Excessive daytime sleepiness in sleep apnea: any role of testosterone or vitamin D?

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Short title: Association of testosterone and vitamin D with excessive daytime sleepiness

Summary:

Background: Recent studies reported association of sleep-disordered breathing (SDB) with testosterone and vitamin D deficiency. Low testosterone and vitamin D levels have been linked to fatigue and excessive daytime sleepiness (EDS). However, the impact of testosterone and vitamin D deficiency on EDS in subjects with SDB remains unknown. The aim of this study was to explore the predictors of EDS in habitual snorers. Role of testosterone, and vitamin D was studied in detail. We also looked for associations between testosterone, vitamin D, and sleep-related indices.

Methods: We prospectively enrolled 291 consecutive male patients with habitual snoring. Baseline clinical characteristics were recorded on admission. Standard overnight polysomnography was performed to detect SDB, and Epworth Sleepiness Scale (ESS) was used to assess EDS. Blood samples were obtained in a fasting condition in the morning after polysomnography to determined levels of testosterone and vitamin D.

Results: Respiratory disturbance index (RDI) (95% CI: 1.004-1.024, p=0.005) and the use of antihistamines (95% CI: 1.083-11.901, p=0.037) were the only independent variables significantly associated with EDS in binary logistic regression analysis. In linear multiple regression analysis, body mass index (BMI) (Beta=-0.282, p <0.001) and oxygen desaturation index (Beta=-0.150, p=0.043) were the only independent variables significantly associated with testosterone levels, and BMI (Beta=-0.142, p =0.016) was the only independent variable significantly associated with vitamin D.

Conclusions: We failed to find any independent association of testosterone and vitamin D with EDS among habitual snorers. Our results suggest an independent association between the magnitude of nocturnal desaturation and testosterone levels.

Key words: Sleep-disordered breathing; Polysomnography; Excessive daytime sleepiness; Testosterone; Vitamin D

Introduction:

Sleep-disordered breathing (SDB) is a frequent condition that affects approximately 25% of adult males (Peppard *et al.* 2013). Typical symptoms and signs of SDB include snoring, apneas during sleep, as well as excessive daytime sleepiness (EDS) and fatigue (Cowie 2017; American Academy of Sleep Medicine 2014; Pagel 2006). Except of SDB, EDS is most commonly caused by sleep deprivation, medication or other medical, and psychiatric conditions. SDB is also associated with other sleep disorders including insomnia, restless legs syndrome (RLS), periodic limb movement disorder, and circadian rhythm disorders (American Academy of Sleep Medicine 2014).

Despite increasing data, the role of testosterone and vitamin D in sleep disorders remains controversial (Bercea *et al.* 2015; McCarty *et al.* 2014). Recent studies reported association of SDB with testosterone and vitamin D deficiency (Viana *et al.* 2017; Bouloukaki *et al.* 2020). Additionally, low testosterone and vitamin D levels have been linked to fatigue and daytime sleepiness (Hyde *et al.* 2010; McCarty *et al.* 2012). However, the impact of testosterone and vitamin D deficiency on EDS in subjects with SDB remains unknown.

The aim of this study was to explore the predictors of EDS in habitual snorers who were referred for sleep apnea evaluation in a sleep laboratory. Clinical characteristics, comorbidities and medication was considered, and the role of testosterone and vitamin D was studied in detail. We also looked for association between testosterone, vitamin D and other sleep related indices.

Methods:

Between May 2016 and May 2017, we prospectively enrolled 291 consecutive adult male patients with habitual snoring who were examined at the sleep laboratory of the 1st Department of Neurology, Comenius University Bratislava for sleep apnea evaluation. Subjects were excluded from a sleep study in a case of acute cardiac/respiratory comorbidity, or a case of acute exacerbation of chronic cardiac/respiratory comorbidity, end stage cancer, liver insufficiency, or if they refused to participate. Subjects were also excluded in a case of testosterone or vitamin D supplement therapy.

