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Relationship between age and cardiovascular complications in obstructive sleep apnoea

Abstract

Introduction: Obstructive sleep apnoea (OSA) is a risk factor for cardiovascular morbidity and mortality. The aim of this study was to assess relations between cardiovascular diseases (CVD) and age in OSA subjects.

Material and methods: Consecutive OSA subjects (AHI/RDI > 10, Epworth score > 9 points) were evaluated. The chest X-ray, spirometry, arterial blood gases, ECG, blood morphology and biochemistry were performed during trial treatment with autoCPAP.

Results: We studied 533 consecutive OSA patients, mean age 55.6 ± 10.3 years (range 24–81), with obesity (BMI 34.4 ± ± 6.6 kg/m^2) and severe OSA (AHI/RDI 37.8 ± 21.8). To evaluate relations between CVD and age, patients were divided into three groups. Group 1 < 50 years (123 subjects, 23.1%), Group 2 aged 50–60 years (250 subjects, 46.9%) and Group 3 > 60 years (160 subjects, 30%). Subjects < 50 years were more obese and had higher AHI/RDI when compared to older groups. Incidence of arterial hypertension, coronary artery disease, atrial fibrillation, heart failure and stroke increased with age (higher in subjects > 60 years).

Conclusions: Cardiovascular diseases were prevalent in OSA patients > 60 years. However the youngest group presented with more severe obesity and higher AHI/RDI.

Key words: obstructive sleep apnoea, cardiovascular complications, age

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Introduction

Previous epidemiological studies confirmed that respiratory disturbances during sleep (RDDS) are more frequent among elderly people (from 30% to 80%) than among middle age subjects (4% of men and 2% of women). In middle age RDDS occurs about twice as often among men as among women. In older age groups (men > 60–65 years and women after menopause without hormonal substitutive therapy — HTZ) the frequency of RDDS occurrence is similar in both sexes [2–4].

Ancoli-Israel et al. [5] assessed RDI occurrence among persons over 65 years in a group of 427 people. Respiratory disturbance index (RDI) > 5 was confirmed among 81% of the study's participants; 62% of the group (70% of men and 56% of women) had RDI > 10. RDDS risk factors: high index of body mass (BMI) and sex (RDDS was more often diagnosed among men).

Elsewhere, the same authors studied relations between the RDDS occurrence and age among 233 occupants of a foster home (151 men and 82 women). The average age was 83.5 ± 8.5 years for women and 79.7 ± 7.5 years for men. RDI > 5 was diagnosed among 70% of subjects, (68% of women and 76% of men).

Bixler et al. [4, 7] assessed the influence of age on the frequency of RDDS occurrence in the po-

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pulation of men and women (1000 women and 741 men over 20 years were chosen to PSG study). The RDDS occurred more than twice as often in the oldest group of men and women (65–100 years) compared to middle aged patients (46–64 years). Among men, AHI ≥ 10 was diagnosed among 23.9% of subjects aged between 65–100 and 11.8% of subjects aged 45–64. Among women AHI ≥ 15 was confirmed in 7% of subjects aged 65–100 and in 2% of subjects aged 45–64. On the basis of polisomnography and daily symptoms, OSA was diagnosed among 3.9% of men and 1.2% of women. The OSA frequency was low among women before menopause (0.6%) and among these who were taking HTZ (0.5%). Among women who were undergoing their menopause without HTZ, the RDDS frequency was significantly higher and amounted to 2.7% ($p = 0.02$).

Bigger differentiation in the RDDS frequency in middle and old age patients were diagnosed by Spanish authors [8, 9]. In these works, two populations were studied: the first aged between 30–70 and the second aged 71–100. AHI ≥ 5 was diagnosed/found among 81% of men and 80% of women aged 30–70. AHI ≥ 15 was diagnosed among 57% of men and 49% of women in the older group and among 14.2% of men and 7% of middle age women.

In Cleveland Family Study [10] the RDDS occurrence was compared among men and women in the following age groups: 25–60 years and > 60 years. AHI ≥ 15 was diagnosed among 4% of women in the first group and 32% of those in the second group and among 22% and 42% of men respectively.

In the Sleep Heart Health Study (SHHS) the percentage of persons with AHI ≥ 15 in the age group between 60–99 years was 1.7 times bigger than among subjects aged 40–60 [11].

The aim of this study is to assess the relations between age and the degree of OSA progression and between obesity and cardiovascular diseases.

