VIA MEDICA

ORIGINAL ARTICLE

Cardiology Journal
2008, Vol. 15, No. 5, pp. 441–445

ISSN 1897–5593

Heart rate turbulence in patients with obstructive sleep apnea syndrome

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Abstract

Background: *Heart rate turbulence (HRT) assessment is used as noninvasive method based on physiological sinus node response to the premature ventricular beat. Blunted HRT may indicate the autonomic nervous system impairment and can be helpful in identifying high-risk patients. Obstructive sleep apnea syndrome (OSAS) leads to cardiovascular complications. Autonomic nervous system and baroreflex dysfunctions may play the main role in the development of cardiovascular diseases. In the present study we aimed to assess HRT parameters in OSAS patients with and without coronary artery disease (CAD) in comparison to control group.*

Methods: *HRT analysis (TO — turbulence onset and TS — turbulence slope) was performed in 22 OSAS patients (confirmed by polisomnography, apnea-hypopnea index ≥ 15) and 21 healthy persons, obtained from 24-hour ECG recordings. CAD was confirmed in 10 OSAS patients, by positive exercise test ECG and coronary angiography.*

Results: *TS was significantly lower in OSAS patients in comparison to control group (1.14 ± ± 2.83* vs. *21.28 ± 16.2, $p < 0.001$). TO didn't differ in both group. Significant negative correlation between TS and apnea-hypopnea index was observed ($r = 0.49$, $p < 0.01$). There were no significant HRT changes in OSAS and CAD patients* vs. *OSAS without CAD patients, although tendency to more impaired HRT in OSAS and CAD patients was observed.*

Conclusions: *In OSAS patients, blunted HRT (especially TS) was observed. This may indicate baro-reflex dysfunction correlated with the severity of sleep disorders. The additional diagnosis of CAD did not significantly influence HRT parameters.* (Cardiol J 2008; 15: 441–445)

Key words: heart rate turbulence, obstructive sleep apnea, coronary artery disease

Introduction

The influence of sleep disturbances on the cardiovascular system function has been studied for the past few years [1, 2]. In 1988 He et al. [3] showed an increased mortality among patients with obstructive sleep apnea syndrome (OSAS). This difference in mortality was related to an apnea-hypopnea index (AHI) — the number of apnea and hypopnea episodes during one hour of sleep. Worse prognosis was associated with AHI > 20 and 50 years of age. Seventy-seven percent of patients are

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Received: 19.02.2008 Accepted: 25.07.2008

30–60 years old, whereas only 19% of them are over 60 [4]. OSAS is a highly prevalent disease in the population, affecting 1–4% of adults [5, 6]. The main reasons of greater mortality in this group are cardiovascular disorders: arterial hypertension [7], heart failure [8], ischemic heart disease [9, 10] and stroke [11]. The mechanism of the cardiovascular complications of OSAS is still poorly understood, however. Hypoxemia and hypercapnia may lead to sympathetic overactivity and baroreflex dysfunctions [12].

Heart rate turbulence (HRT) assessment is used as a non-invasive method, based on physiological sinus node response to the premature ventricular beat.

Blunted HRT may indicate autonomic nervous system impairment and can be helpful in identifying patients with coronary artery disease (CAD) and high risk of sudden cardiac death, especially after myocardial infarction (studies: MPIP, EMIAT, ATRAMI) [13, 14].

The aim of the study was to assess HRT parameters in OSAS patients with and without coronary artery disease in comparison to a control group.

Methods

Thirty patients with sleep-disordered breathing (SDB) were initially included in the study. Eventually, 22 patients with diagnosed OSAS (18 men and 4 women, aged 40–68; mean 51 ± 12 years) and 21 healthy subjects (16 men and 5 women, aged 39–60; mean 51 ± 11 years) were included in the analysis.

All patients gave informed consent and the local ethics committee approved the study.

OSAS was diagnosed by polysomnographic studies. Sleep studies were carried out in the Sleep Unit of the Department of Respiratory Medicine at Poznań University of Medical Sciences. Inclusion criteria were: AHI (apnea-hypopnea index) ≥ 15 and sinus rhythm in ECG.

In patients clinically suspected of coronary artery disease, with positive exercise ECG test, coronary angiography was performed.

The ambulatory 24-h Hotler ECG recordings were processed by Del Mar-Reynolds system — Pathfinder 700 with 3-chanel tape recorders Sherpa 3.

QRS detection, morphology classification (normal, aberrant, premature aberrant) and measurement of the RR interval were automatically performed by the system. All Holter files were reviewed and manually corrected.

Measurements of HRT parameters (onset and slope) require the presence of single ventricular premature beats (VPB) and were performed according to the definitions of Schmidt et al. [14]. The RR intervals before and after ectopic beats were manually transferred to a personal computer.

