Advs Exp. Medicine, Biology - Neuroscience and Respiration (2019) 43: 35–41
https://doi.org/10.1007/5584_2019_376

Published online: 1 May 2019

Anthropometric Factors in the Assessment of Obstructive Sleep Apnea Risk in Patients with Metabolic Syndrome

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Abstract

Metabolic syndrome (MetS) and obstructive sleep apnea (OSA) are related to a higher incidence of cardio-vascular diseases and mortality in patients. The aim of the study was to define the potential use of anthropometric factors for the evaluation of OSA risk in patients with diagnosed MetS. The patient group consisted of 50 obese men with MetS (mean age 49 ± 9 years). The following anthropometric indices were assessed: body mass index (BMI), neck circumference (NC), waist circumference (WC), and waist-to-hip ratio (WHR). In addition, blood glucose and lipid profile were investigated. On the basis of polysomnography, clinical symptoms, and Epworth Sleep Scale, patients were stratified into the OSA group accompanied by MetS (n = 31) and the MetS alone group taken as control (n = 19). OSA was evaluated as severe in 26 out of the 31 patients (>30 apneic episodes *per* hour). We found a significantly larger NC in the OSA with MetS group then that in the MetS alone group. Further, NC associated with the increase in the apnea/hypopnea index. However, the other anthropometric indices investigated failed to differentiate the two groups. We conclude that increased neck circumference in patients suffering from metabolic syndrome is a risk factor for the development of OSA.

Keywords

Anthropometry · Apnea hypopnea index · Metabolic syndrome · Neck circumference · Obesity · Obstructive sleep apnea

1 Introduction

Obstructive sleep apnea (OSA) is a disease based on a multiple repetitions of closure (apnea) or restriction of airflow (hypopnea) through the upper respiratory tract. Untreated OSA affects both length and quality of life of patients. As a result, the disease contributes to the accident rate related to daytime sleepiness and it also increases a risk of serious cardio-vascular and metabolic events. The population cohort studies have estimated the frequency of OSA at 17–24% in

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men and 5–9% in women (Bixler et al. 2001; Bixler et al. 1998; Young et al. 1993), with a growing tendency of 14–55% related to an increasing number of obese people (Peppard et al. 2013). OSA is diagnosed in about 60% of patients suffering from metabolic syndrome (MetS) (Drager et al. 2010). The incidence of MetS is especially high in the patients diagnosed with OSA. In such patients, MetS is found 6–9 times more often than in the general population, due possibly to the shared risk factors for both diseases (Gruber et al. 2006; Coughlin et al. 2004). The mechanisms underlying the development of cardiovascular diseases in both MetS and OSA are similar (Vgontzas et al. 2005; Coughlin et al. 2001). Patients with OSA also more often suffer from alterations that characterize MetS (Gami and Somers 2004; Shamsuzzaman et al. 2003). Thus, hypertension with accompanying sympathetic activation, increased waist circumference, lipid and carbohydrate metabolism disorders, insulin resistance, endothelial dysfunction, general pro-inflammatory propensity, and rheological properties of blood disorders are commonly observed in OSA patients (Tażbirek et al. 2011). In order to emphasize the common pathogenetic pathways in OSA and MetS, the term 'Z syndrome' has been coined (Wilcox et al. 1998).

Both OSA and MetS are closely related to obesity. In case of MetS, an increased waist circumference, associated with the accumulation of adipose tissue is one of the diagnostic criteria. The importance of obesity as a risk factor for OSA has been shown in both population and clinical studies. Approximately 70% the population with body mass index (BMI) $\geq$ 40 kg/m^2 suffer from OSA (Young et al. 1993). The Wisconsin Sleep Cohort Study has revealed that an increase of body weight by 10% in patients with mild OSA yields a sixfold increase in the risk of the appearance of moderate or severe OSA (Peppard et al. 2000). Not only the accumulation of adipose tissue but also its distribution is important for OSA development. A golden standard for the diagnosis of OSA is a polysomnography examination, but it remains of rather limited availability due to involved labor intensity and expenses. Therefore, in the present study we set out to determine whether and which anthropometric obesity characteristics present in patients with MetS could be useful in the optimization of the risk assessment for OSA development.

