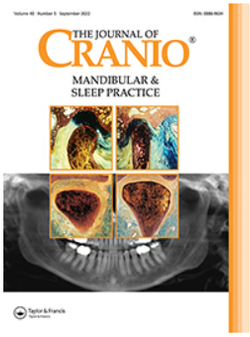

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SLEEP

Association between obstructive sleep apnea syndrome and bone mineral density in adult orthodontic populations

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ABSTRACT

Objective: To determine the association between obstructive sleep apnea syndrome (OSAS) and predicted bone mineral density (BMD) in adults presenting for orthodontic treatment.

Methods: This retrospective cross-sectional study included 38 adults divided into OSAS and non-OSAS groups. Using pre-treatment CBCT images, radiographic density (RD) of left and right lateral regions of the 1st cervical vertebrae and dens of the 2nd cervical vertebrae were measured as an indicator for BMD.

Results: When controlling for age, sex, and BMI, the mean RD was significantly lower in the OSAS group compared to the non-OSAS group (left CV1: 36.69 ± 84.50 vs. 81.67 ± 93.25 Hounsfield Units [HU], respectively, $p = 0.031$; right CV1: 30.59 ± 81.18 vs. 74.26 ± 91.81 HU, $p = 0.045$; dens: 159.25 ± 115.96 vs. 223.94 ± 106.09 HU, $p = 0.038$).

Conclusion: Adults with OSAS have lower values for predicted BMD than those without OSAS.

KEYWORDS

Obstructive sleep apnea; bone density; cone beam computed tomography; cervical vertebrae

Introduction

Obstructive sleep apnea syndrome (OSAS) is a common disorder that affects 9% to 38% of North American and European adults [1]. OSAS is characterized by frequent episodes of partial or complete airway collapse during sleep, leading to hypoxia and recurrent arousals from sleep [1,2]. OSAS is associated with several comorbidities, such as hypertension, cardiovascular disease, and diabetes [1,3]. Recent studies offer new evidence for an association between reduced bone mineral density (BMD) and OSAS [4–6].

Low BMD is a condition that affects the entire skeletal system and is often a consequence of nutritional, hormonal, or renal disease [7]. It can also be linked to systemic conditions such as chronic obstructive pulmonary disease [7]. Dual X-ray absorptiometry (DXA) is the current gold standard for diagnosing BMD by measuring density at the proximal femur and lumbar spine [8,9]. Risk factors for decreased femoral BMD include old age in men, post-menopausal age in women, increased serum calcium levels, and low body mass index (BMI) [9]. Biomarkers of increased bone turnover, such as cross-linked C-terminal telopeptide of type I collagen (CTX), bone sialoprotein, hydroxyproline, cathepsin K, and pyridinium crosslinks have been proposed as predictors of low BMD and fracture risk, but their clinical utility is still debated [10,11].

Orthodontic tooth movement has been shown to reduce alveolar bone density [12,13]. Hsu et al. [12] investigated bone density changes adjacent to teeth during orthodontic treatment and found a mean reduction of 24% after 7 months of non-extraction treatment. While this reduction in density may not be clinically significant in the normal population and would be considered a physiologic process, it is possible that patients with reduced BMD may undergo further reduction with orthodontic treatment [12]. Low BMD may accelerate orthodontic tooth movement due to increased bone turnover in these individuals [14]. It may also negatively impact mini-implant primary stability as well as interdisciplinary treatment such as dental implant failure [15,16].

While the link between OSAS and low BMD has yet to be fully elucidated, it is likely that the intermittent hypoxic events characteristic of OSAS could be responsible for such an association [4,5]. The hypoxia seen in OSAS results in ischemic injury, leading to inflammation and the involvement of a host of hormones and signaling factors that cause a decrease in osteoblastic activity and stimulate osteoclastic activity [4,5]. The

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repetitive deoxygenation of blood seen in OSAS could have a chronic negative effect on bone metabolism and, ultimately, bone density. Orthodontic tooth movement relies on healthy bone metabolism. If the hypoxic environment created by OSAS could negatively affect bone metabolism, it is possible that orthodontic tooth movement could be affected as well. Another theory linking OSAS and low BMD involves gas exchange and rib cage fragility. Polverino et al. [17] found that bone fragility was associated with significant perturbations in gas exchange and shortening of inspiratory time. If low BMD is linked to an alteration in breathing pattern, a person with OSAS may be particularly at risk.

While CBCT images of the head and neck region are not used to diagnose OSAS, they are often obtained for orthodontic diagnostic purposes. If CBCT images could be used to predict low BMD in the rest of the body, the imaging could potentially act as a screening tool for OSAS in the future.

Study aims

The objective of this study was to determine the association between OSAS and BMD in adults presenting for orthodontic treatment. The hypothesis was that subjects in the OSAS group have lower BMD than those in the control group.

Materials and methods

Study design

This retrospective cross-sectional study measured radiographic density (RD) as a means of assessing BMD in adults with and without OSAS. The study was approved by the Institutional Review Board at the University at Buffalo (STUDY 00004421), and informed consent was waived due to the retrospective nature of the study. Pre-treatment records of adults presenting for orthodontic treatment between January 2021 and March 2021 at Get it Straight Orthodontics in Pittsford, NY were evaluated.

Sample size calculation

To detect a difference of 130 gray values in RD on the left side of the first cervical vertebrae (CV1) between individuals with normal versus low BMD at 80% power and a standard deviation of 90 [17], it was estimated that a minimum of 32 subjects would be needed (16 subjects per group).

Subject selection

A list of patients treated in the practice stated above was generated from Dolphin Management and Imaging Software (Version 11.95.8.7, Dolphin Imaging and Management Solutions, Chatsworth, CA, USA). This practice treats adult and growing orthodontic patients with focus on patients with sleep conditions. To select an appropriate OSAS sample, records were searched using the diagnostic group identifiers "Obstructive Sleep Apnea", "Surgery", and "TAP Appliance" (Thornton Adjustable Positioner). The TAP appliance is a mandibular advancement device often used by the practitioner to treat patients with moderate to severe OSAS [18]. From this search criteria, 348 records were initially identified. After applying inclusion and exclusion criteria (Table 1), 19 patients (11 females, 8 males) were included in the OSAS group.

