Original Article

Eur J Gen Med 2015; 13(1): 28-36

DOI : 10.15197/ejgm. 01476

Sleep Quality and Atherogenic Risk in Sleep Apnea Patients

Jarosław Wysocki[2,1], Jarosław Balcerzak[1], Monika Prus[1], Kazimierz Niemczyk[1], Magdalena Lachowska[1]

ABSTRACT

Objective: *Some studies have shown the atherogenic dyslipidemia as being sometimes independent of the obesity; however, with a close relation to the obstructive sleep apnea (OSA). The aim of this study was to investigate a relationship between parameters defining the quality of sleep and the standard lipid profile despite the obesity.* ***Methods:*** *The data of 211 patients with suspected OSA were analyzed prospectively. The following tests were performed: polysomnography, morphometric assessment and serum lipid levels.* ***Results:*** *Value of AHI showed a positive correlation with TG, TG/HDL ratio, BMI, plasma atherogenic index (API), circumference of neck, waist, and hip, and WHR. A negative correlation was found between AHI and HDL. The patients with severe OSA (AHI>30) differ significantly from the patients with moderate and mild OSA in terms of TG, and the ratio of TG /HDL and API and they are, therefore, in the group of much higher risk of cardiovascular disease. Significant predictors of the severity of sleep apnea are as follow: the ratio of TG/HDL, BMI and the neck circumference. The arousal index was the only parameter of the sleep quality significantly associated with the level of TG.* ***Conclusion:*** *The most important parameters of the quality of sleep that determine atherogenic risk are AHI and arousal index that are significantly correlated with TG/HDL ratio. Particularly, high risk of cardiologic problems applies to patients with AHI>30 who substantially differ in terms of lipid profile from the patients with mild or moderate OSA. Arousal index significantly distinguishes patients with AHI> 30 from the other groups of patients.*

Key words: *Obstructive sleep apnea, lipid profile, sleep quality, atherogenic risk*

Uyku Apneli Hastalarda Uyku Kalitesi ve Atherojenik Risk

ÖZET

Amaç: *Bazı çalışmalarda atherojenik dislipideminin obeziteden bağımsız olabileceğini ve uyku apnesi ile yakında bir ilişkisi olduğu gösterilmiştir. Bu çalışmanın amacı obeziteye rağmen uyku apneli hastalarda uyku kalitesi ile lipid profili arasındaki ilişkiyi göstermektir.* ***Yöntem:*** *Prospektif olarak uyku apneli 211 hasta çalışmaya alınmıştır. Polisomnografi, morfometrik ölçümler ve lipid profili ölçülmüştür. Bulgular: AHI ile TG, TH/HDL oranı, BMI, plazma atherojenik indeks (API), boyun, kalça ve bel kalınlığı ile bel/kalça oranı arasında pozitif korelasyon vardı. AHI ile HDL arasında negatif korelasyon vardı. Şiddetli UAS'li hastaların TG, TG/HDL oranı ve API değerleri hafif-orta UAS'lu hastalardan farklı idi. Bu nedenle bu grupya kardiyovasküler hastalık riski daha yüksekti. Şiddetli UAS göstergeleri TG/HDL oranı, BMI ve boyun kalınlığı idi. Uyanma indeksi sadece uyku kalitesini gösteriyordu ve TG düzeyi ile ilişkiliydi.* ***Sonuç:*** *Uyku kalitesini gösteren AHI ve uyanma indeksi kalp hastalıkları göstergesi olarak TG/HDL oranı ile belirgin korelasyon vardı. Özellikle yüksek kalp problemi riski AHI >30 olan hastalara uygulanır. Uyanma riski belirgin olarak AHI >30 olan hastaları diğer gruplardan ayırır.*

Anahtar kelimeler: *Obstrüktif uyku apne, lipid profili, uyku kalitesi, atherojenik risk*

Medical University of Warsaw, Department of Otolaryngology[1], Warsaw, Poland, Institute of Health, Siedlce University of Natural Sciences and Humanities, Department of Dietetics and Food Evaluation[2] , Poland

Received: 2015-02-17, Accepted: 2015-04-12

Correspondence: *Magdalena Lachowska, MD, PhD*
Department of Otolaryngology
Medical University of Warsaw,
ul. Banacha 1a
02-097 Warsaw
Poland

E-mail: mlachowska@wum.edu.pl

INTRODUCTION

In patients with obstructive sleep apnea (OSA), most of which meet the criteria of the metabolic syndrome, dyslipidemia seems to be directly connected with overweight/obesity (1-3). However, some studies demonstrated an independent association between OSA and atherogenic dyslipidemia in non-obese subjects with OSA: increased levels of triglycerides (TG), total cholesterol (TC), and LDL cholesterol (LDL), and lower levels of HDL cholesterol (HDL) (4-6). However still there is relatively small number of clinical trials dealing with the lipid profile in patients with OSA and their results are ambiguous (3,6,7-10). Two of the main polysomnographic parameters, desaturation index and Sat O_2nadir are significantly associated with a reduced level of HDL (3). It was also found that AHI is strongly associated with the level of HDL, regardless of age, sex, body weight, BMI, diabetes or lipid-lowering drugs. (1). However, other studies did not show any relationship between AHI and the standard lipid profile (8-10). Indirect evidence for the association of OSA with dyslipidemia is the positive impact of CPAP therapy on one or more elements of the standard lipid profile (1,11,12). However, several other studies analyzing the lipid parameters (8,13,14) have not shown any effect from CPAP therapy. Perhaps therefore atherogenic dyslipidemia also depends on other factors, including the quality of sleep. In the literature, there is no data whether a pathological structure of sleep, despite respiratory events, might be associated with atherogenic lipid profile in OSA patients.

