Original Article

Bone Metabolic Markers in Patients with Obstructive Sleep Apnea Syndrome

Yan Qiao[1], Bei Wang[1], Jiao-Jiao Yang[2], Yan-Feng Fan[1], Qian Guo[2], Zhan-Jun Dou[2], Ya-Qiong Huang[2], Ting-Ting Feng[2], Shu-Juan Wang[2], Dong-Dong An[2], Xiao-Ling Gao[1]

[1]Department of Respiratory and Critical Care Medicine, The Second Hospital of Shanxi Medical University, Taiyuan, Shanxi 030001, China
[2]Department of the Second Clinical Medicine, Shanxi Medical University, Taiyuan, Shanxi 030001, China

Abstract

Background: Obstructive sleep apnea syndrome (OSAS) is prevalent in obesity and is associated with many metabolic abnormalities. The relationship between OSAS and bone metabolism is still unclear. The aim of this study was to investigate the relationship between the severity of OSAS and bone metabolic markers.

Methods: A total of 119 obese males were enrolled in this study in spring months from 2015 to 2017. All candidates underwent polysomnography, and their bone mineral density (BMD) and the serum levels of total procollagen type 1 N-terminal propeptide (t-P1NP), N-terminal midfragment of osteocalcin (N-MID), β-C-terminal telopeptide of type 1 collagen (β-CTX), vitamin D (VD), and parathyroid hormone (PTH) were measured. The analysis of variance and Pearson correlation analysis were performed for data analyses.

Results: No significant differences in the mean values of BMD were observed among the obesity, mild-to-moderate OSAS, and severe OSAS groups; and the serum levels of t-P1NP and β-CTX in the severe OSAS group were significantly higher than those in the obesity group (48.42 ± 23.78 ng/ml vs. 31.98 ± 9.85 ng/ml, $P < 0.001$; 0.53 ± 0.24 ng/ml vs. 0.41 ± 0.13 ng/ml, $P = 0.011$, respectively). The serum level of VD in the obesity group was significantly higher than those in the mild-to-moderate and severe OSAS groups (both $P < 0.001$), and decreased as the severity of OSAS increased ($P < 0.001$). The serum level of PTH in the severe OSAS group was significantly higher than those in the obesity and mild-to-moderate OSAS groups (both $P < 0.001$). The results of correlation analysis indicated that the level of apnea-hypopnea index (AHI) was correlated with the levels of t-P1NP ($r = 0.396$, $P < 0.001$), VD ($r = –0.404$, $P < 0.001$), and PTH ($r = 0.400$, $P < 0.001$), whereas the level of minimum O_2 saturation (SaO_2min) was correlated with the levels of VD ($r = 0.258$, $P = 0.016$) and PTH ($r = –0.376$, $P < 0.001$).

Conclusions: The levels of bone resorption and formation markers in patients with severe OSAS were significantly increased compared to obese men, and the severity of OSAS was correlated with the serum levels of t-P1NP, VD, and PTH.

Key words: Bone Metabolic Markers; Bone Mineral Density; Obstructive Sleep Apnea Syndrome

Introduction

Obstructive sleep apnea syndrome (OSAS) is a common disorder characterized by repeating episodes of upper airway obstruction during sleep. Previous studies indicated that OSAS was more prevalent among obese people and the incidence of OSAS increased with age.[1-3] At present, OSAS can seriously affect the quality of life in patients and has been considered as an independent risk factor of a variety of systemic diseases including hypertension and metabolic syndrome.[4-8]

Although the relationship between OSAS and bone mineral density (BMD) has been confirmed in many studies, the results are conflicting.[9-11] Only few studies have focused on the relationship between OSAS and bone metabolic markers. The bone is mainly composed of collagen fibers formed by type 1 collagen. Procollagen type 1 N-terminal propeptide (P1NP) is a specific marker for the deposition

