Heart rate variability analysis of single-channel electrocardiogram can help to differentiate high-risk patients with obstructive sleep apnea syndrome - a study on diagnostic accuracy

Tek kanal elektrokardiyografide kalp hızı değişkenliği analizi yüksek riskli obstrüktif uyku apne sendromlu hastaları tanımlamada yardımcı olabilir- Bir doğruluk değeri çalışması

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ABSTRACT

Objective: To evaluate the usefulness of heart rate variability analysis (HRV) analysis from the long duration electrocardiogram (ECG) recordings as a screening test for the diagnosis of moderate-to-severe obstructive sleep apnea syndrome (OSAS).
Methods: Recordings from 87 patients who were admitted to sleep laboratory for polysomnographic study (PSG) were evaluated. Finally 30 cases with apnea-hypopnea index (AHI)≥15/hour included in patient's group (male/female: 22/8; mean age: 49±10 years) and 21 cases with AHI<5 were included in control group (male/female: 10/11; mean age: 48±11 years). From the ECG recordings taken as a part of PSG, time -domain and frequency -domain HRV parameters were evaluated and their accuracy in the diagnosis of OSAS was investigated using ROC analysis.
Results: Statistically significant differences were found in HRV variables in time- domain parameters such as SDNN, SDNN index; frequency-domain parameters VLF, LF, nuLF, nuHF, LF/HF and geometric parameter HRV triangular index values in between groups. Cut- off value of 16 for the HRV triangular index was found to be 50% sensitive and 85.7% specific with a positive likelihood ratio (LR) of 3.50% and negative LR of 0.58% When the total power was higher than 9.611, then the analysis sensitivity was 53.3%, specificity was 95.6%, positive LR was 11.2% and negative LR was 0.49% When the SDNN was higher than 83 then its sensitivity was 80%, specificity was 76.2%, positive LR was 3.36% and negative LR was 0.26% For the cut off value of 62 calculated for SDNN index, sensitivity was 73.3%, specificity was 85.7%, positive LR was 5.13% and negative LR was 0.31%, for the cut off value of 9.12 was calculated for VLF, sensitivity was 90.4% specificity was 50% positive LR was 1.81% and negative LR was 0.19%.
Conclusion: Heart rate variability analysis done over routine single channel ECG data gathered through routine Holter applications may be helpful in distinguishing moderate-to-severe OSAS patients from mild OSAS patients and non-OSAS control subjects.
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Key words: Diagnosis, electrocardiography, heart rate, polysomnography, sleep apnea, sensitivity, specificity

ÖZET

Amaç: Çalışmanın amacı uzun süreli tek kanal elektrokardiyogram (EKG) kaydı üzerinden yapılan kalp atım hızı değişkenliği (HRV) analizinin orta ve ağır tıkayıcı uyku apne hipopne sendromu (TUA) hastalarının taranmasına katkısını araştırmaktır.
Yöntemler: Hastanemizin uyku laboratuvarına başvurarak polisomnografi yapılan 87 hastanın kayıtları değerlendirildi. Değerlendirme sonucunda apne-hipopne indeksi (AHI)≥15/saatin üzerinde bulunan 30 kişi olgu grubuna dahil edildi (erkek/kadın: 22/8;yaş ortalaması: 49±10 yıl) AHI <5 olan 21 kişi de kontrol grubuna dahil edildi (erkek/kadın:10/11; yaş ortalaması: 48±11 yıl). Polisomnografi esnasında kaydedilen EKG kanalı verileri üzerinden zaman-domain ve frekans-domain HRV ölçütleri hesaplanarak bu ölçütlerin TUA olasılığı öngörüsüne katkısı ROC analizi ile değerlendirildi.
Bulgular: Zaman- domain HRV ölçütlerinden SDNN ve SDNN indeksi, frekans-domain ölçütlerden VLF, LF, nuLF, nuHF, LF/HF, geometrik ölçütlerden de HRV trianguler indekste gruplar arasında anlamlı fark saptandı. Daha sonra bu anlamlı ilişkinin katkısını değerlendirmek için yapılan ROC analizinde HRV trianguler indeks için kestirim değeri 16 olarak alındığında %50 duyarlılık ve %85.7 özgüllük, %3.5 pozitif olasılık oranı (LR) ve %0.58