However, it is known that sleep fragmentation and, therefore, both the number of respiratory incidents and their adverse changes during the sleep reflected in the EEG, can reflect in biochemical system disorders. It is known that OSA influences in negative way the hypothalamic-pituitary-adrenal axis by repeated arousals (15). It leads to permanent increase in the activity of the renin-angiotensin-aldosterone-cortisol axis (16,17). Moreover, all the published studies analyzed only the relationship between AHI or SO2nadir and the lipid profile without mentioning the atherogenic indices. It has been proven that the absolute values of the levels of TC, LDL-C, LDL-C, and TG do not always adequately reflect the risk of atherosclerosis. The atherogenic indices have a greater predictive value than do each of the lipid fractions individually (18).

This study aimed to determine whether there is any relationship independent of obesity between the quality of sleep and atherogenic lipid profile in patients with OSA.

MATERIAL AND METHODS

Subjects

The data of 211 patients (176 men and 35 women) with OSA diagnosed on the base of polysomnography (PSG) were analyzed. All the patients gave their informed consent to participate in the study. The Ethics Committee Review Board at the Medical University of Warsaw approved the study protocol. Patients were consecutively included in this prospective study according to the waiting list for a PSG test. In the morning, right after PSG was completed, every patient underwent lipid profile test. For this study, the inclusion criteria were age over 18 years old, no treatment for OSA (no oral medication, no CPAP, no surgical treatment). The exclusion criteria were pregnancy, cancer, diagnosed hyperlipidemia and/or treatment for hyperlipidemia, diabetes, previous tonsillectomy or septoplasty.

Polysomnography

Standardized attended 14-channel laboratory overnight PSG was performed, using an oronasal thermocouple (Grass, USA). Sleep stages were manually scored in 30 seconds sections using standard AASM 2005 criteria. The AHI, arousals, and desaturations were computed and then manually revised. PSG sleep time was obtained by summing the time spent in sections scored as any stage of sleep during the period from "lights off" (approximately 10:00 pm) to "lights on" (approximately 7:00 am). Obstructive sleep apnea is confirmed by AHI≥5. Mild OSA is determined by 5≤AHI≤15, moderate by 15≤AHI≤30, and severe by 30>AHI. Sleep quality was assessed based on proportions of the various stages, the number of EEG activations/ per hour of sleep (arousal index) and the number of awakenings to the state of wake per hour of sleep. The sleepless time (Wake After Sleep Onset - WASO) was assessed by time after the start of stage N2. The duration of the different phases of sleep: NREM (N1, N2, N3) and REM, was determined as a percentage of total sleep time.

Biochemistry

Venous blood sampling was performed between 7:00 am and 8:00 am and an overnight fast. Samples were analyzed at the Clinical Biochemistry Laboratory (analysis using the Roche Diagnostic Laboratory system). Fasting TC, HDL as well as TG were determined by an enzymatic photometric test. The LDL was calculated using the Friedewald formula. Then atherogenic indices: Castellani index TC/HDL, API - Atherogenic Index of Plasma $\log_{10}$ (TG/HDL), LDL/HDL ratio and TG/HDL ratio were calculated.

Table 1. Results of measurements of studied parameters and calculated indices for all the patients with confirmed diagnosis of sleep apnea and grouped for sex.

Variable/ group	General (n:211)		Males (n:176)		Females (n:35)	
	X (SD)	Min-Max	X (SD)	Min-Max	X (SD)	Min-Max
Age	50.35(12.67)	19.0-84.0	49.8 (12.25)	19.0-78.0	52.40 (14.06)	20.00-84.0
Glucose	102.09 (19.7)	71.0-233.0	103.76 (20.6)	71.0-233.0	95.11 (13.04)	74.00-126.0
TC	199.7 (39.38)	104.0-324.0	199.6 (39.74)	104.0-324.0	200.09 (38.9)	123.0-307.0
TG	145.31 (74.5)	31.0-437.0	148.8 (78.28)	31.0-437.0	130.1 (53.24)	43.00-239.0
HDL	51.37 (13.73)	25.0-107.0	50.44 (13.41)	25.0-107.0	55.48 (14.48)	25.00-98.0
LDL	118.9 (35.44)	25.0-223.0	118.98 (35.4)	25.0-223.0	118.4 (36.23)	46.00-214.0
AHI	33.61 (26.59)	0.2-115.7	34.88 (26.26)	0.4-115.7	28.46 (27.50)	0.20-110.40
SO_2nadir	80.71 (12.12)	12.0-96.0	80.92 (10.53)	12.0-93.0	79.88 (17.30)	14.00-96.0
N1	14.63 (13.43)	0.0-70.1	14.88 (13.51)	0.0-70.1	13.64 (13.17)	0.00-62.40
N2	62.79 (20.13)	7.6-94.8	64.42 (19.99)	7.6-94.5	56.26 (19.53)	18.00-94.8
N3	15.73 (16.23)	0.0 -91.2	13.94 (15.08)	0.0-91.2	22.88 (18.69)	0.00-81.0
REM	6.21 (5.94)	0.0-31.5	6.24 (5.45)	0.0-24.8	6.09 (7.65)	0.00-31.50
WASO	75.84 (62.58)	3.5-399.00	73.32 (56.75)	3.5-399.0	87.24 (83.97)	7.00-356.0
Arousal	27.1 (21.43)	2.6 -155.5	25.92 (18.11)	2.6-109.8	32.35 (32.12)	5.30-155.5
WAKE	9.72 (9.59)	0.1-67.0	9.67 (8.91)	0.1-67.0	9.97 (12.31)	0.90-61.40
Neck	41.27 (3.86)	30.0-54.0	42.44 (3.07)	36.0-54.0	36.49 (3.01)	30.00-45.0
Waist	104.03 (14.1)	70.0-155.0	105.94 (12.9)	82.0-155.0	96.62 (16.05)	70.00-136.0
Hip	109.77 (11.2)	87.0-155.0	109.5 (10.09)	87.0-155.0	110.7 (14.69)	93.00-152.0
BMI	30.44 (5.44)	18.93-56.44	30.68 (5.07)	20.81-51.65	29.54 (6.61)	18.93-56.44
WHR	0.95 (0.07)	0.73-1.14	0.97 (0.06)	0.84-1.14	0.87 (0.06)	0.73-1.02
Castellani	4.12 (1.27)	1.65-8.29	4.18 (1.28)	1.65-8.29	3.84 (1.17)	2.08-6.82
API	0.42 (0.29)	-0.36-1.10	0.43 (0.29)	-0.33-1.1	0.35 (0.27)	-0.36-0.97
LDL/HDL	2.47 (0.99)	0.50-5. 82	2.51 (0.99)	0.5-5.82	2.3 (0.97)	0.71-4.78
TG/HDL	3.23 (2.27)	0.44-12.57	3.35 (2.36)	0.46-12.57	2.71 (1.75)	0.44-9.24

