Radiolucent periapical lesions and bone mineral density in post-menopausal women

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Purpose: To investigate the relationship between radiolucent periapical lesions and bone mineral density in post-menopausal women.

Material and methods: Seventy-five post-menopausal women were recruited for the study. Bone mineral density was measured using dual-energy X-ray absorptiometry. Three groups were established: healthy bone group, osteopenic group and osteoporotic group. Periapical radiolucencies were diagnosed on the basis of examination of digital panoramic radiographs. Statistical analysis was carried out using ANOVA and chi-squared tests, and logistic regression analysis.

Results: In both the osteopenic and osteoporotic groups, 25% of women showed at least one periapical radiolucency, whereas this was only 7.4% in the healthy bone group (odds ratio = 4.2; p = 0.061). After multivariate logistic regression analysis adjusting for covariates (age, number of teeth, number of root-filled teeth and number of teeth with coronal restorations), a marginally significant association was evident between bone mineral density and the presence of periapical radiolucencies (odds ratio = 1.9; CI 95% = 1.0–3.8; p = 0.050).

Conclusions: After adjusting for covariates, low bone mineral density is marginally associated with a higher frequency of radiolucent periapical lesions.

Keywords: apical periodontitis, menopause, oral medicine, osteoporosis.

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Introduction

Osteoporosis is a systemic skeletal disease characterised by low bone mass and micro-architectural deterioration with consequent increase in bone fragility and susceptibility to fracture of bones. Although changes in the bone mass and calcium metabolism are evident in the pre-menopausal period, at menopause, the production of oestrogens decreases drastically while follicle-stimulating hormone (FSH) levels rise sharply in parallel, leading to osteoporosis in skeletal bones. Therefore, menopause marks the beginning of a bone loss that continues until the end of life. Loss of bone mass, per se, does not cause symptoms but, once a fracture does occur, pain, loss of function and, in some cases, deformity may result.

Total skeletal mass reduction in post-menopausal women may include jawbones, particularly the mandible. Consequently, osteoporosis has recently received increasing attention in relation to the susceptibility to periodontal disease in post-menopausal women. Osteoporosis has been shown to be a risk indicator that may contribute to the progression of periodontal disease. Moreover, a number of studies showed that bone changes in osteoporosis are associated with loss of periodontal attachment, loss of teeth and reduction in the height of the residual ridge.

Apical periodontitis is an inflammation of the periodontium at the root apex of a tooth consecutive to an infection of the dental pulp, generally provoked by caries. Chronic apical periodontitis develops as a chronic inflammatory process characterised radiographically by the presence of periapical radiolucency, that is, a radiolucent image surrounding the apex of the affected tooth. Both osteoporosis and chronic apical periodontitis are...
diseases characterised by the presence of inflammation-induced osteolysis. In both diseases, inflammatory processes, either within or in the vicinity of the skeleton, affect the remodelling of the nearby bone tissue in such a way that the amount of bone resorbed exceeds that being formed, resulting in net bone loss. This clinical phenotype is observed not only in the alveolar bone surrounding the root of teeth at a site with marginal periodontitis, but also at a site with chronic apical periodontitis. Periapical radiolucency results from the bone loss consecutive to the interaction between a microbial challenge and immune response, involving recruitment of inflammatory cells, generation of cytokines, elaboration of lytic enzymes and activation of osteoclasts, which lead to alveolar bone resorption. It has been reported that the local effects of interleukin IL-1 included enhanced leucocyte adhesion to endothelial walls, stimulation of lymphocytes, potentiation of neutrophils, production of prostaglandins and proteolytic enzymes, enhanced bone resorption and inhibition of bone formation. As a result, the inflammation-induced osteolysis present in post-menopausal osteoporosis could be a systemic aggravating factor in chronic apical periodontitis.

The purpose of this study was to investigate the possible association between the presence of radiolucent periapical lesions and bone mineral density in post-menopausal women.

Material and Methods

The experiments were undertaken with the understanding and written consent of each subject and according to the principles of the Declaration of Helsinki. The protocol was approved by the Ethical Board of the Dental Faculty of Barcelona, Spain.