2 Methods

2.1 Patients and Measurements

The study encompassed 50 male patients, diagnosed with MetS who were hospitalized due to a suspicion of breathing disorders during sleep. Patients were stratified into the OSA group accompanied by MetS (mean age 49.4 $\pm$ 8.8 years; n = 31) and the MetS only group taken as control (mean age 47.1 $\pm$ 6.9 years; n = 19). OSA was diagnosed on the basis of polysomnography examination and clinical symptoms according to the American Academy of Sleep Medicine criteria (AASM 2014). The apnea-hypopnea index (AHI) criterion for OSA was $\geq$4.9 episodes per hour of sleep. Metabolic syndrome was defined as the presence of at least three of the following criteria: (1) waist circumference of $\geq$94 cm; (2) fasting triglycerides (TG) $\geq$150 mg/dL or hypertriglyceridemia treatment; (3) fasting high density lipoprotein (HDL) cholesterol <40 mg/dL; (4) systolic blood pressure $\geq$ 130 mmHg and/or diastolic blood pressure $\geq$ 85 mmHg, or treatment of previously diagnosed hypertension; and (5) fasting glycemia $\geq$100 mg/dL (Jaspinder 2014). The following anthropometric measurements were made at the level of the thyroid: body mass index (BMI), waist circumference (WC), and neck circumference (NC).

2.2 Polysomnography

Polysomnography was conducted in a sleep laboratory, using an Alice (Respironics Inc., Monroeville, PA) sleep diagnosing setup. Computerized data were reanalyzed manually by a trained clinician. Disturbances of sleep

architecture and breathing during sleep were diagnosed according to the AASM (2014) and the Polish Society of Lung Diseases (Pływaczewski et al. 2013) recommendations. Apnea was defined when there was a 90% or greater reduction in airflow, accompanied by a respiratory effort lasting for 10 s or longer. Hypopnea was defined as a 30% or greater reduction in airflow, accompanied by a persistent respiratory effort lasting for 10 s or more and associated with desaturation of 3% or greater. OSA severity was determined by AHI defined as a summary number of obstructive apneas and hypopneas *per* hour of sleep. The severity of OSA was defined as mild, moderate, and severe by AHI of 5–14.9, 15–29.9, and $\geq$ 30 episodes/h, respectively.

2.3 Statistical Analysis

Data were expressed as means ±SD. The Shapiro–Wilk test was used to test normality of data distribution. A two-tailed *t*-test was used for comparisons of normally distributed data and the Mann–Whitney U test for not normally distributed data. The Spearman rank test was used to assess associations between independent parameters. A p-value <0.05 defined statistically significant inter-group differences. The analysis was performed using a commercial Statistica package (StatSoft; Tulsa, OK).

3 Results

Polysomnography results in the patients with OSA accompanied by MetS and in those with MetS alone are shown in Table 1. The mean ESS score in the OSA-MetS group was inappreciably different from that in the MetS alone group. Daytime sleepiness (EES >10 points) was found in 20 (64.5%) and 11 (57.9%) patients in the respective groups. The mean AHI in the OSA-MetS group was 45.1 ± 16.2/h, minimum level of nighttime SaO_2 (SaO_{2min}) of 70.5 ± 10.6%, and the percent of nighttime spent at SaO_2 < 90% was 41.9 ± 3.8%, while in the MetS alone group, AHI was 2.2 ± 1.5/h, SaO_{2min} of 86.2 ± 6.7%, and the percent of nighttime spent at SaO_2 below 90% was 2.2 ± 2.9%; the inter-group differences between the corresponding variables were highly significant ($p < 0.00001$). According to the AHI criteria

Table 1 Polysomnographic characteristics in patients with obstructive sleep apnea (OSA) accompanied by metabolic syndrome (MetS) and in patients with MetS alone

Parameter	OSA with MetS (n = 31)	MetS (n = 19)
AHI ($hour^{-1}$)	45.0 ± 16.2	2.16 ± 1.5**
SaO_2 (%)	90.0 ± 5.1	95.7 ± 1.9**
SaO_{2min} (%)	70.5 ± 10.6	86.2 ± 6.7**
SaO_2 (%)	90.0 ± 5.1	95.7 ± 1.9**
SaO_2 < 90% (%)	41.9 ± 3.8	2.2 ± 2.9**
AI ($hour^{-1}$)	48.4 ± 15.8	11.6 ± 8.0**
REM (%)	5.5 ± 3.6	12.6 ± 7.6*
Non-REM1 (%)	28.8 ± 9.5	25.3 ± 13.1
Non-REM2 (%)	43.8 ± 10.8	39.5 ± 17.9
Non-REM3 (%)	1.9 ± 1.8	5.9 ± 5.8*
ESS	12.5 ± 5.8	11.6 ± 4.3