Age expressed in years; biochemical parameters in mg/dl; AHI, arousal, wake in incidents per hour of sleep; neck, waist, hip circumference in cm; SO_2nadir, NREM and REM in %. Glucose=serum glucose level, TG= serum triglyceride level, TC=serum total cholesterol level, HDL=serum high density lipoproteins level, LDL=serum low density lipoproteins level, AHI= apnoea/hypopnea index, SO_2nadir= the lowest saturartion level during sleep period , N1=duration of N1 sleep pahase as a percent of total sleep time, N2=duration of N2sleep pahase as a percent of total sleep time, N3=duration of N3 sleep pahase as a percent of total sleep time, REM=duration of REM sleep pahase as a percent of total sleep time, WASO=wake after sleep onset in minutes, Arousal=index of arousal incidents per hour, WAKE=index of wake incidents per hour, Neck=neck circumference in cm, Waist=waist circumference in cm, Hip=hip circumference in cm , BMI=body mass index, WHR=waist to hip cirumference ratio, Castellani=Castellani idex of plasma atherogenicity, API=API index of plasma atherogenicity

Anthropometric analysis

Height and weight of participating subjects were obtained using the Tanita Corp. scale (BC 418 MA). Neck, waist, and hip circumferences were measured using a metallic anthropometric tape. All anthropometric measurements were rounded up and expressed in kilograms and centimeters. Waist to hip ratio (WHR) as well as body mass index (BMI) was calculated.

Statistical analysis

Statistical analysis was performed using Statistica software (StatSoft, Inc. 2010, data analysis software system, version 10). To analyzed the data the following tests were used: Student's t-test, the Mann-Whitney test, multivariate analysis of variance (ANOVA), Fisher's (LSD - least significant differences), Scheffe and Newman-Keulus tests, Spearman's rank order and the Pearson correlation coefficient tests. A P-value of <0.05 was considered statistically significant.

***Table 2**. Analyzed parameters in four studied groups according to their AHI.*

Variable/ group	*Group I 5≤AHI≤15*	*Group II 15<AHI≤30*	*Group III AHI>30*	*p value for ANOVA*
	X (SD)	*X (SD)*	*X (SD)*	
N	*47*	*50*	*114*	*211*
Glucose	*103.00 (23.81)*	*102.09 (16.45)*	*103.85 (20.41)*	*0.339*
TC	*201.45 (35.7)*	*198.7 (36.52)*	*198.79 (41.32)*	*0.8639*
TG	*125.96 (48.2)*	*134.16 (72.57)*	*160.03 (80.3)*	*0.0324**
HDL	*53.7 (12.48)*	*52.76 (12.45)*	*48.9 (14.03)*	*0.0566*
LDL	*123.72 (31.91)*	*118.31 (32.55)*	*117.01 (38.28)*	*0.7178*
AHI	*10.7 (2.66)*	*21.6 (4.68)*	*57.8 (19.53)*	
SO_2nadir	*86.87 (3.55)*	*82.58 (4.67)*	*74.87 (15.14)*	*0.0000**
N1	*10.63 (10.23)*	*13.35 (13.73)*	*18.37 (14.62)*	*0.0006**
N2	*67.78 (17.09)*	*62.85 (21.39)*	*63.32 (19.09)*	*0.4645*
N3	*15.11 (13.65)*	*17.7 (19.34)*	*12.84 (14.77)*	*0.2116*
REM	*6.21 (5.05)*	*6.08 (6.35)*	*5.41 (5.45)*	*0.6273*
WASO	*61.36 (38.01)*	*77.38 (66.92)*	*79.88 (60.47)*	*0.357*
Arousal	*21.03 (13.37)*	*22.18 (20.43)*	*33.2 (20.62)*	*0.0004**
WAKE	*6.65 (3.95)*	*8.6 (7.7)*	*12.02 (10.88)*	*0.0029**
Neck	*40.86 (2.92)*	*40.05 (3.04)*	*42.88 (3.62)*	*0.0002**
Waist	*100.9 (9.38)*	*99.31 (10.24)*	*109.86 (14.85)*	*0.0003**
Hip	*107.43 (9.18)*	*107.03 (9.37)*	*113.24 (12.22)*	*0.0096**
BMI	*28.97 (3.77)*	*29.38 (4.38)*	*32.4 (6.0)*	*0.0000**
WHR	*0.94 (0.06)*	*0.93 (0.07)*	*0.97 (0.05)*	*0.0182**
Castellani	*3.95 (1.02)*	*3.91 (1.02)*	*4.34 (1.42)*	*0.1278*
API	*0.35 (0.21)*	*0.36 (0.26)*	*0.48 (0.3)*	*0.0121**
LDL/HDL	*2.44 (0.86)*	*2.35 (0.81)*	*2.57 (1.11)*	*0.5783*
TG/HDL	*2.57 (1.45)*	*2.76 (1.87)*	*3.77 (2.6)*	*0.0054**