Subjects

For two years, all the post-menopausal women greater than 50 years old who were patients at the Dental Clinic of the University of Barcelona, Spain, were invited to participate in the study, and 75 patients who agreed a radiological and densitometry examination were recruited. Questionnaires were filled for each patient, eliciting information on medical and dental history, age at menopause, smoking status and history of oestrogen supplementation. Each woman signed a consent form after being advised of the nature of the study. All the women met the following inclusion criteria: at least eight teeth; at least 12 months since the last menstrual period; no hormone therapy; no medical treatment influencing bone metabolism; and no metabolic diseases. Exclusion criteria were as follows: smokers or former smokers; patients having parathyroid and metabolic bone disease, or cancer, or who are on long-term steroid therapy; patients having early onset of menopause; patients having history of hysterectomy; alcoholics; patients having lumbar spinal deformity (scoliosis), large amount of calcium in blood and multiple fractures. All patients answered a questionnaire on eating habits and focused particularly on food consumption related to the possibility of developing osteoporosis. It also asked the basic questions based on FRAX® (available at: http://www.shef.ac.uk/FRAX/).

Bone mineral density measurements

To diagnose osteoporosis in its early phases, bone mineral density (BMD) was measured in each woman in two standard places: the femoral neck and the lumbar spine, using dual-energy X-ray absorptiometry (QDR 1000, Hologic Inc., Waltham, MA, USA). The World Health Organization defines osteoporosis by a BMD measured as two-and-one-half standard deviations (−2.5 SD) below average peak bone density achieved in young adults, matched by gender and race. Based on the values obtained (g/cm²), three groups were established: healthy bone group (HBG) (BMD ≥ −1 SD), osteopenic group (OEG) (BMD between < −1 SD and > −2.5 SD) and osteoporotic group (OPG) (BMD ≤ −2.5 SD).

Radiographic examination

Periapical radiolucencies were diagnosed on the basis of examination of digital panoramic radiographs of the jaws. Two trained radiographic technician using a digital panoramic radiography machine (Promax®, Planmeca, 80 KV, Planmeca, Helsinki, Finland) took the panoramic radiographs.

Three observers with extensive clinical experience examined the radiographs. Radiolucent periapical lesions were assessed after careful analysis of the periodontal ligament space, the lamina dura, the trabecular pattern and the bone marrow spaces, according to the criteria previously described by Halse and Molven. The changes in the continuity and shape of the periapical lamina dura and the width and shape of the periodontal ligament space were emphasised in order to
decrease interobserver variations and add to correct radiographic diagnosis. Intra-observer and interobservers reproducibility were determined. Intra-observer reproducibility was evaluated by the repeat scoring of the panoramic radiographs of 20 patients, randomly selected, 2 months after the first examination. The intra-observer agreement on the 20 patients produced a Cohen’s kappa ranging 0.84–0.91. The Cohen’s kappa for interobservers variability ranged 0.76–0.83. The consensus radiographic standard was the simultaneous interpretation by the three examiners of all radiographs for each subject.

All teeth were recorded. Teeth were categorised as root-filled teeth if they had been filled with a radiopaque material in the root canal(s). The following information was recorded on a structured form for each subject: (i) number of teeth present; (ii) number and location of root-filled teeth; (iii) number and location of teeth having coronal restorations; and (iv) number and location of teeth having periapical radiolucencies.

Statistical analysis

The minimal sample size was calculated for the comparison of independent proportions with nQuery Advisor® (Version 7.0, Statistical Solutions, Saugus, MA, USA), taking into account a two-sided significance level of 5% (α = 0.05, Zα = 1.960), an 80% power (β = 0.20, Zβ = 0.842) to detect a hypothesised difference between two groups of 25 points.

Data are reported as mean ± standard deviation. Differences between groups in normally continuous variables were assessed by analysis of variance (ANOVA). The comparative analysis of discrete variables was carried out using the chi-squared test. Logistic regression analysis was performed to measure the strength of the association between bone mineral density and the presence of periapical radiolucencies adjusted for the presence of covariates. A value of \( p < 0.05 \) was considered significant.

Results

In the total sample, mean age was 62.5 ± 1.7 years (range 59–68 years) and the mean menopausal age was 47.1 ± 4.1 yrs. The average number of teeth per subject was 20.4 ± 7.6, and the mean number of root-filled teeth and coronal restorations per subject were 1.5 ± 2.1 and 7.0 ± 5.8, respectively (Table 1). According to bone mineral density assessed by densitometry, 27 women (36.0%) were classified as the healthy bone group (HBG), 36 women (48.0%) as the osteopenic group (OEG) and 12 women (16.0%) as the osteoporotic group (OPG) (Table 1). No statistically significant differences between the three groups were observed in age (\( p = 0.52 \)), number of teeth (\( p = 0.36 \)), number of root-filled teeth (\( p = 0.70 \)) or number of teeth with coronal restorations (\( p = 0.52 \)).