Material and methods

During the first consultation, subjects filled in a questionnaire about respiratory disturbances during sleep (the questionnaire referred to such symptoms as snoring, sleep apnoeas, awakening, daily sleepiness [the Epworth Sleepiness Scale or ESS], morning fatigue, nycturia and co-existing diseases, applied drugs, laryngological operations experienced, and smoking). Polisomnography (PSG) was made using Somnostar α (Sensormedics, USA) and Alice 5 (Respironics, USA) equipment. Some people were subjected to polygraphical examination (without the estimation of sleep phases) with the use of apparatus PolyMesam (MAP, Germany). A description of the above studies is presented in another work [12].

AHI/RDI which was associated with excessive daily sleepiness (SSE > 9) was assumed as a criterion for diagnosing OSA [7].

Some 533 people suffering from OSA (412 men, 77.3% and 121 women, 22.7%) aged between 24 and 81 (the average age was 55.6 plus or minus 10.3) were examined. The subjects suffered from moderate and severe forms of the disease (the average AHI/RDI — 37.8 ± 21.8).

Chest spirometry, ECG, arterial blood gasometry and basic blood examinations were made among patients during the hospitalization connected with OSA using autoCPAP apparatus.

Co-existing diseases were diagnosed according to criteria described below.

Arterial hypertension was diagnosed in cases of positive history (previously prescribed hypotensive drugs) and/or increased blood pressure during repetitive measurements. Ischaemic heart disease was diagnosed on the basis of the history (coronary ailments, applied treatment) and/or diagnosed changes in ECG (post-infarction scar. Left bundle branch block — after excluding other reasons — trails of ischemia). Decisive factors in the diagnosis of cardiac insufficiency were: historic data (results of previous examinations from cardiologic/ /internistic units); effort dyspnoea — II–IV class according to NYHA; objective examination — peripheral oedemas; traits of pulmonary haemostasis completed with results of actual echocardiography (ejection fraction < 50% or end-diastolic function) and roentgenoscopy of chest (extended heart silhouette, Karley's lines). Endured stroke was diagnosed on the basis of previous examination results and medical documentation from internistic and neurological units.

The diagnosis of chronic obstructive pulmonary disease (COPD) was confirmed after making spirometry (FEV_1%FVC < low range of norm and negative end-diastolic test) which was most often completed with typical history (chronic cough, effort dyspnoea, exposure to cigarette smoke).

Diabetes was diagnosed when the following factors occurred: glycemia on empty stomach twice > 125 mg% or 'incidental' glycemia > 200 mg% or glycemia > 200 mg% in the 75 g glucose load test (diabetes was diagnosed and was healing before confirmation of OSA among most of the people suffering from diabetes). Hypertriglyceridemia, hypercholesterolemia and mixed hyperlipidemia were diagnosed if: triglycerides concentration in fasting state exceeded 160 mg%, total cholesterol concentration in fasting state was > 200 mg%

and when both criteria occurred at the same time. Hyperuricemia was diagnosed when uric acid concentration in blood serum in fasting state exceeded 5.7 mg% in women and 7 mg% in men.

Statistical analysis

The results obtained were analyzed with the help of statistical program Statistica 6.0. The results of research were presented as mean and standard deviations. The qualitative differences between studied variables were estimated with Pearson's χ^2 test or in Yates's and Fisher's modification for groups of fewer people. The quantitative differences between studied variables in selected sub-groups of patients were estimated with the ANOVA test. The multiple regression test was used to select variables, which significantly influenced AHI/RDI value.

Results

The average index of apneas and shallow-breathing AHI/RDI amounted in the whole group to 37.8 ± 21.8 episodes for an hour of sleeping during the PSG examination and registration time during the PolyMesam examination. The average arterial blood saturation with oxygen (SaO_2 mid.) was 90.3 ± 5.1%. The lowest arterial blood saturation with oxygen (SaO_2 min.) was 74 ± 12%. The subjects were spending almost one third of the night in oxygen deficiency. Most subjects were overweight or obese and had an average BMI of 34.4 ± 6.6 kg/m^2. The score on the Epworth scale was on average 11.9 ± 5.7 (the norm is 9; the range of scale is 0–24).

Diseases of the cardiovascular system were often diagnosed in this subject group. Arterial hypertension was diagnosed in 381 patients and 126 suffered from ischemic heart disease. Heart failure was diagnosed in 63 persons (11.8%). Auricular fibrillation (periodic or fixed) was diagnosed in 45 patients (8.4%). Nineteen subjects (3.6%) had suffered a stroke.

COPD was diagnosed in 91 subjects (17.1%). Among metabolic disorders hypercholesterolemia was most often diagnosed: 251 subjects (47.2%); 230 subjects (43.2%) had hypertriglyceridemic; mixed hyperlipidemia was diagnosed in 149 (28%) and hyperuricemia was diagnosed in 202 (38.5%). Diabetes was confirmed in 87 patients (16.3%).

