TÜBİTAK

Original Article

Turk J Med Sci
2012; 42 (6): 964-969

E-mail: medsci@tubitak.gov.tr
doi:10.3906/sag-1201-52

# Heart rate recovery in patients with obstructive sleep apnea syndrome

Rıza Murat KARAŞEN[1], Bülent ÇİFTÇİ[2], Baran ACAR[1], Ahmet Arif YALÇIN[1], Selma FIRAT GÜVEN[2]

**Aim:** To demonstrate the effects of obstructive sleep apnea syndrome (OSAS) on baroregulatory function by using heart rate recovery (HRR) parameters.

**Materials and methods:** Fifty-four moderate and severe OSAS patients were included in the study. HRR was defined as the difference in heart rate between peak exercise and 1 min later; a value of 18 beats/min was considered abnormal. OSAS patients were enrolled in the study as group 1 (normal HRR; n = 12) and group 2 (abnormal HRR, n = 42). Left ventricular ejection fraction (LVEF, %) and other parameters were also measured by echocardiography in both groups.

**Results:** There was no statistically significant difference between group 1 and group 2 with regard to resting heart rate, or basic clinical and echocardiographic features (P > 0.05). The apnea-hypopnea index (AHI) was negatively correlated with the value of maximal heart rate during exercise (P < 0.05). In group 1, the mean age and coronary artery disease were significantly lower (respectively, 55.68 ± 10.05, 60.50 ± 9.00 years; 47.2% (n = 34), 80% (n = 24): P < 0.05), whereas the mean values of LVEF and maximal heart rate during exercise were significantly higher in comparison to group 2 (respectively 52.13 ± 11.95%, 45.13 ± 11.74%; 141.42 ± 19.70, 121.17 ± 19.01/min).

**Conclusion:** These results indicate that in OSAS baroregulatory function was impaired. This may show that baroreflex dysfunction is correlated with OSAS. The routine inclusion of HRR in the prognostic assessment of patients with OSAS may be warranted.

**Key words:** Heart rate recovery, obstructive sleep apnea syndrome

## Introduction

Obstructive sleep apnea (OSA) is a common disorder associated with an increased risk of cardiovascular disease and stroke. Previous studies showed increased mortality among patients with OSA (1). As it is strongly associated with known cardiovascular risk factors, including obesity, insulin resistance, and dyslipidemia, OSA is an independent risk factor for hypertension and has also been implicated in the pathogenesis of congestive cardiac failure, pulmonary hypertension, arrhythmias, and atherosclerosis. The difference in mortality was related to the apnea-hypopnea index (AHI) — the number of apnea and hypopnea episodes during 1 h of sleep. A worse prognosis was associated with AHI > 20 and 50 years of age.

Reduced cardiac autonomic function has been associated with cardiac vulnerability and may represent an important pathophysiological mechanism linking OSAS and risk of cardiac mortality. The mechanism of the cardiovascular complications of OSAS is still poorly understood, however. Hypoxemia and hypercapnia may lead to sympathetic overactivity and baroreflex dysfunctions (2). Heart rate decrease after exercise is important as it is associated with mortality. It has been thought that the decrease in heart rate occurs as a result of reactivation of the parasympathetic system.

Received: 20.01.2012 – Accepted: 13.02.2012
[1] Department of Otorhinolaryngology, Keçiören Training and Research Hospital, Ankara - TURKEY
[2] Atatürk Chest Diseases & Thoracic Surgery Training and Research Hospital, Ankara - TURKEY
***Correspondence:*** *Baran ACAR, Department of Otorhinolaryngology, Keçiören Training and Research Hospital, Ankara - TURKEY*
*E-mail: drbaranacar@gmail.com*

According to the protocol applied after the first minute of the exercise test, expected reduction is ≥12 beat/min if exercise is ended by slowing down and ≥18 beat/min if exercise is ended suddenly (3). The term abnormal heart rate recovery is used for the results below these values and it has been shown in previous studies that this is an independent mortality predictor in patients with coronary artery disease and normal left ventricular function.

Specifically, our study was conducted to demonstrate the baroregulatory function by using heart rate recovery after an exercise test among OSAS patients.