The relationship between BMD and periapical radiolucencies was analysed. Table 2 shows the distribution of women in relation to bone mineral density and periapical status. In both osteopenic and osteoporotic groups, 25% of women showed at least one radiolucent periapical lesion, whereas this percentage was only 7.4% in the HBG group (odds ratio = 4.2; CI 95% = 0.9–20.3; \( p = 0.061 \)).

Multivariate logistic regressions were run with age (year), number of teeth, number of root-filled teeth, number of teeth with coronal restorations and BMD, assessed using dual-energy X-ray absorptiometry in the femoral neck, as independent variables, and the presence of periapical radiolucency in at least one tooth (present = 1; absent = 0) as the dependent variable (Table 3).

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Dental status of patients in relation to their bone mineral density assessed by densitometry. Results are expressed as mean ± standard deviation.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HBG</td>
</tr>
<tr>
<td>Number of women (%)</td>
<td>27 (36.0)</td>
</tr>
<tr>
<td>Age</td>
<td>62.8 ± 1.6</td>
</tr>
<tr>
<td>Number of teeth</td>
<td>20.1 ± 7.9</td>
</tr>
<tr>
<td>Number of RFT</td>
<td>1.3 ± 2.3</td>
</tr>
<tr>
<td>Number of teeth with CR</td>
<td>6.0 ± 6.4</td>
</tr>
</tbody>
</table>

HBG, healthy bone group; OEG, osteopenic group; OPG, osteoporotic group; RFT, root-filled teeth; CR, coronal restorations.

*p > 0.05
In the multivariate analysis including all the above factors as covariates, BMD correlated marginally significant with the presence of at least one radiolucent periapical lesion (odds ratio $= 1.9; \text{CI } 95\% = 1.0–3.8; p = 0.05$), whereas all other factors were not statistically associated with the presence of periapical radiolucencies.

### Discussion

The present cross-sectional study was carried out to assess the relationship between radiolucent periapical lesions and BMD in post-menopausal women. Results reveal a marginally significant association between the presence of periapical radiolucencies and low BMD.

Osteoporosis is a significant health problem for middle-aged women, and it has been proved that age-related loss of bone is more pronounced in women after menopause$^2$. In the present study, post-menopausal women ($62.5 \pm 1.7$ years old) were selected. Study population were 50 years and above because it has been proved earlier that age-related loss of bone is more pronounced in women after the age of 50 years$^{12}$. Subjects with a range of different levels of BMD (healthy bone, osteopenic and osteoporotic women) were intended therefore severity of these conditions was not a selection criterion.

Systemic factors of bone remodelling may also modify local tissue response to periapical infection, so all subjects having a history of smoking$^{13,14}$, parathyroid disease or cancer were excluded from the study$^{2}$. Moreover, three conditions that falsely can elevate BMD, that is, lumbar spinal deformity (scoliosis), large amount of calcium in blood and multiple fractures, have been taken into account as exclusion criteria.

Dual-energy X-ray absorptiometry in the femoral neck and the lumbar spine was used to obtain BMD and to diagnose osteoporosis. This technique has become very common in the field of primary care and preventive medicine. Some current studies have observed that the BMD of the standard areas of study correlates with that obtained in the mandible$^{15}$. Moreover, it has been proposed that mandibular indices obtained in panoramic radiographs could be used in the early diagnosis of osteoporosis$^{16}$ and as indicators of mandibular osteoporosis by dual-energy X-ray$^{17}$. The role of the dentist in the diagnosis of osteoporosis could become important if it is kept in mind that panoramic radiography is currently performed in dental practices.