Clinical and demographic characteristics, including age, body mass index (BMI), past medical history and current medication, were obtained in all patients as a part of the

baseline evaluation. Medical records of all patients were reviewed to search medical conditions and medications that could contribute to EDS, including hypertension, diabetes mellitus, coronary artery disease, gastrointestinal disorders, renal insufficiency, liver dysfunction, hypothyroidism, cancer, parkinsonism, seizures, depression and the use of anticonvulsants, antidepressants, antiparkinsonian agents, alpha-adrenergic blocking agents, beta-adrenergic blocking agents, antihistamines and anxiolytics (Guilleminault and Brooks 2001; Pagel 2006; Pagel 2009). Subjects with absence of these conditions were considered as apparently healthy.

Overnight polysomnography (using Alice 6 device, Philips-Respironics, Netherlands) was performed in all patients. Standardized criteria were used to score sleep parameters and respiratory events. Apnea was defined as a cessation or a reduction of airflow of ≥ 90% for more than 10 seconds. A reduction in airflow of ≥ 50% for more than 10 seconds associated with oxygen desaturation of > 3% was considered as a hypopnea. RERAs were estimated by flattening of the inspiratory airflow profile associated with an arousal, when airflow changes did not meet apnea or hypopnea criteria (American Academy of Sleep Medicine 2007). A diagnosis of sleep apnea was defined as an apnea-hypopnea index (AHI) ≥ 5. Respiratory disturbance index (RDI) was defined as the total number of apneas, hypopneas and respiratory effort related arousals (RERAs) per hour of sleep. Total sleep time, arousal index (AI), and oxygen desaturation index (ODI) were also recorded. Sleep stages (N1, N2, N3, REM) were scored according to the American Academy of Sleep Medicine sleep scoring rules (Moser *et al.* 2009).

The Epworth Sleepiness Scale (ESS) was used to assess EDS, and ESS score of 10 or more indicated the presence of EDS (Johns 1991). The minimum criteria defined by the International Restless Legs Syndrome Study Group were used to establish the diagnosis of the restless leg syndrome (RLS). To avoid false-positive diagnosis, the questionnaires were applied during an interview with a patient. Diagnosis of RLS was set when all four diagnostic criteria were fulfilled (an urge to move the legs, usually accompanied or caused by uncomfortable and unpleasant sensations in the legs; the urge to move or unpleasant sensations beginning or worsening during periods of rest or inactivity such as lying or sitting; the urge to move or unpleasant sensations partially or totally relieved by movement, such as walking or stretching; the urge to move or unpleasant sensations worse in the evening or night than during the day or only occurring in the evening or night) (Allen *et al.* 2003). Scorers were blinded to the baseline characteristics of the study population and for the results of other laboratory tests.

Blood tests were performed in the morning following polysomnography, and blood samples were obtained in a fasting condition within 1 hour after polysomnography. Serum levels of vitamin D [25(OH)-D vitamin], and total testosterone were assessed. Testosterone levels were assessed by electrochemiluminescence immunoassay, and vitamin D levels were assessed by electrochemiluminescence immunoassay using Roche Cobas assay reagent (Roche Diagnostics, Mannheim, Germany). Testosterone levels were considered as decreased if they are < 9 nmol/l in 18-50-year-old males, or < 7 nmol/l in males older than 50 years. Hypovitaminosis D was defined as vitamin D < 20μg/l, and vitamin D insufficiency as vitamin D < 30 μg/l.

SPSS version 18 (SPSS Inc., Chicago, IL) was used for the statistical analyses. Categorical variables were expressed as numbers (%), continuous variables as means (± standard deviation) or median (interquartile range, range). Chi-squared test, Student t test, and Mann–Whitney test were used for group comparison of particular variables. Pearson or Spearman correlation coefficients were used to determine relationships between testosterone, vitamin D, and characteristics of the study population. To identify factors that contributed to the EDS, binary logistic regression was used. Stepwise multiple linear regression analysis was used to identify factors that contributed to testosterone and vitamin D. All tests were 2-sided. P values < 0.05 were considered statistically significant.

The study was approved by the institutional ethics committee and all patients provided an informed consent.

