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ANTHROPOMETRIC PREDICTORS OF HIGH RISK OF OBSTRUCTIVE SLEEP APNEA SYNDROME IN A RURAL POPULATION

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Abstract

Objective. *To evaluate which anthropometric parameter better predicts the high risk of obstructive sleep apnea syndrome (OSA) in a rural population.* ***Material and Method.*** *254 subjects were enrolled. We measured weight, height, waist circumference (WC) and neck circumference (NC) and calculated body mass index (BMI), waist-to-height ratio (WHtR) and neck circumference/height ratio (NC/Height). The risk of OSA was assessed by using Berlin Questionnaire.* ***Results.*** *Subjects with high risk of OSA had a significant higher BMI, WC, WHtR, NC, and NC/Height. A higher percentage of those with large WC (≥80cm and ≥94cm for women and men, respectively) (p<0.001), WHtR ≥0.5 (p<0.001), NC ≥40cm (p=0.004), NC/Height ratio ≥0.23 (p=0.002) had a high risk of OSA. Using ROC curves of anthropometric parameters studied we found that WHtR was the best predictor for high risk of OSA, with AUC of 0.760, 95% CI: 0.699 to 0.815.* ***Conclusions.*** *WHtR was the best predictor for high risk of OSA as assessed by the Berlin Questionnaire.*

key words: *obstructive sleep apnea syndrome, waist-to-height ratio, Berlin questionnaire, anthropometric measures.*

Background

The American Academy of Sleep Medicine clinically defines OSA as the occurrence of daytime sleepiness, loud snoring, witnessed breathing interruptions, or awakenings caused by gasping or choking in the presence of at least 5 obstructive respiratory events per hour [1]. The prevalence of sleep apnea has been estimated to be about 2 to 5% of men and 2% of women [2]. According to a more recent study,

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Young's group found that one in six people over 50 years old had at least mild apnea, with one-fourth of those cases severe [3].

A survey by the National Sleep Foundation [4] found that 26% of the population has a high probability of having OSA. In a study conducted among primary care offices, 32% of adults were estimated to be at high risk (HR) for OSA [5]. OSA is a common medical condition that is under-recognized and under diagnosed in many adults, approximatively 80% of OSA patients remaining without diagnosis [2] and estimates show that up to 5% of western population could have undiagnosed OSA [3]. Population based studies have demonstrated the increase of mortality in subjects with moderate and severe OSA [6, 7].

Obesity is probably the most important risk factor for the development of OSA. The prevalence of OSA among obese patients is much higher than in general population, exceeding 30% [8] and reaching up to 50-98% in morbidly obese individuals [9, 10]. An estimated 58% of patients with OSA have a BMI higher than 30 kg/m^2 [11] and approximatively 60-90% of adults with OSA are overweight [12]. Numerous studies have shown the development or worsening of OSA with increasing weight, as opposed to substantial improvement with weight reduction. Several studies have long demonstrated the implication of obesity in the pathogenesis of sleep apnea; both generalized obesity as reflected by BMI [13], as well as regional obesity, meaning abdominal obesity as reflected by WC [14] and upper-truncal obesity as reflected by parapharingeal fat deposits [15] or neck circumference [16, 17, 18]. While early studies of sleep apnea emphasized the importance of obesity, as a significant determinant of sleep-disordered breathing, subsequent investigations pointed out the importance of regional, rather than over-all obesity. Waist circumference is a better measure than BMI or neck circumference to predict sleep disordered breathing [19]. Davies and Stradling [18] were the first to note that NC corrected for height was a better correlate of apnea severity than BMI or other indexes of obesity, therefore being a better predictor of obstructive sleep apnea than general obesity, results also confirmed by other studies [17, 20]. Dancey et al., in their study carried out to see the gender differences in sleep apnea, found that both in men and women, people with higher NC/Height ratio were older, had greater BMI and had more severe sleep apnea [20].

Conversely, OSA may itself predispose individuals to worsening obesity because of sleep deprivation, daytime somnolence and disrupted metabolism. OSA is associated with increased sympathetic activation, sleep fragmentation, ineffective sleep and insulin resistance, potentially leading to diabetes and aggravation of obesity [21].

Polysomnography is the golden standard for diagnosing OSA [22]. However, polysomnography is a time-consuming and costly procedure. Increasing awareness that OSA left untreated could lead to numerous complications has augmented the number of solicitations for sleep studies [23]. Also the increasing epidemic of obesity is most likely to rise the prevalence of OSA, putting a heavy burden on health care systems.