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Address for correspondence: Dr. Xiao-Ling Gao, Department of Respiratory and Critical Care Medicine, The Second Hospital of Shanxi Medical University, Taiyuan, Shanxi 030001, China
E-Mail: 937658284@qq.com

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of type 1 collagen, whereas β-C-terminal telopeptide of type 1 collagen (β-CTX) is a degradation product of type 1 collagen. P1NP and CTX are recommended by the International Osteoporosis Foundation and the International Federation of Clinical Chemistry and Laboratory Medicine as the markers of bone formation and bone resorption, respectively.[12,13] N-terminal midfragment of osteocalcin (N-MID) is a degradation product of osteocalcin and its level in the peripheral blood can reflect the activity of osteoblasts and the rate of bone mineralization. Vitamin D (VD) is one of the essential and fat-soluble vitamins in the human body. Adequate daily intake of VD can increase the absorption of intestinal calcium and phosphorus by 30–40% and 80%, respectively. VD can also inhibit the secretion of parathyroid hormone (PTH), and the reduced PTH can mediate bone resorption and maintain the health of bone. Therefore, VD deficiency can now be considered as a high-risk factor of osteoporosis.[14] In this study, obesity was designed as the control group, we compared both the above bone metabolic markers and BMD in obesity and obese OSAS patients, and correlation analysis was performed to determine whether the levels of these bone metabolic markers and BMD in OSAS patients are correlated with the severity of OSAS, which is rarely seen in the previous studies.

Methods

Ethical approval

The study was conducted in accordance with the *Declaration of Helsinki* and was approved by the Ethics Committee of the Second Hospital of Shanxi Medical University. Written informed consent was signed by all the participants before the study enrollment.

Patients

A total of 119 obese male individuals were enrolled in this study in spring months from 2015 to 2017. Polysomnography (PSG) and the collection of serum samples were conducted at the physical examination center, and the multi-guide sleep monitoring center of the Second Hospital of Shanxi Medical University. The age of the subjects ranged from 30 to 65 years, and after detailed medical history, physical and auxiliary examinations (including blood routine, urinalysis, electrocardiography, color Doppler echocardiography, thyroid color ultrasonography, abdominal color ultrasonography, chest radiography, pulmonary function test, serum biochemicals, and thyroid function test), candidates with smoking habit, alcoholism, cold, stuffy nose, acute illness, chronic obstructive pulmonary diseases, any other respiratory disorder, diabetes, hypertension, coronary heart diseases, heart failure, hyperthyroidism, hypothyroidism, hyperparathyroidism, hypoparathyroidism, Cushing syndrome, hypogonadism, hypopituitarism, growth hormone deficiency, acromegaly, gastrointestinal diseases, chronic renal disease, multiple myeloma, malignancy, bone metastasis, Paget's disease, rheumatologic disorders, stroke, paraplegia, hemiplegia, dementia, schizophrenia, depression, or a history of fractures were excluded from this study. In addition, the patients with positive airway pressure therapy were also excluded, as well as the candidates with a medication history that might affect bone metabolism, such as calcium, VD, bisphosphonates, corticosteroid, parathormone, calcitonin, antiepileptics, Vitamin K antagonist, and heparin. Moreover, all the participants were requested to avoid exercise for 48 h before blood collection. Before PSG monitoring, all participants wore loose clothes and maintained good personal hygiene. They were prohibited from using alcohol, coffee, tea, and sedative drugs.

Polysomnographic test

Among these 119 individuals, 32 subjects (based on the "Guidelines for prevention and control of adult obesity in China") with body mass index (BMI) ≥28 kg/m^2 were assigned into the obesity group and the 87 OSAS patients were diagnosed by the multi guide sleep monitor (Sandman 64 guide sleep monitor, USA; Compumedics-E Type 44 guide sleep monitor, Australia). The OSAS patients were further divided into two groups based on their apnea-hypopnea index (AHI): the mild-to-moderate OSAS group contained 32 patients with 5 events/h ≤ AHI <30 events/h, and the severe OSAS group contained 55 patients with AHI ≥30 events/h. All subjects underwent PSG monitoring performed by experienced doctors, and their blood samples were collected on the following morning for further analysis.