To assess the relationship between age and the degree of OSA progression, obesity and cardiovascular disease, the subjects were divided into three sub-groups according to age. The first group consisted of 123 patients (23.1%) aged < 50 years, the second of people aged 50–60 (250 people, 46.9%), and the third aged > 60 years (160 people, 30%).

The progression of OSA in the age groups

The highest AHI/RDI values and the highest score on the Epworth scale were found in the youngest age group. In all groups, the average BMI exceeded 30 kg/m^2 (the lowest was in the third group). Minimal and average SaO_2 were lowest, and time of night oxygen deficiency/anoxia (T90) the shortest, in the oldest group. The results of PSG/Poly-Mesam examination, BMI and Epworth scale of sleepiness in the age groups are presented in Table 1.

Co-existing diseases

Arterial hypertension, ischemic heart disease and auricular fibrillation were most often diagnosed in the third group and most rarely in the first group. Significant differences were found between all groups. Similar results were observed for heart failure (significant differences only between groups 1 and 3) and stroke (in the first group nobody had a stroke and significantly important differences were between groups 1 and 2 and groups 1 and 3). Detailed results are presented in Table 2.

Table 1. Comparison of PSG/PolyMesam, BMI, Epworth score in age groups 1, 2 and 3

Variable	Group 1	Group 2	Group 3	p
BMI [kg/m^2]	35.5 ± 7*	35.1 ± 6.6$^{\#}$	32.3 ± 5.7*$^{\#}$	*p = 0.0003 $^{\#}$p = 0.0004
AHI/RDI (n/h)	44 ± 24.8*	38.8 ± 21.2$^{\#}$	31.4 ± 18.4*$^{\#}$	*p < 0.0001 $^{\#}$p = 0.005
Mean SaO_2 (%)	89.9 ± 5.6	89.9 ± 5.2*	91.3 ± 4.2*	*p = 0.045
Lowest SaO_2 (%)	74.4 ± 11.5	73 ± 13	75.4 ± 10.6	NS
T90 (%)	35.5 ± 31.5*	33 ± 31.2	25.8 ± 27.3*	p = 0.03
Epworth Sleepiness Score (points)	13.4 ± 5.6*	12.6 ± 5.6$^{\#}$	9.7 ± 5.2*$^{\#}$	*p < 0.0001 $^{\#}$p < 0.0001

Explanations of abbreviations in the text

Table 2. Cardiovascular diseases in groups 1, 2 and 3

Variable	Group 1	Group 2	Group 3	p
Arterial hypertension (n/%)	70 (56.9%)*#	182 (72.9%)*	129 (80.6%)#	*p = 0.002 #p = 0.00002
Coronary artery disease (n/%)	8 (6.5%)*#	53 (21.2%)*+	65 (40.6%)#+	*p = 0.0003 #p < 0.0001 +p < 0.0001
Heart failure (n/%)	8 (6.5%)*	28 (11.2%)	27 (16.9%)*	*p = 0.008
Atrial fibrillation (n/%)	2 (1.6%)*#	20 (8%)*+	23 (14.4%)#+	*p = 0.01 #p = 0.0001 +-p = 0.04
Stroke (n/%)	0 (0%)*#	8 (3.2%)*	11 (6.9%)#	*p = 0.04 #p = 0.003

Explanations of abbreviations in the text

Table 3. Other concomitant diseases in groups 1, 2 and 3

Variable	Group 1	Group 2	Group 3	P
COPD (n/%)	14 (11.4%)	47 (18.8%)	30 (18.8%)	NS
Diabetes (n/%)	11 (8.9%)*#	47 (18.8%)*	29 (18.1%)#	*p = 0.01 #p = 0.03
Hypertriglicerydaemia (n/%)	62 (50.4%)*	116 (46.4%)#	52 (32.7%)*#	*p = 0.002 #p = 0.007
Hypercholesterolaemia (n/%)	62 (50.4%)*	128 (51.2%)#	61 (38.4%)*#	*p = 0.04 #p = 0.01
Mixed hyperlipidaemia (n/%)	40 (32.5%)*	80 (32%)#	29 (18.2%)*#	*p = 0.004 #p = 0.003
Hyperuricaemia (n/%)	52 (42.6%)	93 (37.8%)	57 (36.5%)	NS

Diabetes was diagnosed significantly more often in groups 2 and 3 compared to group 1. COPD was most rarely diagnosed in the first group (the differences between groups were not statistically significant). Hypercholesterolemia, hypertriglyceridemia and mixed hyperlipidemia were significantly more often diagnosed in groups 1 and 2 than in group 3. Hyperuricemia was diagnosed most often in group 1, but the differences were not statistically significant. Detailed results are presented in Table 3.