To select an appropriate non-OSAS control sample, records from the same practice were searched by medical history to determine patients who fit the inclusion and exclusion criteria (Table 1). From this search criteria, 156 records qualified and were then screened for their Epworth Sleepiness Scale (ESS) and STOP-Bang Questionnaire (SBQ) scores. An ESS score below 10 and an SBQ score of less than 3 were used to suggest the absence of OSAS [19,20]. The 49 records that met

Table 1. Inclusion and Exclusion Criteria.

Inclusion Criteria
• Male and female patients 18 years or older
• Diagnosed with moderate to severe OSAS by overnight polysomnography according to the American Academy of Sleep Medicine classification[a]
• Large field of view CBCT taken between 2010 and the present
• CBCT of adequate quality that shows up to the second vertebrae in its entirety
Exclusion Criteria
• Images of undiagnostic quality
• Systemic diseases that affect bone density such as diabetes, thyroid disorders, and chronic obstructive pulmonary disease
• Osteopenia or bone diseases such as osteoporosis
• Current smoking
• Moderate to severe periodontal disease
• Prior diagnosis and treatment for OSAS (for the non-OSAS group only)

[a]The American Academy of Sleep Medicine (AASM) classifies OSA severity in adults according to AHI, where mild is ≥ 5,but < 15 events per hour, moderate is ≥ 15, but < 30 events per hour, and severe is ≥ 30 events per hour

CBCT: Cone beam computed tomography; OSAS: Obstructive sleep apnea syndrome.

these criteria were then sorted into age range categories: 30–39, 40–49, 50–59 and 60–69 years. To match the non-OSAS sample to the OSAS sample by age range in a 1:1 ratio, the appropriate number of records were chosen from each age range by selecting every other record for improved random selection until the number of subjects needed was fulfilled. A total of 19 records (3 males, 16 females) were included. Age, sex, BMI [21], smoking history, medical conditions, and prescribed medications were recorded for both groups. Medications were categorized into antidepressant, antihypertensive, and lipid-lowering drugs. The Apnea-Hypopnea Index (AHI) was recorded for the OSAS group, and ESS and STOP-BANG scores were recorded for the non-OSAS group.

Study outcomes

CBCT imaging was used to measure bone density in the head and neck as a proxy for BMD in the remainder of the body. The RD values, reported as Hounsfield Units (HU), of the left side of CV1, the right side of CV1, and dens or odontoid process of the 2nd cervical vertebrae (CV2), were measured in patients with and without OSAS. These measurement sites were validated in previous studies [17,22]. All study measurements were conducted by one investigator (M.D.).

CBCT acquisition and analysis

Pre-treatment CBCT images were taken by one of the three trained technicians using an i-CAT scanner (Version 17–19, Imaging Sciences International, Hatfield, PA, USA). Scans were made using a 16 × 13 cm field-of-view (FOV), 4.8 s scan, at 5 mA and 120 kV. Each image data set included 328 slices with a 0.4 mm voxel size. All scans were obtained using natural head position with teeth in maximal intercuspation while the patient was seated in an upright position.

CBCT image files were de-identified prior to transfer and analysis. Images were then exported in Digital Imaging and Communications in Medicine (DICOM) format and uploaded in a computer running a Windows 7 (Microsoft, Redmond, WA, USA) operating system with a Dell LCD monitor with 2560 × 1440 resolution (Model U2713, Dell Computer Corp., Round Rock, TX, USA). All measurements were conducted using ACTEON® Imaging Suite (AIS) Software 3D Application (Version 5.20191206, de Götzen® S.r.l by Acteon Group, Olgiate Olona, Italy). Image files were reordered randomly to ensure blinding.

The full volume CBCTs were oriented so that the vertebral column was perpendicular to the axial plane, and the trimming tool was used to crop the image to include CV1 and CV2 in their entirety (Figure 1a). The axial view was oriented so that the plane dissected the middle of the

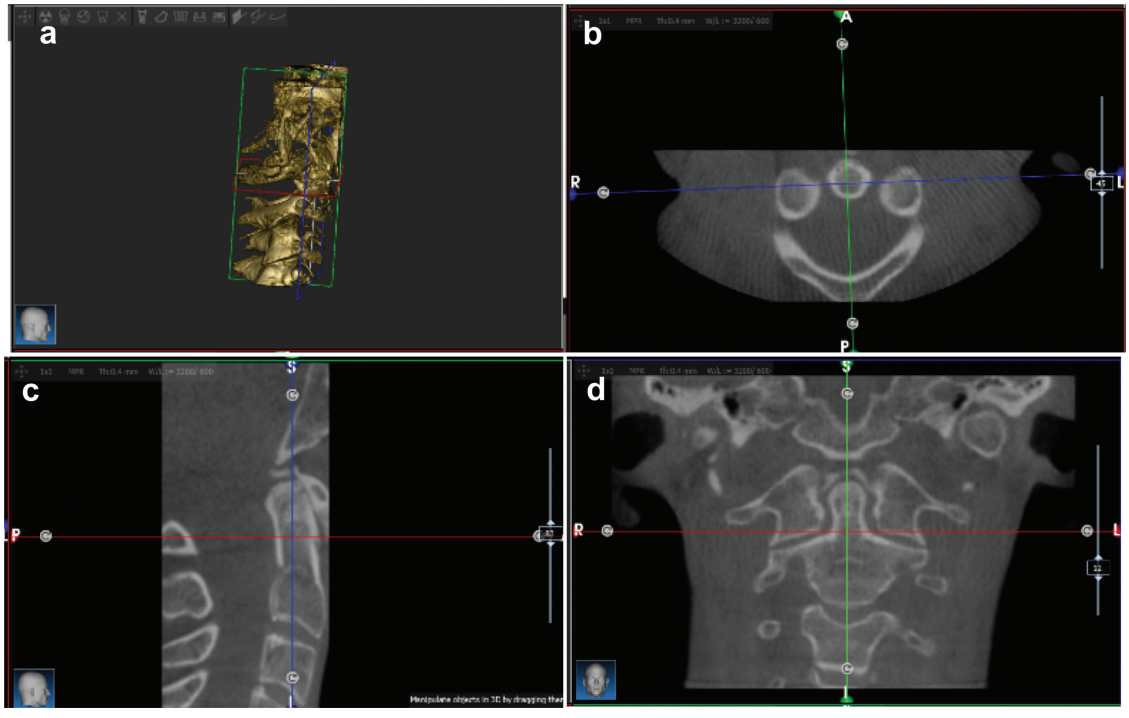

Figure 1. Orientation of a slice of a cone beam computed tomography (CBCT) image. (a) 3D representation of the image cropped to focus on the cervical vertebrae of interest. (b) Axial view of the image with the left and right regions of CV1 and the dens of CV2. (c) Sagittal view of the image. (d) Coronal view of the image, as used for measurements.