To deal with this issue, a number of screening questionnaires and clinical screening models have been developed to help identify patients with high risk of OSA. This kind of approach could actually increase the rate of diagnosis of OSA, by improving the cost-efficiency in sleep centers. One of the most widely used questionnaires is the Berlin questionnaire, validated for primary care patients [24] and some non-primary care settings [25-27]. The sensitivity ranges from 54% to 86% and the specificity ranges from 43% to 87% [27, 28] among primary care patients. The Berlin Questionnaire asks about risk factors for sleep apnea, namely snoring behavior, day time sleepiness or fatigue and the presence of obesity or hypertension [24], being a useful screening tool for sleep apnea in a primary care population and may be more convenient and less costly than polysomnography. The sensitivity of 86% for an apnea-hypopnea index (AHI) >5 is higher than that of most strategies currently used in clinical practice [29].

Material and Method

We performed a cross-sectional study on 254 subjects, aged 18 or older, both men and women, randomly selected out of the 3248 people who participated at the National Health Program held during 2007-2008 and, therefore, were registered in a database. The site of the study was Deleni, a representative rural community in Iaşi County. Subjects were convoked through their general practitioners and all of them provided written informed consent before enrolling in the study. Also ethical approval was obtained from the University Ethics Committee.

The data collected included age, gender and anthropometric measures: weight, height, waist circumference, neck circumference. Body weight and height were recorded in all subjects while wearing light clothes and no shoes, using standard techniques and equipment. We calculated BMI as body weight/height^2 (kg/m^2) and we used World Health Organization (WHO) criteria to define BMI categories: underweight, normal weight, overweight and obesity. Waist circumference was measured midway, between the lower rib margin and the anterior superior iliac spine, with the patient standing at the end of a gentle expiration. Normal WC was defined as WC<80 cm for women and <94 cm for men. We then calculated the waist-to-height ratio by dividing WC by height and defined the normal value as <0.5. Neck circumference was measured at mid-neck height, between the mid-cervical spine to mid-anterior neck. In men with a laryngeal prominence (Adam's apple), it was measured just below the prominence. Since taller people are expected to have larger necks, we normalized NC for body height by calculating the neck circumference/height ratio, achieving also the effect of minimizing the differences between genders.

The risk of OSA was assessed using Berlin Questionnaire (Table 1) which consists of 10 items organized in 3 categories. The first category refers to snoring and witnessed apneas (questions 1 to 5), the second one is referring to daytime sleepiness (3 or 4 questions), including napping on the wheel, and the last category evaluates the presence of either hypertension or a BMI≥30 kg/m^2. Inside each item some „positive" answers are defined and these are given 1 point. The only item that is an exception is question 5, which receives 2 points for a positive answer. In category three, the answers that confirm the presence of hypertension or obesity are considered positive and also transform this category into a positive one. The first two categories are considered to be positive if the total points ≥2. The risk for OSA is high if two or more categories are positive and, by opposite, the risk is low if less than two categories are positive.

Table 1. Berlin Questionnaire.

CATEGORY 1 QUESTIONS	CATEGORY 2 QUESTIONS
Do you snore?	6. Are you tired after sleeping?
Yes ** No	Almost every day **
I don't know	3 - 4 times per week **
How loud is your snoring?	1 - 2 times per week
My snoring is as loud as breathing	1 - 2 times per month
My snoring is as loud as talking	Never or almost never
My snoring is louder than talking **	7. Are you tired during waketime?
My snoring is very loud **	Almost every day **
How frequently do you snore?	3 - 4 times per week **
Almost every day **	1 - 2 times per week
3 - 4 times per week **	1 - 2 times per month
1 - 2 times per week	Never or almost never
1 - 2 times per month	8. Have you ever nodded off or falling asleep while driving a vehicle?
Never or almost never	Yes ** No
Does your snoring bother other people?	If yes, how often does it occur?
Yes** No	Almost every day **
How often have your breathing pauses been noticed?	3 - 4 times per week **
Almost every day **	1 - 2 times per week
3 - 4 times per week **	1 - 2 times per month
1 - 2 times per week	Never or almost never
1 - 2 times per month	CATEGORY 3 QUESTIONS
Never or almost never	Do you have high blood pressure?
	Yes ** No
	10. BMI (body mass index) > 30?
	Yes ** No

Any answer followed by double asterisks (**) is a positive response.

