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## Prevalence of metabolic syndrome diagnosis in patients with obstructive sleep apnoea syndrome according to adopted definition

Częstość rozpoznawania zespołu metabolicznego u chorych na obturacyjny bezdech senny w zależności od zastosowanej definicji

The Authors declare no financial disclosure.

### Abstract

**Introduction:** Metabolic syndrome (MS), which is connected with enlarged cardiovascular risk, is common in patients with OSAS. The aim of the study was to estimate the prevalence of MS in patients with OSAS according to two definitions of MS (criteria from NCEP-ATP III from 2001 versus criteria from IDF 2005).

**Material and methods:** Materials consisted of 155 males and 18 females with OSAS (mean AHI  $44 \pm 22 \text{ h}^{-1}$ ), obesity (BMI  $31.8 \pm 5.0 \text{ kg/m}^2$ ), aged  $53.9 \pm 9.3$  years (mean  $\pm$  SD). Serum lipids, glucose, body mass index (BMI), waist circumference (WC) and waist-to-hip ratio (WHR) were measured in all patients.

**Results:** According to first definition (NCEP — ATP III from 2001), MS was diagnosed in 98 patients (56% of the whole group — MS1 group) compared to 120 patients (69% of the whole group — MS2 group) diagnosed according to the second definition (IDF from 2005),  $p < 0.05$ . No differences in BMI and WC between the groups were found. Significant differences in WHR were noted (MS1 group:  $1.005 \pm 0.05$  vs. MS2 group:  $1.027 \pm 0.06$ ,  $p < 0.05$ ). Patients from the MS2 group had higher cholesterol HDL compared to the MS1 group ( $52.3 \pm 12.1 \text{ mg/dl}$  vs.  $42.3 \pm 12.1 \text{ mg/dl}$ ,  $p < 0.05$ ). Serum triglyceride concentrations were significantly higher in the MS1 group than in the MS2 group ( $228 \pm 122 \text{ mg/dl}$  vs.  $122 \pm 49 \text{ mg/dl}$ ,  $p < 0.05$ ). There were no differences in OSAS severity between the MS1 and MS2 group. In both groups weak correlations between diagnosis of MS and AHI were found ( $r = 0.19$  for MS1 and  $r = 0.21$  for MS2,  $p < 0.05$ ) They are, however, clinically insignificant.

**Conclusions:** The IDF definition from 2005 of metabolic syndrome indeed increases the frequency of diagnosis of metabolic syndrome in patients with OSAS. We did not observe essential clinical correlation among the degree of OSAS severity and recognition of metabolic syndrome in the MS1 or in the MS2 group.

**Key words:** definition, metabolic syndrome, obstructive sleep apnoea

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### Streszczenie

**Wstęp:** Zespół metaboliczny (ZM) jest związany ze zwiększonym ryzykiem chorób sercowo-naczyniowych i występuje często u chorych na OBS.

Celem pracy jest ocena częstości ZM w zależności od zastosowanej definicji (NCEP-ATP III z 2001 oraz IDF z 2005 roku) u chorych na OBS.

**Materiał i metody:** Materiał stanowiło 155 mężczyzn i 18 kobiet z OBS (AHI  $44 \pm 22 \text{ h}^{-1}$ ), w większości otyłych (BMI  $31,8 \pm 5,0 \text{ kg/m}^2$ ), w wieku  $53,9 \pm 9,3$  roku (średnie  $\pm$  SD).

U badanych oznaczano w surowicy: lipidogram, stężenie glukozy oraz wykonano pomiar wskaźnika masy ciała (BMI), obwodu w pasie (OP) oraz wskaźnik talia-biodra (WHR).