Lung function tests

The results of FVC and FEV_1 (expressed in percentage of predicted value) were similar in all groups. FEV_1%FVC was significantly higher in group 1. PaO_2 measured during the day (while breathing with atmospheric air) was also significantly higher in group 1. The results of spirometry and gasometry are presented in Table 4.

The analysis of multiple regression (the following factors were taken into consideration in the model: BMI, sex, age, SSE, neck circumference, COPD, ischaemic heart disease, arterial hypertension, heart failure, auricular fibrillation, diabetes) showed significant correlations ($R = 0.49$, $R^2 = 0.24$) between AHI/RDI and BMI ($\beta = 0.37$, $p < 0.0001$), Epworth scale ($\beta = 0.12$, $p = 0.01$) and age ($\beta = 0.12$, $p = 0.02$).

Discussion

Among the 533 suffering from OSA, the most severe forms of the disease were diagnosed among patients aged under 50 years and cardiovascular complications were most often found among subjects aged over 60 years.

Previous results of epidemiologic studies confirm more frequent occurrence of RDDS among older age groups [1, 2, 4, 5, 7–10]. The results of studies pertaining to RDDS's influence on the occurrence of cardiovascular complications and death rate in elderly age are unequivocal.

Bliwise et al. [13] observed 198 subjects over 12 years (average age 66 ± 8.2 years). Among subjects with RDDS confirmed (RDI > 10) the risk of

Table 4. Comparison of spirometry and arterial blood gases in groups 1, 2 and 3

Variable	Group 1	Group 2	Group 3	P
FVC (%n)	94.2 ± 16.5	93.4 ± 18.1	95.7 ± 18.1	NS
FEV_1 (%n)	89.6 ± 17.2	87.8 ± 19.8	90.3 ± 21.1	NS
FEV_1%FVC (%)	77.2 ± 7.4*#	74.2 ± 8.1*	72.2 ± 9.1#	*p = 0.01 #p < 0.0001
PaO_2 [mm Hg]	74.1 ± 9.1*#	70 ± 8.2*	71.2 ± 8.4#	*p < 0.0001 #p = 0.02
$PaCO_2$ [mm Hg]	39.2 ± 3.9	39.5 ± 4.2	39.2 ± 4.6	NS

Explanations of abbreviations in the text

death was 2.7 times higher in comparisson with subjects without respiratory disturbances during sleep. Cardiovascular diseases were most often the death cause in this subject group.

Ancoli-Israel et al. [14] analyzed death causes among 426 elderly persons (average age while beginning the study 72.5 years). Subjects with RDI > 30 lived significantly shorter than persons with RDI ≤ 30 (p = 0.0034). The independent factors of death risk were age, diseases of the circulatory system/ /cardiovascular system and of the respiratory system.

He et al. [15] evaluated the survival time among 385 sufferers from OSA over eight years. Those with advanced forms of the disease (AI > 20 than AI < 20; p < 0.05), who were not treated for OSA, died significantly more often. The above phenomenon was especially found among those aged under 50 (significant differences in the length of survival were observed between the second and eighth year of observation). In the group of patients aged over 50, a significant influence of AI > 20 on survival shortening was found only in the eighth year of observation.

Lavie et al. [16] studied the RDDS influence on the general death rate in a large group of 14 589 men aged between 20 and 93 years. The average length of observation was 4.6 years. The subjects with RDI > 30 had a significantly higher risk of death in comparison to persons with RDI ≤ 10. The biggest death rate was observed among obese patients (BMI ≥ 31) with RDI > 40 (11.47/1000 persons/year). In the group of people with RDI > 30, after considering age, a significantly higher risk of death was found in the group aged 20–29 years — hazard ratio (HR) 5.8 (95% CI, 1.45–23.42) and among those ≥ 80 years — HR 1.92 (95% CI, 1.19––3.09) in comparison to control groups selected according to age. In the group of patients with RDI > 50 the increased risk of death in comparison to the general population was stated for the following age groups: 20–29, 30–39, 40–49 years (HR was appropriately 9.8% [95% CI, 2.44–39.25], 3.12 [95% CI, 1.17–8.35] and 1.89 [95% CI, 1.04–3.44]).

According to some authors, OSA is an independent (also from age) risk factor of arterial hypertension, ischaemic heart disease and stroke [17]. However in other studies, the RDDS influence on the development of cardiovascular diseases was not confirmed.