## Clinical material and methods

### Study population

Fifty-four consecutive OSAS patients (confirmed by polysomnography, apnea-hypopnea index (AHI) ≥ 15)) (30 male, 24 female) presenting to our clinic and who asked to undergo an exercise stress test were included in our study. OSAS patients were enrolled in the study as group 1 (normal HRR; n = 12; 7 males and 5 females; mean age, 49.9 ± 6.6 years) and group 2 (abnormal HRR; n = 42; 23 males and 18 females; mean age, 42.0 ± 6.1 years).

Definition of hypertension was established as having a blood pressure of ≥140 mmHg and/or diastolic pressure of ≥90 mmHg or having a previous hypertension diagnosis. Using hypoglycemic agents and/or having fasting blood glucose of ≥126 mg/dL was sufficient for a diabetes mellitus diagnosis. In order to be diagnosed with coronary artery disease, history of myocardial infarction or epicardial coronary artery lesions having angiographic evidence or a history of unstable angina pectoris was a must. Patients were classified as smokers if they had smoked regularly during the previous 1 year.

A complete physical and echocardiographic examination was performed before the study. All participants gave their informed consent, and the institutional review board approved the study protocol.

### Polysomnography

Polysomnography is the gold standard diagnostic tool for assessing sleep-disordered breathing. Full-night polysomnography (PSG) was performed in all patients by a computerized system (Somnostar alpha; Sensormedics, USA) and included the following variables: electrooculogram, electroencephalogram, electromyogram of submental muscles, electromyogram of the anterior tibialis muscle of legs, an electrocardiogram, and airflow (with an oro-nasal thermistor). Chest and abdominal efforts were recorded using inductive plethysmography and arterial oxyhemoglobin saturation by pulse oximetry with a finger probe. Arousals were scored according to accepted definitions based on the American Sleep Disorders Association criteria for measurements, definitions, and severity ratings of the Sleep Related Breathing Disorders Task Force Report (4). Obstructive apneas were defined as absence of airflow for longer than 10 s, and obstructive hypopneas as a 50% decrease in airflow or a clear but lesser decrease in airflow if coupled with either a desaturation of >3% or an arousal in the context of ongoing respiratory effort. The apnea-hypopnea index (AHI) was defined as the number of obstructive apneas and hypopneas per hour of sleep. Patients with an AHI < 15 were assigned to the control group. Patients with an AHI ≥ 16 were considered as having OSAS. Patients with sleep disorders except OSAS, such as upper airway resistance syndrome (UARS), central sleep apnea syndrome (CSAS), periodic limbs movement (LPMs), or narcolepsy, were excluded. All records were scored manually for sleep stage, arousals, apneas, and hypopneas.

### Cardiopulmonary exercise test

A symptom (dyspnea or fatigue) limited exercise test was done without asking the patients to stop taking their medications. Blood pressure was measured every 3 min before and during the test and also at the end of the test. Heart rate was measured at rest, once every 2 min of the test, during maximum exercise, and at the end of the first minute of recovery after the test. The chronotropic response was calculated as (maximum heart rate – heart rate at rest)/(220 – age – heart rate at rest)) and ≤0.80 was regarded as chronotropic incompetence. The test was finished when maximum exercise exertion was achieved and patients were allowed to sit and rest without a cooling down period. Heart rate reserve was defined as the difference between maximum exercise heart rate and heart rate after 1 min of rest, and rates ≤ 18 were interpreted as abnormal values.

### Statistical analysis

Parametric data were expressed as mean ± SD and categorical data as percentages. All statistical procedures were performed using SPSS 15.0. Parametric data were compared using Student's t-test and categorical data with the chi-square test. Relations between the nicotine dependence index and HRR parameters were assessed by Pearson's correlation coefficient. A P value < 0.05 was considered to be statistically significant.

## Results

Clinical characteristics of both groups are shown in the Table. There was no significant difference between the groups in demographics of age, blood pressure, or body mass index (P > 0.05). The baseline heart rate tended to be significantly higher in group 2 than in group 1 (82.25 ± 6.67 vs. 71.87 ± 7.44 beats/min, P < 0.001).

Heart rate at rest was 71.87 ± 7.44/min in group 1 and 82.25 ± 6.67/min in group 2 (P > 0.05). Maximum heart rate of patients during the effort test was 141.42 ± 19.70/min and 121.17 ± 19.01/min in group 1 and group 2, respectively, and patients in group 1 had significantly higher heart rates (P < 0.001). A significant negative correlation was found in the correlation test between maximum heart rate reached during the effort test and the value of AHI (r = –0.201; P < 0.05). Values obtained during the effort tests were 9.48 ± 2.28 and 8.36 ± 2.50 in group 1 and group 2, respectively, and the difference between these values was statistically significant (P < 0.05). Average body mass index was 27.75 ± 3.71 in group 1 and 26.15 ± 3.13 in group 2 (P < 0.05).