Data are means ±SD

AHI apnea-hypopnea index, *SaO_2* arterial oxygen saturation; *SaO_{2min}* minimum level of nighttime arterial oxygen saturation, *SaO_2 < 90%* percent of nighttime spent at SaO_2 below 90%, *AI* arousal index – number of arousals *per* hour of sleep, *REM* rapid eye movement sleep stages – percent of sleep time spent at a given sleep stage, *ESS* Epworth sleepiness scale

*p < 0.001; **p < 0.00001

outlined in the methodological section, severe OSA was diagnosed in 26 (83.8%) and moderate in 5 (16.1%) patients. A significantly higher arousal index (AI) *per* hour of sleep and a decrease in the percent of time spent in in REM sleep also were noticed. Disturbed sleep architecture was accompanied by a tendency for shorter non-REM 3 and 4 sleep phases. The OSA-MetS and MetS alone groups did not differ in terms of total cholesterol (TC), LDL, HDL, or TG, and blood glucose levels (Table 2). CRP, however, was significantly higher in the former group. There were no appreciable relationships among AHI, SaO_{2min}, percent of nighttime spent at $SaO_2 < 90\%$, and metabolic parameters.

Concerning the anthropometric measurements we noticed an outstandingly greater neck circumference in OSA-MetS than that MetS alone group; neck circumference was greater, on average, by more than 3 cm in the former group ($p < 0.001$). The other parameters, such as height, body mass, BMI, and WC, were not different between the two groups (Table 3). In addition, neck circumference associated with the severity of OSA, positively with the AHI index ($r = 0.37$; $p = 0.02$) and inversely with SaO_{2min} ($r = -0.26$; $p = 0.03$).

4 Discussion

The major finding of this study was that patients with OSA accompanied by MetS significantly differed from those with MetS alone on one essential count, which was a greater neck circumference. Further, neck circumference was associated with the severity of OSA. Therefore, increased neck circumference in patients suffering from metabolic syndrome could be considered as a risk factor for the development of OSA. Apart from the desaturation and enhanced AHI and AI indices, pathognomonic for OSA, there were hardly any other distinguishing features between the OSA-MetS and MetS alone patients. Both groups had similar changes in the main anthropometric indices of obesity, lipid and

Table 2 Laboratory characteristics in patients with obstructive sleep apnea (OSA) accompanied by metabolic syndrome (MetS) and in patients with MetS alone

Parameter	OSA with MetS (n = 31)	MetS (n = 19)
TC (mg/dL)	202.9 ± 40.4	203.6 ± 47.4
LDL (mg/dL)	123.4 ± 30.3	120.9 ± 30.9
HDL(mg/dL)	36.3 ± 7.3	41.2 ± 10.4
TG (mg/dL)	218.3 ± 102.4	190.6 ± 84.3
Glucose (mg/dL)	92.5 ± 24.2	99.5 ± 25.7
C-reactive protein (mg/L)	7.2 ± 4.4	4.3 ± 2.7*

Data are means ±SD
TC total cholesterol, *LDL* low density lipoprotein, *HDL* high density lipoprotein, *TG* triglycerides
*p < 0.01

Table 3 Demographic and anthropometric data in patients with obstructive sleep apnea (OSA) accompanied by metabolic syndrome (MetS) and in patients with MetS alone

Parameter	OSA with MetS (n = 31)	MetS (n = 19)
Age (years)	49.4 ± 8.8	47.1 ± 6.9
Height (cm)	171.6 ± 5.8	173.5 ± 6.6
Body mass (kg)	105.1 ± 19.0	100.0 ± 15.5
BMI (kg/m^2)	35.7 ± 6.2	33.1 ± 3.8
WC (cm)	119.6 ± 14.9	116.3 ± 14.0
NC (cm)	46.2 ± 3.2	43.0 ± 2.6*

Data are means ±SD
BMI body mass index, *WC* waist circumference, *NC* neck circumference
*p < 0.001

glucose blood profiles, or daytime sleepiness. Likewise, both groups suffered from disordered sleep architecture, which appeared somehow worse in OSA-MetS in terms of shorter REM and non-REM3 sleep phases compared with MetS alone.

A growing percentage of obese people results in increased incidence of OSA as well as metabolic syndrome (Gaines et al. 2018; Formiguera and Canton 2004), which contributes to cardiovascular morbidity. A co-occurrence of OSA and MetS is common in clinical practice. Metabolic syndrome is diagnosed in 23–80% patients with obstructive sleep apnea (Bonsignore et al. 2013), while OSA is diagnosed in approximately 60–87% patients with MetS (Drager et al. 2009, 2010; Venkateswaran and Shankar 2007). In the present study, OSA was diagnosed in 31 (62%) out of the 50 obese patients with metabolic syndrome. Further, OSA was severe (AHI >30 episodes/h) in 25 (84%) out of the 31 patients.