*Age expressed in years; biochemical parameters in mg/dl; AHI, arousal, wake in incidents per hour of sleep; neck, waist, hip circumference in cm; SO2nadir, NREM and REM in %; p values <0.05 are marked in bold numerals and *. lucose=serum glucose level, TG= serum triglyceride level, TC=serum total cholesterol level, HDL=serum high density lipoproteins level, LDL=serum low density lipoproteins level, AHI= apnoea/hypopnea index, SO_2nadir= the lowest saturartion level during sleep period , N1=duration of N1 sleep pahase as a percent of total sleep time, N2=duration of N2sleep pahase as a percent of total sleep time, N3=duration of N3 sleep pahase as a percent of total sleep time, REM=duration of REM sleep pahase as a percent of total sleep time, WASO=wake after sleep onset in minutes, Arousal=index of arousal incidents per hour, WAKE=index of wake incidents per hour, Neck=neck circumference in cm, Waist=waist circumference in cm, Hip=hip circumference in cm , BMI=body mass index, WHR=waist to hip cirumference ratio, Castellani=Castellani idex of plasma atherogenicity, API=API index of plasma atherogenicity*

RESULTS

The results of sleep analysis as well as the anthropometric and biochemical parameters regarding gender are presented in Table 1. The analysis revealed significant differences between females and males in the fasting glucose levels (p = 0.0027), HDL (p=0.0082), AHI (p=0.0351), relative duration of N2 (p=0.0016) and N3 phase (p=0.0003), neck circumference (p<0.0000), waist circumference (p=0.0001), WHR (p<0.0000), and BMI (p=0.0276).

To determine the impact of OSA severity on the individual parameters, subjects were divided into subgroups according to AHI. Group I included subjects with AHI index 5≤AHI≤ 15, group II with index 15<AHI≤30, and group III those with index AHI>30 (Table 2). Significant differences between these subgroups were found in TG, TG/HDL, BMI index, API SO2nadir, N1, arousal index, wake index, neck, waist, hip circumferences, and WHR. Group III was significantly different from both groups I and II in terms of TG levels (p=0.0324) and TG/HDL (p=0.0054). Furthermore, group III was significantly different from I and II in terms of BMI (p<0.0000) and API (p=0.0121). The parameter SO2nadir showed a significant difference be-

tween group III and I and II (p<0.0000), and between I and II (p= 0.0379). The relative duration of N1 phase in subjects in group III differed significantly from subjects in the remaining groups: I (p=0.0005) and II (p=0.0189). Similarly, the arousal index significantly differentiated group III from group I (p=0.0007), and II (p=0.002). Wake index was significantly different between group III and group I (p = 0.001) and II (p = 0.00316). Neck circumference was significantly different between group III and I (p=0.016) and II (p=0.0001). Waist circumference significantly differentiated group IV from II (p=0.0068) and II (p=0.0001); hip circumference group III from I (p = 0.0329) and II (p=0.0063); and the WHR between groups III and II (p=0.0028).

To determine the influence of body weight on the examined parameters the subjects were divided into three groups relating to the BMI: Group A included subjects with BMI≤25, group B with index 25<BMI≤ 30, and group C with BMI>30 (Table 3). Significant differences in ANOVA were found between mentioned groups in terms of AHI, SO2nadir, fasting glucose, N2, N3, HDL, TG, Castellani index, TG/HDL ratio, API index, circumference of the neck, waist and hips. Post hoc analysis showed significant differences between the group C and A and B separately in terms of: AHI (for both p<0.0000), glucose (p=0.0332 and p=0.019 respectively) and HDL (p=0.001 and p=0.0068 respectively). Significant differences between groups A and B, A and C showed the Castellani ratio (p=0.0279, p=0.0011 respectively). Between groups A and B, A and C, and B and C separately, the API index (p=0.001, p<0.0000, p=0.0001 respectively), TG (p=0.0165, p<0.0000, p=0.0001 respectively), as well as TG/HDL ratio (p=0.042, p<0.0000, p=0.0002 respectively) were significantly different.