vertebrae at a 90° angle (Figure 1b). The sagittal view was oriented so that the plane dissected the middle of the CV2 body perpendicular to its superior and inferior borders (Figure 1c). These steps enabled the coronal slice to be oriented on the central portion of the dens (Figure 1d). To standardize the appearance of the slice and to show the greatest amount of contrast between bone and other tissues, the default window width and level were adjusted. The window width, which is the range of HU values that an image displays and controls the contrast in an image, was set to 850 HU (Figure 2a,b) [23]. The window level, which is the center of the window width and controls image brightness, was set to 150 HU (Figure 2a,b) [23].

The left and right CV1 and the dens of CV2 were analyzed in the coronal view. The left and right CV1 were outlined in their entirety, and the dens was outlined with a line drawn across its base to separate the dens from the body of CV2. For measurement of radiodensity, five consecutive slices were chosen, 0.4 mm in thickness, and in each slice, the "ROI" tool was used to outline each area of interest. Using the AIS software, mean HU measurements were determined for each area of interest (Figure 2c), and the final value for each area was calculated by averaging measurements from the five slices.

Statistical analysis

Ten randomly selected CBCT images from each treatment group were re-measured 2 weeks apart by one investigator. Intraclass correlation coefficients (ICC) and the Dahlberg's formula [24] were used to calculate reproducibility and measurement error.

Descriptive statistics were calculated, and the Shapiro–Wilk test was used to assess data normality. Independent sample *t*-tests were conducted to compare the mean RD values of the left and right CV1 and dens between groups. A two-factor Analysis of Variance (ANOVA) was used to assess the relationship between OSAS status and sex. An Analysis of Covariance (ANCOVA) was used to evaluate the relationship between OSAS status and age, as well as OSAS status and BMI. Lastly, ANCOVA was used to compare mean RD values between groups after adjusting for sex, age, and BMI. All tests were two-tailed and performed at the 5% level using SPSS for

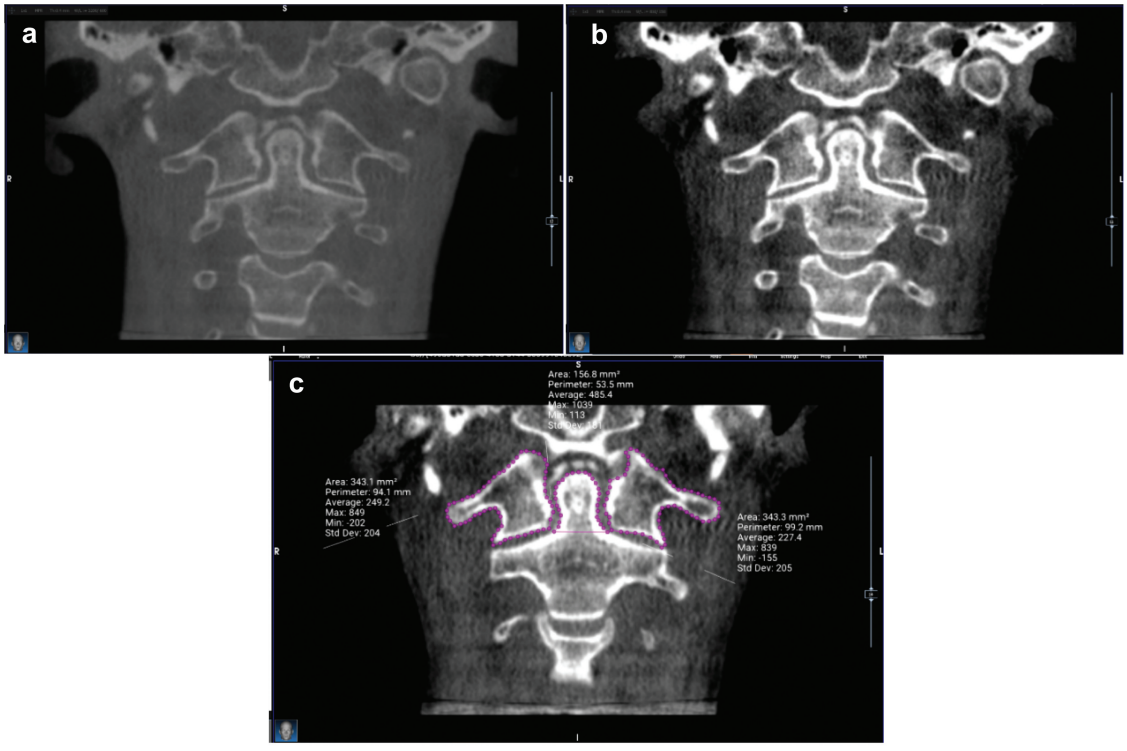

Figure 2. (a) Coronal cone beam computed tomography (CBCT) slice at default window width and window level of the software. (b) The same slice as seen using the adjusted window width and window level to increase the contrast of the image and differentiate bone from other tissues. (c) Outlines of the regions of interest and where the measurements were made.

Windows (Version 24, IBM Corporation, Armonk, NY, USA).

Results

Intra-rater reliability

The ICC estimates for the RDs of the left and right CV1 and dens were 0.99, indicating a high level of reproducibility. Measurement error according to Dahlberg's formula was 0.52, 0.84, and 0.88 HU for the left CV1, right CV1, and dens, respectively.