The statistical package SPSS version 16.0 for Windows (Chicago, IL, USA) and MedCalc statistical software 11.5.1 were used for data analysis. A *p* value <0.05 was considered as statistically significant. The significance of differences between continuous variables was assessed by using the Student's *t* test and One-way ANOVA test. To find the optimal, maximal sensitivity and specificity of anthropometric indicators in predicting high risk of OSA we used receiver operating characteristic analysis (ROC curves) with the determination of cut-off values, and we used area under the curve (AUC) to evaluate which anthropometric parameter most accurately predicted the high risk of OSA. AUC is a measure of the diagnostic power of a test. A perfect test will have an AUC of 1.0, and an AUC equal to 0.5 means that the test performs no better than chance [30].

Results

We studied 254 subjects, 152 women (59.84%) and 102 men (40.15%).The mean age of the whole study population was 55±16.28 years and the mean BMI was 27.55±5.29kg/m^2 (Table 2). The mean BMI, WC and NC/Height ratio were similar for men and women. Men had a larger neck and a higher WHtR (p<0.001 in both) (Table 3).

When assessing the results of the Berlin Questionnaire, we found that 29.4% of men and 36.8% of women had high risk of OSA, with no statistically significant difference between sexes (p=0.220). We found statistically significant global differences in percentage of normal weight (15.5%), overweight (24.0%) and obese (67.6%) with high risk of OSA (p<0.001). When comparing by pairs, the difference was not between normal weight and overweight (p=0.156), but between overweight and obese (p<0.001). In men, 2.9% of normal weight, 22% of overweight and 74.1% of obese had a high risk of OSA (p<0.001) – between normal weight and overweight (p=0.016) and between overweight and obese also (p<0.001). In women, 24% of normal weight, 25.5% of overweight and 63.8% of obese had high risk of OSA (p<0.001 between overweight and obese; no difference between normal weight and overweight – p=0.863).

A statistically significant higher percentage of those with large WC had a high risk of OSA (40.5%) than those with normal WC (6.1%), p<0.001. The level of significance is maintained also when analysing separately for genders. In men, 6.1% of those with normal WC and 40.6% of those with large WC have high risk of OSA (p<0.001). In women, 6.3% of those with normal WC and 40.4% of those with large WC had high risk of OSA (p=0.007).

Table 2. The characteristics of the study population.

Variables	Mean	Minimum	Maximum	Standard deviation
Age, years	55,04	21	91	16,28
Weight, kg	72,90	23	126	15.52
Height, m	1,62	0,90	1,89	0,10
BMI, kg/m^2	27,55	16,1	51,1	5,29
WC, cm	97,83	66	141	13,34
WHtR	0,60	0,40	0,88	0,09
NC, cm	37,63	29,5	54,5	3,49
NC/Height	0,23	0,19	0,58	0,03

Table 3. The comparison between genders.

Variables		Mean	Standard deviation	95% CI	Minimum	Maximum	*P* value
BMI, kg/m^2	*men*	27.325	4.57	26.42-28.22	16.7	41.8	0.566
	women	27.715	5.74	26.79-28.63	16.1	51.1	
WC, cm	men	98.56	11.55	96.29-100.83	71	130	0.645
	women	97.35	14.44	95.03-99.66	66	141	
WHtR	men	0.57	0.07	0.56-0.59	0.41	0.86	<0.001
	women	0.62	0.09	0.60-0.63	0.39	0.88	
NC, cm	*men*	40.12	2.69	39.54-40.69	35	47	<0.001
	women	36.06	2.99	35.55-36.56	30	55	
NC/Height	men	0.23	0.018	0.23-0.23	0.20	0.30	0.074
	women	0.23	.0024	0.22-0.23	0.19	0.38	

A statistically significant higher percentage of those with large WHtR have a high Berlin risk (38.3%) than those with normal WHtR (3.1%), p<0.001. No men with normal WHtR had high Berlin risk, but 34.1% of those with high WHtR had high Berlin risk (p=0.009). In women, 5.6% of those with normal WHtR and 41% of those with high WHtR had high Berlin risk (p=0.003). Statistically significant more of those with NC≥40cm had a high risk of OSA: 28% of those with NC<40cm and 48.3% of those with NC≥40cm (p=0.004). This was seen both in men (15% vs. 42.6%, p=0.005) and in women (12.5% vs. 36.5%, p=0.029). Among subjects with a NC/Height ratio≥0.23, significantly more had a high risk of OSA (40.4%) than among those with a NC/Height ratio <0.23 (19.5%), p=0.002. The same was seen in men (69.2% vs. 32.3%, p=0.008) and women (43.4% vs. 22.6%, p=0.14).