Significant differences in SO2nadir parameter were found between groups C and A (p=0.0001) and B (p=0.0001). Relative duration of stage N2 in group I differed from group B (p=0.0044) and A from C (p=0.0023). As for relative duration of N3 the significant difference was noticed between groups A and B (p=0.0097) and between A and C (p=0.0054). Furthermore, the neck, waist and hip circumferences the differences were significant between each of the groups (p<0.0000). Correlation analysis showed many significant correlations in general, and between males and females (Table 4). A significant correlation has been proven between AHI and TG (positive), and HDL (negative). A positive correlation was also demonstrated between AHI and the anthropometric parameters: neck circumference, waist, hip, WHR and BMI. A model of stepwise regression created for HDL and for TG showed that among females as well as among males, and for all subjects in general, total explanatory variables are neck circumference for TG (β =0.406, p<0.0000) and the WHR ratio for HDL (β=0.33, p=0.0005). A model created for AHI as the dependent variable for OSA patients (AHI≥5), the explanatory variables were SO2nadir (β=-0.37, p<0.0000), arousal index (β=0.16, p=0.012), BMI (β=0.2, p=0.003), and TG/HDL (β=0.23, p<0.0000). With respect to the males, AHI as a dependent variable was determined mostly by SO2nadir (β=0.37, p<0.0000), and by the neck circumference (β=0.41, p<0.0000). In females, the strongest explanatory variable was also SO2nadir (β=-0.42, p=0.005), and the BMI index (β=0.33, p=0.025). Results of the final calculation of regression analysis are presented in Table 5.

DISCUSSION

A clinically significant correlations between AHI and the level of TG (0.19), and HDL (-0.21) were demonstrated, however this correlation was not strong. Atherogenic lipid profile is associated with a number of considerations than just the quality of sleep, therefore value of r>0.5 should not be expected. To support this statement it is worth mentioning that a similar relationship was found between AHI and the atherogenic plasma profile. Our rank correlation coefficients (Spearman) as well as linear (Pearson - not included in this paper) were comparable with the results of other authors. A significant correlation between the AHI count and the TG level (0.146) and a negative one with the level of HDL (-0.283) was found by Börgel et al. (1). Newman et al. (6) showed a negative correlation between AHI and HDL (-0.172)

The group of patients with severe OSA, however, also had significantly higher BMI compared to patients with milder forms of OSA. This may suggest that the atherogenic dyslipidemia is caused mainly by overweight/obesity that is very common in patients with OSA. The significantly higher neck, waist, and hip circumferences, as well as WHR ratio in patients with severe OSA compared to the other three groups (without OSA, mild and moderate OSA) also support this hypothesis. The relationship between OSA and serum lipids is not simply linear. According to some authors, OSA besides body mass is associated in particular with atherogenic LDL-B phenotype, but only in non-obese patients (19). The results of some other studies showed that there is no relationship between the levels of the

***Table 3**. Analyzed parameters in three studied groups of patients according to their BMI.*

Variable/ group	Group A BMI≤25 X (SD)	Group B 25>BMI≤30 X (SD)	Group C BMI>30 X (SD)	p value for ANOVA test
N	29	91	91	211
Glucose	94.85 (14.39)	99.48 (20.36)	107.55 (19.76)	0.0192*
TC	182.44 (34.73)	201.05 (36.68)	197.73 (44.2)	0.2111
TG	89.05 (46.77)	134.18 (65.08)	178.61 (83.47)	0.0000*
HDL	57.67 (14.21)	52.06 (13.93)	83.47 (11.35)	0.0009*
LDL	106.78 (34.8)	122.34 (32.23)	114.11 (39.41)	0.1569
AHI	19.36 (15.81)	28.85 (21.5)	45.07 (29.16)	0.0000*
SO_2nadir	86.3 (5.29)	82.85 (9.06)	76.15 (15.03)	0.0000*
N1	14.58 (14.43)	14.51 (13.83)	15.2 (11.86)	0.9318
N2	52.31 (20.42)	64.89 (18.58)	65.64 (18.24)	0.0076*
N3	23.8 (20.65)	14.23 (15.37)	13.59 (14.58)	0.0173*
REM	8.38 (5.97)	6.37 (5.65)	5.54 (5.57)	0.0911
WASO	79.46 (74.17)	71.53 (57.1)	84.92 (74.28)	0.4295
Arousal	26.68 (34.27)	23.76 (14.91)	30.83 (23.93)	0.1092
WAKE	7.05 (5.37)	9.04 (8.88)	11.95 (11.94)	0.0744
Neck	37.14 (3.24)	40.21 (2.36)	43.78 (3.44)	0.0000*
Waist	86.35 (7.98)	98.58 (6.64)	115.23 (12.65)	0.0000*
Hip	99.85 (4.26)	105.08 (5.78)	117.85 (12.11)	0.0000*
BMI	23.47 (1.54)	27.799 (1.41)	35.12 (4.64)	
WHR	0.86 (0.07)	0.94 (0.05)	0.98 (0.06)	0.0000*
Castellani	3.36 (1.11)	4.08 (1.15)	4.43 (1.35)	0.0034*
API	0.15 (0.27)	0.38 (0.25)	0.55 (0.27)	0.0000*
LDL/HDL	2.02 (0.97)	2.51 (0.92)	2.56 (1.05)	0.1088
TG/HDL	1.7 (1.05)	2.9 (2.02)	4.24 (2.58)	0.0000*