There is no convincing evidence that obesity is a common denominator for both OSA and MetS or OSA is just an additional factor that has an influence on metabolic dysfunction and pro–inflammatory propensity. There are data to suggest the existence of an independent influence of OSA, which could explain why patients with obesity and severe OSA show worse metabolic, inflammatory, and vascular profile than those without OSA having a similar level of obesity. It is known that dysregulation of glycemic profile also is present in non-obese OSA patients (Bonsignore et al. 2013). Episodes of hypoxia and sleep fragmentation are indicated as the most likely elements that link OSA to MetS due to oxidative stress, and impact on glucose and lipid metabolism (Drager et al. 2015). There also is evidence that both MetS (Ridker et al. 2003) and OSA (Lui et al. 2009) are independently related to increased levels of CRP. In the present study, we found an enhanced level of CRP in patients with OSA accompanied by MetS, which points to a role of breathing disorders in upholding pro-inflammatory propensity. A meta–analysis of 10 cross–sectional studies has concluded that OSA is related to MetS regardless of BMI (Qian et al. 2016).

Although there are different definitions of metabolic syndrome, suggesting different cut-off levels of blood pressure, and blood glucose and lipid content (Huang 2009), it seems that the presence of abdominal obesity, defined by waist circumference, is key to all of them. Waist circumference is highly dependent on the quantity of visceral adipose tissue (Vgontzas et al. 2000). However, increased amount of visceral fat, along with lipid content and acute phase markers, also is noticed in non-obese men with OSA (Kritikou et al. 2013, 2014). Visceral fat corresponds to 5–8% of total body fat in women, increasing after menopause, and to 10–20% of total body fat in men (Wajchenberg 2000), which could pertain to the gender dimorphism in OSA prevalence. It is worth noting that excessive body fat, especially in then abdominal region, is related to the accumulation of fat tissue in the neck region. That hampers respiratory function (Lubrano et al. 2012), increases the risk of upper respiratory tract collapse, decreases the effectiveness of pharyngeal muscles' contraction (Deegan and McNicholas 1995), and contributes to expression of inflammatory genes (Poelkens et al. 2013).

Factors that would enable the presage of risk of OSA co-occurrence in patients with MetS are not yet fully unraveled. The risk of OSA can be estimated using specific surveys, such as the Berlin Questionnaire, STOP-Bang, or NoSAS scale. These questionnaires are, however, of limited usefulness in patients with metabolic syndrome as also are clinical symptoms of snoring and breathing pauses noticed by family members or the assessment of daytime sleepiness. Excessive daytime sleepiness is known to strongly associate with not only with OSA but also with obesity and metabolic syndrome (Vgontzas 2008; Bixler et al. 2005). In the present study, snoring and ESS scores were similar in both OSA-MetS and MetS alone syndromes, and thus could not distinguish between these two disease entities or be a presage of OSA development in patients with metabolic syndrome. The only significant factor of a bearing, we found in this study, that could help presage the risk of OSA development in

obese patients with metabolic syndrome appeared the neck circumference, which amounted to about 46 cm; 3 cm more than in obese patients with MetS alone. The increased amount of fat in the neck region may distort the mandible and uvula position during sleep, decreasing the respiratory lumen. Further we found that neck circumference associated with OSA severity. This result is in line with previous studies that have reported that the neck circumference, apart from BMI and waist circumference, seems a risk factor for OSA development in obesity (Soylu et al. 2012; Davies et al. 1992). Flemons et al. (1994) have reported that patients with neck circumference of <37 cm have a lower risk for OSA. On the other side, patients with >48 cm of neck circumference have a 20–fold chance for OSA development. In a study of 1000 Brazilian adults, neck circumference associated with triglyceride levels and insulin resistance (Stabe et al. 2013). Neck circumference might thus be a useful addition to the routine diagnostics of obese patients, as suggested by Cizza et al. (2014).

In conclusion, we believe this study has provided confirmatory evidence for a high incidence of OSA in obese patients with metabolic syndrome. A routine assessment toward the presence of OSA should be routinely implemented in such patients. One of the valuable and easy, albeit preliminary, screening tool in this assessment seems the measurement of the neck circumference, which could help raise the awareness of OSA accompanying obesity.

Conflicts of interest The authors declare no conflicts of interest in relation to this article.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by the Bioethics Committee of Medical University of Silesia.

Consent Written informed consent was obtained from all individual participants included in the study.

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