Table 4. Characteristics of the subgroups with Low Risk and with High Risk of OSA.

		Low Risk	High Risk	Sig.
BMI	Total	25.908 ±4.2862	30.784± 5.6160	p<0.001
	Men	25.788 ± 3.9427	31.012 ± 3.8469	p<0.001
	Women	25.997 ± 4.5451	30.661 ± 6.3950	p<0.001
WC	Total	93.77 ± 12.051	105.77 ± 12.182	p<0.001
	Men	94.96 ± 10.611	107.20 ± 8.927	p<0.001
	Women	92.88 ± 13.011	105.00 ± 13.624	p<0.001
WHtR	Total	0.575 ±0.082	0.661 ± 0. .078	p<0.001
	Men	0.559 ± 0.073	0.628 ± 0.0527	p<0.001
	Women	0.587 ± .0865	0.678 ± 0.085	p<0.001
NC	Total	37.19 ± 3.348	38.51 ±3.628	p = 0.008
	Men	39.43 ± 2.458	41.73 ± 2.576	p<0.001
	Women	35.64 ± 2.995	36.80 ± 2.865	p=0.03
NHtR	Total	0.228 ± 0.0196	0.241 ± 0.025	p<0.001
	Men	0.232 ± 0.017	0.244 ± 0.017	p=0.003
	Women	0.225 ± 0.021	0.239 ± 0.028	p=0.001

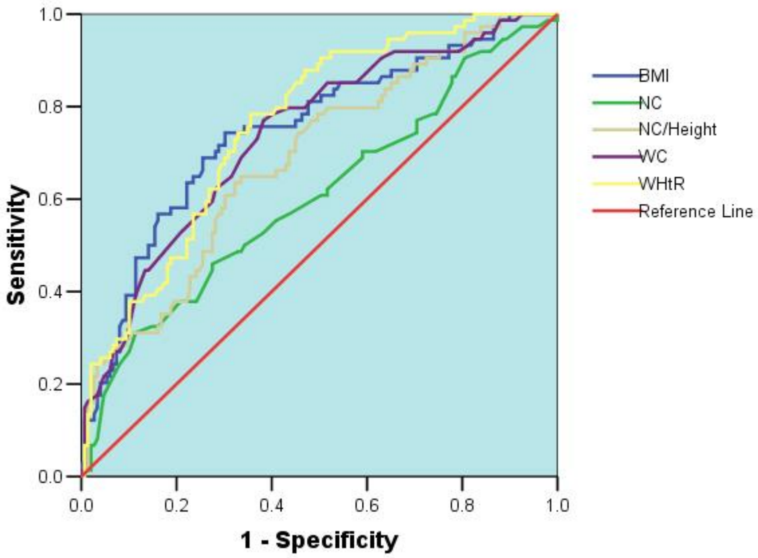

Fig. 1. ROC curves of anthropometric indicators for high risk of OSA.

We found statistically significant differences between the subjects who, according to Berlin Questionnaire, were at high risk of OSA compared to those with low risk, in terms of BMI, WC, WHtR, NC and NC/Height and the significance remained even when analysing data for gender. People having high risk of OSA, as assessed by the Berlin Questionnaire, had a higher BMI, WC, NC, WHtR and NC/ Height (Table 4).

Using ROC curves (Figure 1) with AUC and 95% confidence intervals of the assessed anthropometric parameters- BMI, WC, NC, WHtR and NC/ Height we found that WHtR was the best predictor for high risk of OSA, followed by BMI and WC. NC/Height ratio was proved to be a better predictor than NC uncorrected for height (Table 5).

Table 5. The values of AUC and 95% CI of evaluated parameters.

Parameters assessed	AUC	*P* value	95%CI
BMI	0.747	<0.0001	0.685 to 0.803
WC	0.738	<0.0001	0.675 to 0.794
WHtR	0.760	<0.0001	0.699 to 0.815
NC	0.604	0.0092	0.537 to 0.669
NC/Ht	0.687	<0.0001	0.622 to 0.747

Table 6. Anthropometric indices cut-off levels for determining subjects with high risk of OSA.

