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Relationship between the Mandibular Inferior Cortical Bone Thickness and The Second Cervical Vertebra Density in Women Relative to Menopause Using Cone-Beam Computed Tomography

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Objectives This study aimed to assess the association between the second cervical vertebra (C2) density and the mandibular inferior cortical bone thickness at the mental foramen in women before and after menopause on cone-beam computed tomography (CBCT) scan as a predictor for the risk of osteoporosis.
Methods This retrospective cross-sectional study analyzed 176 CBCT scans from a sample of 88 post-menopausal women and 88 pre-menopausal women. The thickness of the mandibular inferior cortical bone was assessed using cross-sectional CBCT images at the mental foramen, a measurement referred to as the mental index (MI), using the NNT viewer software. Additionally, the density of the C2 vertebra was measured on both coronal and axial CBCT sections. The collected data were then analyzed using the independent t-test, ANOVA, Tukey's test, and Pearson's correlation test, with a significance level set at α=0.05.
Results No significant difference was found in the mean density of the C2 vertebra or the mean MI between post-menopausal and pre-menopausal women. However, a significant correlation was found between the C2 density and MI in all women (r=0.445, P<0.001) and also in pre-menopausal women (r=0.704, P<0.001); this correlation was more pronounced in younger age groups.
Conclusion The standalone evaluation of CBCT is not recommended for predicting the risk of osteoporosis. The relationship between C2 density and mandibular inferior cortical bone thickness may be more applicable in younger women.
Keywords Bone Density; Cone-Beam Computed Tomography; Cortical Bone.

Introduction

The cervical spine, situated between the skull base and the thoracic spine in the trunk, consists of seven cervical vertebrae located in the neck region from C1 (the most superior) to C7 (the most inferior). [1] The cervical spine, which consists of the narrowest and most fracture-prone vertebrae, protects the spinal cord and facilitates the movement of the head and neck. The C1 vertebra, also known as the atlas, supports the skull; while the C2 vertebra, referred to as the axis, provides a pivot point for skull rotation. [1]

Osteoporosis is a condition characterized by a widespread decrease in bone mass, degradation of bone tissue, and weakened bone strength. It is prevalent among middle-aged and elderly women, with approximately 30% of post-menopausal women being affected. [2] Reduction in bone density starts at 35-45 years of age in both males and females; however, it is aggravated after menopause in women. Women lose about 5% to 7% of their bone strength within 5-7 years after menopause. The reduction in bone density is age-dependent, and 0.5-1% of bone density is lost per year in both males and females, starting from the age of 40. [3]

The reduction in bone mass continues for life and may be affected by a number of parameters, such as the body mass index, smoking, alcohol consumption, immobility, impaired synthesis and metabolism of vitamin D, and hyperparathyroidism. [4] According to a recent systematic review, the prevalence of osteoporosis is 34% in individuals over 60 years of age in Iran, and the prevalence of osteopenia is 47% among Iranians over 60 years of age.[5] An epidemiological study conducted in Iran showed that approximately 28% of women over 50 years of age had osteoporosis, and approximately 53% of women over 50 years had osteopenia. [6]

A variety of factors contribute to the development of osteoporosis. These factors can be categorized into two groups of modifiable and non-modifiable. [7] The non-modifiable risk factors include, but are not limited to age, gender, genetics, race, body size, and early or surgically-induced menopause. Aging is among the most prominent causes of osteoporosis. Females are more susceptible to osteoporosis, and the prevalence of osteoporosis considerably increases after menopause. [8] Individuals of Asian or Caucasian descent, as well as those with a small body size, are at an elevated risk for osteoporosis. A decrease in bone density also contributes to the development of this condition.