Descriptive statistics

Of the 19 subjects included in the OSAS and age-matched non-OSAS samples, 1 (5%) was in the 30–39 year category, 4 (21%) were in the 40–49 age category, 11 (58%) were in the 50–59 age category, and 3 (16%) were in the 60–69 category. The mean BMI was significantly higher in the OSAS group compared to the non-OSAS group (31.0 ± 4.2 vs. 23.5 ± 2.9 kg/m^2, respectively; $p < 0.001$; Table 2).

In the OSAS group, nine (47%) subjects were on anti-depressants, eight (42%) were on lipid-lowering drugs, and five (26%) were on anti-hypertensive drugs. In the non-OSAS group, one (5.3%) subject was on anti-depressants and two (11%) were on anti-hypertensive drugs. Two subjects were current smokers, both of whom were in the OSAS group.

The majority (58%, n = 11) of subjects in the OSAS sample were in the obese category (Figure 3). In contrast, in the non-OSAS sample, the majority (68%, n = 13) of subjects were in the normal weight category, while none were in the obese category. There was a statistically significant difference in distribution of BMI categories between the groups ($p < 0.001$).

In the OSAS group, the mean AHI of the male subjects was 36.2 (95% CI [26.0, 46.4]), indicating severe OSAS, while for the females, the mean AHI was 22.8 (95% CI [17.7, 27.9]), indicating moderate OSAS, where the difference between groups was significant ($p = 0.032$). Table 3 presents the AHI severity according to BMI category in the OSAS group. There was a significant association between the two variables ($p = 0.005$).

Bone radiodensity

The mean RD at the left and right CV1 and dens are presented in Table 4. Based on the independent sample

Table 2. Sample demographics (N = 19 per group).

	Non-OSAS Group	OSAS Group	
Variable	N (%)	N (%)	Total
Female	16 (59)	11 (41)	27 (100)
Male	3 (27)	8 (73)	11 (100)
Age, years (Mean ± SD)	52.6 ± 7.4	53.7 ± 8.3	53.2 ± 7.8
BMI, kg/m^2 (Mean ± SD)	23.5 ± 2.9	31.0 ± 4.2	27.3 ± 5.2

OSAS: Obstructive sleep apnea syndrome; BMI: Body mass index.

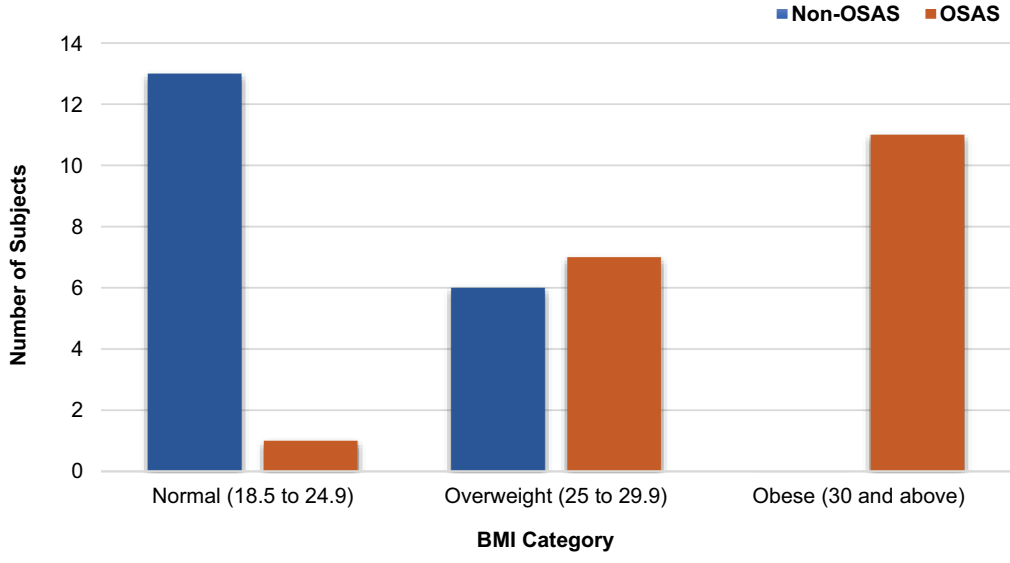

Figure 3. Number of subjects in each body mass index (BMI) category according to obstructive sleep apnea syndrome (OSAS) group.

Table 3. OSAS severity according to BMI category.

		BMI Category		
		Normal to Overweight (≦ 29.9)	Obese (≧ 30)	
		N (%)	N (%)	Total
OSAS severity	Moderate (AHI ≥ 15 to < 30)	8 (67)	4 (33)	12 (100)
	Severe (AHI ≥ 30)	0 (0)	7 (100)	7 (100)
	Total	8 (42)	11 (58)	19 (100)

OSAS: Obstructive sleep apnea syndrome; BMI: Body mass index.

Table 4. Mean Radiodensity (HU) of left and right 1st cervical vertebrae and dens in the Non-OSAS and OSAS groups.

	Group	Mean Radiodensity (HU)	SD	*p*-Value*
Left CV1	Non-OSAS	81.67	93.25	0.128
	OSAS	36.69	84.51	
Right CV1	Non-OSAS	74.26	91.81	0.129
	OSAS	30.59	81.18	
Dens	Non-OSAS	223.94	106.09	0.081
	OSAS	159.25	115.96	

*Statistical significance set to $p < 0.05$ using Independent sample *t*-test.
OSAS: Obstructive sleep apnea syndrome.

t-tests, there was no statistically significant difference between the OSAS and non-OSAS groups in mean RD of the left CV1, right CV1, or dens (Figure 4).

There was no statistically significant interaction between OSAS status and sex at the left CV1 or right CV1, whereas the interaction was significant at the dens ($p = 0.032$). The mean RD of males at the dens was 67.24 ± 60.50 HU in the OSAS group and 234.22 ± 135.12 HU in the non-OSAS group (Figure 5).

When controlling for age, sex, and BMI, there was a statistically significant difference in mean RD values at the left CV1 ($p = 0.031$), right CV1 ($p = 0.045$), and dens ($p = 0.038$) between the OSAS and non-OSAS groups (Table 5). The interaction of OSAS status and sex was maintained in the model because it was statistically significant at the dens. No significant interaction was seen between OSAS status and BMI or between OSAS status and age. The adjusted R^2 values displayed in Table 5 indicate that approximately 24% of the variance seen in the mean RD values at the left CV1, 21% at the right CV1, and 27% at the dens can be explained by the variables included in the model.

