Sultan Qaboos University Medical Journal
March 2008, Volume 8, Issue 1, p. 21-25
Sultan Qaboos University©
Submitted - 23rd January 2008
Accepted - 2nd February 2008

Screening of Patients with Snoring and Obstructive Sleep Apnoea using Heart Rate Variability Indices

Omar Al Rawas,[1] Bazdawi Al-Riyami,[1] Christopher Goddard,[2] *Mohammed O Hassan[3]

تحري المرضى المصابين بالشخير وانْقِطاعُ النَفَس الانْسِدادِيُّ النَّومِيّ باستخدام مَناسِب تغير نبضات القلب

عمر الرواس، بزدوي الريامي، كرستوفر قودارد محمد عثمان حسن

الخلاصة: الشخير وانْقِطاعُ النَفَس الانْسِدادِيُّ النَّومِيّ هما من الاضطرابات واسعة الانتشار. الشخير مصحوبا بفرط النعاس أثناء النهار هو العرض الأكثر انتشارا لانْقِطاعُ النَفَس الانْسِدادِيُّ النَّومِيّ . يرتبط تغير سرعة نبضات القلب بشدة انْقِطاعُ النَفَس الانْسِدادِيُّ النَّومِيّ . استخدمت حديثا تقنية تَخْطيطُ سُرْعَة نبضات القلب لمدة 24 ساعة للتحري عن المرضى المصابين بانْقِطاعُ النَفَس الانْسِدادِيُّ النَّومِيّ . من الممكن بشكل معول عليه دراسة مكونات الجهاز العصبي اللا إرادي التي تسبب تغيرا في سرعة نبضات القلب بالتحليل الطيفي باستعمال برنامج فورير التحويلي. **الطريقة :** شملت الدراسة 23 شخصا متقاربون في الوزن والعمر . 13 منهم مصابون بانْقِطاعُ النَفَس الانْسِدادِيُّ النَّومِيّ و 10 أشخاص يعانون من الشخير تم تشخيصهم في مختبر النوم بمستشفى جامعة السلطان قابوس . تم تسجيل تخطيط القلب لمدة 24 ساعة في المنزل ابتداءا من الساعة العاشرة ليلا . وقمنا بالتحليل الطيفي لنبضات القلب المستخرجة من مختبر النوم ومن تخطيط القلب بالمنزل باستعمال برنامج فورير التحويلي السريع. **النتائج:** تبين في تخطيط القلب أن الفترات الزمنية لنبضات القلب عند مرضى انْقِطاعُ النَفَس الانْسِدادِيُّ النَّومِيّ أقصر بكثير من مرضى الشخير لوحده ($p<0.01$) . التَّرَدُّدُ المُنْخَفِض لكثافة الطيف لسرعة نبضات القلب أعلى بشكل معتد إحصائيا عند المصابين بانقطاع النفس الانسدادي النومي عنه في المصابين بالشخير ($p< 0.0001$) . كانت نتائج طاقة كثافة الطيف لحزم الذبذبة العالية متساوية في المجموعتين . استطاع جهاز تخطيط القلب خلال الليل التعرف على 13 مريضا مصابا بالشخير وانقطاع النفس الانسدادي. **الخلاصة:** يمكن الاستفادة من استخدام طاقة الطيف للحزمة الترددية المنخفضة باستعمال برنامج فورير التحويلي لقياس نبضات القلب أثناء النوم . لمعرفة الأشخاص الذين يعانون من الشخير المصحوب بانقطاع النفس الانسدادي النومي .

مفتاح الكلمات: انقطاع النفس الانسدادي النومي . تغير سرعة نبضات القلب.