Meanwhile, the modifiable risk factors include, but are not limited to body weight, exercise, smoking, alcohol consumption, diet, hormone replacement therapy, and immobility. Systemic diseases, such as hypogonadism, endocrine disorders, gastrointestinal diseases, rheumatologic disorders, congenital diseases, hematological disorders, and malignancies, can also cause osteoporosis. [9]

Osteoporosis imposes a substantial personal and economic

burden on those affected. In Europe, the disability resulting from osteoporosis surpasses that caused by tumors (excluding lung cancer) and is comparable to, or even exceeds, the disability from various chronic diseases, such as rheumatoid arthritis, asthma, and hypertensive heart disease. Given these implications, early diagnosis of osteoporosis and the initiation of preventive or therapeutic measures are of utmost importance. [10] It has been confirmed that osteoporosis is irreversible; however, prompt interventions can prevent its progression in the majority of cases. [11] The impact of osteoporosis on the density of cervical vertebrae, especially the C2 vertebra, has been established in prior studies. Overall, the assessment of the C2 vertebra density can yield valuable insights into the presence of osteoporosis. [6, 12-15]

The measurement of bone mineral density (BMD) using dual-energy X-ray absorptiometry (DEXA) scan is considered the "gold standard" for diagnosing osteoporosis in post-menopausal women. When BMD results are reported, the DEXA scan provides a metric known as the T-score. Osteoporosis is diagnosed when the T-score value of BMD is more than 2.5 standard deviations (SDs) below the mean for young, healthy, normal adult women (i.e., T-score <-2.5). Patients with BMD values that fall between 1 and 2.5 SDs below the mean for young adults (T-score of -1.0 to -2.5) are categorized as having osteopenia. While the DEXA scan is globally recognized for its high reliability and low radiation dose in assessing BMD, it is not always accessible and may not be cost-effective for screening low-risk demographics, such as younger individuals. [16]

Cone-beam computed tomography (CBCT) can accurately depict anatomical details [17] and allow for a three-dimensional evaluation of anatomical structures in all planes with a lower exposure dose than computed tomography (CT). [18] Several indices, including the mental index (MI), mandibular cortical index, panoramic mandibular index, and antegonial index, have been suggested as potential diagnostic markers for identifying osteoporosis. [19] The MI has been suggested as one of the most accurate indices for determining the risk of osteoporosis. [20] Moreover, a significant correlation has been reported between the mandibular inferior cortical bone width and BMD. [21] A significant correlation has been also documented between the cortical thickness at the mental region and the mineral density of the lumbar vertebrae. [22] Therefore, assessment of the C2 density on CBCT scans may aid in the detection of osteoporosis.

In this regard, a literature review was undertaken to explore the application of CBCT examinations in predicting the risk of osteoporosis. The review revealed that the most accurate results were obtained in a study that identified the risk of osteoporosis by quantifying the gray values of the first and second cervical vertebrae. [23] Therefore, the present study aimed to assess the correlation of the C2 density with the mandibular inferior cortical bone thickness at the mental foramen in women before and after menopause on CBCT scans.

Methods and Materials

This retrospective cross-sectional study evaluated 176 CBCT scans of 88 menopausal and 88 non-menopausal women, retrieved from the archives of a private radiology clinic in Isfahan, Iran, in 2021. The study protocol was approved by the Ethics Committee of the School of Dentistry, Islamic Azad University, Khorasgan Branch (Isfahan, Iran) (IR.IAU.KHUISF.REC.1400.342).

Eligibility criteria:

The inclusion criteria for the study were as follows: CBCT scans of individuals aged between 30 and 70 years, images of good diagnostic quality, optimal visualization of the mandibular inferior cortex in the images, complete visibility of the C1, C2, and C3 vertebrae within the field of view, and the availability of patient information, such as age, gender, and history of systemic diseases in their medical records.

The exclusion criteria for the study were as follows: a history of mandibular or cervical vertebral fractures, jaw lesions, surgery in the body of the mandible, presence of developmental or congenital anomalies, and a history of bone diseases, renal diseases, hyperparathyroidism, Cushing's syndrome, thyrotoxicosis, rheumatoid arthritis, organ transplantation, diabetes, and hypocalcemia. Women who experienced early menopause (before the age of 45) or due to surgery were also excluded. Additionally, women with a history of present or past consumption of medications influencing bone metabolism (e.g., glucocorticoids, bisphosphonates, strontium ranelate, selective estrogen receptor modulators, hormone replacement therapy, calcitonin, active vitamin D metabolites, and teriparatide), except for calcium (at doses <1000 mg/day) and vitamin D (at doses <800 IU/day) supplements, were excluded from the study.