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negatif LR değeri bulundu. Total güç 9.611 üzerinde hesaplandığında duyarlılık ise %53.3, özgüllük %95.6, pozitif LR %11.2 ve negatif LR %0.49'du. SDNN değeri 83'ün üzerinde olduğunda ise duyarlılık %80, spesifivite %76.2, pozitif LR %3.36 ve negatif LR %0.26 idi. SDNN indeksi için sınır değeri 62 olarak hesaplandığında duyarlılık ise %73.3, özgüllük %85.7, pozitif LR %5.13 ve negatif LR %0.31 bulundu, VLF için kestirim değeri 9.12 olarak kabul edildiğinde duyarlılık %90.4 özgüllük %50 pozitif LR 1.81 negatif LR 0.19 olarak hesaplandı. Bu değerlerin yüksek pozitif LR ve düşük negatif LR ile OSAS öngörüsünde kullanılışlı olabileceği düşünüldü.

Sonuç: Rutin Holter uygulamaları sırasında elde edilen tek kanal EKG verileri üzerinde yapılan HRV analizi ciddi risk arz eden orta ağır şiddette TUA hastalarının ayırt edilerek öncelikle uyku laboratuvarına refere edilmeleri burada da öncelikle değerlendirilmeleri konusunda yol gösterici olabilir.
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Anahtar kelimeler: Tanı, elektrokardiyografi, kalp hızı, polisomnografi, tıkayıcı uyku apnesi, duyarlılık, özgüllük

Introduction

Obstructive sleep apnea hypopnea syndrome (OSAS) is one of the major health problems due to its high incidence (2% to 4% of general population) and its cardiovascular consequences. One third of essential hypertension patients have OSAS and 1/3 of OSAS patients die due to cardiovascular events such as acute myocardial infarction, cerebrovascular ischemia, coronary heart disease and heart failure (1-3). Polysomnography (PSG) is the gold standard for diagnosis. However, this is a costly and time-consuming examination. Long backlog lists have been increasingly retarding diagnostic studies and this is probably inflating the prediagnostic health costs of OSAS patients. Unfortunately, there is not a screening test with proven validity supporting OSAS pre-diagnosis to enable patients with high risk to be primarily evaluated in the sleep laboratory. The early detection and prevention of cardiovascular events, which is the most common cause of mortality and morbidity, is important to not only decrease maintenance costs but also for the patient benefit.

Rhythm Holter monitoring is a method often used in the cardiology applications to establish the diagnosis for rhythm disturbances and ischemia. Advances in technology allow analysis of the simple electrocardiogram (ECG) recordings with different algorithms. Complex spectral analysis like heart rate variability (HRV) has become quite easy owing to these technological developments. HRV can be measured by different methods. Time- domain, frequency -domain and geometrical methods are the most common ones. In the time- domain methods heart rate taken at any time or distance between consequent normal complexes are determined. In the frequency-domain analysis recordings are evaluated in 2 to 5 minutes or 24 hours' time intervals and three main spectral component is calculated. These components are very low frequency band (VLF), low frequency band (LF) and high frequency band (LF). From these VLF is the least defined variable physiologically, and thought to be related to long-term control mechanisms (like as heat and humoral factors). Some investigators accepted LF to be an indicator for sympathetic activity. In direct contradiction, HF is determined by vagal effect and respiratory sinus arrhythmia. LF/HF ratio derived from these values though to show sympathomimetic balance. In the geometrical approach, N-N distance transformed to a geometric model. HRV could be effected from cardiac diseases like as acute myocardial infarction but also could be effected from paralysis, multiple sclerosis, diabetes mellitus, alcoholism, cancer, glaucoma and pharmacological treatment targeting autonomic nervous system (4). Therefore, information on sympathovagal balance as well as arrhythmia and ischemia can be obtained from the standard Holter records. The data pointing to the changes revealing in the sympathoadrenergic balance can be reached by this way. This additional information obtained from the routine Holter monitoring suggesting the presence of OSAS, can enable patients to be guided and their PSGs to be primarily held.