*Age expressed in years; biochemical parameters in mg/dl; AHI, arousal, wake in incidents per hour of sleep; neck, waist, hip circumference in cm; SO2nadir, NREM and REM in %; p values <0.05 are marked in bold numerals and *. Glucose=serum glucose level, TG= serum triglyceride level, TC=serum total cholesterol level, HDL=serum high density lipoproteins level, LDL=serum low density lipoproteins level, AHI= apnoea/hypopnea index, SO_2nadir= the lowest saturartion level during sleep period , N1=duration of N1 sleep pahase as a percent of total sleep time, N2=duration of N2sleep pahase as a percent of total sleep time, N3=duration of N3 sleep pahase as a percent of total sleep time, REM=duration of REM sleep pahase as a percent of total sleep time, WASO=wake after sleep onset in minutes, Arousal=index of arousal incidents per hour, WAKE=index of wake incidents per hour, Neck=neck circumference in cm, Waist=waist circumference in cm, Hip=hip circumference in cm , BMI=body mass index, WHR=waist to hip cirumference ratio, Castellani=Castellani idex of plasma atherogenicity, API=API index of plasma atherogenicity*

individual serum lipids and AHI. More important are the proportions of the individual components of the lipid profile (8-10). In this study, the significant parameters associated with the AHI were just TG/HDL ratio and API index, which are considered the most important for cardiovascular risk prediction.

Stepwise regression models constructed for AHI, HDL and TG showed that the values of these three parameters did not depend significantly on most of the sleep parameters (except arousal) but on the neck circumference, WHR ratio and BMI index. Our study did not confirm the initial assumptions about the relationship of atherogenic dys-

lipidemia with relative shortening of the duration of SWS or the wake index, showed in particular in the linear correlation analysis and stepwise regression model where the relative duration of SWS was not a significant explanation for the AHI parameter or serum lipid levels as dependent variables. However, it is known that SWS is a recovery period of intense cardiovascular and hormonal secretion, and its quality determines the level of leptin. Both obesity and OSA are significantly associated with a resistance to leptin, which may generate (by an unspecified mechanism) a reduction of airway muscle tension (20, 21). However, leptin levels did not significantly determine the value of the AHI alone, but only the association with BMI and percentage of fat in the body, which are the strongest predictors of OSA (22). Perhaps the calculated total time of slow-wave sleep, despite its considerable fragmentation induced by excitations, showed no differences large enough to reach a level of significance. This issue should be analyzed in larger number of EEG recordings.

WHR ratio, significantly higher in participants with severe OSA, puts these patients in the particularly high risk of cardiovascular disease group, because WHR is a strong predictor of these diseases (23, 24). Results of our study showed that patients with severe OSA differ significantly from patients with moderate and mild OSA in the level of TG and the ratio of TG/HDL and the API index. Thus, the limit of 30 apnea/hypopnea counts per hour of sleep is once again the rationale for the clinical classification of severe OSA. It should be noted that this group (III) had a significantly higher arousal index compared with other groups (I or II, or I and II together). Data in Table 4 show arousals incidents as not direct result of high AHI, since the coefficient of linear correlation between AHI and arousals was 0.46. It seems that the greatest impact on the quality of sleep is therefore the number of arousal incidents. Arousal index has a significant effect on the activity of the adrenergic system (25). Sleep fragmentation and repeated EEG excitation may also affect the ejection of free fatty acids (8). In this study, for analyzing all subjects as one group (but not for men and women separately) we identified a weak but statistically significant correlation between the arousal index and the level of TG (0.15). It should also be mentioned that in some subsets created during stepwise regression analysis, arousal index appeared as an equally strong explanatory variable for the TG levels as a dependent variable as BMI was. This may suggest the need for further clinical trials, in which the arousal index would be evaluated in conjunction with the secretion profile of selected hormones.

It seems that there are two distinct phenomena: incidents of arousal and incidents of apnea/hypopnea (measured with AHI and SO2nadir respectively), both causing sleep fragmentation. While respiratory incidents usually lead to arousals, the arousal incidents mainly lead to shallow sleep, interrupting a deep sleep, in particular REM and slow-wave. The correlation between the number of respiratory events with atherogenic lipid profile is well understood, but the fragmentation of sleep due to arousals is mentioned only as a possible cause of the activation of the hypothalamic-pituitary-adrenal axis. The authors did not find any data in the literature that would confirm a relationship between AHI and elevated TG and therefore increased atherogenic risk. This issue should be further investigated in a larger group of patients, and including sleep fragmentation index in each of its phases caused by arousals. The authors did not find any data in the literature analyzing patients with severe sleep apnea and proving them in particular vulnerable of developing cardiovascular diseases. In those patients, the lipid levels and atherogenic indexes are very abnormal. In our study, the arousal incidents in this group of patients were found to be significantly more frequent. Probably AHI> 30 is a certain limit, and above it, the sleep fragmentation is so serious that normal homeostatic functioning of the organism is no longer possible.

In conclusion, the most important parameters of the quality of sleep that determine atherogenic risk are AHI and arousal index that are significantly correlated with TG/HDL ratio. Particularly high risk of cardiologic problems applies to patients with AHI>30 who substantially differ in terms of lipid profile from the patients with mild or moderate OSA. Arousal index significantly distinguishes patients with AHI> 30 from the other groups of patients.

Ethical standarts statement: All the patients gave their informed consent to participate in the study. The Ethics Committee Review Board at the Medical University of Warsaw approved the study protocol. Conflictof interest statement: The authors state that there is no conflict of interest including any financial interest or financial support to be disclosed.

REFERENCES

1. *Börgel J, Sanner BM, Bittlinsky A, et al. Obstructive sleep apnoea and its therapy influence high-density lipoprotein cholesterol serum levels. Eur Respir J 2006;27:121-7*
2. *Marin JM, Carrizo SJ, Vicente E, et al. Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: an observational study. Lancet 2005;365:1046-53*

Table 4. Values of Spearman's rank order coefficients in all patients (without any subdivisions). Significant correlations are marked in bold numerals.