The proportion of those having coronary artery disease was 47.2% in group 1 and 80% in group 2; the difference between the groups with respect to the said parameter was statistically significant (P < 0.05). The proportion of smokers was 27.8% in group 1 and 40% in group 2, which is also a statistically significant difference (P < 0.05).

The proportions of hypertension and diabetes mellitus were 50% (n = 36) and 6.9% (n = 5) in group 1 and 43.3% (n = 13) and 10% (n = 3) in group 2, respectively. Regarding the said parameters, there was no significant difference between the groups (P > 0.05).

## Discussion

OSAS is a common disorder associated with an increased risk of cardiovascular disease and stroke. Previous studies showed increased mortality among patients with OSAS (1). OSAS is part of a spectrum

Table. The comparison of general features, and echocardiographic and Holter parameters between group 1 and group 2.

| | Group 1 (n = 64) | Group 2 (n = 30) | P value |
|---|---|---|---|
| Age (years)* | 49.9 ± 6.6 | 42.0 ± 6.1 | N.S. |
| Sex (male) % * | 54.7% | 53.3% | N.S. |
| BMI (kg/m$^2$)* | 25.54 ± 3.17 | 24.86 ± 3.22 | N.S. |
| Systolic BP (mmHg)* | 110.17 ± 14.14 | 105.50 ± 11.32 | N.S. |
| Diastolic BP (mmHg) * | 65.70 ± 9.18 | 65.33 ± 6.68 | N.S. |
| Heart rate (bpm) * | 71.87 ± 7.44 | 82.25 ± 6.67 | P < 0.001 |
| LVEF (%) * | 51.32 ± 5.23 | 51.92 ± 5.68 | N.S. |
| LVEDD (cm) * | 4.32 ± 0.31 | 4.28 ± 0.33 | N.S. |

of sleep-related breathing disorders that includes snoring, upper airway resistance syndrome (increased respiratory effort without apnea or hypopnea), and central sleep apnea (CSA) (apnea without respiratory effort) (4). OSAS is the combination of obstructive apneas with daytime tiredness or recurrent awakenings or gasping episodes (5). As it is strongly associated with known cardiovascular risk factors, including obesity, insulin resistance, and dyslipidemia, OSAS is an independent risk factor for hypertension and has also been implicated in the pathogenesis of congestive cardiac failure, pulmonary hypertension, arrhythmias, and atherosclerosis (6). OSAS is characterized by repetitive partial or complete closure of the upper airway during sleep. Acute physiologic stresses occur during these episodes of asphyxia, including arterial oxygen desaturation, surges in sympathetic activity, and acute hypertension. In a patient with moderate-to-severe OSAS, these cycles may occur hundreds of times a night. The association between OSA and cardiovascular disease was first raised by observational studies linking snoring, a surrogate for OSAS, with increased cardiac events (7). Previous studies have demonstrated a clear relationship between the presence and severity of OSAS and both systemic hypertension and increased cardiovascular disease (8-10). OSAS is thought to play a role in the pathogenesis of systemic hypertension and congestive cardiac failure, as well as possibly acute coronary syndromes, pulmonary hypertension (PHT), arrhythmias, and cerebrovascular events (11). Previous studies showed that treatment of OSAS reduces cardiovascular mortality (12).

Recent studies have shown that heart rate recovery (HRR) has prognostic value in healthy volunteers and in coronary artery patients with preserved left ventricular function (3,13-15). Moreover, delayed HRR measured during the 2 min after maximal exercise has been suggested to be a predictor of all-cause mortality with respect to cardiovascular diseases in high-risk people (16,17). In normal people, cardiac output increases as a result of an increase in heart rate and pulse volume. Heart rate increases due to removal of vagal tonus and predominance of sympathetic tonus. The decrease in heart rate just after the exercise ends can be explained by re-activation of the parasympathetic system. Activation of the parasympathetic system not only causes a decrease in heart rate but also a decrease in myocardial response and occurrence of peripheral vasodilatation. Although factors regulating HRR are not known clearly, it has been thought that altered venous return, increased stretch of atrial receptors, and impaired balance of sympathetic/parasympathetic stimulation balance in favor of the parasympathetic system are the main factors (18-20).