Results:

Our study population consisted of 291 male habitual snorers with the mean age 53.4±13.1. Sleep apnea was present in 265 (91.1%) and EDS in 83 (28.5%) of the subjects. Median ESS was 6 (range: 0-24). Decreased testosterone levels were present in 41 subjects (14.1%) and insufficient vitamin D levels in 231 subjects (79.4%). Other characteristics are presented in Table 1. Subjects with EDS had significantly higher use of antihistamines (8.4% vs. 2.4%), significantly higher frequency of sleep apnea (97.6% vs. 88.5%), significantly higher values of multiple SDB-specific indices, and significantly higher rate of decreased testosterone levels (20.5% vs. 11.5%), compared to subjects without EDS (see Table 1). The only variables significantly associated with EDS in binary logistic regression analysis were RDI (95% CI: 1.004-1.024, p=0.005) and use of antihistamines (95% CI: 1.083-11.901, p=0.037). Characteristics of 85 apparently healthy subjects are shown in Table 2. In

subpopulation of apparently healthy subjects, snorers with EDS had significantly higher AI (median 18.6 vs. median 12.4), see Table 2. Among apparently healthy subjects, AI (95% CI: 1.004-1.060, p=0.027) was the only independent variable significantly associated with EDS in binary logistic regression analysis.

There were significant negative correlations between testosterone levels and both BMI and nocturnal saturation of blood with oxygen, and significant positive correlations between testosterone and the presence of SDB, AHI, RDI, ODI, and AI (see Table 3). BMI (Beta=-0.282, p <0.001) and ODI (Beta=-0.150, p=0.043) were the only independent variables significantly associated with the levels of testosterone in linear multiple regression analysis.

There was no significant correlation between vitamin D levels and sleep-related indices (see Table 4). We found a significant negative correlation between vitamin D levels and BMI, and BMI (Beta=-0.142, p =0.016) was the only independent variable that was significantly associated with vitamin D levels in linear multiple regression analysis.

Discussion:

Despite a high frequency of vitamin D insufficiency (79.4%), and relatively high frequency of decreased testosterone levels (14.1%), we failed to find any independent association of either testosterone or vitamin D with EDS in habitual snorers. Our results suggest, that testosterone and vitamin D deficiency do not seem to play important role in EDS among subjects with SDB. Further results of our study suggest an independent association between severity of SDB and testosterone levels. BMI (Beta=-0.282, p <0.001) and ODI (Beta=-0.150, p=0.043) were the only independent variables that were significantly associated with testosterone levels in linear multiple regression analysis. We failed to find any significant association of vitamin D levels with sleep-related indices. BMI (Beta=-0.142, p =0.016) was the only independent variable that was significantly associated with vitamin D levels in the regression analysis.

Despite limited data on testosterone status in general Slovak population, decreased testosterone levels (<10 nmol/l) were observed in 40.2% of males with abdominal obesity (Fillo *et al.* 2012). Despite similar populations, prevalence of testosterone deficiency was even higher when compared to our study (40.2% vs. 14.1%). This finding may suggest important link between obesity and testosterone deficiency. This is in accordance with our results, where inverse association of testosterone with BMI was found.

Most of the studies so far studied the association of testosterone with SDB, and data regarding the association of testosterone with other sleep disorders are limited (Wittert 2014). Low testosterone levels in SDB patients have been attributed to hypoxia, sleep deprivation, sleep fragmentation or obesity (Feldman *et al.* 2002; Luboshitzky *et al.* 2003; Schmid *et al.* 2012). On the other hand, the causal role of SDB in decreased testosterone levels remains controversial and the evidence in humans is mixed. While some authors have found an independent association of testosterone with some measures of SDB, other researchers have concluded that the low testosterone levels in men with SDB is primarily related to obesity (Clarke *et al.* 2020; Bercea et al. 2015; Canguven *et al.* 2010; Luboshitzky *et al.* 2005). In a recent study, Clarke et al. suppose, that testosterone concentration is determined by obesity, rather than by sleep apnea per se. This statement is supported by graded effect of weight loss, but limited effect of continuous positive airway pressure therapy to increase testosterone levels and highlights the importance of obesity in men with low testosterone levels (Clarke *et al.* 2020).