Measurement of bone metabolic markers

The serum samples were collected between 08:00 a.m. and 09:00 a.m. after an overnight fast, and the levels of t-P1NP, N-MID, β-CTX, VD, and PTH were measured using a Roche Cobase601 electrochemical luminescence instrument (Roche Diagnostics, Mannheim, Germany), and the lumbar BMD was measured using a radiation absorption method.

Statistical analysis

Statistical analysis was performed using SPSS version 17.0 (SPSS Inc., Chicago, IL, USA). Data were expressed as mean ± standard deviation (SD). The analysis of variance was used to compare the difference among different groups based on the least significant difference. Pearson correlation analysis was performed to study the correlation among the data. A $P < 0.05$ was considered statistically significant.

Results

Evaluation of clinical information of the participants

As shown in Table 1, the mean age of the individuals was 50.1 ± 7.3 years, 51.8 ± 8.1 years, and 48.2 ± 9.9 years for the obesity, mild-to-moderate OSAS, and severe OSAS groups, respectively, without significant difference ($P > 0.05$). The mean values of BMI in the obesity ($t = 3.519$, $P = 0.001$), and the severe OSAS groups ($t = 5.277$, $P < 0.001$) were greater than that in the mild-to-moderate OSAS group.

Evaluation of the bone metabolic markers of the individuals

Subsequently, to investigate the effect of OSAS on bone metabolism, some serum bone metabolic markers were evaluated [Table 2]. No significant differences were found in terms of the mean BMD values among the obesity, mild-to-moderate OSAS, and severe OSAS groups ($P > 0.05$). The N-MID values among the three groups also showed no significant differences ($P > 0.05$). The serum levels of t-P1NP in the obesity and mild-to-moderate OSAS groups were significantly lower than that in the severe OSAS group ($t = -4.138$, $P < 0.001$; and $t = -3.421$, $P = 0.001$, respectively). The mean value of β-CTX in the severe OSAS group was significantly higher than that in the obesity group ($t = 2.575$, $P = 0.011$), whereas the levels of β-CTX and t-P1NP between the obesity and mild-to-moderate OSAS groups showed no significant difference ($t = -1.839$, $P = 0.069$; and $t = -0.637$, $P = 0.525$, respectively). In terms of serum VD levels, the mild-to-moderate and severe OSAS groups showed markedly lower results as compared to the obesity group ($t = -5.660$, $P < 0.001$; and $t = -10.862$, $P < 0.001$, respectively), and the VD level in the mild-to-moderate OSAS group was significantly higher than that in the severe OSAS group ($t = 4.498$, $P < 0.001$). The PTH level in the severe OSAS group was significantly higher than that in the mild-to-moderate OSAS and obesity groups ($t = 4.945$, $P < 0.001$; and $t = 7.056$, $P < 0.001$, respectively), whereas no significant difference was observed in the mean values of PTH between the obesity and mild-to-moderate OSAS groups ($t = -1.877$, $P = 0.063$).

Correlation between the polysomnographic and bone metabolic markers in Obstructive sleep apnea syndrome patients

In the next step, a correlation analysis was performed to investigate the relationship between the severity of OSAS and bone metabolic markers in the OSAS patients. As shown in Table 3, BMI was positively correlated with AHI ($r = 0.572$, $P < 0.001$) and PTH ($r = 0.292$, $P = 0.006$), but negatively correlated with minimum O_2 saturation (SaO_2min) ($r = -0.339$, $P = 0.001$) and BMD ($r = -0.261$, $P = 0.015$) in OSAS patients. In addition, AHI was positively correlated with PTH ($r = 0.400$, $P < 0.001$) and t-P1NP ($r = 0.396$, $P < 0.001$) but negatively correlated with SaO_2min ($r = -0.673$, $P < 0.001$) and VD ($r = -0.404$, $P < 0.001$). SaO_2min was positively correlated with VD ($r = 0.258$, $P = 0.016$) but negatively correlated with PTH ($r = -0.376$, $P < 0.001$). PTH was positively correlated with t-P1NP ($r = 0.270$, $P = 0.011$), but negatively correlated with VD ($r = -0.363$, $P = 0.001$). The β-CTX was positively correlated with N-MID ($r = 0.616$, $P < 0.001$) and t-P1NP ($r = 0.614$, $P < 0.001$), and N-MID was positively correlated with t-P1NP ($r = 0.560$, $P < 0.001$).

