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ORIGINAL ARTICLE

Association of osteoporosis and bone medication with the periodontal condition in elderly women

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Abstract
Summary This study investigated whether osteoporosis and its treatment may affect periodontal condition in elderly women. The findings highlighted that women with osteoporosis had a higher chance to present severe periodontitis than women with normal bone mineral density (BMD), particularly those who were not treated for osteoporosis.
Introduction This study investigated whether osteoporosis increases the frequency and severity of chronic periodontitis in elderly women and evaluated the influence of vitamin D and osteoporosis treatment in the periodontal condition.
Methods In this cross-sectional study, elderly women were selected among 1266 subjects evaluated for lumbar spine and proximal femur bone mineral density (BMD) using dual energy X-ray absorptiometry. Sociodemographic, clinical characteristics, and complete periodontal examination were recorded. Serum 25-hydroxyvitamin D levels were measured by chemiluminescence.
Results Forty-eight elderly women with normal BMD and 86 with osteoporosis were selected. Women with osteoporosis presented higher frequency of sites with clinical attachment level ≥6 mm (p=0.003) and gingival recession ≥3 mm (p=0.002) than those with normal BMD and were more than twice as likely to present severe periodontitis (odds ratio (OR)=2.49, 95 % CI [1.14 to 5.43]). Osteoporotic women who were not treated for the condition had more chance to present severe periodontitis (OR=3.16, 95 % CI [1.28 to 7.82]) than those who did use bisphosphonates (OR=2.04, 95 % CI [0.85 to 4.89]). Among the participants who presented low levels of vitamin D, those with osteoporosis exhibited a higher chance to present severe periodontitis than those with normal BMD (p=0.027), but the association between vitamin D levels and osteoporosis was not statistically significant after adjustment (p=0.198).
Conclusions Elderly women with osteoporosis have a greater chance to present periodontitis, with higher severity than those with normal BMD. Osteoporosis treatment provides protection for periodontitis.

Keywords Bisphosphonates · Bone density · Elderly · Osteoporosis · Periodontitis · Vitamin D

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Introduction

Osteoporosis and periodontitis are frequent conditions that affect bone mass and share some risk factors [1, 2]. In osteoporosis, bone loss is generalized, whereas in periodontal disease, it may be localized in the alveolar bone of the jaw [3]. Bone changes resulting from osteoporosis may potentially aggravate periodontal disease [1].

Osteoporosis is characterized by reduced bone mass and disruption of bone microarchitecture, resulting in increased bone fragility and fracture risk [4]. The prevalence of osteoporosis depends on the geographic area, ethnicity, and age range, and it is a serious public health concern [5, 6].

Periodontitis is a biofilm-induced infection caused by components of the indigenous oral microbiota. Host inflammatory-immunologic responses to bacteria are responsible for most of the observed tissue damage, like periodontal attachment loss and alveolar bone destruction. Periodontal disease is one of the most common causes of tooth loss, and periodontal therapy is effective as long as patients comply with maintenance programs. Therefore, prevention and early detection of periodontal disease are essential to reduce further damage to the periodontium [7].

One possible link between osteoporosis and severe periodontal destruction is the simultaneous systemic and alveolar bone resorption. Moreover, systemic factors in bone remodeling could modify the local tissue response to periodontal infection. Individuals with systemic bone loss may react to periodontitis with increased production of cytokines and inflammatory mediators [8].

Studies using clinical periodontal parameters to verify the possible association of periodontal disease with low systemic BMD found controversial results [9–21]. Different methodologies are the main reason for the contradictory data reported in the studies. Thus, some studies involve only elderly women [9–13, 17], some have small samples [11, 22], and some include subjects with osteopenia in the osteoporosis group [14, 15] or in the normal BMD group [20]. The use of medication for osteoporosis was an exclusion criteria for some studies [19, 21], while others evaluated medication effects in the periodontium [15, 17].