The biggest strength of our study compared to these earlier studies is our larger sample size. In 291 consecutive male habitual snorers, BMI (Beta=-0.282, $p < 0.001$) and ODI (Beta=-0.150, $p=0.043$) were the only independent variables significantly associated with levels of testosterone in linear multiple regression analysis. Our results suggest an independent role of both obesity and nocturnal desaturations with low testosterone levels. However, the study is not designed to address any causal relationship between SDB and low testosterone levels. To elucidate this relationship, future studies should also focus on the treatment of testosterone deficiency and its impact on sleep characteristics.

Vitamin D deficiency (≤20 ng/ml) was observed in 41.9% and vitamin D insufficiency (≤30 ng/ml) in 79.4% of subjects in this study. Despite the data on vitamin D status in general Slovak population are not available, vitamin D deficiency was observed in 15%, and vitamin D insufficiency in 41% of apparently healthy volunteers, suggesting higher prevalence of decreased vitamin D levels in subjects with SDB (Sebekova *et al.* 2016).

The relationship between sleep disorders and vitamin D seems to be complex and bidirectional (McCarty et al. 2014). In cross-sectional studies, lower serum vitamin D levels were associated with higher odds of short sleep duration (< 5 h), and SDB and short sleep duration were independently associated with the risk of vitamin D deficiency (Massa *et al.* 2015; Piovezan *et al.* 2017). Mete et al. found no statistically significant difference in serum vitamin D levels between SDB subjects and controls. However, patients with severe SDB had significantly lower levels of vitamin D compared with other groups

(Mete *et al.* 2013). Serum vitamin D has also been assessed in patients with EDS or RLS. In a consecutive series of 81 sleep clinic patients, McCarthy et al. found an inverse correlation of ESS with vitamin D levels in subjects without vitamin D deficiency (McCarty et al. 2012). Data from a study of 36 patients with RLS and 38 healthy controls also suggest a significant inverse correlation between vitamin D levels and disease severity in female subjects (Balaban *et al.* 2012).

Multiple mechanisms could link vitamin D deficiency with SDB, including immune dysregulation with subsequent development of chronic rhinitis, tonsillar hypertrophy, and impaired contractility and remodeling of airway smooth muscle (Britt *et al.* 2016; McCarty et al. 2014). Inadequacy of vitamin D is also associated with other conditions, including nonspecific pain and noninflammatory myopathy (Bischoff *et al.* 1999; Plotnikoff and Quigley 2003). These conditions could directly contribute to sleep disruption or, conversely, their symptoms could negatively impacted by poor sleep quality (McCarty et al. 2014).

Compared to these earlier studies on vitamin D, our study is unique in its prospective design as well as consecutive enrollment of patients during a one-year period. In a group of 291 male habitual snorers, we failed to find any significant association of vitamin D with sleep-related indices of SDB, EDS and presence of RLS. Our results are in accordance with the findings of recent well designed study, where no association was found between severity of sleep apnea and vitamin D levels (Yassa et al. 2019). Future controlled studies are needed to explore the relationship between vitamin D and sleep disorders, and effects of vitamin D supplementation on sleep parameters should also be investigated.

The primary aim of this study was to explore the predictors of EDS in habitual snorers who were referred for sleep apnea evaluation. The role of testosterone and vitamin D was studied in detail. Despite increasing data linking vitamin D insufficiency and decreased testosterone levels with EDS and fatigue, their role in sleep disorders remains controversial (Bercea et al. 2015; McCarty et al. 2014). Fatigue and "lack of energy" have been described in non-SDB subjects with low testosterone level (Bassil 2011; Hyde et al. 2010). Bercea et al., in a study of 15 SDB patients and 15 controls, found a strong association of SDB-related fatigue with serum testosterone (Bercea et al. 2015). As previously mentioned, McCarthy et al. found an inverse correlation of ESS with vitamin D levels in subjects without vitamin D deficiency (McCarty et al. 2012). Our study failed to find any significant independent association of testosterone and vitamin D levels with EDS, suggesting minor role of testosterone and vitamin D deficiency in EDS among subjects with SDB. RDI (95% CI: 1.004-1.024, p=0.005) and use of antihistamines (95% CI: 1.083-11.901, p=0.037) were the

only variables significantly associated with EDS in binary logistic regression analysis. Similarly, among apparently healthy subjects, AI (95% CI: 1.004-1.060, p=0.027) was the only independent variable significantly associated with EDS in binary logistic regression analysis.