Our study was aimed to investigate the contribution of the information obtained from ECG recording with HRV analysis to the pre-diagnosis of OSAS. We hypothesized that HRV analysis have the potential for distinguishing moderate-to-severe OSAS patients who are at increased risk for cardiovascular events.

Methods

Study design

The study was planned as retrospective cohort study on diagnostic accuracy.

Study population

Total 87 patients who admitted to the sleep laboratory of our hospital with the complaints of snoring and PSG were performed between October 2006 and March 2008 was examined. None of the patients had been referred to a sleep laboratory previously. The patients who known to have cardiovascular, renal or hepatic diseases, who had abnormalities in thyroid functions, diabetic and hypertensive patients those with a history of drug use that interact with the autonomic nervous system functions were excluded from the protocol.

Patients without exclusion criteria, with symptoms of snoring, witnessed apnea or daily sleepiness and have indication for PSG after the primary evaluation were included as the order of admission. According to these criteria, records of 66 patients who included to the protocol were analyzed. At this stage, HRV analysis was performed in 51 patients, excluding 15 cases that had not an ECG segment defined with technical competence of 5 minutes convenient for HRV analysis. On PSG, 30 patients with apnea/hypopnea index (AHI) ≥15 were assigned to the study

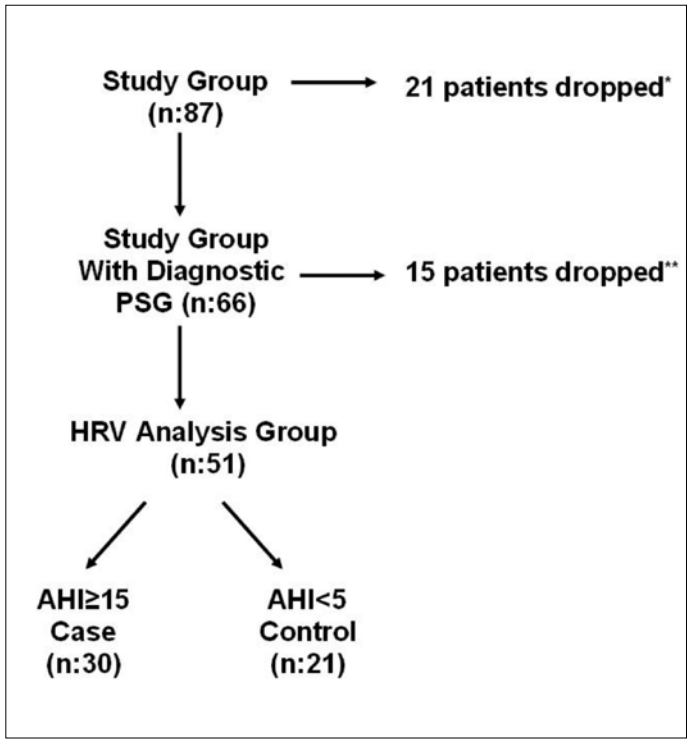

Figure 1. Study flow chart
*21 patients were dropped from the study due to cardiovascular disease history and use of the drugs affecting the autonomic nervous system
**15 patients were dropped from the study, because technically appropriate segment was not found for HRV analysis
AHI - apnea/hypopnea index, HRV - heart rate variability, PSG - ploysomnography

group and 21 patients with AHI <5 assigned to the control group (Fig. 1).

Clinical and laboratory examinations records

Medical history regarding sleep habits, cardiovascular disease presence and alcohol or drug abuse was taken from all patients. Respiratory function test, postero-anterior chest X-ray and electrocardiography were performed at all patients after the physical examination. Complete blood count, arterial blood gas, fasting glucose, liver function test, urea, creatinine levels and thyroid functions were studied.

