact, Guilleminault et al.<sup>5</sup> already described such heart rate oscillations and their quantitative relationship with the apnea or hypopnea severity. Le Heuzey et al.<sup>14</sup> described enlarged HRVs in OSAS patients. Both studies suggest the use of cardiac autonomous nervous system response to sleep disorders to diagnose OSAS, although without using a standard HRV approach. Recent data on time-domain measurement published by the authors<sup>6</sup> clearly demonstrated the performance of time-domain HRV variables in OSAS screening. Nevertheless, after further analysis, it was found that repetitive low frequency oscillations could better be expressed using spectral analysis of the interbeat interval increment.

More specifically, Shiomi et al.<sup>7</sup> had already observed a decrease in the VLF component of HRV after treatment of OSAS patients by prosthetic mandibular advancement. However, standard HRV frequency-domain analysis did not appear appropriate to properly quantify variations in VLF oscillations. By contrast, the present results showed that frequency analysis of the interbeat interval increment allowed a precise identification and quantification of VLF components. Furthermore, the highly discriminant power of the new variables, %VLF<sub>I</sub>, was not dependant from an operator selection of day and night periods, unlike the  $\Delta[D/N]$  SDNN index and  $\Delta[D/N]$  r-MSSD.<sup>6</sup> In addition, %VLF<sub>I</sub>, automatically summarized by a simple number, was the most powerful predictor of OSAS as shown by an adjusted OR of 8.4. The accuracy of PS3I variables in OSAS detection is further reinforced by the linear relationship between %VLF<sub>I</sub> and the AHI. Although weak, this correlation is statistically significant and reinforces confidence in the diagnosis of OSAS since, the lower the %VLF<sub>I</sub>, the lower the severity of the sleep related breathing disorder. Interestingly enough, the relationship between the AHI and %VLF<sub>I</sub> opens the possibility to use this parameter as a simple indicator of treatment efficacy, that could reduce the overload in sleep laboratories and the financial burden of the disease.

The observed enhanced HRV should not be confused with an isolated central drive in parasympathetic activity.<sup>16</sup> Rather, it reflects the struggle against upper airway occlusion, associated first with a strong increase in the parasympathetic arm of the autonomous nervous system, followed by an abrupt sympathetic activation due to the consecutive hypoxia;<sup>5,15</sup> this sequence dramatically enhances RR variability. In fact, the repeatability of the abnormal and typical cycle

length probably reflects loop response of the cardiopulmonary chemo- and baroreceptors. These responses could be compared with the primary slow oscillations in heart rate generated by the central nervous system during Cheyne-Stokes or periodic breathing patterns.<sup>8</sup>

Altered respiratory patterns are not restricted to patients with OSAS, but also occur frequently in mild to severe chronic heart failure.<sup>17</sup> Increased spectral power in the VLF band has been found to be a marker for poor prognosis after myocardial infarction as well.<sup>16</sup> The results are similar to those observed in short-term recordings obtained in chronic heart failure patients with Cheyne-Stokes respiration.<sup>18</sup> One should be aware that, in such patients, HRV can be artificially enhanced by associated periodic breathing disorders, thus masking the pejorative prognostic information associated to the lowering of VLF oscillations.

Patients with autonomic disorders were excluded to limit false-negative results. However, complete polysomnography and continuous nocturnal oxygen saturation monitoring, also carry some limitations: transducer position, failure, and displacement; artefacts due to movements; and alteration of the sleep characteristics because technical environment. Similarly, even though arterial oxyhemoglobin saturation appears to be the only simple reference variable, it could be misleading by being unable to identify nonapneic nocturnal hypoventilation, and underestimate the severity of sleep related breathing disorders. Stradling et al.,<sup>19</sup> underlined that the autonomic arousals related to OSAS were better quantified using blood pressure variability.<sup>20,21</sup> They described classical polysomnography as a flattened criterion standard because measuring apneas, hypopneas, or hypoxemic events was only logging some of the respiratory abnormalities.<sup>20,21</sup> If autonomous associated microarousals should even be better than HRV analysis in establishing the diagnosis and the severity of respiratory abnormalities remains to be determined.

## Conclusion

Frequency-domain analysis of HRV using spectral power of the interbeat interval increment could represent an efficient tool for the screening of OSAS. Its added ease of use and of interpretation is of interest, considering the high prevalence of sleep related breathing disorders in a general middle-aged population. Furthermore, it could represent an interesting tool for monitoring treatment efficacy on an ambulatory basis.

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