Discussion

The purpose of this study was to determine the association between OSAS and BMD. The findings suggested that those with OSAS had significantly lower BMD than their non-OSAS counterparts when controlling for age, sex, and BMI. Therefore, the initial hypothesis, that

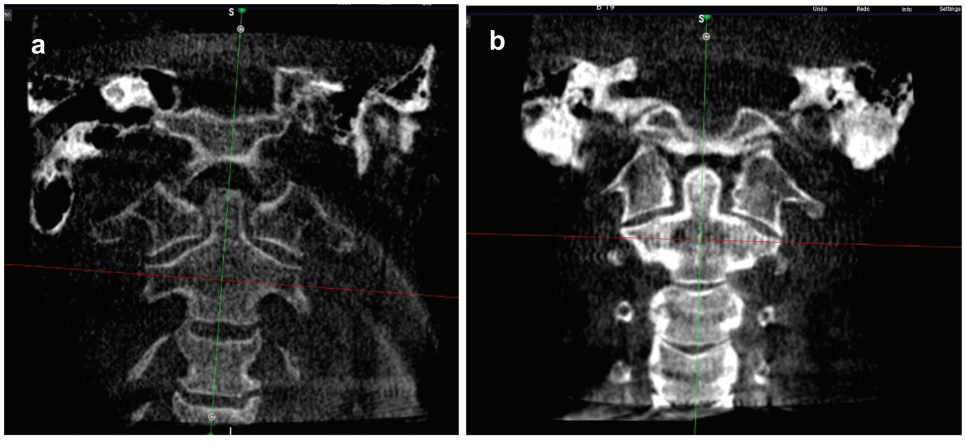

Figure 4. Coronal views of cone beam computed tomography (CBCT) slices showing radiodensity in an (a) OSAS subject and a (b) non-OSAS subject.

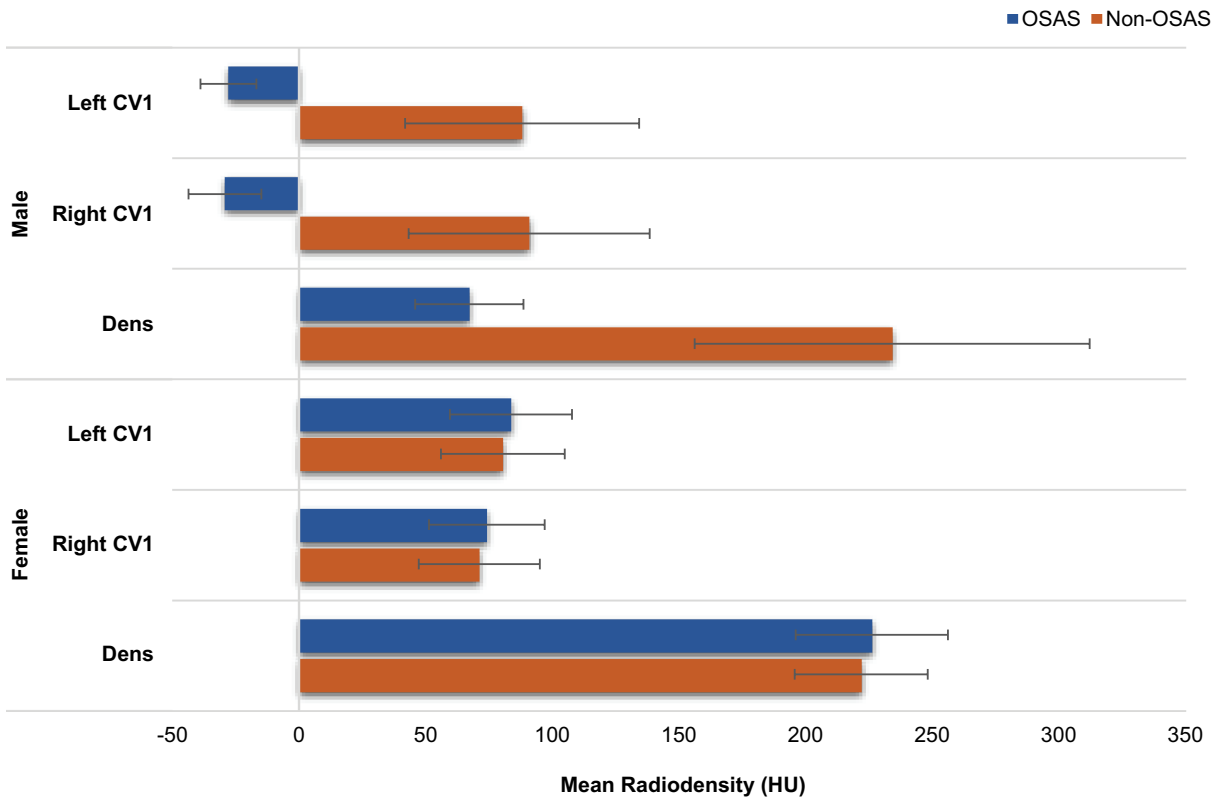

Figure 5. Mean radiodensity (HU) of the left and right 1st cervical vertebrae and dens in the non-obstructive sleep apnea syndrome (OSAS) and OSAS groups separated by sex.

Table 5. Significance levels of mean difference in RD between OSAS groups after adjusting for sex, age, and BMI.

	p-Value		
Variable	Left CV1	Right CV1	Dens
Age	0.075	0.090	0.184
BMI	0.201	0.352	0.421
OSAS status	0.031*	0.045*	0.038*
Sex	0.065	0.154	0.063
OSAS status*Sex	0.154	0.125	0.068
Adjusted R^2	0.24	0.21	0.27

OSAS: Obstructive sleep apnea syndrome; BMI: Body mass index; RD: Radiographic density.
*Statistically significant at $p < 0.05$ using Analysis of Covariance (ANCOVA).

subjects in the OSAS group would have a lower BMD than those in the control group, was not rejected.