Panoramic digital images were used to diagnose periapical radiolucencies. It has been reported that an underestimation of lesions occurred when panoramic radiography was used$^{18}$, but the difference with periapical radiography was not statistically significant$^{19,20}$. The advantages of panoramic radiography when compared to full-mouth periapical radiography are numerous: its relatively low exposure to ionising radiation, the fact that all teeth can be seen on one panoramic radiograph,

### Table 2

<table>
<thead>
<tr>
<th></th>
<th>HBG (%)</th>
<th>OEG (%)</th>
<th>OPG (%)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>At least one PRL</td>
<td>2 (7.4)</td>
<td>9 (25.0)</td>
<td>3 (25.0)</td>
<td>14</td>
</tr>
<tr>
<td>No PRL</td>
<td>25 (92.6)</td>
<td>27 (75.0)</td>
<td>9 (75.0)</td>
<td>61</td>
</tr>
<tr>
<td>Total</td>
<td>27</td>
<td>36</td>
<td>12</td>
<td>75</td>
</tr>
</tbody>
</table>

Chi-squared test: overall fit; $p = 0.172$.
HBG vs (OEG + OPG); $p = 0.061$.
HBG, healthy bone group; BMD $\geq – 1$ SD.
OEG, osteopenic group; BMD between $< – 1$ SD and $> – 2.5$ SD.
OPG, osteoporotic group; BMD $\leq – 2.5$ SD.

### Table 3

Multivariate logistic regression analysis of the influence of the independent variables age (year), number of teeth, number of root-filled teeth, number of teeth with coronal restorations and bone mineral density assessed using dual-energy X-ray absorptiometry in the femoral neck (BMD), on the dependent variable 'periapical radiolucent lesion in at least one tooth' (present $= 1$; absent $= 0$).

<table>
<thead>
<tr>
<th>Independent variables</th>
<th>B</th>
<th>$p$</th>
<th>Odds Ratio</th>
<th>CI 95% Inf. Limit</th>
<th>CI 95% Sup. Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.2182</td>
<td>0.2551</td>
<td>1.2438</td>
<td>0.8542</td>
<td>1.8111</td>
</tr>
<tr>
<td>No. Teeth</td>
<td>0.0327</td>
<td>0.4843</td>
<td>1.0332</td>
<td>0.9428</td>
<td>1.1323</td>
</tr>
<tr>
<td>No. RFT</td>
<td>-0.0408</td>
<td>0.8279</td>
<td>0.9601</td>
<td>0.6648</td>
<td>1.3864</td>
</tr>
<tr>
<td>Coronal restorations</td>
<td>-0.0272</td>
<td>0.6728</td>
<td>0.9732</td>
<td>0.8579</td>
<td>1.1040</td>
</tr>
<tr>
<td>BMD</td>
<td>0.6634</td>
<td>0.0504</td>
<td>1.9413</td>
<td>0.9988</td>
<td>3.7733</td>
</tr>
</tbody>
</table>

Overall model fit. Chi-square $= 5.8503$; df $= 5$; $p = 0.3211$. 

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the convenience of panoramic radiography and its easy and quick obtaining. Thus, panoramic radiography is a highly viable tool to implement studies in a rapid fashion, and many epidemiological studies have been carried out using panoramic radiographs. Moreover, it has been proposed that panoramic radiography could be useful for confirming individuals who present with low bone mineral density.

Chronic apical periodontitis (CAP) is an asymptomatic inflammation of the apical periodontium of a tooth. Due to the encasement of the root in bone and the relatively greater resistance of the root to resorption, the spreading of the inflammatory process usually occurs at the expense of the surrounding bone. There is a firm evidence that the loss of bone seen around the apex in teeth with CAP can be attributed to increased bone resorption.

Current evidences support an association of osteoporosis with the onset and progression of periodontal disease in humans. Several studies have shown low bone mass to be independently associated with loss of alveolar crestal height and tooth loss. Recently, it has been reported that, after adjusting for smoking and menopausal status, subjects with osteoporosis presented with greater clinical attachment loss and had greater gingival recession than subjects with normal BMD. Nevertheless, others have found no correlation between periodontal disease and osteoporosis.