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**Wyniki:** Postępując się definicją pierwszą (NCEP-ATP III z 2001), zespół metaboliczny rozpoznano u 98 chorych (56% całej grupy — grupa ZM1), stosując definicję IDF z 2005 — u 120 osób (69% całej grupy — grupa ZM2) ( $p < 0,05$ ). Pomiedzy grupami nie stwierdzono istotnych różnic wielkości BMI i OP. Natomiast statystycznie istotną różnicę stwierdzono w WHR (ZM1:  $1,005 \pm 0,05$  v. ZM2:  $1,027 \pm 0,06$ ,  $p < 0,05$ ). W grupie ZM2 stwierdzono istotnie wyższe stężenie HDL w porównaniu z grupą ZM1 ( $52,3 \pm 12,1$  mg/dl v.  $42,3 \pm 12,1$  mg/dl,  $p < 0,05$ ). W grupie ZM1 istotnie wyższe w porównaniu z grupą ZM2 było stężenie triglicerydów w surowicy ( $228,2 \pm 122,5$  mg/dl v.  $122,5 \pm 49,1$  mg/dl,  $p < 0,05$ ). Grupy ZM1 i ZM2 nie różniły się istotnie stopniem ciężkości OBS. Zaobserwowano korelacje pomiedzy rozpoznaniem zespołu metabolicznego a wartością AHI ( $r = 0,19$  dla ZM1 i  $r = 0,21$  dla ZM2,  $p < 0,05$ ). Są one jednak klinicznie nieistotne.

**Wnioski:** Definicja zespołu metabolicznego IDF z 2005 roku istotnie zwiększa częstość rozpoznawania zespołu metabolicznego u chorych na OBS. Nie zaobserwowano znamienych klinicznie korelacji pomiedzy stopniem ciężkości OBS a rozpoznaniem zespołu metabolicznego.

**Słowa kluczowe:** definicja, zespół metaboliczny, obturacyjny bezdech senny

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## Introduction

Metabolic syndrome (MS) is a significant cause of development of cardiovascular system diseases and type 2 diabetes [1]. It doubles the risk of cardiovascular diseases and increases the risk of development of type 2 diabetes by five times [2]. Several definitions of this syndrome have been elaborated in recent years. In the USA in 2001 the Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (NCEP-ATP III) used for the first time clinical aspects in the definition of metabolic syndrome [3]. According to the NCEP-ATP III criteria, diagnosis of MS is based on the occurrence of at least three out of five components of the syndrome, such as: elevated fasting plasma glucose (or previously diagnosed type 2 diabetes), abdominal obesity measured by waist circumference, elevated triglycerides, decreased HDL-cholesterol and increased arterial blood pressure (Table 1). In 2005 the International Diabetes Federation (IDF) proposed a new definition (Table 1) based on the assumption that the presence of abdominal obesity and, additionally, two out of four remaining components, as defined in the NCEP-ATP III definition, are necessary conditions for the diagnosis of metabolic syndrome. While evaluating abdominal obesity the IDF definition considers racial and ethnic factors and assumes different criteria for the European and for the Asian population (except for the Japanese) [4]. A value over 100 mg% was assumed as impaired fasting plasma glucose, and it was also assumed that patients treated for dyslipidaemia, hyperglycaemia or type 2 diabetes and arterial hypertension meet criteria for diagnosis of metabolic syndrome.

In 2005 the American Heart Association (AHA) and National Heart, Lung and Blood Institute (NHLBI) took into account the position of IDF and presented the modified NCEP-ATP III definition of 2001 [5]. It took into consideration recommendations of IDF concerning ethnic differences and distinguished separate criteria for obesity for people of American or Asian origin. A value over 100 mg% was also assumed as impaired fasting glycaemia, and the possibility of diagnosis of metabolic syndrome was also allowed in patients with dyslipidaemia, hyperglycaemia or arterial hypertension. The main difference between the NCEP-ATP III and IDF definitions was still an obligatory incidence of abdominal obesity in the latter (Table 1).

In 2009 the IDF, NHLBI, AHA, World Heart Federation (WHF), International Atherosclerosis Society (IAS) and International Association for the Study of Obesity (IASO) published a common statement concerning the definition of metabolic syndrome [6]. Consensus among the organizations assumed that in order to diagnose metabolic syndrome three out of five previous IDF criteria would be sufficient, without the necessity of obesity perceived as a main criterion. This definition is presently recommended and used.

In 1998 Wilcox attached metabolic syndrome (syndrome X) to OSAS and created the notion of syndrome Z [7]. Metabolic syndrome occurs from 5 to 9 times more frequently in patients with OSAS than in control groups [8, 9], and its prevalence varies from 19% among the snoring population in Korea to 87% of patients with OSAS in Great Britain [10]. The majority of studies report that the prevalence of metabolic syndrome in patients with OSAS reaches 30–77% and it increases together with severity of OSAS [8, 11–15]. Many researchers [10] showed an independent relation between OSAS and hyperinsulinaemia and