Polysomnography

Overnight PSG was performed using Embla A-10 (Embla; Medcare Flaga; Reykjavik, Iceland) data acquisition and analysis system in the attended setting of the sleep laboratory in baseline conditions. Physiological signals monitored included electroencephalography (C4-A1, C3-A2, O2-A1, O1-A2); electrooculography; sub mental electromyography; ribcage and abdominal effort measured by respiratory inductive plethysmography (RIP) (XactTrace Medcare Flaga; Reykjavik, Iceland); body position measured by calibrated sensor; snoring sound measured with piezoelectric sensor, oro-nasal flow measured with a nasal pressure cannula (Medcare Flaga; Reykjavik, Iceland), SpO2 (8000J, Nonin Medical, Plymouth, MN, USA) with averaging time set at 3 seconds; ECG (lead II) was sampled at 512 Hz. Sleep stages and arousals were scored using Somnologica Studio software package (Medcare Flaga; Reykjavik, Iceland) according to standard criteria by a skilled pulmonary physician (LK). Respiratory events were scored as follows: apnea was defined as a cessation of airflow ≥10 seconds, classified as obstructive in the presence of continued movement in the RIP and as central in the absence of movement in the RIP. Hypopneas were defined as a ≥50% reduction in oro-nasal flow amplitude ≥10 seconds, accompanied by ≥3% desaturation and/or arousal. Hypopneas were classified as obstructive if there was evidence of upper airway resistance such as snoring, paradoxical motion in the respiratory bands, or inspiratory flow limitation on nasal pressure signal.

HRV analysis

Lead 2 ECG recordings from the overnight PSG study were used for HRV analyzes. Overnight ECG recording was analyzed first, using Somnologica Studio software package (Medcare Flaga; Reykjavik, Iceland) in accordance with the guidelines (4) issued by The European Society of Cardiology and The North American Society of Pacing and Electrophysiology in 1996. Standard deviation of all NN intervals (SDNN), SDNN index, square root of the mean of the sum of the squares of differences between adjacent NN intervals (RMSSD) and standard deviation of the averages of NN intervals in all 5-min segments of the entire recording (SDANN) from the time -domain criteria were calculated. Frequency-domain criteria were recorded calculating as total power (TP), average VLF, average LF, average high HF and average LF/HF ratio. Normalized values of HF (nuHF) and LF (nuLF) bands were re-calculated using the formulas of nuLF=LF/HF+LF and nuHF=HF/HF+LF. HRV triangular index (Tr.Ind) was defined as the total number of all NN intervals divided by the height of the histogram of all NN intervals measured on a discrete scale with bins of 7.8125 ms (1/128 s) (4).

Statistical analysis

Data of 51 patients were statistically analyzed by MedCalc 9.6 pocket program MedCalc for Windows 7.0 (MedCalc Software, Mariakerke, Belgium). Age, body mass index (BMI), and AHI data were evaluated by Student's t- test and sex distribution was evaluated by Chi-square test. HRV variables that were not normally distributed (TP, LF, and HF) were log transformed prior to statistical analysis and for data presentation (5). Transformed data obtained from both of the groups were compared with unpaired samples Student's t-test. Further ROC analysis was applied for HRV variables presenting significance and the relationship was evaluated in terms of the contribution to the diagnostic decision. Area under curve (AUC), 95% confidence intervals (95% CI) and sensitivity, specificity, positive, negative likelihood rates (LR) were assessed. A p value lower than 0.05 was accepted as statistically significant.

Results

Clinical and HRV characteristics

Eight of the cases were females and 22 were males while 11 of the controls were females and 10 were males. Mean age of our study group was 49±10 years and of controls was 48±11 years. BMI of the study group was 29.4±4.7 kg/m^2 and of the controls was 27.4±1.4 kg/m^2. There was no statistically significant difference between the groups in terms of gender (p=0.1152), age (p=0.847) and BMI (p=0.059). The difference between the study and control groups was significant in HRV variables of SDNN, SDNNindex, LF, nuLF, LF/HF, HRV triangular index and VLF (p<0.05 for all). A significant difference was not found in terms of RMSSD, SDANN, HF and VLF (Table 1).

Diagnostic accuracy of HRV

In order to investigate the contribution of the difference defined between the case and control groups to the diagnostic decision, cut off values were calculated with ROC analysis for each significant criterion.