The lack of fatigue assessment is one of several limitations of our study. The impact of low testosterone levels on fatigue may be more significant than its effect on daytime sleepiness, and this association should be investigated in future prospective studies (Hossain *et al.* 2005). Another limitation is a tool used for EDS assessment. Although the ESS is a reliable instrument, its self-rating character belongs to the most important limitations of this study. Objective assessment by The Multiple Sleep Latency Test, the gold standard for measuring EDS, is highly warranted in the future studies. Search strategy for EDS predictors also belongs to limitations. Despite the extensive search was performed, we used only the data from the medical records. No additional imaging, functional, or laboratory tests were used. For example, due to absence of thyroid hormones testing, it was not able to clearly assess the control of the hypothyroidism. Future studies should also focus more closely on wider spectrum of comorbid sleep disorders. Insomnia, periodic limb movement disorder, and circadian rhythm disorders were not assessed in this study. In our study, both testosterone and vitamin D levels were inversely associated with BMI. Since BMI might be related to fitness levels, future studies should also assess the impact of physical activity on EDS as well as on testosterone and vitamin D levels (Basta *et al.* 2008). Association of antihistamines with sleepiness is also well known, and antihistamines were independently associated with EDS despite their use in only 4.1% of the subjects in this study (Murri *et al.* 1992).

Association of sleep disruption with obesity, as well as their adverse consequences are extensively studied (Cibičková *et al* 2019; Rácz *et al.* 2018). Regarding the inverse independent association of BMI with both, testosterone and vitamin D levels, future studies should evaluate the role of obesity related hypoventilation in testosterone and vitamin D deficiency. We suppose, that obesity related hypoventilation could play more important role than sleep apnea per se. Due to absence of capnography, we were not able to assess nocturnal hypoventilation. We have to admit one more limitation. Diagnosis of sleep apnea was found in relatively high proportion of enrolled habitual snorers (91.1%). Enrollment of habitual snorers who were referred for sleep apnea evaluation in sleep laboratory setting could cause selection bias, so prevalence of sleep apnea was higher as expected among “real-world” habitual snorers.

Despite high frequency of vitamin D and testosterone insufficiency, our study failed to find any independent association of testosterone and vitamin D with EDS in patients with habitual snoring. Our results suggest, that testosterone and vitamin D deficiency do not seem to play important role in EDS in subjects with SDB. No association was found between vitamin D levels and any of the observed sleep-related parameters. While an independent association was found between testosterone levels and the magnitude of nocturnal desaturation, the study is not designed to address any causality in this relationship. Future prospective randomized studies should elucidate any impact of SDB therapy on testosterone and vitamin D levels. The effects of testosterone and vitamin D supplementation on sleep parameters should be also investigated.

Abbreviations:

AHI: apnea-hypopnea index
AI: arousal index
BMI: body mass index
EDS: excessive daytime sleepiness
ESS: Epworth Sleepiness Scale
ODI: oxygen desaturation index
RDI: respiratory disturbance index
RERAs: respiratory effort related arousals
RLS: restless leg syndrome
SDB: sleep-disordered breathing

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Tables:

Table 1: Characteristics in the population with excessive daytime sleepiness and in the population without excessive daytime sleepiness.