Sample size:

The sample size was determined to be 80 menopausal and 80 non-menopausal women, based on assumptions of α=0.05, β=0.2, a study power of 80%, and a minimum correlation coefficient of 0.3 for a significant correlation.[24] Considering a potential 10% dropout rate, a total of 176 CBCT scans (88 for each group) were selected for the study.

Measurements:

All CBCT scans were conducted using the NewTom VGi EVO CBCT system (NewTom, Verona, Italy), adhering to standard exposure settings (11×16 cm^2 field of view, 0.3 mm voxel size, 110 kV, 3.6–5.4 s). The milliamperage was automatically adjusted (using the safe-beam feature) based on each patient's anatomy, ranging from 1 mA to 20 mA. All measurements were made using the NNT Viewer software (NNT 2.21; NewTom, Verona, Italy) on an LCD monitor (Barco, Kortrijk, Belgium) with a diagonal dimension of 30 inches and a resolution of 3280×2048 pixels (pixel size, 0.20 mm). The NNT Viewer enables measurements with 0.1-mm accuracy.

All CBCT scans were viewed by an experienced oral and maxillofacial radiologist and an endodontist in a semi-dark room, using the NNT Viewer software twice in a one-week

interval. The ruler feature of the software was used to measure the thickness of the mandibular inferior cortical bone at the MI on cross-sectional images, visualizing the mental foramen. The width of the mandibular inferior cortical bone at each point of the mental foramen was measured, and then, the mean value was calculated. Patients with a cortical thickness ≤3 mm had a high risk of osteoporosis (Figures 1 & 2). [25]

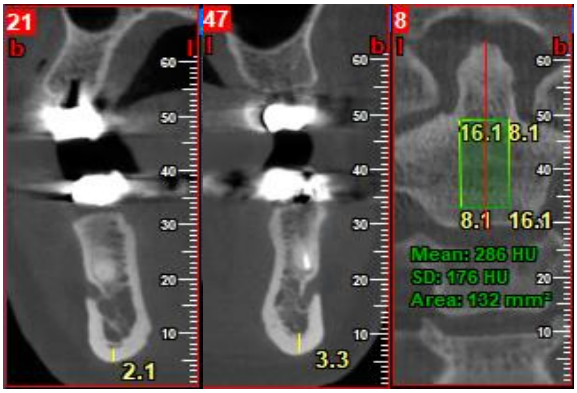

Figure 1. Mandibular inferior cortical bone thickness and position of mental foramen in a non-

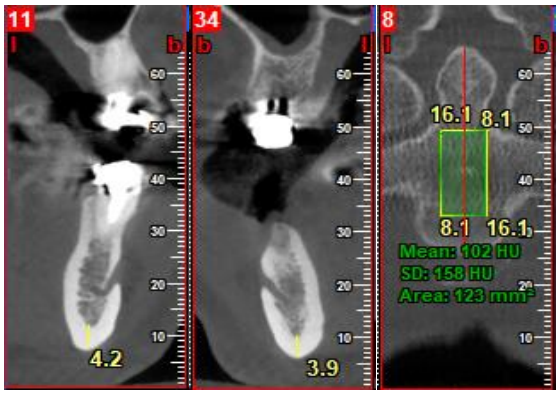

Figure 2: Mandibular inferior cortical bone thickness and position of mental foramen in a menopaused woman

To assess the C2 density on coronal images, the central point of the C2 vertebra was identified and marked on both axial and sagittal images. A coronal section was created at this point. Subsequently, a rectangle measuring 16.1×8.1 mm^2 was delineated from the base of the dens process of C2 to the body of C2, using the software's measure distance tool. The density of C2 was then measured using the software's Hounsfield Unit (HU) feature. [25-29] Finally, the mean value was recorded (Figures 3 & 4). [16]

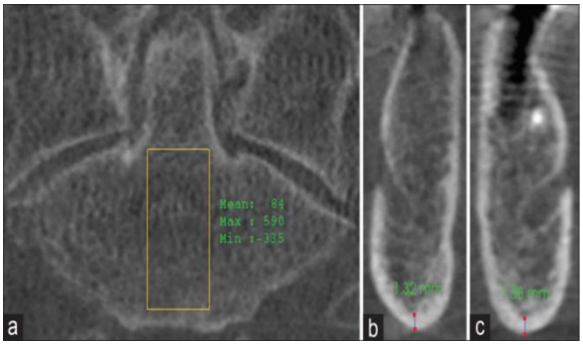

Figure 3: CBCT scan of a patient at high risk of osteoporosis; (a) C2 density; (b) MI at the right side of the mandible; (c) MI at the left side of the mandible

Statistical analysis:

Data were analyzed in SPSS Version 26, using independent t-test, ANOVA, Tukey's test, and Pearson's correlation test at a significance level of 0.05.