Bisphosphonate (BP) therapy is commonly employed for osteoporosis treatment [23] and has been associated with decreased alveolar bone loss in the periodontium of postmenopausal women. Thus, BPs might be useful in treating periodontal disease [24, 25], being an appropriate adjunctive therapy to preserve periodontal bone mass [26]. Postmenopausal women with osteoporosis/osteopenia presented periodontitis more frequently than women with normal BMD, particularly among those women which were not treating osteoporosis [15]. There are few data about the effect of antiresorptive and osteoanabolic drugs in periodontal therapy, but it seems to be promising [27].

Vitamin D is unique among hormones, because it is produced in the skin after exposure to sunlight and then transformed in the liver to its most abundant circulating metabolite 25-hydroxyvitamin D and finally to 1,25-dihydroxyvitamin D, mostly in the kidneys. In patients with vitamin D deficiency, only 10 to 15 % of dietary calcium and about 60 % of phosphorus are absorbed, which limits bone mineralization [28]. Vitamin D has a wide range of biological actions, and D-deficiency has been associated with an increased risk of cancers, autoimmune disease, types 1 and 2 diabetes, infectious disease, rheumatoid arthritis, cardiovascular disease, and others [28]. Periodontal disease seems more common in women with osteoporosis and associated with lower concentration of serum 25-hydroxyvitamin D [3]. Furthermore, patients in periodontal maintenance programs taking vitamin D and calcium supplementation exhibited a trend for better periodontal health compared with patients not taking the supplementation [29].

The association between osteoporosis and periodontitis, and the eventual benefits of vitamin D and anti-osteoporosis drugs for the periodontium deserve further investigation, especially considering the increase of elderly people in a global perspective and, consequently, of osteoporosis and periodontal disease. The aim of this study was to test the hypothesis that osteoporosis is associated to a higher frequency and severity of periodontal disease in a population of elderly women. In addition, the influence of vitamin D levels and osteoporosis medications in the periodontal condition was explored.

Methods

Study design

This was a cross-sectional study which compared the prevalence and severity of periodontal disease between elderly woman with normal BMD and elderly woman with osteoporosis. The influence of low vitamin D levels and bisphosphonate use on the periodontal status was also investigated.

Research subjects

The sample size calculation of 127 subjects for the study was based on preliminary data, in which the prevalence of periodontitis in 96 elderly women was 47 % in subjects with osteoporosis and 22 % in controls. The confidence interval (CI) used was 95 % with a power study of 80 %.

Aging women were selected from the whole population of individuals submitted to bone density assessment from December 2013 to January 2015 at the Hospital Naval Marcilio Dias (HNMD), in Rio de Janeiro, Brazil. This hospital is a military institution that serves Brazilian Navy military and dependents. To be eligible for the study, subjects should be 65 to 80 years old and have a densitometry report of normal BMD or osteoporosis within the last 6 months (those with osteopenia were excluded).

Subjects were excluded if presented conditions affecting the bone (Paget disease, diabetes mellitus, or malignancies), if they were current smokers, or if they were using medication which may affect the bone (corticosteroid, immunosuppressive, or chemotherapy), except subjects using antiosteoporosis

drugs. Potential participants were contacted by phone, when they were informed about the study and asked about their willingness to participate. If the answer was positive, participants were asked about other eventual exclusion criteria: if they had less than six teeth, underwent previous periodontal treatment and/or antibiotics use within the last 6 months, and if they could attend a dental appointment at the Odontoclínica Central da Marinha (OCM). Participants signed the informed consent form when they attended the dental appointment. This study was approved by the Hospital Clementino Fraga Filho/Universidade Federal do Rio de Janeiro and Hospital Naval Marcilio Dias Research Ethics Committees, in Rio de Janeiro, Brazil, protocols 453.319 and 489.507, respectively, and was in accordance with the ethical standards established by the Declaration of Helsinki.