**Table 1. Definitions of metabolic syndrome (NCEP-ATP III i IDF)**

Definition of MS	NCEP-ATP III 2001 Presence of $\geq 3$ of the following:	IDF 2005 WC above the presented limit plus any 2 of the following:
Abdominal obesity	WC: F: $\geq 88$ cm M: $\geq 102$ cm	WC: F: $\geq 80$ cm M: $\geq 94$ cm
Triglycerides	$\geq 150$ mg% (1.7 mmol/l)	$\geq 150$ mg% (1.7 mmol/l) or taking medication for lipid disorder
HDL-C	HDL-C F: $< 50$ mg/dl (1.03 mmol/l) M: $< 40$ mg/dl (1.29 mmol/l)	HDL-C F: $< 50$ mg/dl (1.03 mmol/l) M: $< 40$ mg/dl (1.29 mmol/l) or taking medication for lipid disorder
High blood pressure (BP)	BP $\geq 130/\geq 85$ mm Hg	BP $\geq 130/\geq 85$ mm Hg or diagnosis of hypertension
Fasting plasma glucose (FPG)	FPG $\geq 110$ mg/dl ( $\geq 6.1$ mmol/l)	FPG $\geq 100$ mg/dl ( $\geq 5.6$ mmol/l) or diagnosis of diabetes type 2

F — female, M — male; abbreviations in the text

lipid metabolism disorders. Most of them show a significant correlation between Apnea-Hypopnea Index (AHI) and the occurrence of metabolic syndrome; however, such a relationship was not observed between transient hypoxaemia and MS [10, 16]. Due to the fact that AHI in patients with OSAS correlates with visceral fat tissue more strongly than with BMI, it was suggested that obstructive sleep apnoea was an element of metabolic syndrome [17]. One of the studies demonstrated that symptoms such as loud snoring and excessive daytime sleepiness may be predictors of development of metabolic syndrome, and OSAS is its inherent element [18]. Therefore, an appropriate definition of metabolic syndrome used for early diagnosis and treatment of MS in patients with OSAS seems to be a significant clinical problem.

The aim of this study was to assess the prevalence of metabolic syndrome in patients with OSAS depending on the applied definition of MS (the one formulated by the NCEP-ATP III in 2001 or that specified by the IDF in 2005), and to try to evaluate which of them correlates better with OSAS severity, and which one is a better clinical tool to diagnose metabolic syndrome in this group of patients.

### Material and methods

The examined group was selected from the patients of the Clinic of Sleep-Disordered Breathing in the Autonomous Public Clinical Hospital in Warsaw. All patients gave consent to their participation in the research. Additionally, a physical examination consisted of measurement of waist-to-hip ratio with the use of standard me-

thod, i.e. measurement of waist circumference (in centimetres) in half the distance between the lower edge of the ribs and the upper iliac crest, and hip circumference (in centimetres) indicating the widest measurement at the height of the greater trochanter [19]. Based on these two values, the waist-to-hip ratio (WHR) was defined. The degree of obesity was determined by body mass index (BMI) according to the WHO classification [20]. Metabolic syndrome was diagnosed pursuant to the NCEP-ATP III definition of 2001 and the IDF definition of 2005 [3, 4].

### Diagnostics of OSAS

A polysomnography test (PSG) was executed with the help of Alice 4 apparatus from RESPIRONICS, USA. After the test, qualified laboratory staff verified the results of the automatic analysis by using the software supplied by the producer.

The tests were conducted between 11 p.m. and 6 a.m. the following day, in a soundproof room. They were supervised by a physician or a trained student of the faculty of medicine of the Medical University of Warsaw. OSAS was diagnosed based on the criterion defined in the report of the American Academy of Sleep Medicine (AASM) [21], i.e. total apnoea-hypopnoea index (AHI)  $\geq 5$  episodes of breathing disorders during one-hour sleep in the case of typical symptoms of OSAS, or  $\geq 15$  episodes of breathing disorders during sleep without characteristic of ailments of this disease. A total of 155 men and 18 women with mean age  $53.9 \pm 9.3$  years were examined, with AHI  $44.3 \pm 22.1$  h<sup>-1</sup> and BMI  $31.8 \pm 5.0$  kg/m<sup>2</sup>. Arterial hypertension was diagnosed in 94 patients, 53 were treated for dyslipidaemia and 13 for type 2 diabetes.