ABSTRACT ***Objective:*** Snoring and obstructive sleep apnea (OSA) are common disorders. Snoring associated with excessive daytime sleepiness is the most prevalent symptoms of OSA. Heart rate variability (HRV) is altered in patients with OSA and the degree of alteration may be linked to the severity of OSA. Alterations in HRV in 24 hour tachograms have recently been used in screening OSA patients. Autonomic components causing HRV can be reliably studied using spectral analysis techniques involving fast Fourier transformation (FFT). ***Methods:*** Twenty-three subjects, 13 with severe OSA and 10 controls matched for age and body mass index, were selected from patients who had undergone polysomnography (PSG) for snoring at Sultan Qaboos University Hospital, Oman. A 24- hour electrocardiogram (ECG) Holter recording was done at home, starting at 10am. Spectral analysis of ECG from sleep Holter and PSG recordings was analysed using fast Fourier transformation (FFT). ***Results:*** The ECG RR intervals of snorers with OSA were significantly shorter than in snorers without OSA ($p<0.01$). The low frequency (LF) spectral densities of HRV from polysomnography and Holter were significantly higher in OSA patients than in snorers, ($p< 0.0001$). The power spectral density of the high frequency bands was similar in the two groups. The overnight ECG Holter accurately identified all 13 snorers with severe OSA. ***Conclusion:*** The spectral power of the LF band obtained using FFT of sleep HRV from Holter tachograms may be a useful and cost effective test in identifying snorers with severe OSA.

Key words: Obstructive Sleep Apnea; Heart Rate Variability.

Departments of [1]Medicine, [2]Medical Physics Unit, [3]Physiology, College of Medicine & Health Sciences, Sultan Qaboos University, Muscat, Sultanate of Oman

**To whom correspondence should be addressed. Email: mhassan@squ.edu.om*

Advances in Knowledge

- *Learn how to utilize heart rate variability for advanced diagnostics*
- *Perform signal processing on heart rate intervals by using spectral analysis software which is available free in the web*
- *Develop awareness that sleep apnea can affect heart rate variability.*
- *Sleep apnea can also present with snoring.*

Applications to Patient Care.

- *Short listing of patients for full sleep studies*
- *Holter ECG can be performed at home*
- *Polysomnography is essential for the definitive diagnosis of sleep apnea*

Snoring and obstructive sleep apnea (OSA) are common disorders that affect both men and women. Snoring and excessive daytime sleepiness are the most prevalent symptoms of sleep apnea, which in turn is associated with cardiovascular and cerebrovascular complications. [1, 2, 3] The recognition of OSA and snoring as a health problem has grown worldwide and the number of subjects who seek medical help for problems with snoring and with concern about OSA and daytime sleepiness is increasing. In the general population, the greatest challenge for primary care providers lies in determining which patients with these symptoms warrant further evaluation, as most patients with OSA snore, but most snorers do not have OSA.[4] In developed countries, the cost of investigating these symptoms has increased considerably during the last decade as the only reliable method for the diagnosis of OSA until now has been overnight polysomnography (PSG),[5] which is a cumbersome, time consuming and expensive procedure requiring specially trained polysomnographers, despite evolving newer software which allows rapid analysis. This, together with long waiting lists of patients, has lead to the search for faster and less expensive diagnosis. Heart rate variability, or short-term changes in the RR intervals, of a continuously recorded electrocardiogram (tachogram), is the consequence of various influences of the autonomic nervous system on heart rate.[7, 8] Heart rate variability (HRV) is altered in patients with OSA and this alteration is evident even in the absence of hypertension, heart failure, or other diseases.[9, 10] The degree of alteration in HRV variability may be linked to the severity of OSA.[11] Alterations in HRV in 24 hour tachograms have recently been used in screening patients with OSA.[12]

Autonomic components causing HRV can be reliably studied using spectral analysis techniques. After Akselrod[13] introduced power spectral analysis (PSA) of short-term heart rate fluctuations as a non-invasive quantitative probe of beat-to-beat cardiovascular autonomic control, the study of HRV has become a rapidly expanding field in clinical research[14, 15] The analysis gives selective information on sympathetic and parasympathetic functions and the reproducibility of HRV findings in OSA have been confirmed by several studies.[16, 17]

Power spectral density (PSD) provides the basic information of how power, or variance, is distributed as a function of frequency. Fast Fourier transformation (FFT) is the most widely used nonparametric method for the calculation of PSD.[16, 17] The advantages of FFT are the simplicity of the algorithm used, the high processing speed, and no data pre-processing is required. In addition, FFT software is readily available in most cardiovascular analyses packages and end-users are not required to have advanced computer knowledge.