Data collection

A structured questionnaire was applied to obtain sociodemographic, medical, and dental history. Women were considered physically active individuals if they exercised at least twice a week. The type, dosages, and duration of medications were recorded. History of low-impact fracture was checked for all participants. Nonclinical vertebral fractures were checked using lateral thoracic and lumbar spine X-rays.

Bone mineral density (BMD) was measured by dual-energy X-ray absorptiometry (DXA) at the lumbar spine (L1 to L4), femoral neck, and total femur. All the assessments were performed in a standardized way, by trained technologists, using a GE Lunar DPX-NP (GE Health Care Clinical Systems Medical Equipment). The lowest T-score of each patient was considered to classify as normal BMD (T-score≥−1 SD from peak BMD at all sites) or osteoporosis (T-score≤−2.5 SD at any site), according to the criteria established by the World Health Organization [30]. These results were only revealed to clinical investigator after the periodontal examination.

All patients were oriented to collect blood for 25-hydroxyvitamin D levels (assayed by electrochemiluminescence, Elecsys kit 2010 Roche, Berlin, Germany; normal range 30–100 ng/mL). According to the Endocrine Society guidelines, patients were considered D-sufficient if levels were ≥30 ng/mL, D-insufficient between 21 and 29 ng/ml, and D-deficient if levels were below 20 ng/mL [28]. For statistical analysis, all women with 25(OH)D level below 30 ng/mL were considered as having low vitamin D levels. The study was held in a city with tropical climate, and thus, seasonal variations were not a concern.

Evaluation of periodontal conditions

An oral exam was performed in each subject, with full-mouth periodontal assessment. Probing depth (PD) and clinical attachment level (CAL) were measured at six sites (mesial, distal, and middle sites of the buccal and lingual sides) on each tooth, using a North Caroline periodontal probe (Hu-Friedy®, USA). The probing depth was measured as the distance from the gingival margin to the position of greatest penetration of the probe. The CAL was measured as the distance from the cement-enamel junction (CEJ) to the base of the periodontal pocket. Gingival recession (GR) was obtained by the difference between CAL and PD. Third molars were excluded from the examinations. Additional assessments of periodontal status included the presence of biofilm and bleeding on probing (BOP). Biofilm was recorded using the plaque index (PI) by a dichotomous way: the absence of biofilm received score 0 (nonvisible) and its presence received score 1 (visible). Also, BOP was determined as absent (0) or present (1), and considered present if bleeding occurred up to 15 s after removing the periodontal probe of the periodontal site.

Oral examinations were performed by one calibrated and blinded examiner. Measurement reliability was determined by intra-class correlation for PD and CAL measurements, and was, respectively, 0.82 and 0.83. Women were considered to have periodontitis if they presented ≥2 interproximal sites with CAL ≥6 mm (not on same tooth) and at least ≥1 interproximal site with PD ≥5 mm [31].

Data analysis

Descriptive statistics was performed for sociodemographic, clinical, densitometry, and laboratory data. Regarding periodontal parameters, the frequency of bleeding sites and visible biofilm was calculated for each patient. Probing depth, CAL, and GR variables were categorized into PD and CAL ≥4 mm and ≥6 mm, and GR ≥3 mm. The mean frequency of sites of PD and CAL ≥4 mm and ≥6 mm, and GR ≥3 mm was then calculated for each group: normal BMD and osteoporosis. The osteoporosis group was separated into two subgroups: women who did not take any medication for osteoporosis and women undergoing osteoporosis treatment. Mean values of the lowest BMD T-scores were calculated for the two osteoporotic subgroups. Statistical differences between groups were evaluated using the chi-square test for categorical variables, and Mann-Whitney and Kruskal-Wallis for continuous variables, with a 5 % significance level. Stratified analyses were performed in order to explore whether low levels of vitamin D increased the severity of periodontitis in elderly women with osteoporosis. A univariate and multivariate logistic regression was performed to explore the association of independent variables with periodontitis: osteoporosis (with medication/without medication), 25(OH)D levels (low/sufficient), and BMI.