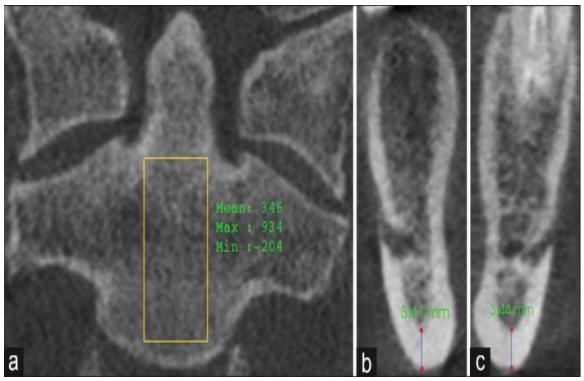

Figure 4: CBCT scan of a patient at low risk of osteoporosis; (a) C2 density; (b) MI at the right side of the mandible; (c) MI at the left side of the mandible

Results

Age range of the participants:

The age range for non-menopausal women was 31-50 years, with the majority (53.4%) falling within the range of 41-50 years. The age range of menopausal women was 51-70 years, with the majority (59.1%) being 61-70 years old.

Measurements of the C2 density and mandibular inferior cortical bone thickness:

Table 1 presents the central dispersion measurements for the C2 density and the mandibular inferior cortical bone thickness. According to the results of independent t-test, no significant difference was found in the mean density of C2 (P=0.333) or the mean MI (P=0.943) between menopausal and non-menopausal women. A significant correlation was detected between the C2 density and MI in all women (r=0.445, P<0.001) and also in non-menopausal women (r=0.704, P<0.001). However, this correlation was not significant in menopausal women (r=0.190, P=0.076).

Measurement of C2 density in different age groups:

Table 2 presents the central dispersion measurements for the C2 density in different age groups. One-way ANOVA indicated a significant difference in the C2 density among different age groups (P=0.005). Also, pairwise comparisons based on the Tukey's test showed that the mean C2 density was significantly lower in females aged 61-70 years compared to women in the age range of 51-60 years (P<0.05). However, no other significant differences were observed (P>0.05).

Measurement of MI in different age groups:

Table 3 shows the central dispersion measurements for the MI in different age groups. One-way ANOVA test showed no significant difference in terms of MI among different age groups (P=0.519).

Correlations:

The Pearson's correlation test showed a significant correlation between the C2 density and MI in the age groups of 31-40 years (r=0.593, P<0.001) and 41-50 years (r=0.785, P<0.001). No such correlation was found in the age groups of 51-60 years (r=0.289, P=0.087) or 61-70 years (r=0.088, P=0.536).

Table 1. Measures of central dispersion for C2 density and mandibular inferior cortical bone thickness

Variable	Group	Number	Minimum	Maximum	Mean	Std. deviation	t	P value
C2 density	Non-menopaused	88	-37.00	318.00	155.61	91.74	.971	.333
	Menopaused	88	-35.00	306.00	142.78	83.41		
	Total	176	-37.00	318.00	149.20	87.66		
MI	Non-menopaused	88	1.90	4.50	3.07	.61	-.071	.943
	Menopaused	88	1.60	4.70	3.08	.66		
	Total	176	1.60	4.70	3.08	.63		

MI: Mental index

Table 2. Measures of central dispersion for the C2 density in different age groups

Variable	Age group (yrs.)	Number	Minimum	Maximum	Mean	Std. deviation	F	P value
C2 density	31-40	41	-10.00	299.00	163.83[ab]	77.53	4.367	.005
	41-50	47	-37.00	318.00	148.45[ab]	102.84		
	51-60	36	-27.00	306.00	179.64[b]	76.08		
	61-70	52	-35.00	272.00	117.27[a]	79.19		
	Total	176	-37.00	318.00	149.20	87.66		

*Different superscripted letters indicate presence of a significant difference, and similar letters indicate no significant difference between different age groups.