Discussion

There are many factors affecting bone metabolic markers, such as age, gender, menstrual variation, seasonal variation, circadian variation, fasting and food intake, physical activity, diseases, and drugs.[15,16] To eliminate the effects of these factors, we set strict exclusion criteria. In our study, only men were included, and no significant differences were found in terms of the mean age among the obesity, mild-to-moderate OSAS, and severe OSAS groups. We also excluded the patients with diseases and drugs that affect bone metabolic markers, such as thyroid and parathyroid diseases, Cushing syndrome, growth hormone deficiency, acromegaly, gastrointestinal diseases, chronic renal disease, multiple myeloma, malignancy, bone metastasis, and Paget's disease. In addition, in order to reduce the variability, samples were collected between 08:00 a.m. and 09:00 a.m. after an

Table 1: Clinical information and polysomnographic parameters of all participants in this study

Items	Obesity group ($n = 32$)	Mild-to-moderate OSAS group ($n = 32$)	Severe OSAS group ($n = 55$)
Age (years)	50.1 ± 7.3	51.8 ± 8.1	48.2 ± 9.9
BMI (kg/m^2)	32.1 ± 2.2†	30.1 ± 1.4	32.7 ± 2.7†
AHI (events/h)	2.46 ± 0.96	15.93 ± 7.44*	72.07 ± 22.14*†
SaO_2min (%)	93.56 ± 2.38	79.44 ± 11.31*	56.33 ± 13.34*†

The data are shown as mean ± SD. *P<0.05, compared with obesity group; $^\dagger P$<0.05, compared with mild-to-moderate OSAS group. BMI: Body mass index; AHI: Apnea-hypopnea index; SaO_2min: Minimum O_2 saturation; OSAS: Obstructive sleep apnea syndrome; SD: Standard deviation.

Table 2: Evaluation of the bone metabolic markers of all participants in this study

Items	Obesity group ($n = 32$)	Mild-to-moderate OSAS group ($n = 32$)	Severe OSAS group ($n = 55$)
BMD (g/cm^2)	1.02 ± 0.07	1.04 ± 0.19	0.99 ± 0.09
t-P1NP (ng/ml)	31.98 ± 9.85	34.83 ± 10.66	48.42 ± 23.78*†
N-MID (ng/ml)	16.87 ± 4.43	17.73 ± 5.93	18.26 ± 7.11
β-CTX (ng/ml)	0.41 ± 0.13	0.50 ± 0.17	0.53 ± 0.24*
VD (ng/ml)	27.23 ± 7.59	17.62 ± 5.88*	10.83 ± 6.80*†
PTH (pg/ml)	28.29 ± 13.89	37.02 ± 6.94	57.47 ± 24.60*†

The data are shown as mean ± SD. *P<0.05, compared with obesity group; $^\dagger P$<0.05, compared with mild-to-moderate OSAS group. BMD: Bone mineral density; t-P1NP: Total procollagen type 1 N-terminal propeptide; N-MID: N-terminal midfragment of osteocalcin; β-CTX: β-C-terminal telopeptide of type 1 collagen; VD: Vitamin D; PTH: Parathyroid hormone; OSAS: Obstructive sleep apnea syndrome; SD: Standard deviation.