	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
Age	**0,25**	-0,10	-0,06	0,10	**-0,13**	**0,12**	**-0,20**	**0,24**	0,01	**-0,24**	-0,07	**0,24**	**0,17**	**0,25**	-0,03	-0,02	-0,04	0,02	0,03	**-0,17**	-0,09	**-0,17**	-0,09
Glucose		-0,02	**0,33**	**-0,17**	-0,08	**0,19**	**-0,21**	0,10	0,03	**-0,20**	0,04	0,07	**0,20**	0,05	**0,46**	**0,34**	**0,26**	**0,29**	**0,35**	0,11	**0,31**	0,02	**0,31**
TC			**0,31**	**0,16**	**0,92**	-0,06	0,07	-0,09	0,12	-0,02	-0,05	-0,09	0,05	-0,10	-0,06	-0,06	-0,07	0,02	0,04	**0,49**	**0,17**	**0,58**	**0,17**
TG				**-0,52**	**0,16**	**0,19**	**-0,13**	0,04	0,02	-0,08	-0,01	0,07	**0,15**	**0,14**	**0,46**	**0,42**	**0,32**	**0,42**	**0,35**	**0,66**	**0,94**	**0,43**	**0,94**
HDL					0,01	**-0,21**	**0,16**	0,02	0,01	-0,03	0,03	-0,12	-0,02	**-0,18**	**-0,31**	**-0,31**	-0,17	**-0,26**	**-0,31**	**-0,75**	**-0,76**	**-0,61**	**-0,76**
LDL						-0,10	0,10	**-0,16**	0,12	0,05	-0,05	-0,13	-0,02	**-0,15**	-0,18	-0,14	-0,14	-0,06	-0,02	**0,58**	0,12	**0,75**	0,12
AHI							**-0,70**	**0,32**	-0,01	**-0,21**	**-0,15**	0,09	**0,46**	**0,27**	**0,43**	**0,46**	**0,46**	**0,37**	**0,26**	0,12	**0,21**	0,03	**0,21**
SO_2nadir								**-0,25**	0,05	0,11	**0,13**	-0,12	**-0,34**	**-0,24**	**-0,27**	**-0,43**	**-0,43**	**-0,44**	**-0,24**	-0,08	**-0,14**	-0,02	**-0,14**
N1									**-0,35**	**-0,39**	0,07	**0,34**	**0,39**	**0,40**	**0,22**	0,16	0,09	0,07	**0,19**	-0,10	0,03	**-0,14**	0,03
N2										**-0,54**	**-0,43**	-0,11	**-0,23**	**-0,15**	0,10	0,05	0,06	0,12	0,01	0,08	0,02	0,09	0,02
N3											**0,13**	**-0,17**	**-0,14**	**-0,23**	**-0,19**	-0,11	-0,05	-0,10	-0,13	0,04	-0,06	0,08	-0,06
REM												**-0,15**	0,01	**-0,18**	-0,04	-0,11	-0,13	**-0,17**	-0,02	-0,08	-0,03	-0,07	-0,03
WASO													**0,23**	**0,76**	0,12	0,13	0,10	0,14	0,12	0,02	0,10	-0,04	0,10
Arousal														**0,35**	**0,25**	**0,24**	0,17	**0,17**	**0,23**	0,03	0,11	-0,02	0,11
WAKE															**0,19**	**0,23**	**0,20**	**0,17**	**0,19**	0,06	**0,17**	-0,02	**0,17**
Neck																**0,79**	**0,57**	**0,67**	**0,69**	**0,21**	**0,46**	0,04	**0,46**
Waist																	**0,80**	**0,84**	**0,72**	**0,23**	**0,43**	0,08	**0,43**
Hip																		**0,79**	**0,23**	0,12	**0,30**	0,00	**0,30**
BMI																			**0,50**	**0,21**	**0,41**	0,09	**0,41**
WHR																				**0,25**	**0,37**	0,16	**0,37**
Castellani																					**0,78**	**0,93**	**0,78**
API																						**0,56**	1,00
LDL/HDL																							**0,56**
TG/HDL																							

Glucose=serum glucose level, TG= serum triglyceride level, TC=serum total cholesterol level, HDL=serum high density lipoproteins level, LDL=serum low density lipoproteins level, AHI= apnoea/hypopnea index, SO_2nadir= the lowest saturartion level during sleep period , N1=duration of N1 sleep pahase as a percent of total sleep time, N2=duration of N2sleep pahase as a percent of total sleep time, N3=duration of N3 sleep pahase as a percent of total sleep time, REM=duration of REM sleep pahase as a percent of total sleep time, WASO=wake after sleep onset in minutes, Arousal=index of arousal incidents per hour, WAKE=index of wake incidents per hour, Neck=neck circumference in cm, Waist=waist circumference in cm, Hip=hip circumference in cm , BMI=body mass index, WHR=waist to hip cirumference ratio, Castellani=Castellani idex of plasma atherogenicity, API=API index of plasma atherogenicity

***Table 5**. Results of calculations of final models for stepwise regression analysis for TG and HDL as dependent variables; p values <0.05 are marked in bold numerals and *.*