Turbulence onset (TO) was defined as the difference between the mean of the first two sinus RR intervals after a VPB, and the last two sinus RR intervals before the VPB divided by the mean value of the last two sinus RR intervals before the VPB. The value of TO is expressed as a percentage. Positive values of TO (> 0%) indicate sinus rhythm deceleration after VPB, and negative values (< 0%) indicate acceleration. The optimal is TO < 0%.

Turbulence slope (TS) is a measurement of the following heart rate deceleration. TS is the maximum positive slope of a regression line assessed over any sequence of five subsequent sinus rhythm RR intervals within the first 20 sinus rhythm intervals after VPB. The value of TS is expressed in milliseconds per RR interval. The normal value is over 2.5 ms/RR.

TO values were calculated in several episodes of VPB (at least 1), and values were averaged for each patient. The subjects without ventricular extrasystoly were excluded. TS were obtained from averaged tachogram.

HRT parameters were calculated in 100 episodes of VPB in OSAS patients and in 100 episodes in the control group. TO and TS values were compared between all analyzed groups i.e. OSAS *vs*. control, OSAS CAD (+) *vs*. OSAS CAD (–).

Statistical analysis

For the analysis of the remaining Holter parameters, a Mann-Whitney U-test was used because of the skewed distribution of these variables. Spearman's rank correlation was performed to assess the relation between parameters. A value $p < 0.05$ was considered statistically significant.

Results

Patient characteristics

The clinical characteristics of the OSAS patients are listed in Table 1.

AHI values in OSAS patient were 15.4–71.1 (mean 56.2). In 15 (75%) patients AHI was estimated above 30, which indicate severe sleep apnea.

Coronary angiography results in CAD (+) patients confirmed significant changes in 3 vessels in 3 patients, in 2 vessels in 3 patients and in 1 vessel in 1 patient.

Diabetes mellitus was recognized in 5 (50%) CAD (+) patients. In the OSAS CAD (–) group diabetes mellitus was observed in 5 (41%) patients.

Table 1. Obstructive sleep apnoea syndrome patient characteristics.

Age (years)	40–68 (mean 51)
Male gender	16 (73%)
Apnea-hypopnea index > 30	15 (75%)
Diabetes mellitus	10 (45%)
Hypertension	18 (81%)
Coronary artery disease	10 (45%)
Myocardial infarction	2 (10%)
Body mass index > 30 kg/m^2	18 (81%)

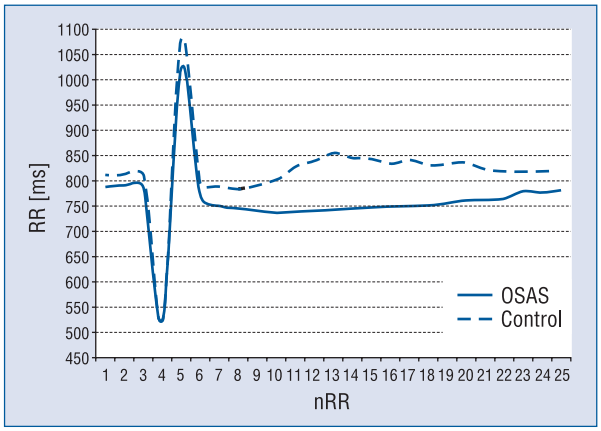

Figure 1. Heart rate turbulence curves in obstructive sleep apnea syndrome (OSAS) patients and in healthy control subjects.

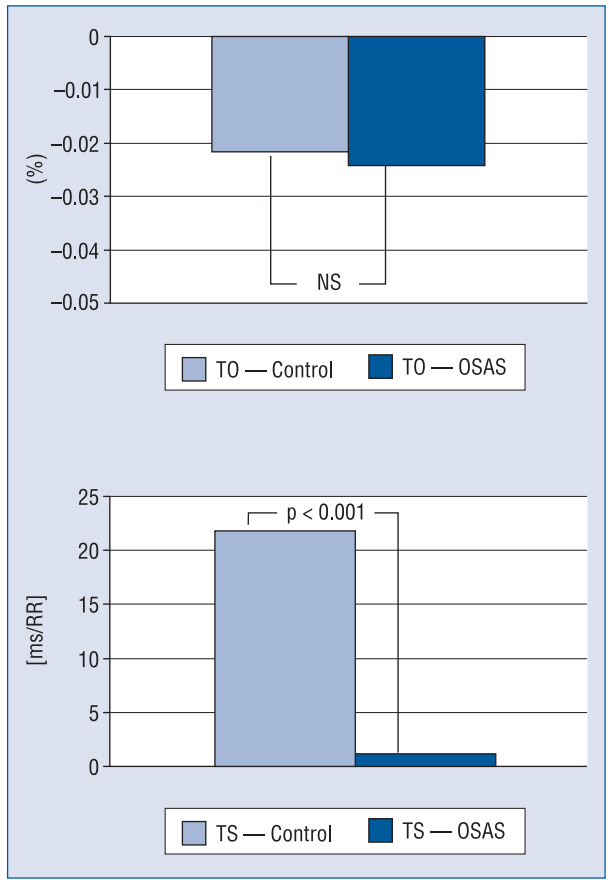

Figure 2. Turbulence onset (TO) and turbulence slope (TS) values comparison in obstructive sleep apnea syndrome (OSAS) patients and control healthy subjects.