	All subjects	Excessive daytime sleepiness		P
		Present	Absent	
N	291	83	208	
Age (years)	53.4±13.1	53.5±12.4	53.3±13.4	0.942
Body mass index (kg/m^2)	32.2±6.2	32.6±6.4	32.1±6.1	0.502
Hypertension	162 (55.7%)	43 (51.8%)	119 (57.2%)	0.402
Diabetes mellitus	43 (14.8%)	17 (20.5%)	26 (12.5%)	0.083
Coronary artery disease	27 (9.3%)	8 (9.6%)	19 (9.1%)	0.894
Cancer	7 (2.4%)	1 (1.2%)	6 (2.9%)	0.398
Hypothyroidism	13 (4.5%)	5 (6.0%)	8 (3.8%)	0.417
Liver dysfunction	26 (8.9%)	11 (13.3%)	15 (7.2%)	0.103
Gastrointestinal disturbances	38 (13.1%)	10 (12.0%)	28 (13.5%)	0.747
Epilepsy	8 (2.7%)	0 (0%)	8 (3.8%)	0.070
Parkinsonism	3 (1%)	1 (1.2%)	2 (1.0%)	0.853
Depression	25 (8.6%)	9 (10.8%)	16 (7.7%)	0.386
Alpha-adrenergic blockers	35 (12%)	6 (7.2%)	29 (13.9%)	0.112
Beta-blockers	93 (32%)	25 (30.1%)	68 (32.7%)	0.671
Antihistamines	12 (4.1%)	7 (8.4%)	5 (2.4%)	0.020*
Anxiolytics	9 (3.1%)	1 (1.2%)	8 (3.8%)	0.240
Total sleep time (min)	410.9±45.0	415.3±41.6	409.2±46.3	0.292
AHI (n/h)	30.0 (0.1-107.3)	38.0, 45.7 (0.4-101.1)	26.7, 39.3 (0.1-107.3)	0.003**
Sleep apnea (AHI ≥ 5) - Obstrustive sleep apnea - Central sleep apnea	265 (91.1%) 237 (89.4%) 28 (10.6%)	81 (97.6%) 73 (90.1%) 8 (9.9%)	184 (88.5%) 164 (89.1%) 20 (10.9%)	0.014* 0.809 0.809
RDI (n/h)	33.0 (0.4-108.0)	42.5, 43.9 (3.0-103.9)	30.2, 41.7 (0.4-108.0)	0.002**
ODI (n/h)	26.3 (0.1-	36.3, 46.7 (0.1-	23.0, 33.7 (0.8-	0.005**

	135.5)	113.0)	135.5)	
Average SaO_2 (%)	87.8±6.5	87.2±6.7	88.0±6.5	0.332
Minimal SaO_2 (%)	77.0±13.5	74.2±15.6	78.1±12.5	0.026*
AI (n/h)	16.8 (2.6-108.0)	24.3, 24.8 (4.4-75.0)	15.9, 22.3 (2.6-108.0)	0.004**
RLS	43 (14.8%)	16 (19.3%)	27 (13.0%)	0.172
Testosterone (nmol/l)	13.5±6.0	13.2±6.2	13.7±5.9	0.478
Decreased testosterone (%)	41 (14.1%)	17 (20.5%)	24 (11.5%)	0.048*
D vitamin (µg/l)	22.7±9.8	21.8±9.7	23.1±9.8	0.310
Hypovitaminosis D (%)	122 (41.9%)	47 (56.6%)	122 (58.7%)	0,752
Insufficient vitamin D (%)	231 (79.4%)	68 (81.9%)	163 (78.4%)	0.498
SDB: sleep-disordered breathing, EDS: excessive daytime sleepiness, AI: arousal index, RDI: respiratory disturbance index, ESS: Epworth sleepiness scale, AHI: apnea hypopnea index, ODI: oxygen desaturation index, SaO_2: saturation of blood with oxygen, RLS: restless leg syndrome, *: $p < 0.05$, **: $p < 0.001$. Decreased testosterone < 9 nmol/l in 18-50-year-old; < 7 nmol/l in > 50-year-old. Hypovitaminosis D < 20µg/l. Insufficient vitamin D < 30 µg/l. Categorical variable are expressed as numbers and proportions (%), continuous variables as means ± standard deviation or median, minimal-maximal values.				

Table 2: Characteristics of apparently healthy snorers in the population with excessive daytime sleepiness and in the population without excessive daytime sleepiness.