For the case of LF/HF >2.51, AUC was found as 0.75 (95% CI: 0.61-0.86), sensitivity as 73.3%, specificity as 71.4%, positive likelihood rate (LR) as 2.57 and negative likelihood rate as 0.37 for OSAS diagnosis. For HRV triangular index, AUC was found as 0.69 (95% CI: 0.55-0.81), sensitivity as 50%, specificity as 85.7%, positive LR as 3.50 and negative LR as 0.58. For nuHF <0.261 AUC was found as 0.75 (95% CI: 0.55-0.81), sensitivity as 73.3%, specificity as 71.4%, positive LR as 2.57% and negative LR as 0.37% for OSAS diagnosis. For nuLF >0.676 AUC was found as 0.74 (95% CI: 0.60-0.85), sensitivity as 76.7%, specificity as 66.7%, positive LR as 2.30% and negative LR as 0.35%. When the total power was above 9.611, AUC of the analysis was 0.76 (95% CI: 0.62-0.87), sensitivity 53.3%, specificity 95.6%, positive LR 11.2% and negative LR 0.49%. When SDNN elevated above 83, AUC was found as 0.74 (95% CI: 0.59-0.85) sensitivity as 80%, specificity as 76.2%, positive LR as 3.36% and negative LR as 0.26%. While cut-off value calculated for SDNN index was 62, AUC was found as 0.77 (95% CI: 0.63-0.87) sensitivity as 73.3%, specificity as 85.7%, positive LR as 5.13% and negative LR as 0.31%, for the cut off value of 9.12 was calculated for VLF, sensitivity was 90.4% specificity was 50% positive LR was 1.81% and negative LR was 0.19%.

Of these values, total power, SDNN index, Tr.Ind. and SDNN values respectively were remarkable with high positive LR and low negative LR values (Table 2).

Table 1. Demographic and HRV parameters of case and control groups

Variables	Case (n=30)	Control (n=21)	*p
Age, years	49±10	48±11	>0.05
Gender, f/m ratio	8/22	11/10	>0.05
BMI, kg/m^2	27.4±1.41	29.4±4.7	>0.05
AHI	56.7±26.1	2.8±0.3	<0.01
SDNN, ms	98±32	75±25	<0.01
SDNNindex, ms	76±30	52±25	<0.01
RMSSD, ms	57±45	39±34	>0.05
SDANN, ms	76±43	62±37	>0.05
TP, ms^2 (ln)	9.61±0.38	9.26±0.29	<0.01
VLF, ms^2 (ln)	9.08±0.08	8.80±0.33	<0.05
LF, ms^2 (ln)	9.08±0.48	8.8±0.33	<0.01
nuLF, ms^2 (n.u)	0.75±0.12	0.66±0.09	<0.01
HF, ms^2 (ln)	7±0.64	7.02±0.53	>0.05
nuHF, ms^2 (n.u)	0.22±0.11	0.31±0.09	<0.01
LF/HF, ms^2/ ms^2	4.79±3.63	2.46±1.33	<0.01
Tr. Ind	17±5	13±3	<0.01

Data are presented as mean±SD and numbers

*Unpaired Student's t and Chi-square tests

AHI - apnea/hypopnea index, BMI (kg/m^2)-body mass index, f - female, HF (ms^2)- power in high frequency range (0·15–0·4 Hz), HRV - heart rate variability, LF (ms^2)- power in low frequency range (0·04–0·15 Hz), LF/HF-ratio of LF (ms^2)/HF (ms^2), m- male, nuHF- HF power in normalized units (nuHF=HF/HF+LF), nuLF-LF power in normalized units (nuLF=LF/HF+LF), RMSSD (ms)- the square root of the mean of the sum of the squares of differences between adjacent NN intervals, SDANN (ms)-standard deviation of the averages of NN intervals in all 5 min segments of the entire recording, SDNN (ms)-standard deviation of all NN intervals, SDNN index (ms)- mean of the standard deviations of all NN intervals for all 5 min segments of the entire recording, this variant is possible counting all such NN intervals pairs or only pairs in which the first or the second interval is longer, TP - total power (ms^2), variance of all NN intervals, Tr.Ind- HRV triangular index is total number of all NN intervals divided by the height of the histogram of all NN intervals measured on a discrete scale with bins of 7.8125 ms (1/128 s), VLF (ms^2) -power in the very low frequency range 0.003-0.04 Hz

Discussion

This study is one of the few studies demonstrating guidance of HRV analysis performed on the long term ECG records to OSAS diagnosis and its contribution to the clinical decision. Results of our study showed that HRV data, especially SDNN index, triangular index and SDNN values respectively were remarkable with high positive LR and low negative LR values, could help differentiation of OSAS patients.