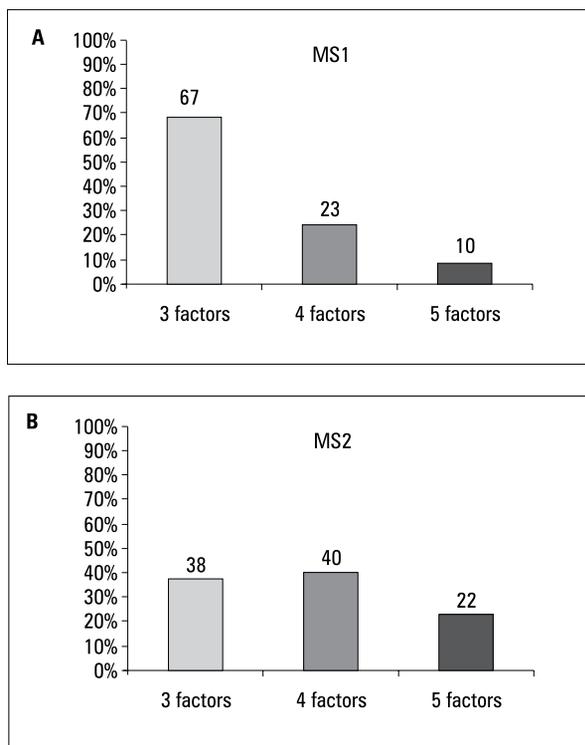
In order to determine glucose and lipidogram, all examined patients had fasting venous blood samples taken after a full night's rest. Determinations were taken in the Central Laboratory of the Autonomous Public Clinical Hospital in Warsaw using suitable methods.

### Statistical analysis

Statistical analysis of the obtained data was made with the help of the program StatSoft, Inc. (2007) STATISTICA (data analysis software system), version 8.0. www.statsoft.com. To compare independent groups, due to the parameter values that assume rank or nominal values, non-parametric Mann-Whitney U tests were employed. The tables include the values concerning nominal variables, given as mean  $\pm$  SD (standard deviation). Relations between two nominal or rank variables, or between one nominal and a second ordinal value, were calculated with the use of Spearman's rank correlation. When two variables were qualitative or binary, Chi-square contingency table analysis was applied, and in a special case for the table  $2 \times 2$  (consisting of two rows and two columns) depending on calculated expected values, a version of this test with McNemar's alteration was used. In order to define the compatibility of the two definitions of metabolic syndrome, the Kappa coefficient was calculated.

### Results

Based on the first definition (NCEP-ATP III of 2001), metabolic syndrome was diagnosed in 98 patients (56% of the whole group — the MS1 group) in comparison to 120 patients (69% of the whole group — the MS2 group) diagnosed according to the IDF definition of 2005,  $p < 0.05$ . The value of the Kappa coefficient at the level of 0.71 proves the high compatibility of the two methods, and a significant result of McNemar's test, i.e.  $p < 0.001$ , suggests that these definitions assess the prevalence of metabolic syndrome in a different way. All criteria of the NCEP-ATP III were met by 10 out of 98 patients (10.2%) and in the case of the IDF definition — by 26 out of 120 patients (21.7%) (Fig. 1). The most frequent criterion was abdominal obesity: in the case of the NCEP-ATP III definition it was diagnosed in 90 out of 98 patients (91.8%). In the IDF definition it is an obligatory criterion. The most frequent among the four remaining criteria was hypertriglyceridaemia (in 104 out of 120 patients — 86.6%). Significant differences in the occurrence of metabolic syndrome depending on definition were also influenced by glucose concentration (impaired fasting plasma



**Figure 1.** Prevalence of metabolic syndrome including the number of its components

glucose was diagnosed in 37 patients (37.7%) according to the NCEP-ATP III definition, and in 70 patients (58.3%) according to the IDF definition). However, the absolute values of glucose did not differ (Table 2). A statistically significant difference was discovered in the WHR values (MS1:  $1.005 \pm 0.05$  vs. MS2:  $1.027 \pm 0.06$ ,  $p < 0.05$ ).