Table 3: Correlation analysis of association between polysomnographic and bone metabolic markers in OSAS patients

Items	BMI	AHI	SaO_2min	BMD	PTH	β-CTX	VD	N-MID	t-P1NP
BMI	–	0.572*	−0.339*	−0.261†	0.292*	0.016	−0.168	−0.111	0.120
AHI		–	−0.673*	−0.205	0.400*	0.133	−0.404*	0.030	0.396*
SaO_2min			–	0.143	−0.376*	−0.005	0.258†	0.117	−0.124
BMD				–	−0.103	−0.059	0.058	0.016	−0.084
PTH					–	0.171	−0.363*	0.081	0.270†
β-CTX						–	−0.135	0.616*	0.614*
VD							–	−0.058	−0.136
N-MID								–	0.560*
t-P1NP									–

*P<0.01; †P<0.05. BMI: Body mass index; AHI: Apnea-hypopnea index; SaO_2min: Minimum O_2 saturation; BMD: Bone mineral density; PTH: Parathyroid hormone; β-CTX: β-C-terminal telopeptide of type 1 collagen; VD: Vitamin D; N-MID: N-terminal midfragment of osteocalcin; t-P1NP: Total procollagen type 1 N-terminal propeptide; OSAS: Obstructive sleep apnea syndrome; –: Not applicable.

overnight fast only in spring, and exercise was avoided for 48 h before the collection.

The relationship between OSAS and obesity has been confirmed by many previous studies, and obesity is now considered as an independent risk factor for OSAS.[17] Zhang and Si[18] have reported that when body weight increased, the frequency of respiratory events would also increase during sleep. Some studies have suggested that if body weight gained by 10%, the value of AHI might increase by 32% and the risk of OSAS might also increase by 5 folds. In addition, obesity might also cause problems in bone metabolism by affecting the secretion of cytokines and hormones.[19] On the other hand, sleep disorders and chronic intermittent hypoxia (CIH) in OSAS patients might cause metabolic disorders, which could further aggravate the condition of obesity.[20] In this study, individuals with obesity were assigned into the control to reduce the influence of obesity. As expected, the results showed that the BMI in the severe OSAS group was higher than that in the mild-to-moderate OSAS group, and the correlation analysis indicated that BMI was positively correlated with AHI and PTH but negatively correlated with SaO_2min and BMD. The results of this study showed no significant difference of BMD in subjects among the obesity, mild-to-moderate OSAS, and severe OSAS groups. The correlation analysis suggested no relationship between BMD and AHI or between BMD and SaO_2min. The data obtained from this study were consistent with those shown in a previous report about BMD.[10] In summary, these results indicated that BMI was correlated to the severity and BMD of OSAS patients.

Previous studies have indicated that during osteoporosis, the changes in the levels of bone metabolic markers occurred much earlier than the change in BMD, suggesting that these metabolic markers might have an important value for the early diagnosis of osteoporosis. To investigate the role of bone metabolic markers in OSAS, the serum levels of these markers were compared among individuals from different groups. As mentioned above, our results indicated no significant differences in BMD among the obesity, mild-to-moderate OSAS, and severe OSAS groups, but some bone metabolic markers made the differences. As shown in Table 1, the severe OSAS and obesity groups had the similar BMI, but the levels of β-CTX and t-P1NP shown in Table 2 were higher in the severe OSAS group than those in the obesity group. Many studies have reported that OSAS was associated with an increased level of bone resorption. In this study, it was also observed that the serum level of β-CTX, a marker of bone resorption, in the severe OSAS group was significantly higher compared to the obesity group. These results demonstrated that the activity of osteoclasts, bone resorption, and the release of β-CTX in the severe OSAS group were all increased. Tomiyama *et al*.[21] found that OSAS could be characterized by "an uncoupled state" between bone formation and bone resorption, because they observed that the level of urinary CTX was higher in severe OSAS patients than that in mild OSAS patients and controls, however, no such change was observed for bone formation markers (bone-specific alkaline phosphatase and osteocalcin). In this study, the severe OSAS group showed a higher level of t-P1NP, a marker of bone formation, than the obesity and mild-to-moderate OSAS groups. Although no significant differences were observed in the levels of N-MID among the obesity, mild-to-moderate OSAS, and severe OSAS groups, the N-MID level was on the uptrend in OSAS patients. These results indicated that the severe OSAS group was associated with an increased rate of bone collagen deposition. In addition, this study demonstrated that AHI and t-P1NP were positively correlated in OSAS patients, suggesting that the severity of OSAS might be associated with bone formation. In summary, all these results suggested an increased rate of bone turnover in the severe OSAS group. The correlation analysis also showed that β-CTX was positively correlated with N-MID and t-P1NP, and N-MID was positively correlated with t-P1NP, indicating "a coupled state" between bone formation and bone resorption in OSAS. Nevertheless, large-scale clinical studies are still needed to clarify the relationship between bone formation and bone resorption in OSAS patients.