The autonomic nervous system and baroreflex dysfunctions may play the main roles in the development of cardiovascular diseases. HRR has been reported to be a useful tool with reproducibility sufficient to evaluate cardiac autonomic modulation. HRR impairment reflects cardiac autonomic dysfunction, in particular impaired baroreflex sensitivity and reduced parasympathetic activity. Impaired HRR is associated with an increased risk of mortality and susceptibility to life-threatening arrhythmias. In our study we found a strong correlation between OSAS and impaired HRR. Our results support previous studies (21-23). Maeder et al. found that the severity of OSAS expressed as higher AHI is independently associated with lower HRR, a measure of autonomic dysfunction. The common point of the underlying reason is mostly cardiac autonomic system dysfunction. Our findings suggested that as the OSAS gets worse the cardiac rhythm disorders increase. Several previous studies have focused on the effect of OSAS on the cardiac autonomic system. Several investigators have reported that reduced heart rate variability (HRV) and heart rate turbulence (HRT) in OSAS subjects is a strong indicator for autonomic disturbances that may be involved in the mechanism promoting arrhythmias and sudden death in OSAS subjects (24-26). Park et al. (25) showed that the LF/HF ratio can be an appropriate index estimating the severity of OSAS symptoms and that it can be a good candidate for a screening tool with oximetry for apnea-hypopnea syndrome. Wiklund et al. (27) showed that the total HRV parameters were significantly lower in OSAS than in healthy subjects. Syzmanowska et al. showed that HRT parameter abnormalities (especially TS) were observed in patients with proven OSAS (26). Roche et al. (28) found that the time domain parameters of HRV (SDNN and RMSSD) are decreased in severe OSAS when compared to mild OSAS. Together with the previous results, our findings suggest that impairment of the cardiovascular

autonomic system in OSAS patient may be a possible component of the deleterious effect of OSAS.

### Limitation

The main limitation of our study seems to be the small sample size. Because the small sample size results in low statistical power for equivalency testing, negative results may be simply due to chance. However, it should be taken into account that establishing an OSAS group is difficult.

### Conclusion

We think that the autonomic modulation of the heart is reduced in OSAS patients and it becomes apparent particularly during parasympathetic maneuver, and that the impaired autonomic cardiac control may in part explain the mechanism promoting arrhythmias and sudden death in OSAS subjects. To achieve a meaningful reduction in mortality, OSAS must be targeted for treatment.