Sympathovagal balance presents variability as to sleep arousal cases and sleep stages. There are numerous methods enabling evaluation of sympathovagal balance using technological facilities. Pulse transit time (PTT), peripheral arterial tonometry (PAT) and HRV analysis are the most remarkable ones of these methods (6). Of these methods, PAT and PTT required using of dedicated devices. As it is known, PTT requires recording of both pulse oximetry and ECG channels at the same time. Many of the PSG configurations can be produced after recording of PTT channel. However, PTT is not a current transaction for screening at OSAS patients. On the other hand, although PAT has been subject to the reports as a screening test with its high compliance with PSG, a completely dedicated device and software are needed (7-10). The association between OSAS and

Table 2. Cut- off values of some HRV parameters with significant difference found between the groups and specificity, sensitivity, positive likelihood and negative likelihood rates of these values

HRV variables	Cut-off value	Sens. (95% C.I.)%	Spec. (95% C.I.)%	+LR%	-LR%
SDNN, ms	>83	80 (61.4-92.2)	76.2 (52.8-91.7)	3.36	0.26
LF/HF	>2.51	73.3 (54.1-87.7)	71.4 (47.8-88.6)	2.57	0.37
Tr. Ind	>16	50 (31.3-68.7)	85.7 (63.6-96.8)	3.50	0.58
nuHF, n.u	<0.26	73.3 (54.1-87.7)	71.4 (47.8-88.6)	2.57	0.37
nuLF, n.u	>0.67	76.7 (57.7-90)	66.7 (43-85.4)	2.3	0.35
Total power, ln	>9.61	53.3 (34.3-71.6)	95.2 (76.1-99.2)	11.20	0.49
VLF(ln)	<9.12	90.48 (69.5-98.5)	50 (31.3-68.7)	1.81	0.18
SDNN	>62	73.3 (54.1-87.7)	85.7 (63.6-96.8)	5.13	0.31

HRV - heart rate variability, LF/HF-ratio LF (ms^2)/HF(ms^2), +LR-positive likelihood ratio, -LR -negative likelihood ratio, nuHF-HF power in normalized units (nuHF=HF/HF+LF), nuLF- LF power in normalized units (nuLF=LF/HF+LF), SDNN (ms)-standard deviation of all NN intervals, SDNN index (ms)-mean of the standard deviations of all NN intervals for all 5 min segments of the entire recording, this variant is possible counting all such NN intervals pairs or only pairs in which the first or the second interval is longer, Sens -sensitivity, Spec-specificity, total power (ms^2) - variance of all NN intervals, Tr.Ind-HRV triangular index is total number of all NN intervals divided by the height of the histogram of all NN intervals measured on a discrete scale with bins of 7·8125 ms (1/128 s), VLF (ms^2)- power in the very low frequency range 0.003-0.04 Hz