Several studies examining the link between OSAS and BMD have reported conflicting results. Tomiyama et al. [25] were the first group to report evidence of a relationship between OSA and low BMD by measuring a bone resorption marker in a sample of 50 males with OSA. They found that serum and urinary levels of cross-linked C-terminal telopeptide of type I collagen (CTX) was higher in patients with OSA than in patients without OSA and that levels of CTX were reduced when CPAP therapy was administered [25]. Uzkeser et al. [26] were the first to directly measure BMD in OSAS patients by DXA. They compared 21 male patients with OSAS to 26 male controls and found that OSAS patients had significantly lower lumbar and femoral neck BMD values compared to controls. Wang et al. [27] found BMD in those with OSA to be significantly lower than those without OSA. Terzi and Yilmaz [5] reported significantly lower BMD measurements in the femoral neck of patients diagnosed with OSAS and significantly higher levels of serum CTX compared to non-OSAS controls. Therefore, results of the present study are consistent with multiple studies on this topic.

In contradiction with the above studies, Mariani et al. [28] found that BMD did not differ among obese patients regardless of OSAS status, and that AHI and BMD were not correlated. However, this study did not use a control population and compared BMD among mild, moderate, and severe OSAS groups. Sforza et al. [29] evaluated 833 patients with a mean age of 68.6 ± 0.6 years and found that patients with OSAS had a significantly higher femoral and spinal BMD than patients without OSAS. The mean age of all subjects in the present study was 53.2 ± 7.8 years, and thus, it is possible the results from these two studies were dissimilar because of differences in the age groups studied.

Reduced BMD in patients with OSAS may be caused by a confluence of several factors [26,30]. Inflammation,

oxidative stress, and hypoxia are all risk factors for osteoporosis and are also mediators in the pathophysiology of OSAS [27,30]. Several inflammatory mediators, such as TNF-α, IL-1, and IL-6, are elevated in patients with OSAS and have been shown to potentiate osteoclastogenesis and bone resorption [27,30,31]. Moreover, in patients with OSAS, oxidative stress occurs as a result of the repetitive oxygenation and deoxygenation, resulting in the increased production of reactive oxygen species (ROS) [26,32]. ROS induce the apoptosis of osteoblasts and favor osteoclastogenesis, which in turn, inhibits bone mineralization and osteogenesis [26,32]. In addition, intermittent hypoxia, a hallmark characteristic of OSAS, has been shown to enhance the activity of osteoclasts and inhibit bone formation [33,34]. It is possible that increased amounts of inflammatory cytokines, ROS, and hypoxia seen in OSAS patients could lead to reduced bone formation and result in low BMD.

This study showed that males in the OSAS group had a lower predicted BMD than females. Similar results were found by Hamada et al. [35], who, using CT scans to compare BMD between an OSA and non-OSA population, discovered that BMD was lower in males with severe OSA compared to females. In fact, in the population studied, they found that BMD and OSA had no association among females. These investigators also found a significant association between hypertension and reduced BMD in males. OSAS has been shown to cause secondary hypertension due to intermittent hypoxia increasing sympathetic nervous system activity [35,36]. Evidence shows that through the nuclear factor kappa B (NF-κB) and RANK/RANKL pathway, sympathetic activation results in bone loss [37,38]. Increased sympathetic activity causes an increase in bone resorption through the formation and activation of osteoclasts and a decrease in bone formation [37]. In the current study, 50% of male subjects in the OSAS group were using anti-hypertensive medications, while only one female in the same group had diagnosed hypertension. Therefore, the higher proportion of male patients with hypertension in the OSAS group could provide a possible explanation for why males with OSAS had reduced BMD relative to females. Subjects in the control group were age-matched, as bone density tends to decrease with increasing age, especially in women of post-menopausal age [39].

BMI was significantly higher in the OSAS group than the non-OSAS group, a finding that was expected because of the well-established link between obesity and OSAS. However, there was not a significant relationship between mean RD and BMI at any of the measurement sites. This could be attributed to the increased mechanical loading in obesity, where elevated loading is associated with increased bone formation [40]. However, obesity itself is an inflammatory disease and has been shown to result in the production of higher levels of TNF-α and IL-6, cytokines that are associated with increased bone resorption [40]. Because these same inflammatory cytokines are also elevated in patients with OSAS, it could be that their effects are additive and negatively influence bone density. Overall, it is likely that a larger sample size was needed in this study to elucidate the relationship between BMI and BMD.

Although DXA is the gold standard for measuring BMD, it has been shown to be less accurate in patients with a BMI over 25 kg/m^2 [41,42]. Obese patients have a larger proportion of soft tissue that causes attenuation of the X-ray beam and a beam hardening artifact, resulting in elevated BMD measurements [41,42]. Hamada et al. [35] cited the limitations of DXA in measuring BMD as the reason for using computed tomography (CT) scans to compare BMD between OSA and non-OSA populations. As seen in this study, most subjects in the OSAS group were obese, with all but one patient having a BMI over 25 kg/m^2, which justified the use of CT as an imaging modality over DXA. When comparing CBCT to CT, several studies have found strong positive correlations between gray values of CBCT and conventional CT [43,44]. While the dimensional accuracy of CBCT is comparable to that in medical CT, the gray density values of CBCT images are not absolute, and as such, HU values are not consistent between different CBCT machines and software [45]. The present study was based upon a study by Barngkei et al. [17], in which RD of the left and right parts of the CV1 and dens of CV2 were measured using CBCT. These investigators determined HU reference standards for osteopenia based on the CBCT imaging using a FOV of 13 × 15 cm and a voxel size of 0.25 mm, whereas the present study used a FOV of 16 × 13 cm and a voxel size of 0.4 mm. Due to differences in machine settings, it was not appropriate to apply the reference standards used by Barngkei et al. [17] to the results in the current study. Therefore, measurement of BMD using CBCTs should be interpreted with caution until a formula has been created to standardize measurements among different CBCT machines. Once this conversion formula has been established, threshold values can be determined that will enable future research to categorize patients into osteopenia and osteoporotic categories.