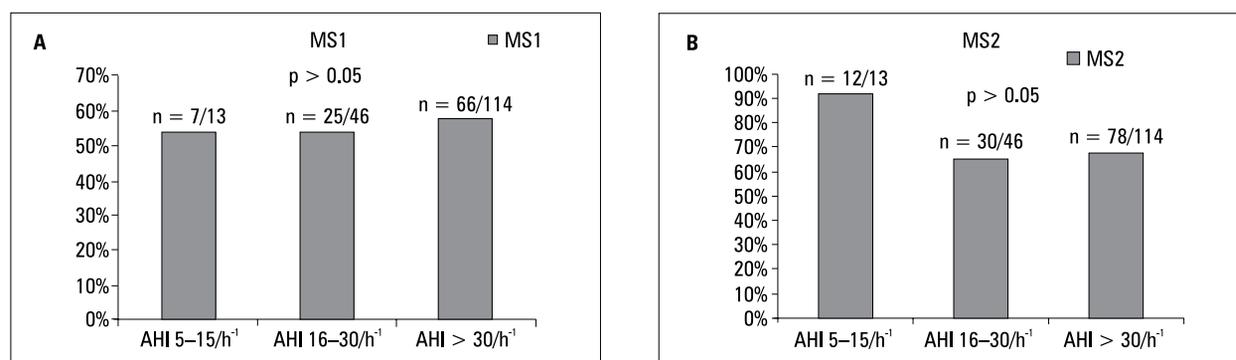
A significantly higher concentration of HDL was noted in the MS2 group in comparison with the MS1 group ( $52.3 \pm 12.1$  mg/dl vs.  $42.3 \pm 12.1$  mg/dl,  $p < 0.05$ ). Triglyceride concentration in serum was significantly higher in the MS1 group than in the MS2 group ( $228.2 \pm 122.5$  mg/dl vs.  $122.5 \pm 49.1$  mg/dl,  $p < 0.05$ ).

After division of groups MS1 and MS2 into 3 subgroups according to OSAS severity — mild (AHI  $5-15/h^{-1}$ ), moderate (AHI  $16-30/h^{-1}$ ) and severe (AHI  $> 30$ ) — it was discovered that the prevalence of metabolic syndrome did not depend on OSAS severity, irrespective of the applied MS definition (Fig. 2). Merely weak, clinically insignificant correlations between diagnosis of metabolic syndrome and AHI were noted ( $r = 0.19$  for MS1 and  $r = 0.21$  for MS2,  $p < 0.05$ ). The occurrence of MS1 correlated significantly with minimal saturation (min SaO<sub>2</sub>) and mean saturation during sleep (mean SaO<sub>2</sub>) ( $r = 0.15$  for min SaO<sub>2</sub>,  $r = 0.18$  for mean SaO<sub>2</sub> during sleep,  $p < 0.05$ ). Similar dependencies were not observed in

**Table 2. Demographic data of the study subjects**

Variables	MS1 group	MS2 group	P
Age (yrs)	55.2 ± 8.9	52.6 ± 8.7	ns
Sex (M/F)	86/12	107/13	ns
AHI (h <sup>-1</sup> )	45.7 ± 22.5	44.6 ± 22.7	ns
Systolic BP [mm Hg]	128 ± 14	127 ± 14	ns
Diastolic BP [mm Hg]	81 ± 10	80 ± 10	ns
WC [cm]	112.3 ± 10.8	110.7 ± 11	ns
WHR	1.005 ± 0.05	1.027 ± 0.06	P < 0.05
BMI [kg/m <sup>2</sup> ]	33.4 ± 8.4	32.8 ± 7.8	ns
FPG [mg/dl]	107.2 ± 28.7	106.1 ± 27.9	ns
HDL-C [mg/dl]	52.3 ± 12.1	42.3 ± 12.1	P < 0.05
TG [mg/dl]	228.0 ± 122.0	122.0 ± 49.0	P < 0.05

F — female, M — male; abbreviations in the text



**Figure 2.** Differences in prevalence of MS1 and MS2 in mild, moderate and severe OSAS patients

MS2; however, in this case correlation with excessive sleepiness measured with the use of the Epworth sleepiness scale (ESS) occurred ( $r = 0.2$ ,  $p < 0.05$ ).