It is well known that OSAS is related to obesity, a disorder closely associated with VD deficiency. Increased influx of 25-hydroxyvitamin D into adipose tissues is a plausible explanation for VD deficiency in obesity. A recent study has shown that if children suffered from both obesity and OSAS,

their VD levels would be further reduced.[22] In this study, a lower VD level was also shown in the severe OSAS group, although it had a similar BMI as compared with that in the obesity group. Consistent with the findings from a previous study,[23] it was observed in this study that as the severity of OSAS increased, the level of VD would decrease and might be associated with the high bisphenol A (BPA) levels in OSAS patients. Erden *et al*.[24] found that the BPA level in the severe OSAS group was significantly higher than those in the mild-to-moderate OSAS and control groups, and the level of BPA was negatively correlated with VD level. BPA might be involved in the etiopathogenesis of OSAS by inducing obesity, androgen antagonist activities, estrogenic activities, and muscular dysfunctions. In addition, OSAS is associated with insulin resistance and diabetes, whereas a low level of VD can lead to glucose intolerance and IR, suggesting that VD may also play an important role in the pathophysiology of OSAS. The correlation analysis in this study also indicated that VD was negatively correlated with AHI but positively correlated with SaO_2min in the OSAS patients, suggesting that the severity of OSAS might affect the level of VD in the body.

VD deficiency could also increase the secretion of PTH, while an increased level of PTH could induce bone resorption and bone loss.[25] Barceló *et al*.[26] reported that PTH was positively correlated with AHI. The results from this study also confirmed that PTH was positively correlated with AHI, but negatively correlated with SaO_2min in the OSAS patients. In addition, the level of PTH in the severe OSAS group was significantly higher than that in the mild-to-moderate OSAS and obesity groups, suggesting that the patients with severe OSAS might have more active bone resorption.

Although the causes of increased bone resorption and formation markers in severe OSAS patients are still unclear, it has been considered that hypoxia, oxidative stress, inflammation, and increased sympathetic tone might be the contributing factors.

OSAS is characterized by CIH. Hypoxia could accelerate the resorption of bone by affecting the proliferation and differentiation of osteogenic cells as well as the activity of osteoclasts.[27-29] However, some studies showed that hypoxia could promote osteoblasts differentiation into osteocytes and inhibit sclerostin expression,[30,31] which was a negative regulatory factor for bone formation. Acidosis induced by hypoxia could inhibit mineral deposition and activate osteoclasts.[32,33] Oxidative stress which is also present in OSAS patients can affect bone health through increasing bone resorption. In addition, CIH can activate the NF-kB signaling pathway and induce inflammatory conditions through up-regulating the expression of downstream cytokines including interleukin 6 (IL-6) and tumor necrosis factor-alpha (TNF-alpha), which are called osteolytic cytokines, and subsequently increase the risk of bone mineral loss. Repeated intermittent hypoxia and micro arousal during the sleep of OSAS patients could increase the sympathetic tone.[34,35] Most scholars believe that the excitation of sympathetic nerves could inhibit the activity of osteoblasts, thus leading to reduce bone formation and ultimately lowering the bone mass and BMD.[36]