Philips et al. [18] observed a group of 82 healthy persons aged between 50 and 80 over five years. After the first polisomnography, AHI > 5 was diagnosed in 16 subjects. After five years, control examinations were done among 42 persons (including ten people with AHI > 5 from the initial examination). Neither a significant increase in BMI nor blood pressure among people with AHI < 5 and AHI > 5 were observed.

Enright et al. [19] assessed the relation between snoring, apnoea's occurrence and the functioning of the circulatory system in 5201 people > 65 years. Snoring was declared by 33% of men and 19% of women; apnoeas were observed among 13% of men and 4% of women. Snoring, observed apnoeas and daily excessive sleepiness were not in the subject group connected with arterial hypertension nor other diseases of the cardiovascular system.

Hass et al. [20] assessed the influence of age on arterial hypertension occurrence among 6120 subjects participating in the Sleep Heart Health Study (SHHS). The authors compared two groups of subjects: the first consisting of 2477 people aged between 40–59 years, and the second of people aged 60 and above. In the first group, significant connections between AHI and arterial hypertension were diagnosed (for AHI from 15 to 39.9, OR was 2.38, 95% CI, 1.30–4.38; for AHI ≥ 30 OR was 2.24, 95% CI, 1.10–4.54). In the group of subjects ≥ 60 years the connections between AHI and arterial hypertension were not observed.

Other studies of RDDS, with a sizeable proportion of persons over 60 years of age, confirm more

frequent occurrence of cardiovascular diseases among elderly people [21–26].

Nieto et al. [21] studied the connections between RDDS and arterial hypertension in the group of 6132 people ≥ 40 years (46.7% of them were persons ≥ 65 years; SHHS). The subjects with AHI ≥ 30, in comparison to persons with AHI < 1.5, had a 1.37 times bigger risk of arterial hypertension occurrence (p = 0.005) (after considering body mass, neck circumference, waist index, cigarette smoking, alcohol consumption). The subjects ≥ 65 years (AHI ≤ 30 vs. AHI < 1.5, (after considering sex and race) had a 1.69 times greater risk of arterial hypertension.

Peker et al. [22] assessed OSA occurrence in a group of 62 diseased in middle age, who were admitted to an intensive care unit because of ischemic heart disease exacerbation and among 62 subjects from a control group (chosen according to age, sex and BMI). OSA (RDI ≥ 10) was found among 19 people with ischemic heart disease exacerbation and among eight persons from the control group (p = 0.017). The analysis of multifactorial regression showed that actual cigarette smoking (OR 4.2, 95% CI, 1.1–17.1) and OSA (OR 3.1, 95% CI, 1.2–8.3) were independent factors of CVD risk.

Yaggi et al. [23] examined at the risk of a stroke and death among 697 subjects with confirmed OSA (average age 60.9, average AHI 35) and in a control group of 325 people (average age 58.7, average AHI 2). After having concidered age, sex, race, cigarette smoking, alcohol consumption, BMI, occurrence of diabetes, arterial hypertension, hyperlipidemia and atrial fibrillation, OSA was a significant factor of stroke or death risk (HR 1.97, 95% CI, 1.12–3.48, p = 0.01).

Stohs et al. [24] examined 140 men in older age suffering from arterial hypertension. RDDS (RDI > 10) was found among 80% of subjects and RDI > 30 was diagnosed among 34%. Subjects who had been diagnosed with episodes of raised blood pressure despite the application of hypotensial drugs had significantly higher RDI index (p = 0.047).

Zamarron et al. [25] studied RDDS occurrence in 76 people aged 50–70. RDDS (AHI ≥ 5) was diagnosed among 28.9% of subjects. The subjects with RDDS had significant higher systolic blood pressure (p < 0.05).

In another study, the hypoxemia influence on vessels endothelium damage and development of cardiovascular complications was diagnosed among older patients. Nieto et al. [26] assessed relations between OSA and disorders of endothelium vessels functions in the group of 1037 SHHS study participants > 68 years. The authors studied the diastolic activity of a brachial artery stimulated by brachial flow-mediated vasolidation. The authors observed significant correlations between the time spent in oxygen deficiency < 90% and initial arterial average (p < 0,01). The relations listed above were strongest among those aged < 80 years and among subjects with arterial hypotension.

Conclusions

In the group of 533 patients with moderate or severe OSA, the most severe form of the disease was diagnosed among patients aged under 50, who at the same time had higher BMI than the other groups. The frequency of cardiovascular complications occurring increased with age (diseases of cardiovascular systems were most often diagnosed among subjects > 60 years).

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