## Discussion

The IDF definition of metabolic syndrome of 2005 significantly influenced the prevalence of metabolic syndrome in OSAS patients. If the NCEP-ATP III definition of 2001 had been used, metabolic syndrome would not have been diagnosed in 22 (12.7%) patients among the study subjects, and the appropriate measures would not have been adopted. Although we did not note significant strong correlations between degree of severity of OSAS and diagnosis of metabolic syndrome, a higher prevalence of metabolic syndrome in the study subjects with OSAS (56% according to the NCEP-ATP III and 69% according to IDF) compared to the population of adult Poles suggests that there is some relation between MS and OSAS. On the grounds

of the NATPOL III research it was estimated that the prevalence of metabolic syndrome in Poles above 18 years of age reaches 20% according to the criteria of the NCEP-ATP III of 2001 [22]. In the WOBASZ research (Polish National Multicentre Research on the Population's Health) of 2005 the NCEP-ATP III criteria of 2001 were met by 19.5% of men and 18.6% of women, and according to the modified criteria of 2005, metabolic syndrome was observed in 23% of men and 20% of women [23].

In the present paper the prevalence of MS in OSAS patients was 56% according to the NCEP-ATP III definition and 69% according to the IDF definition of 2005.

Lam et al. [11] used the NCEP-ATP III definition of 2005 and they diagnosed MS in 58% of patients with OSAS. Sasanabe et al. [12] noted the presence of metabolic syndrome in 50% of 819 examined OSAS patients. While Kono et al. [24] diagnosed MS (the NCEP-ATP III definition of 2005) in just 19% of patients with OSAS.

Peled et al. also noted a smaller prevalence of MS than in the present paper. Using the NCEP-ATP III definition of 2001, they discovered MS in 30% of examined severe OSAS patients [13]. However, Coughlin et al. [9] discovered MS (the NCEP-ATP III definition of 2001) in 87% of examined severe OSAS patients.

A higher prevalence of MS (the IDF definition of 2005) in OSAS patients than in the present paper was given by Tkacova et al. [15]: MS was diagnosed in 77% of patients with AHI > 30. Similar results based on the same definition were obtained by Gruber et al. [8] (74% of the study subjects were diagnosed with MS). Available literature does not provide thus far any comparison of the two definitions of MS (NCEP and IDF) in OSAS patients or assessment of their clinical usefulness.

These differences seem to be significant in population studies, and typically different prevalences of MS are obtained, depending on the applied definition. In the NHANES research [25] conducted in the USA between 1992 and 2002 on a group of 3601 people, the occurrence of MS was noted in 34.5% of the studied population (the NCEP-ATP III definition) in comparison to 39% (the IDF definition). In the Greek population [26] the presence of MS was diagnosed in 24.5% of the 9669 adults, according to the NCEP-ATP III definition in comparison to 43.4% when the IDF definition was applied. Mancina et al. [27] stated that the IDF definition is more sensitive than the NCEP-ATP III definition while diagnosing metabolic syndrome, which allows the early introduction of appropriate measures.

We did not observe significant dependence of the occurrence of MS on the degree of severity of OSAS; only weak correlations between AHI and MS occurred. Diagnosis of MS1 correlated significantly but also weakly with min SaO<sub>2</sub> and mean SaO<sub>2</sub>; in the case of MS2 a characteristic dependence on ESS was discovered.

Parts of the mentioned reports confirm the relation between OSAS and MS. In the study conducted by Peled et al. [13] the prevalence of MS was increasing together with severity of OSAS; moreover, a significant dependence of MS and AHI and min SaO<sub>2</sub> was noted. In the research conducted by Sasanabe et al. [12] a correlation between the degree of OSAS severity and prevalence of MS was discovered (the Japanese definition). In the study carried out by Gruber et al. [8] OSAS was connected independently with the presence of metabolic syndrome, and the prevalence of MS (IDF 2005) was 5.9 times greater in the group of

OSAS patients than it was in the control group. Kono et al. [24] discovered a significant relation between the occurrence of MS and AHI but not with min SaO<sub>2</sub>. In the study conducted by Grandi et al. [28] there was no significant difference in occurrence of MS (the NCEP-ATP III definition of 2005) in mild, moderate or severe forms of OSAS, and the prevalence of MS amounted to 68.7%, 72.2% and 68.4%, respectively. In the recently published study by Bonsignore et al. [29] significant correlations of MS (the IDF definition of 2009) and AHI were observed, but when multiple factor analysis was used a significant dependence on AHI was noted only for arterial hypertension.

To sum up, it seems that defining metabolic syndrome in OSAS patients with the use of the IDF definition is justified by the greater sensitivity of this method, which enables more frequent diagnosis of MS in this group of patients. The relation between OSAS and MS remains unexplained and needs further thorough studies.

### Conflict of interest

The Authors declare no conflict of interest.

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