Although some differences are evident, apical periodontitis of an endodontic origin shares with periodontal disease important similitudes such as similar micro-organisms (gram-negative anaerobic bacteria, P. gingivalis, F. nucleatum, P. intermedia, and so on); the periodontal ligament; neighbouring spongiosa; resorptive process; and, finally, chronic inflammatory host response to an infectious condition. Consequently, periapical radiolucent lesions consecutive to CAP could also be associated with low BMD and osteoporosis, as the results of the present investigation suggest. The marginally significant association between the presence of at least one radiolucent periapical lesion and low BMD found in this study could be explained in two ways. Firstly, in women with low BMD, osteopenic and osteoporotic groups, oestrogen deficiency depending bone resorption increases inflammatory bone resorption in the periapical lesions, resulting in a higher net bone loss and an intensification of the lesion radiolucency that facilitates its diagnosis. This possibility is supported by the report that evaluated the bone density of periapical lesions in the area of maxillary incisors and canines, finding a correlation between lower densitometric values and osteoporosis and radiolucency areas. A two-year longitudinal study has shown that alveolar bone density decreases more rapidly in post-menopausal women compared with women with normal BMD, indicating that bone tissue in the jaws is also affected by oestrogen deficiency. The visibility of periapical lesions on a radiograph is determined by the diameter of the lesion, the density of the spongiosa and the erosion of either the cortex or the junction area between cortex and spongiosa. Therefore, the changes in alveolar bone in osteopenic and osteoporotic women increase the likelihood of radiographically detect periapical radiolucenties, explaining the association between low BMD and periapical radiolucenties. Secondly, however, it cannot be excluded that reduced bone trabeculation in the jaws in women with low BMD causes false positives in the radiological assessment of the periapical regions. There are studies indicating a correlation between low bone mass in the skeleton in general and in the mandible. Moreover, it has been investigated the diagnostic accuracy of visual assessment of the trabecular pattern in intra-oral periapical radiographs to identify female subjects at risk of having osteoporosis, finding sparse trabecular pattern as indicative of osteoporosis.

In the present study, several factors have been analysed and used as covariates in the logistic regression model to avoid bias in the results. The average number of teeth per patient was similar in the three groups. This comparable average number of teeth cannot be regarded a sufficient estimation of identical risk exposure for pulpal disease, root canal infection and subsequent apical periodontitis in the three groups. Nevertheless, it has been concluded that the number of teeth per patient performed well as an indicator of oral health status. As a result, it could be considered...
that the oral health status of osteoporotic, osteopenic and healthy bone women analysed in this study was comparable. On the other hand, root-filled teeth have been shown to be significantly more frequently affected by radiolucent periapical lesions than non-treated teeth, some of them may represent persistent CAP, while others may be incomplete healed lesions after root canal treatment. Likewise, the probability of CAP, and its periapical radiolucency, increased significantly after coronal filling. However, in the present study, both the average number of root-filled teeth and the number of teeth with coronal restorations per subject were similar in the three groups. Moreover, in the multivariate logistic regression analysis run with age, number of teeth, number of root-filled teeth, number of teeth with coronal restorations as independent variables, the three factors were not statistically associated with the presence of periapical radiolucenties.

The present study has the following limitations: (i) there are factors not recorded, such as prevalence of diabetes, which could affect both the incidence of periapical radiolucenties and osteoporosis, acting as confounding factor; (ii) it has not been taken into account the level of education and socioeconomic status of the study population that may influence both the periapical status and skeletal BMD; and (iii) finally, the quality of root canal filling and coronal restorations, which have not been considered when evaluating the presence of periapical radiolucenties, has been shown to be associated with the prevalence of CAP and could act as confounding factor.

Within the limits of the present study, the following conclusion can be drawn: after adjusting for covariates, low BMD is associated with a higher frequency of detection of radiolucent periapical lesions in panoramic radiographs. However, the cause(s) and significance of finding a greater number of radiolucent periapical lesions in the patients with osteoporosis must be substantiated by determining whether or not these abnormalities are associated with any pulpal and/or periodontal disease, confirmed clinically. Therefore, future clinical investigations must be developed in post-menopausal women, analysing the association between radiolucent periapical lesions and pulpal and periodontal states of the affected teeth. Epidemiologic longitudinal studies comparing the endodontic and periapical states of post-menopausal women with and without low BMD are also required. On the other hand, further studies to better understand the underlying biological mechanisms that may link systemic bone loss and periapical inflammation may provide more insights into their inter-relationship.

The main finding of this investigation, that is, the marginally association between radiolucent periapical lesions and BMD in post-menopausal women, has practical and clinical relevance. First of all, when a woman sought dental care, dentists must always include in the anamnesis questions about osteoporosis and BMD. In addition, dentists must take in mind that some periapical radiolucenties observed in the panoramic radiographs of post-menopausal women can be only reduced bone trabeculation images in the jawbones of the osteoporotic women. Consequently, after the detection of a radiolucent periapical lesion, a thorough clinical examination of the affected tooth must be carried out to determine the pulpal state and the right treatment option.

References

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