Limitations

There are several limitations with the present study. There was an unequal distribution of subjects in each

age group. In future research, a larger sample size that includes a balanced age and sex [39,46] distribution should be investigated to provide more generalizable results. Daily physical activity was not considered in this study. Physical activity is thought to maintain bone mass and stimulate bone growth, especially in post-menopausal women and individuals over the age of 50 [47,48]. Finally, BMD was measured only via the CBCT-imaged structures. Using another imaging modality, such as DXA or CT, to measure the same area may provide a useful frame of reference through which results could be compared. In the same way, it may be useful to correlate BMD measurements using CBCT with biomarkers of bone turnover in future research.

Implications for orthodontic treatment

The results of this study have several implications for orthodontic treatment. If a patient has been diagnosed with OSAS and may be prone to lower BMD, this can influence patient treatment planning and management. The results of this study also show that these implications may be of greater relevance in male patients. Because CBCT imaging has become an integral part of daily orthodontic practice, the imaging could be used as a screening tool for low BMD. Orthodontists could then inform their patients of their propensity for low BMD and encourage the patient to seek further consultation with their physician. When treatment planning, knowing a patient may have lower BMD will help the practitioner warn the patient of possible adverse outcomes, increased risks, and effects on treatment time. There have been several studies that show a link between osteoporosis and decreased alveolar bone height and density [14,49]. In osteoporotic individuals, both bone resorption and formation are accelerated; however, the rate of resorption exceeds the rate of formation, resulting in net bone loss [14,50]. Hashimoto et al. [51] found an increase in tooth movement correlated with a decrease in BMD in female Wistar rats. Reduced bone density in orthodontic patients could lead to accelerated tooth movement, an imbalance in bone modeling patterns, and loss of alveolar bone as a result [14,50,52].

Conclusion

This study found that males with OSAS had lower BMD than females and lower BMD than both males and females in the non-OSAS groups. Adults with OSAS had a significantly lower predicted BMD than non-OSAS patients when controlling for age, sex, and BMI. The mechanisms underlying OSAS and BMD association are still unknown and warrant further investigation.

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Disclosure statement

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List of abbreviations

OSAS	Obstructive sleep apnea syndrome
BMI	Body mass index
DXA	Dual X-ray absorptiometry (DXA)
CBCT	Cone beam computed tomography
BMD	Bone mineral density
RD	Radiographic density
ESS	Epworth Sleepiness Scale
SBQ	STOP-Bang Questionnaire
CV1	1st cervical vertebrae
CV2	2nd cervical vertebrae
AHI	Apnea-Hypopnea Index
CTX	C-terminal telopeptide of type I collagen

References

[1] Senaratna CV, Perret JL, Lodge CJ, et al. Prevalence of obstructive sleep apnea in the general population: a systematic review. Sleep Med Rev. 2017;34:70–81.
[2] Flemons WW. Clinical practice. obstructive sleep apnea. New Engl J Med. 2002;347(7):498–504.
[3] Calvin AD, Albuquerque FN, Lopez-Jimenez F, et al. Obstructive sleep apnea, inflammation, and the metabolic syndrome. Metab Syndr Relat Disord. 2009;7(4):271–278.
[4] Eimar H, Saltaji H, Ghorashi S, et al. Association between sleep apnea and low bone mass in adults: a systematic review and meta-analysis. Osteoporos Int. 2017;28(4):1835–1852.
[5] Terzi R, Yılmaz Z. Bone mineral density and changes in bone metabolism in patients with obstructive sleep apnea syndrome. J Bone Miner Metab. 2016;34(4):475–481.
[6] Upala S, Sanguankeo A, Congrete S. Association between obstructive sleep apnea and osteoporosis: a systematic review and meta-analysis. Inter J Endorinol Metab. 2016;14(3):e36317.
[7] Polverino F, de Torres JP, Santoriello C, et al. Gas exchange and breathing pattern in women with post-menopausal bone fragility. Respir Med. 2018;137:141–146.