The healthy control group was similar to the OSAS patient group (gender, age) but body mass index was significantly lower in this group. In 6 subjects (28%) body mass index was above 30.

Heart rate turbulence evaluation

Blunted HRT was observed in the OSAS group (Fig. 1). TS was significantly lower in OSAS patients in comparison to the control group (1.14 ± 2.83 *vs*. 21.28 ± 16.2, $p < 0.001$). TO did not differ in either group (Fig. 2). A significant negative correlation between TS and AHI was observed ($r = –0.49$, $p < 0.01$). There were no significant HRT changes in OSAS CAD (+) patients *vs*. OSAS CAD (–) patients, although a tendency towards more impaired HRT in OSAS CAD (+) patients was observed (Table 2).

Table 2. Turbulence onset (TO) and turbulence slope (TS) values in obstructive sleep apnea syndrome (OSAS) patients with (+) coronary artery disease (CAD) and without (–) CAD; p = NS

	OSAS CAD (–)	OSAS CAD (+)
TS [ms/RR]	1.99 ± 4.4	0.90 ± 1.78
TO (%)	–0.007 ± 0.07	0.016 ± 0.22

Discussion

The phenomenon of heart rate turbulence is assessed in Holter ECG in order to predict sudden death. The value of this method was confirmed by Schmidt et al. [14] after myocardial infarction.

Recent studies suggest that HRT, especially TS, has a predictive value in patients with chronic heart failure [15, 16].

Heart rate turbulence reflects the change of the sinus cycle length in baroreceptor responses to hemodynamic fluctuations after ventricular premature beat. Impaired baroreflex regulation in cases of blunted HRT was experimentally and clinically confirmed [17, 18]. Different provocative tests and noninvasive methods were based on baroreceptor response. The gold standard is the phenylephrine test, as a pharmacological stimulation. The ratio of

heart rate response to blood pressure stimulus (baroreflex sensitivity) is a useful prognostic marker.

Among noninvasive methods measuring the effects of small spontaneous changes of blood pressure, 24-hour Holter ECG assessment of heart rhythm variation and heart rhythm turbulence are used. A dysfunction of autonomic nervous system has proved to be responsible for high cardiac and arrhythmic mortality in patients after myocardial infarction [19]. Analogically, diminished baroreceptor reflex may be the connection between OSAS and cardiovascular complications.

In our study, HRT parameter abnormalities were observed in patients with proven OSAS. Additional diagnosis of CAD had no significant influence on HRT worsening. It must be noted, however, that only 2 patients in the study group had myocardial infarction, and that was the sub-group in which HRT suppression was expected to be most frequent. Pathological HRT parameters, potentially indicative of baroreceptor function failure, were observed by Cygankiewicz et al. [20] in 38% of patients with multivessel CAD. Among HRT parameters, TS correlates better with cardiovascular pathology incidence than TO. In the study by Young et al. [21], as well as in our own, abnormal TS proved to be a more sensitive marker of disturbance in the autonomic nervous system than heart rhythm variation. In patients with OSAS it correlates with sleep-disordered breathing (SDB) severity. This correlation occurs in patients without cardiovascular disease, potentially prior to their occurrence.

In patients with OSAS, several undesirable effects resulting from SDB are observed: temporary hypoxia, hypercapnia and autonomic nervous system activation secondary to awakening, and significant negative intrapleural pressure variation [22, 23]. Moreover, neurohormonal and inflammatory activation occurs, promoting the development of arterial hypertension, heart failure and CAD. Recent studies confirm the connection between cardiovascular diseases and OSAS [1, 2].

Common pathological mechanisms underlying OSAS and cardiovascular diseases, leading to baroreceptor reflex suppression, may cause abnormal heart rhythm turbulence in both OSAS and CAD patients. It is difficult to evaluate the degree of influence of OSAS alone, as well as the influence of coexisting diseases, on baroreceptor function. However, disturbed baroreceptor performance is a common factor adversely influencing long-term prognosis in both groups of patients.

Limitations of the study

The study group was relatively small. Typically for OSAS, most of the patients were male, aged over 40, in many cases with coexisting diseases: diabetes, arterial hypertension, CAD and obesity. These diseases might have influenced the vegetative nervous system in specific cases. Selection of a patient group without any of the above comorbidities but with confirmed OSAS is virtually impossible.

Conclusions

In OSAS patients, blunted HRT (especially TS) was observed. This may indicate baroreflex dysfunction correlated with the severity of sleep disorders. The additional diagnosis of CAD did not significantly influence HRT parameters.

Acknowledgements

Grant no. 501-2-02-24, University of Medical Sciences, Poznań, Poland.

The authors do not report any conflict of interest regarding this work.

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