Table 3. Measures of central dispersion for the MI in different age groups

Variable	Age group (yrs.)	Number	Minimum	Maximum	Mean	Std. deviation	F	value p
MI	31-40	41	1.90	4.50	3.15	.61	.759	.519
	41-50	47	1.90	4.00	3.01	.60		
	51-60	36	1.90	4.20	3.17	.61		
	61-70	52	1.60	4.70	3.02	.69		
	Total	176	1.60	4.70	3.08	.63		

MI: Mental index

Discussion

Osteoporosis is a pervasive global problem and is considered a major public health concern, with an estimated 200 million individuals believed to be afflicted by the condition worldwide. [30] As the population continues to age, it is anticipated that the number of osteoporosis cases among postmenopausal women will significantly increase. [31] Due to increased life expectancy, dental clinics are witnessing a rise in patients with osteoporosis. Consequently, CBCT scans could potentially serve as a valuable tool for assessing the risk of osteoporosis. [32] The present study assessed the correlation of C2 density with the mandibular inferior cortical bone thickness at the mental foramen in women before and after menopause on CBCT scans. The results indicated that there was no significant difference in the MI across different age groups, a finding that contradicts those of previous studies on this subject. [33, 34] This difference may be due to variations in the study population, sample size, and dietary habits. Also, the current study examined the CBCT scans of patients requiring dental implants due to tooth loss. This requirement could potentially reflect their socioeconomic status, which in turn might influence their diet and overall health; possibly affecting their bone density. Overall, this context could account for the observed lack of significant difference in terms of MI between younger and older women in this study.

The HU is a quantitative scale used to denote radiographic density. In CT scan, it is known as the CT number and is considered highly reliable. However, its reliability in CBCT is a subject of debate due to the presence of high scattered radiation and increased artifacts. [35,36] In this regard, in 2015, Barngkgei et al. [23] compared CBCT and DEXA and concluded that radiographic density in CBCT can serve as a reliable tool for the detection of osteoporosis risk. A systematic review reported that the radiomorphometric indices measured on CBCT scans are promising tools for screening osteoporotic patients, although further studies are still required in this area. [13] The available findings indicate no significant difference in

the C2 density across various age groups according to CBCT scans. This could be attributed to variations in imaging protocols, study populations, environmental factors, and diet. Additionally, environmental conditions affecting vitamin D absorption, which directly impacts bone density, especially in post-menopausal women, as well as socioeconomic status, could contribute to these results. [37-42]

The present results revealed a significant correlation between the C2 density and MI on CBCT scans in all women and also in non-menopausal women (31-40 and 41-50 years old). This finding is in agreement with the results of a study by Alkhader et al. [12], which found a similar correlation and also reported a lower C2 density in patients at risk of osteoporosis. Furthermore, this study uncovered a moderate correlation between the C2 density and MI in the CBCT scans of post-menopausal women. This finding underscores the need for additional research involving a larger sample size, as well as individuals with standardized physical status, diet, and race.

Furthermore, the present findings revealed that the C2 density in CBCT scans of females aged 61-70 years was significantly lower than that of females aged 51-60 years. However, this difference was not significant among other age groups; this finding can be attributed to menopause in older females. The correlation between the C2 density and the serum level of vitamin D and BMD should also be investigated in future studies.

Conclusion

The current findings indicated that there was no significant difference in terms of the C2 density and the inferior cortical bone thickness of the mandible between menopausal and non-menopausal women. A significant correlation was observed between the C2 density and the thickness of the mandibular inferior cortical bone in all women, as well as in non-menopausal women, based on the CBCT scans. However, this correlation diminished with age, suggesting that this parameter may be more applicable in younger women. To apply this method in a broader context, it is essential to develop a dependable validation technique for gray values between different CBCT devices. Additionally, using CBCT to predict the risk of osteoporosis is not recommended. This approach should solely rely on pre-existing CBCT images acquired during assessments for other indications.

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Data availability: The data that support the findings of this study are available from the corresponding author upon reasonable request.
Conflict of Interest: The authors declare that they have no conflict of interest.

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