[8] Guerra ENS, Almeida FT, Bezerra FV, et al. Capability of CBCT to identify patients with low bone mineral density: a systematic review. Dentomaxillofac Radiol. 2017;46(8):20160475.
[9] Ando A, Mitsuhashi T, Honda M, et al. Risk factors for low bone mineral density determined in patients in a general practice setting. Acta Med Okayama. 2019;73(5):403–411.
[10] Dai Z, Wang R, Ang L-W, et al. Bone turnover biomarkers and risk of osteoporotic hip fracture in an Asian population. Bone. 2016;83:171–177.
[11] Shetty S, Kapoor N, Bondu JD, et al. Bone turnover markers: emerging tool in the management of osteoporosis. Indian J Endocrinol Metab. 2016;20 (6):846–852
[12] Hsu JT, Chang HW, Huang HL, et al. Bone density changes around teeth during orthodontic treatment. Clin Oral Investig. 2011;15(4):511–519.
[13] Chang HW, Huang HL, Yu JH, et al. Effects of orthodontic tooth movement on alveolar bone density. Clin Oral Investig. 2012;16(3):679–688.
[14] Sidiropoulou-Chatzigiannis S, Kourtidou M, Tsalikis L. The effect of osteoporosis on periodontal status, alveolar bone and orthodontic tooth movement. A literature review. J Int Acad Periodontol. 2007;9(3):77–84.
[15] Pan CY, Liu PH, Tseng YC, et al. Effects of cortical bone thickness and trabecular bone density on primary stability of orthodontic mini-implants. J Dent Sci. 2019;14 (4):383–388.
[16] Radi IA, Ibrahim W, Iskandar SMS, et al. Prognosis of dental implants in patients with low bone density: a systematic review and meta-analysis. J Prosthet Dent. 2018;120(5):668–677.
[17] Barngkgei I, Joury E, Jawad A. An innovative approach in osteoporosis opportunistic screening by the dental practitioner: the use of cervical vertebrae and cone beam computed tomography with its viewer program. Oral Surg Oral Med Oral Pathol Oral Radiol. 2015;120 (5):651–659.
[18] Cavarra F, Boffano P, Tricarico G, et al. The use of mandibular advancement devices in adult patients affected by obstructive sleep apnea syndrome: our experience with "Thornton adjustable positioner. TAP Splint Minerva Dent Oral Sci. 2022;71(3): 163–167
[19] Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep. 1991;14 (6):540–545.
[20] Chung F, Yegneswaran B, Liao P, et al. STOP questionnaire: a tool to screen patients for obstructive sleep apnea. Anesthesiology. 2008;108(5):812–821.
[21] World Health Organization. Obesity and overwight. Geneva Switzerland; 2006.
[22] Barngkgei I, Al Haffar I, Shaarani E, et al. Assessment of jawbone trabecular bone structure amongst osteoporotic women by cone-beam computed tomography: the OSTEOSYR project. J Investig Clin Dent. 2016;7 (4):332–340.
[23] Murphy A, Baba Y. Windowing (CT): Radiopaedia. [Accessed on 2021 Jul 20 10.53347/rID-52108.
[24] Kim H-Y. Statistical notes for clinical researchers: evaluation of measurement error 2: Dahlberg's error, Bland-Altman method, and Kappa coefficient. Restor Dent Endod. 2013;38(3):182–185.
[25] Tomiyama H, Okazaki R, Inoue D, et al. Link between obstructive sleep apnea and increased bone resorption in men. Osteoporos Int. 2008;19(8):1185–1192.
[26] Uzkeser H, Yildirim K, Aktan B, et al. Bone mineral density in patients with obstructive sleep apnea syndrome. Sleep Breath. 2013;17(1):339–342
[27] Wang TY, Lo YL, Chou PC, et al. Associated bone mineral density and obstructive sleep apnea in chronic obstructive pulmonary disease. Int J Chron Obstruct Pulmon Dis. 2015;10:231–237.
[28] Mariani S, Fiore D, Varone L, et al. Obstructive sleep apnea and bone mineral density in obese patients. Diabetes Metab Syndr Obes. 2012;5:395–401.
[29] Sforza E, Thomas T, Barthélémy JC, et al. Obstructive sleep apnea is associated with preserved bone mineral density in healthy elderly subjects. Sleep. 2013;36 (10):1509–1515.
[30] Chen YL, Weng SF, Shen YC, et al. Obstructive sleep apnea and risk of osteoporosis: a population-based cohort study in Taiwan. J Clin Endocrinol Metab. 2014;99(7):2441–2447.
[31] Boyle WJ, Simonet WS, Lacey DL. Osteoclast differentiation and activation. Nature. 2003;423 (6937):337–342.
[32] Domazetovic V, Marcucci G, Iantomasi T, et al. Oxidative stress in bone remodeling: role of antioxidants. Clin Cases Miner Bone Metab. 2017;14 (2):209–216.
[33] Arnett TR. Acidosis, hypoxia and bone. Arch Biochem Biophys. 2010;503(1):103–109.
[34] Utting JC, Flanagan AM, Brandao-Burch A, et al. Hypoxia stimulates osteoclast formation from human peripheral blood. Cell Biochem Funct. 2010;28 (5):374–380.
[35] Hamada S, Ikezoe K, Hirai T, et al. Evaluation of bone mineral density by computed tomography in patients with obstructive sleep apnea. J Clin Sleep Med. 2016;12 (1):25–34.
[36] Foster GE, Poulin MJ, Hanly PJ. Intermittent hypoxia and vascular function: implications for obstructive sleep apnoea. Exp Physiol. 2007;92(1):51–65.
[37] Togari A, Arai M. Pharmacological topics of bone metabolism: the physiological function of the sympathetic nervous system in modulating bone resorption. J Pharmacol Sci. 2008;106(4):542–546.
[38] Togari A. Adrenergic regulation of bone metabolism: possible involvement of sympathetic innervation of osteoblastic and osteoclastic cells. Microsc Res Tech. 2002;58(2):77–84.
[39] Dy CJ, Lamont LE, Ton QV, et al. Sex and gender considerations in male patients with osteoporosis. Clin Orthop Relat Res. 2011;469(7):1906–1912
[40] Cao JJ. Effects of obesity on bone metabolism. J Orthop Surg Res. 2011;6(1):30.
[41] Binkley N, Krueger D, Vallarta-Ast N. An overlying fat panniculus affects femur bone mass measurement. J Clin Densitom. 2003;6(3):199–204.
[42] Link TM. Osteoporosis imaging: state of the art and advanced imaging. Radiology. 2012;263(1):3–17.

[43] Kim D-G. Can dental cone beam computed tomography assess bone mineral density? J Bone Metab. 2014;21(2):117–126.
[44] Reeves TE, Mah P, McDavid WD. Deriving Hounsfield units using grey levels in cone beam CT: a clinical application. Dentomaxillofac Rad. 2012;41(6):500–508.
[45] Cassetta M, Stefanelli LV, Pacifici A, et al. How accurate is CBCT in measuring bone density? A comparative CBCT-CT in vitro study. Clin Implant Dent Relat Res. 2014;16(4):471–478.
[46] Cawthon PM. Gender differences in osteoporosis and fractures. Clin Orthop Relat Res. 2011;469(7):1900–1905.
[47] Daly RM, Via JD, Fyfe JJ, et al. Effects of exercise frequency and training volume on bone changes following a multi-component exercise intervention in middle aged and older men: secondary analysis of an 18-month randomized controlled trial. Bone. 2021;148:115944.
[48] Kitsuda Y, Wada T, Noma H, et al. Impact of high-load resistance training on bone mineral density in osteoporosis and osteopenia: a meta-analysis. J Bone Miner Metab. 2021;39(5):787–803.
[49] Wactawski-Wende J, Grossi SG, Trevisan M, et al. The role of osteopenia in oral bone loss and periodontal disease. J Periodontol. 1996;67(10 Suppl):1076–1084.
[50] Miyajima K, Nagahara K, Iizuka T. Orthodontic treatment for a patient after menopause. Angle Orthod. 1996;66(3):173–180.
[51] Hashimoto M, Hotokezaka H, Sirisoontorn I, et al. The effect of bone morphometric changes on orthodontic tooth movement in an osteoporotic animal model. Angle Orthod. 2013;83(5):766–773.
[52] Tyrovola JB, Spyropoulos MN. Effects of drugs and systemic factors on orthodontic treatment. Quintessence Int. 2001;32(5):365–371.