## References


1. He J, Krygier MH, Zorick FJ, Conway W, Roth T. Mortality and apnea index in obstructive sleep apnea. Experience in 385 patients Chest 1988; 94: 9-14.
2. Wilkund U, Olfsson B-O, Franklin K, Blom H, Bjerle P, Niklasson U. Autonomic cardiovascular regulation in patient with obstructive sleep apnoea: A study based on spectral analysis of heart rate variability. Clini Physiol 2000; 20: 234-241.
3. Cole CR, Blackstone EH, Pashkow FJ, Snader CE, Lauer MS. Heart-rate recovery immediately after exercise as a predictor of mortality. N Engl J Med 1999; 341: 1351-7.
4. Handan İ, Çiftçi TU, Köktürk O. The clinical and polysomnographic features in complex sleep apnea syndrome. Turk J Med Sci 2010; 40: 693-699.
5. The Report of an American Academy of Sleep Medicine Task Force. Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. Sleep 1999; 22: 667-689.
6. Şahin M, İnal BB, Öğreden Ş, Yiğit Ö, Aral H, Güvenen G. Metabolic profile and insulin resistance in patients with obstructive sleep apnea syndrome. Turk J Med Sci 2011; 41: 443-454.
7. Koskenvuo M, Kaprio J, Partinen M, Langinvainio H, Sarna S, Heikkila K. Snoring as a risk factor for hypertension and angina pectoris. Lancet 1985; 1: 893-6.
8. Hung J, Whitford EG, Parsons RW, Hillman DR. Association of sleep apnoea with myocardial infarction in men. Lancet 1990; 336: 261-4.
9. Peker Y, Kraiczi H, Hedner J, Loth S, Johansson A, Bende M. An independent association between obstructive sleep apnea and coronary artery disease. Eur Respir J 1999; 14: 179-84.
10. Mooe T, Franklin KA, Wiklund U, Rabben T, Holmstrom K. Sleep-disordered breathing and myocardial ischemia in patients with coronary artery disease. Chest 2000; 117: 1597-602.
11. Leung RS, Bradley TD. Sleep apnea and cardiovascular disease. Am J Respir Crit Care Med 2001; 164: 2147-65.
12. Golbin JM, Somers VK, Caples SM. Obstructive sleep apnea, cardiovascular disease, and pulmonary hypertension. Proc Am Thorac Soc 2008; 5: 200-206.
13. Cole CR, Foody JM, Blackstone EH, Lauer MS. Heart rate recovery after submaximal exercise testing as a predictor of mortality in a cardiovascularly healthy cohort. Ann Intern Med 2000; 132: 552-5.
14. Lauer MS, Okin PM, Larson MG, Evans JC, Levy D. Impaired heart rate response to graded exercise: prognostic implications of chronotropic incompetence in the Framingham Heart Study. Circulation 1996; 93: 1520-6.
15. Nishime EO, Cole CR, Blackstone EH, Pashkow FJ, Lauer MS. Heart rate recovery and treadmill exercise score as predictors of mortality in patients referred for exercise ECG. JAMA 2000; 284: 1392-8.
16. Shetler K, Marcus R, Froelicher VF, Vora S, Kalisetti D, Prakash M et al. Heart rate recovery: validation and methodologic issues. J Am Coll Cardiol 2001; 38: 1980-7.
17. Diaz LA, Brunken RC, Blackstone EH, Snader CE, Lauer MS. Independent contribution of myocardial perfusion defects to exercise capacity and heart rate recovery for prediction of all-cause mortality in patients with known or suspected coronary heart disease. J Am Coll Cardiol 2001; 37: 1558-64.
18. Sabin WM, Davidson DM, Haskell WL. Autonomic contribution to heart rate recovery from exercise in human. J Appl Physiol 1982; 53: 1572-5.
19. Arai Y, Saul JP, Albrecht P, Hartley LH, Lilly LS, Cohen RJ et al. Modulation of cardiac autonomic activity during and immediately after exercise. Am J Physiol 1989; 256: H132-141.
20. Imai K, Sato H, Hori M, Kusuoka H, Ozaki H, Yokoyama H et al. Vagally mediated heart rate recovery after exercise is accelerated in athletes but blunted in patients with chronic heart failure. J Am Coll Cardiol 1994; 24: 1529-35.
21. Maeder MT, Ammann P, Schoch OD, Rickli H, Wolfgang K, Hürny C et al. Determinants of postexercise heart rate recovery in patients with the obstructive sleep apnea syndrome. Chest 2010; 137: 310-7.

22. Maeder MT, Münzer T, Rickli H, Schoch OD, Korte W, Hürny C et al. Association between heart rate recovery and severity of obstructive sleep apnea syndrome. Sleep Med. 2008; 9: 753-61.

23. Bayram NA, Çiftçi B, Güven SF, Bayram H, Diker HE, Duraz T et al. Prevalence of cardiac arrhythmia in obstructive sleep apnea syndrome. Turk J Med Sci 2010; 40: 843-850.

24. Gil E, Mendez M, Vergara JM, Cerutti S, Bianchi AM, Laguna P. Discrimination of sleep-apnea-related decreases in the amplitude fluctuations of PPG signal in children by HRV analysis. Trans Biomed Eng 2009; 56: 1005-14.

25. Park DH, Shin CJ, Hong SC, Yu J, Ryu SH, Kim EJ et al. Correlation between the severity of obstructive sleep apnea and heart rate variability indices. J Korean Med Sci 2008; 23: 226-31.

26. Szymanowska K, Piatkowska A, Nowicka A, Cofta S, Wierzchowiecki M. Heart rate turbulence in patients with obstructive sleep apnea syndrome. Cardiol J 2008; 15: 441-5.

27. Wiklund U, Olofsson BO, Franklin K, Blom H, Bjerle P, Niklasson U. Autonomic cardiovascular regulation in patients with obstructive sleep apnoea: a study based on spectral analysis of heart rate variability. Clin Physiol 2000; 20: 234-41.

28. Roche F, Gaspoz JM, Court-Fortune I, Minini P, Pichot V, Duverney D et al. Screening of obstructive sleep apnea syndrome by heart rate variability analysis. Circulation 1999; 100: 1411-5.