A summary of the dependent variable regression: Trigl R= .40607806 R^2= .16489939 Corr. R2= .15776178, F(1.117)=23.103 p<.00000 Estimation error: 75.266						
n: 210	*BETA*	*Error*	*B*	*Error.*	*t(117)*	*p value*
Polynominal			*-250.621*	*83.72*	*-2.994*	*0.0034**
Neck	*0.406*	*0.08*	*9.602*	*2.00*	*4.807*	*0.0000**
A summary of the dependent variable regression: HDL ; R= .32967012 R^2= .10868239 Corr. R2= .10035232, F(1.107)=13.047 p<.00046 Estimation error: 11.035						
n: 210	*BETA*	*Error*	*B*	*Error*	*t(107)*	*p value*
Polynominal			*110.963*	*17.04*	*6.510*	*0.0000**
WHR	*-0.330*	*0.09*	*-64.019*	*17.72*	*-3.612*	*0.0005**

3. *Roche F, Sforza E, Pichot V, et al. Obstructive sleep apnoea/hypopnea influences high-density lipoprotein cholesterol in the elderly. Sleep Med 2009;10:882-6*
4. *McArdle N, Hillman D, Beilin L, Watts G. Metabolic risk factors for vascular disease in obstructive sleep apnea: a matched controlled study. Am J Respir Crit Care Med 2007; 175:190-5*
5. *Muraki I, Tanigawa T, Yamagishi K, et al. Nocturnal intermittent hypoxia and metabolic syndrome; the effect of being overweight: the CIRCS Study. J Atheroscler Thromb 2010;17:369-377*
6. *Newman AB, Nieto FJ, Guidry U, et al. Sleep Heart Health Study Research Group. Relation of sleep-disordered breathing to cardiovascular disease risk factors: the Sleep Heart Health Study. Am J Epidemiol 2001;154:50-9*
7. *Drager L, Jun J, Polotsky VY. Obstructive sleep apnea and dyslipidemia: implications for atherosclerosis. Curr Opin Endocrinol Diabetes Obes 2010;17:161-5*
8. *Coughlin SR, Mawdsley L, Mugarza JA, et al. Obstructive sleep apnoea is independently associated with an increased prevalence of metabolic syndrome. Eur Heart J 2004;25:735-41*
9. *Irwin M, Thompson J, Miller C, et al. Effects of sleep and sleep deprivation on catecholamine and interleukin-2 levels in humans: clinical implications. J Clin Endocrinol Metab 1999; 84:1979-85*
10. *Tan KC, Chow WS, Lam JC, et al. HDL dysfunction in obstructive sleep apnea. Atherosclerosis 2006;184:377-82*
11. *Chin K, Shimizu K, Nakamura T, et al. Changes in intra-abdominal visceral fat and serum leptin levels in patients with obstructive sleep apnea syndrome following nasal continuous positive airway pressure therapy. Circulation 1999;100:706-12*
12. *Dorkova Z, Petrasova D, Molcanyiova A, et al. Effects of continuous positive airway pressure on cardiovascular risk profile in patients with severe obstructive sleep apnea and metabolic syndrome. Chest 2008;134:686-92*
13. *Bixler EO, Vgontzas AN, Lin HM, et al. Prevalence of sleep-disordered breathing in women: effects of gender. Am J Respir Crit Care Med 2001;163:608-13*
14. *Comondore VR, Cheema R, Fox J, et al. The impact of CPAP on cardiovascular biomarkers in minimally symptomatic patients with obstructive sleep apnea: a pilot feasibility randomized crossover trial. Lung 2009; 187:17-22*
15. *Bonnet MH, Arand DL. Hyperarousal and insomnia: state of the science. Sleep Med Rev 2010;14: 9-15.*
16. *Buckley TM, Schatzberg AF. On the interactions of the hypothalamic-pituitary-adrenal (HPA) axis and sleep: normal HPA axis activity and circadian rhythm, exemplary sleep disorders. J Clin Endocrinol Metab 2005;90: 3106-14.*
17. *Golbidi S, Badran M, Ayas N, Laher I. Cardiovascular consequences of sleep apnea. Lung 2012;190: 113-32.*
18. *Millán J, Pintó X, Muñoz A, et al. Lipoprotein ratios: Physiological significance and clinical usefulness in cardiovascular prevention. Vasc Health Risk Manag 2009;5:757-65*
19. *Luyster FS, Kip KE, Drumheller OJ, et al. Sleep apnea is related to the atherogenic phenotype, lipoprotein subclass B. J Clin Sleep Med 2012;8:155-61*
20. *O'Donnell CP, Schwartz AR, Smith PL. Upper airway collapsibility. The importance of gender and adiposity. Am J Respir Crit Care Med 2000;162:1606-7.*
21. *O'Donnell CP, Tankersley CG, Polotsky VP, et al. Leptin, obesity, and respiratory function. Respir Physiol 2000;119:163-70*
22. *Schäfer H, Pauleit D, Sudhop T, et al. Body fat distribution, serum leptin, and cardiovascular risk factors in men with obstructive sleep apnea. Chest 2002;122:829-39*
23. *Seidell JC, Perusse L, Despres JP, et al. Waist and hip circumference have independent and opposite effects on cardiovascular disease risk factors: the Quebec Family Study. Am J Clin Nutr 2001;74:315-21*
24. *Snijder MB, Zimmet PZ, Visser M, et al. Independent and opposite associations of waist and hip circumferences with diabetes, hypertension and dyslipidemia: the AusDiab Study. Int J Obes Relat Metab Disord 2004;28:402-9*
25. *Narkiewicz K, Somers VK. Sympathetic nerve activity in obstructive sleep apnoea. Acta Physiol Scand 2003;177:385-90*