Anthropometric indices	Cut-off level	Sensitivity	95% CI	Specificity	95% CI
BMI, kg/m^2	*>28.72*	68.60	57.7 - 78.2	77.38	70.3 - 83.5
WC, cm	>97	80.23	70.2 - 88.0	61.90	54.1 - 69.3
WHtR	>0.60	79.07	69.0 - 87.1	67.26	59.6 - 74.3
NC ,cm	>40.5	30.67	20.5 - 42.4	88.59	82.4 - 93.2
NC/Height	>0.23	64.86	52.9 - 75.6	66.44	58.3 - 74.0

We used receiver operating characteristic analysis (ROC curves) for the determination of cut-off values in order to find the optimal, maximal sensitivity and specificity of anthropometric indicators in predicting high risk of OSA (Table 6). Our results showed that in the population studied a BMI>28.72 kg/m^2, a WC>97 cm, a WHtR>0.6, a NC>40.5 cm, and NC/Height>0.23 were the best cut-off levels for determining a high risk of OSA, as evaluated by the Berlin Questionnaire.

Discussions

Obstructive sleep apnea is known to diminish quality of life and is associated with many common comorbid conditions. Studies have documented an increased incidence of cardiovascular diseases and glucose metabolism disorders in OSA patients [31, 32]. Early detection of patients suffering from OSA may prevent the occurence or improve the outcome for several important diseases, and this should be given more importance, as there is a treatment with high benefits for these patients. OSA is underdiagnosed [3] both in general population and in high risk population as obese, hypertensive or diabetic patients.

Our study aimed to assess the risk of OSA and its features in a rural population and to find simple clinical measures that may predict the high risk of OSA and point out the subjects who need further sleep investigation and are more likely to get a positive diagnosis. The relation between obesity and OSA is well established and the mechanisms through which obesity leads to sleep disturbances are multiple. These include reduced pharyngeal lumen size due to fatty tissue, decreased upper airway muscle protective force due to fatty deposits in the muscle and reduced upper airway size secondary to mass effect of the large abdomen on the chest wall and tracheal traction. These mechanisms emphasize the great importance of fat accumulated in the abdomen and neck regions compared with the peripheral one. Greater attention should be payed to the “type” of obesity. Several studies have assessed the relationship between truncal obesity and OSA and some studies have observed a correlation between this type of obesity and the severity of OSA. For example, the study of 85 men by Shäfer et al. [33], showed that AHI could be correlated with intraabdominal and subcutaneous abdominal fat measured by MRI. A correlation was also found in the Sleep Heart Health Study [34]. Using a multiple linear regression model, adjusted for age and BMI, that study found a relationship between AHI and the waist-to-hip ratio. In our study we did not measure waist-to-hip ratio because of the fact that it is inconsistent with reflecting the actual body weight and also because a good value of this ratio does not automatically exclude a large WC which triggers many health risks. Instead we assessed WC and WHtR, as an expression of abdominal visceral adiposity. WC correlates with OSA [35] and in the same study BMI correlated with severe OSA, which is consistent with our results, that measures of waist are better predictors for high risk of OSA.

Some investigators concluded that WC is a better measure than BMI or neck circumference to predict sleep disordered breathing [19]. In the study we performed, WHtR was the best predictor for increased risk of OSA, closely followed by BMI and then WC.

Neck circumference is believed to be an indicator of upper truncal obesity, with pathphysiological implication on OSA. NC is a good predictor of both overweight and obesity [36], has been associated with cardiovascular risk factors in the general population [37, 38] and correlates with OSA [18, 20], being nowadays a common clinical measure in evaluating a patient with sleep apnea [39]. Indeed in our study also people with higher NC had a greater risk of OSA. An increased neck circumference (corrected for height) has been suggested as a better predictor of obstructive sleep apnea than other clinical indices [16]. Our results showed that NC/Height was better than NC uncorrected for height in determining a high risk for OSA, but was not better than other indices. However, the literature is inconsistent on this subject. Our findings may indicate that neck circumference and BMI are measures of general obesity like subcutaneous fat or skin folds and it confirms that WHtR and WC are a measure of visceral obesity, which is involved in obstructive sleep disturbances [40].

Our results suggest that BMI is not the best predictor of OSA in a group of patients with an overweight range BMI, but rather accurate measurements of visceral obesity like WHtR are, as other studies have already showed [41, 42].

Conclusions

In our study, WHtR was a better predictor of high risk of OSA (assessed by using the Berlin Questionnaire) than BMI and even than WC and NC.

Our study shows that indices of visceral obesity are better than BMI for evaluating obesity as a related or risk factor for OSA.

Obtaining simple clinical measurements such as WHtR may help prioritize the use of polysomnography in patients with a greater risk of OSA.

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