Three main spectral components can be distinguished in a spectrum calculated from short (2-5 minutes) and long segment (24 hours) of electrocardiographic recordings: very low frequency (VLF, 0.0008-0.04 Hz), low frequency (LF, 0.04-0.14 Hz) and high frequency (HF, 0.15-0.45 Hz). The distribution of the power and the central frequency of LF and HF are not fixed, but may vary in relation to changes in autonomic modulations of heart rate. In normal humans, short-term RR interval variability occurs predominantly at LF which may be due to baroreceptor, sympathetic and parasympathetic modulations and HF which is synchronous with the respiratory frequency.[16] The physiological explanation of the VLF component is much less defined, and the existence of a specific physiological

Table 1: ***Characteristics of the study subjects***

	OSA N:13 (8M, 5F)	Snorers N:10 (7M, 3F)
Age (years)	37.3 (4.2)	38.1 (3.9)
BMI (kg/m^2)	34.6 (5.2)	33.1 (6.0)
AHI/ hour	35.3 (4.5)	4.0 (1.2)
R-R (msec)	792 (45)	811 (56)

Values expressed as mean (SD); AHI: Apnea hypopnea index

process attributable to these heart period changes has been questioned. However, using FFT and sub-band decomposition of overnight HRV in patients with OSA, we and other workers have shown that the VLF band is augmented in snorers with OSA as compared to snorers without OSA.[18, 19]

The aim of this study was to evaluate the use of FFT for the spectral analysis of HRV as a method for screening patients presenting with snoring as the only symptom, in an attempt to identify those who might have OSA and short list them for polysomnography.

The accuracy of the identification algorithm depends mainly on the accuracy of the electrocardiogram QRS waveform detection (R peak detector), that is used to obtain the R-R intervals (RRI) in milliseconds from the raw electrocardiogram (ECG) data. Data are the normal-to-normal (NN) intervals obtained directly from the QRS detector without any smoothing and filtering steps; therefore, it could contain false intervals, missed and/or ectopic beats. The QRS detection is accomplished by Open Source ECG Analysis Software, an arrhythmia detection software, available on the PhysioNet website.[16] The basis of this simple approach to exclude false RRI by binding RRI within lower and upper limits, is typically 400-2000 msec so that all RR intervals beyond these limits are excluded.

METHODS

Overnight PSG was performed using a digital polygraph (Heritage Model 15 Astro-Med Inc, MA, USA). The PSG recording included an electroencephalogram (EEG), ocular and leg electromyography, heart rate tachogram, oxygen saturation, snoring and body position.

Sleep stages and apnea/hypopnea index (AHI) identification were verified manually by a qualified polysomnographer who used 30-second epochs according to standard criteria. Scoring of all computerised studies was done manually in a manner identical to that used for paper studies.[20] Subjects with OSA episodes with an AHI > 30/ hour were considered as having severe OSA while those with an AHI of < 5/ hour were considered as normal.

The study subjects were snorers with no other symptoms. They were selected from the pool of all polysomnography studies performed in our laboratory between the year 1998- 2003 (total 187 studies). The selection of subject was based on the following:

A. OSA group
   a. Severe OSA (AHI>30/hour)
   b. No OSA treatment
   c. No evidence of hypertension, heart failures, diabetes or hypothyroidism

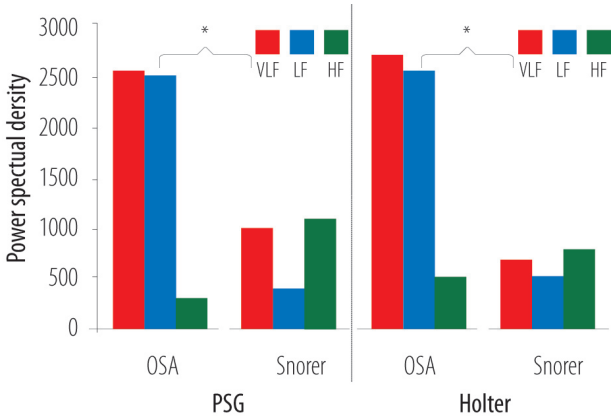
B. Control group (snorers without OSA)
   a. No OSA (AHI <5/hour)
   b. No evidence of hypertension, heart failure, diabetes or hypothyroidism

A total of twenty-three subjects were included for this study (13 with severe OSA and 10 age and body mass index matched controls). Subject characteristics are shown in Table 1.