cardiovascular diseases such as hypertension, ischemic heart disease, and congestive heart failure has been demonstrated quite well. Therefore, OSAS probability in the patients examined with prediagnosis of cardiovascular disease is very high. Tension rhythm Holter is routinely applied at most of these patients. On the other hand, documented data for the relation of respiratory disorders and cardiovascular diseases related to sleep also indicate the arrhythmogenic properties of the sleep related respiratory diseases. In the current study done by Khositseth et al. (11) QT dispersion and corrected QT dispersion values were higher in children with OSAS compared to normal population. As known in general, QT dispersion points to arrhythmogenic potential (12). In consequence, in a patient evaluated for it could be valuable to take sleep related respiratory disorder in to the differential diagnosis. Coexistence of cardiovascular disease and sleep related disorder was thought to be poor prognostic factor. Sleep related disorders are in one way cause structural changes in the myocardium and in another way, they are arrhythmogenic (13). By knowing this close relation and due to the cost and time consuming of the classical diagnostic methods, search for a cheaper, easier, and repeatable standard technique was obvious. Due to the supplied information for the detection of sleep-awake cycles and apnea attacks, electrocardiography and electrocardiogram gives us possibility to work on for analytic evaluations as HRV. By the algorithm, that combines ECG and frequency-domain analysis of respiratory signals Bianchi et al. (14) reported a very high compatibility as 89.9% in detecting sleep stages and 88% in detecting apneic episodes. In addition, our study showed that without detail algorithms just by routine long time ECG monitorization important data about sleep related respiratory disorders could be obtained. Consequently, HRV analysis seems more applicable than the methods like PTT and PAT requiring additional device and software. Today, Holter devices using in rhythm monitoring, enable various analyses on standard ECG data with high sampling rates and the wide support of technology. HRV analysis of nocturnal ECG record is one of these easily made analyses through these devices. HRV analysis can be used for evaluation of the sympathovagal balance. HRV analysis can provide obtaining of the information on sleep arousal, sleep stages and sleep fragmentation from single channel ECG. Pitson and Stradling (15), have pointed out that HRV identified with ECG present a close relationship with electroencephalographic micro arousals, even this relationship is stronger than apnea hypopnea index. Bonnet et al. (16) have reported that heart rate decreases during the sleep, goes in parallel with the body heat during the day and may be also associated with the sleep stages, arousal and major body movements. Interesting results of this study have been supported with the subsequent report by Ferri et al. (17).

Demonstration of the analyses related to heart rhythm and its associations with sleep arousal and major body movements, have paved the way for discussion for adaptability of these findings to the sleep disturbances and in particular, to OSAS diagnosis. Effects of the sleep arousal situation and sleep stages on HRV reveals as well as the changes in the sympathovagal balance because of the factors such as reflexes caused by the upper airway due to OSAS, hypoxia-reoxygenation cycle and intrathoracic pressure. HRV parameters show the difference in people with OSAS compared to the normal population as a result of sympathovagal balance changes (18-20). These negative effects on sympathovagal balance are also considered to play an important role at the known complications of OSAS (3, 21). Changes in the autonomic nervous system caused by sleep arousal state and the evidence indicating these changes show a difference compared to the healthy population; while, on the one hand, provide new knowledge to explain physiopathology of the cardiovascular results of OSAS, on the other hand, draw attention on some methods for OSAS diagnosis more inexpensive and

practical than PSG, basically evaluating the function of the autonomic nervous system. In their study which they investigated HRV parameters in patients with OSAS, Gula et al. (22) similarly to our study pointed out to the association of frequency-domain parameters, particularly LF/HF parameter indicating sympathovagal balance with OSAS diagnosis.