	All subjects	Excessive daytime sleepiness		P
		Present	Absent	
N	85	23	62	
Age (years)	43.0±10.3	44.3±10.8	42.5±10.2	0.496
Body mass index (kg/m^2)	29.9±4.7	29.4±4.5	30.1±4.8	0.548
Total sleep time (min)	405.0±40.0	406.3±41.3	404.6±39.8	0.857
AHI (n/h)	17.3, 38.0 (0.4-101.1)	27.6, 51.2 (0.4-101.1)	15.4, 33.7 (0.9-100.3)	0.133
Sleep apnea (AHI ≥ 5)	71 (83.5%)	21 (91.3%)	50 (83.3%)	0.239
- Obstructive sleep apnea	65 (91.5%)	19 (90.5%)	46 (92%)	0.833
- Central sleep apnea	6 (8.5%)	2 (9.5%)	4 (8%)	0.833

RDI (n/h)	21.8, 37.1 (1.4-101.3)	30.3, 29.1 (3.0-101.3)	20.0, 31.2 (1.4-98.7)	0.115
ODI (n/h)	15.4, 33.8 (0.1-110.1)	24.5, 39.4 (0.1-110.1)	13.8, 28.2 (0.8-100.8)	0.168
Average SaO_2 (%)	89.1±7.0	89.2±5.4	89.1±7.5	0.974
Minimal SaO_2 (%)	81.4±10.6	79.6±11.4	82.0±10.3	0.355
AI (n/h)	13.0, 21.8 (2.6-75.0)	18.6, 30.1 (6.1-75.0)	12.4, 15.8 (2.6-56.5)	0.025*
RLS	9 (10.6%)	1 (4.3%)	8 (12.9%)	0.255
Testosterone (nmol/l)	15.0±6.0	15.0±6.2	15.0±6.1	0.958
Decreased testosterone (%)	12 (14.1%)	3 (13.0%)	9 (14.5%)	0.862
D vitamin (µg/l)	22.7±9.9	23.5±9.1	22.4±10.2	0.675
Hypovitaminosis D (%)	39 (45.9%)	9 (39.1%)	30 (48.4%)	0.447
Insufficient vitamin D (%)	69 (81.2%)	19 (82.6%)	50 (80.6%)	0.837
SDB: sleep-disordered breathing, EDS: excessive daytime sleepiness, AI: arousal index, RDI: respiratory disturbance index, ESS: Epworth sleepiness scale, AHI: apnea hypopnea index, ODI: oxygen desaturation index, SaO_2: saturation of blood with oxygen, RLS: restless leg syndrome, *: $p < 0.05$. Decreased testosterone < 9 nmol/l in 18-50-year-old; < 7 nmol/l in > 50-year-old. Hypovitaminosis D < 20µg/l. Insufficient vitamin D < 30 µg/l. Categorical variable are expressed as numbers and proportions (%), continuous variables as means ± standard deviation or median, minimal-maximal values.				

Table 3: Correlations of testosterone with sleep-related indices.

	R	P
Age	-0.065	0.268
Body mass index	-0.403	<0.001***
Total sleep time	-0.037	0.528
AHI	-0.352	<0.001***
Sleep apnea	-0.168	0.004**
RDI	-0.346	<0.001***
ODI	-0.365	<0.001***
Average SaO_2	0.370	<0.001***

Minimal SaO_2	0.384	<0.001***
AI	-0.249	<0.001***
ESS	-0.053	0.369
EDS	-0.049	0.405
RLS	0.050	0.397
EDS: excessive daytime sleepiness, AI: arousal index, RDI: respiratory disturbance index, ESS: Epworth sleepiness scale, AHI: apnea hypopnea index, ODI: oxygen desaturation index, SaO_2: saturation of blood with oxygen, RLS: restless leg syndrome. ***: p value below 0.001, **: p value below 0.01.		

Table 4: Correlations of vitamin D with sleep-related indices.

	R	P
Age	0.080	0.176
Body mass index	-0.126	0.031*
Total sleep time	-0.010	0.870
AHI	-0.025	0.676
Sleep apnea	-0.011	0.846
RDI	-0.021	0.726
ODI	-0.055	0.354
Average SaO_2	0.066	0.259
Minimal SaO_2	0.065	0.267
AI	-0.016	0.789
ESS	-0.081	0.166
EDS	-0.056	0.345
RLS	-0.091	0.120
EDS: excessive daytime sleepiness, AI: arousal index, RDI: respiratory disturbance index, ESS: Epworth sleepiness scale, AHI: apnea hypopnea index, ODI: oxygen desaturation index, SaO_2: saturation of blood with oxygen, RLS: restless leg syndrome. ***: p value below 0.001, **: p value below 0.01.		