All study subjects had a 24 hour ECG recording at home using an ECG analyser with an analogue to digital converter (Pathfinder 4, RR tools, Reynolds). ECG data from the time the patient recorded going to bed until the time of awakening were selected for the analysis.

Thirty segments of 5 minutes each of Lead II of the ECG from PSG and from Holter recordings were selected by an ECG technologist who was blind to the study. Ectopic beats, movement artifacts and RR intervals +100 msec were manually removed. Another set of data was analysed without visual editing. ECG data was then analysed using the Matlab software (Mathworks, USA) with a sampling frequency of 200 msec and a validated QRS detector identification algorithm with an automated rejection of ectopic beats and missing data artifacts.[21, 22]

Student's one-tailed t-test was used to compare the PSD of the different frequencies while the 95% confidence interval was used to compare the LF bands of PSG and Holter records in the two groups.



*P= 0.0001 for difference between the LF band of OSA and snorer subjects.

Figure 1: ***Very low (VLF), low (LF) and high (HF) frequency bands from polysomnography and Holter ECGs in snorers with and without obstructive sleep apnea (OSA)***

RESULTS

Figure 1 shows the power spectral densities in absolute values obtained from RR values of tachograms recorded during sleep using PSG and Holter recordings in snorers with and without OSA. The RR intervals of snorers with OSA are significantly shorter than in snorers without OSA ($p<0.01$). There was no difference in the VLF, LF or HF spectral densities in the manually edited and unedited ECGs. The LF frequency spectral densities of HRV from PSG and Holter recordings were significantly higher in OSA patients than in snorers, ($p<$ 0.0001). The PSD of the HF bands were similar in the two groups. The overnight ECG Holter accurately identified all 13 snorers with severe OSA. The VLF components, however, had very high spectral densities in both methods, and showed a very wide scatter and overlap with the LF bands in most patients. Nonetheless, the VLF from PSG and Holter recordings accurately identified the same 13 snorers with OSA.

DISCUSSION

The main findings of this study are that the LF frequency spectral densities of HRV from PSG and Holter recordings were significantly higher in OSA patients than in snorers. Second, patients with severe OSA, who are likely to have or develop complications can be detected early for full PSG. Third, complications of OSA such as heart failure, hypertension and obesity have been shown to contribute to the PSD of the LF band in OSA[9, 23] and therefore these complications can only increase the sensitivity of the test. Using this method, shorter periods of Holter recordings can be used in patients hospitalized for continuous positive airway pressure (CPAP) titration or other reasons and several patients can be studied per night. The main strengths of this method are that it is simple, cost effective, non-invasive and can be performed at home; in addition, manual editing is not required as the software is capable of removing movement artifacts, ectopic beats and extremes of tachycardia and bradycardia, which are characteristic of OSA episodes and are known to interfere with the spectral analysis.

Although the ECGs were recorded using two different methods and under different conditions in the laboratory (PSG) and at home (Holter), they clearly demonstrate that the method and the environment of recording do not influence the outcome as both contain ECGs recorded during all sleep stages. The results also show that the LF using FFT and the VLF using sub-band decomposition as shown in our previous study[18] were accurate in identifying snorers with OSA. FFT, as compared to other algorithms, is commercially available in most HRV software and does not require advanced computer knowledge as does sub-band decomposition. Although the VLF band was found to be augmented in OSA in this and another study, [18, 19] we found it had a very wide scatter as compared to the LF band. Apart from ranking patients for PSG, this method may be useful in centres where there are no PSG facilities and in patients with clearly reported and observed symptoms, or when some patients refuse this cumbersome procedure. In spite of this valuable scientific observation, this method will not replace the full PSG of the diagnosis of OSA. The study of HRV using Holter ECG after CPAP treatment in OSA patients warrants further investigation.

The main limitation of this test is that it has been limited only to small number of severe cases of OSA and controls and this was due to the stringent criteria we used for the selection of subjects. The power spectral densities in this study were not converted to normalised units so as to show the importance of the VLF component; this may be important in less severe cases of OSA, but it requires lengthy data processing. Further studies, using simple techniques on less severe cases, will be required.

CONCLUSION

The LF band obtained using FFT for spectral analysis of HRV obtained from overnight Holter tachograms may

be a useful and cost effective test in identifying snorers with severe OSA.

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