Many studies have been reported evaluating the benefit of HRV analysis for OSAS screening. Guilleminault et al. (23) have reported that computer based analysis of the bradycardia tachycardia cycle seen in OSAS can be used in sleep apnea syndrome screening. In their first report in 1999, Roche et al. have indicated that time-domain HRV analysis can be used as an inexpensive screening method and, in their subsequent report, they have pointed out that diagnostic value of HRV can be increased using time frequency wavelet analysis (24, 25). Combining HRV analysis and oximetry, Raymon et al. (26) found a very strong relationship between apnea hypopnea index and desaturation, and combined index they obtained through HRV. Park et al. (27) also have reported that of time-domain criteria, LF/HF could be a good indicator of OSAS severity. Data obtained analyzing of ECG records can provide quite valuable information not only in the patients with OSAS, but also in screening of the Cheyne-Stokes respiration (CSA) (21). CSA is an important but usually overlooked clinical diagnosis. Litman et al. (28) evaluated the telemetric ECG from three patients admitted to the hospital due to cardiovascular reasons and looked for sinus rhythm changes, AV conduction deficiency and contribution of respiratory artifact to the suspicion of sleep related respiratory disease and reported that in all three cases, sinus bradycardia and sudden tachycardia episodes following AV block attacks occurring time to time. Respiratory artifact showing itself by micro oscillations was accompanying these cycles. CSA was diagnosed in all three patients by further investigations done later. Apneic bradycardia and postvagal tachycardia that occurs later on compose the occult additional diagnostic findings that was on the telemetric ECG recordings (28). Upon the increase of the knowledge on the analysis of ECG data using different analytic methods could be helpful in recognizing of the sleep related respiratory disturbances, recent studies investigating the availability of ECG in OSAS screening have focused on the analysis of the different segments of ECG such as QT dispersion and the contribution of various algorithms to the diagnosis (11). Current studies for the OSAS survey evaluating different algorithms and data from these algorithms from the spectral analysis of one channel ECG due exist. Poupard et al. (29) tried to make an OSAS survey through the very low frequency power spectral density of heart rate increment and end up with acceptable sensitivity and specificity values. Both of the two studies from Chine using same parameters like our study but evaluating 24 hour Holter recordings, resulted with parallel values to our sensitivity and specificity values (30, 31). On the other hand, in some centers by the help of the internet, significant data collection was done and from the analytic evaluations of the ECG data, analytic implications were enriched. In the study done by Nemati et al.(32) on the T wave alternans (TWA) activity from the internet derived ECG database reported that TWA showed an increase with hearth rate in healthy individuals while no increase was observed in patients with OSAS.

Study limitations

Although our study demonstrates that HRV analysis can be helpful in differentiation of the patients with high risk for the possibility of OSAS, it has some limitations. First, using of the shorter ECG records instead of 24-hour records makes difficult using of particularly time-domain parameters. On the other hand, it is a more important limitation that the difference between the day and night data could not be evaluated due to lack of the diurnal ECG records. However, separately analysis of the night data part obtained through Holter monitoring is technically possible. Further studies evaluating 24 hours ECG records together with the results of polysomnography are needed to propound the sufficiency for these types of analyses. On the other hand, contrary to be expected from a screening test, HRV parameters obtained in our study indicate relatively lower sensitivity but higher specificity values.

Beside all these, there are significant limitations of our study. One of the most important limitations is the retrospective design through a limited number of cases and controls. Also addition of daytime ECG recordings of the patients accompanying PSG findings to the study could be probably more effective by giving change to evaluate the day and night sympathovagal balance difference.

Not only our study but also other studies evaluating the use of HRV parameters from one channel electrocardiography show that these values were not convenient for the diagnosis of OSAS (17-22). The reason for this is that the expectation from a screening test is high sensitivity rather than specificity. But this situation will turn to an advantage of evaluating patients in respect of referring them for sleep laboratory and give priority in handling these patients whom already monitored for another cardiovascular disease other than OSAS. In addition, as it was shown in our study, parameters like triangular index have high positive likelihood ratios. Just a brief glance at these parameters will make us think that OSAS will be the cause of rhythm disturbance or hypertension.

An important part of OSAS patients admits to cardiology clinics for rhythm disturbances, hypertension, ischemic heart disease and congestive heart failure because of the close relationship of OSAS with the cardiovascular diseases. HRV analysis of the long-term ECG records in these patients can provide the differentiation of the patients with high risk for OSAS and primarily evaluation of these patients in sleep laboratory.

Conclusion

OSAS and other sleep related respiratory deficiencies are a wide group of diseases, which are frequently seen and effect many other systems being especially cardiovascular. Although new diagnostic methods are still being evaluated, PSG is the only accepted diagnostic method. Patients were admitted to different clinics with various complaints and referred to sleep laboratories in case of suspicion. One of the most important clinics is cardiology clinics. Holter monitorization is one of the frequently used methods in detection of various rhythm disturbances and ischemic changes or for the diagnosis and follow up of the hypertension. HRV analysis of the data accumulated by Holter evaluation could not give the diagnosis of OSAS but could help the patients preferentially referred to the sleep laboratories and could cause them to be given priority in laboratories with long waiting list.

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