As seen in our study, the levels of bone resorption and formation markers in patients with severe OSAS were significantly increased compared to obese men, while no significant differences were found in terms of the mean BMD values among the obesity, mild-to-moderate OSAS, and severe OSAS groups. This was mainly because age, gender, and weight were more important for BMD. In our study, all participants were obese men and age-matched, and there was no significant difference in terms of BMI between the obesity and severe OSAS groups. In the obese people included in our study, the BMI values in the obesity and severe OSAS groups were higher than that in the mild-to-moderate OSAS group, it seemed that the mean BMD levels in the obesity and severe OSAS groups were lower than that in the mild-to-moderate OSAS group, but no significant differences were found among the three groups. On the other hand, the changes in bone metabolic markers are much earlier than the change in BMD, so clinical follow-up will have to be done to disclose the truth.

There were some limitations in our study. The sample was small, and it was mainly because of the strict exclusion criteria. The concentrations of IL-6 and TNF-alpha which are related to bone metabolism and CIH existed in OSAS should be measured and analyzed. Follow-up evaluation was not involved in the present study, long-term follow-up of OSAS patients will provide more evidence, and may also help us investigate the bone metabolism in OSAS patients with positive airway pressure therapy.

In conclusion, increased bone resorption and formation markers in patients with severe OSAS compared to obese men indicated high bone turnover, and the severity of OSAS was correlated with the serum levels of t-P1NP, VD, and PTH. In the future, large-scale clinical studies are needed, and the specific mechanisms underlying such observations remain to be further clarified.

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Conflicts of interest

There are no conflicts of interest.

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阻塞性睡眠呼吸暂停综合征患者骨代谢标志物的研究

摘要

背景：阻塞性睡眠呼吸暂停综合征（obstructive sleep apnea syndrome，OSAS）多见于肥胖人群，且与多种代谢性疾病相关，而OSAS与骨代谢的关系至今仍未明确。此研究旨在探讨OSAS严重程度与骨代谢标志物的关系。

方法：纳入了2015年至2017年春季来诊的119名肥胖男性。所有参与者行多导睡眠监测，并测量骨密度（bone mineral density，BMD）及血清总I型胶原氨基端延长肽（total procollagen type1 N-terminal propeptide，t-P1NP）、N-端骨钙素（N-terminal midfragment of osteocalcin, N-MID）、β-胶原特殊序列（β-C-terminal telopeptide of type 1 collagen，β-CTX）、维生素D（vitamin D，VD）和甲状旁腺激素（parathyroid hormone，PTH）的水平。数据分析采用方差分析及Pearson相关分析。

结果：肥胖对照组、轻中度OSAS及重度OSAS组患者的BMD水平无明显差异，而重度OSAS组血清t-P1NP和β-CTX的水平均明显高于肥胖对照组 (48.42±23.78 ng/ml vs. 31.98±9.85 ng/ml, P<0.001; 0.53±0.24 ng/ml vs. 0.41±0.13 ng/ml, P =0.011)。肥胖组的VD水平明显高于轻中度OSAS组 (P <0.001)和重度OSAS组 (P <0.001)，且重度OSAS组的VD水平低于轻中度OSAS组 (P <0.001)。重度OSAS组的PTH水平明显高于轻中度OSAS组（P <0.001）及肥胖组 (P <0.001)。相关性分析显示睡眠呼吸暂停低通气指数（apnea-hypopnea index，AHI)与t-P1NP（r=0.396, P <0.001）、VD（r=–0.404, P <0.001）、PTH（r=0.400, p<0.001）相关，夜间最低血氧（minimum O_2 saturation，SaO_2min)与VD（r=0.258, P =0.016）和PTH（r=–0.376, P <0.001）相关。

结论：与男性肥胖人群相比，男性重度OSAS患者的骨吸收及骨形成标志物明显升高，OSAS的严重程度与血清t-P1NP、VD及PTH相关。