The frequency of patients with severe chronic periodontitis was calculated in each group. The association between periodontitis and osteoporosis (for the whole group and for two subgroups) was evaluated using odds ratios (ORs) and their

respective 95 % confidence intervals. All data processing and analyses were performed using the software SPSS version 21.0 (*Statistical Package for the Social Sciences*, SPSS Inc., Chicago, USA).

Results

Out of 1266 files of patients aged 65–80 years who had their bone densitometry assessed in the HNMD from December 2013 to January 2015, 330 women were eligible for the study. Under the imposed study criteria, 134 women were included in the study: 86 of them with osteoporosis and the remaining 48 presenting normal BMD. Figure 1 shows a flowchart of the enrolment process applied to the study subjects.

Sociodemographic and clinical data of studied participants are shown in Table 1. Groups were relatively homogeneous regarding most of the features, except for the body mass index (BMI), which was lower in those women with osteoporosis. Low-impact fractures were identified in 12.8 % of the osteoporotic women, but not in those with normal BMD. Mean values of the lowest T-scores were not different between the two osteoporotic subgroups: −2.94 for treated osteoporosis and −2.87 for nontreated (Mann-Whitney test, $p=0.713$).

Among the 86 patients with osteoporosis, 47 were undergoing osteoporosis treatment with the following medications: alendronate 70 mg/weekly ($n=34$), risedronate 35 mg/weekly ($n=9$), and ibandronate 150 mg/monthly ($n=1$); two women had changed to strontium ranelate 60 mg/daily; and one changed to teriparatide 20 mcg/daily in the previous year.

Laboratory results of serum 25(OH)D were available for 113 participants. Vitamin D insufficiency was observed in 54 women (47.8 %) and deficiency in 33 (29.2 %) of them. Thus, 77 % presented 25(OH)D below 30 ng/ml, and the mean 25 (OH)D value of these subjects was closer to the cutoff point which defined vitamin D deficiency (21.95±4.3 ng/ml). Among these women with low vitamin D levels, 55 (63.2 %) were affected by osteoporosis. Low levels of this hormone were more frequently observed in women who were not taking vitamin D supplements (58.6 %); however, it was also frequent among those who were taking these supplements (41.4 %).

The mean percentages of periodontal clinical parameters are listed in Table 2. Comparison between groups with normal BMD and osteoporosis showed that the frequency of sites of CAL≥6 mm (Mann-Whitney test, $p=0.003$) and GR ≥3 mm (Mann-Whitney test, $p=0.002$) was significantly higher for the group of osteoporotic women. Worse periodontal conditions were observed particularly in the subgroup of women not using medication for osteoporosis. There was no significant difference in the plaque and bleeding index between women with normal BMD and osteoporosis.

Comparison between the group of women with normal BMD and the two subgroups of osteoporosis (treated and nontreated for osteoporosis) also showed higher frequency of sites of CAL ≥6 mm (Kruskal-Wallis test, $p=0.010$) and GR ≥3 mm (Kruskal-Wallis test, $p=0.007$) for osteoporotic women. However, participants not treated for osteoporosis presented higher means and medians of PD and CAL, and showed worse periodontal condition than those women with normal BMD and those with osteoporosis under treatment.

Among women with osteoporosis, the chance of presenting periodontitis was more than twice as high as among those with normal BMD (OR=2.49; 95 % CI [1.14–5.43]; $p=0.020$) (Table 3). The association between osteoporosis and periodontitis increased when the group of women not treated for osteoporosis was separately analyzed (OR=3.16; 95 % CI [1.28–7.82]; $p=0.011$). However, for the group of osteoporotic women under osteoporosis treatment, the magnitude of the association with periodontal disease was reduced, losing statistical significance (OR=2.04; 95 % CI [0.85–4.89]; $p=0.109$).

Among the 87 participants with low levels of vitamin D, those with osteoporosis were more than three times as likely to present severe periodontitis as were those women with normal BMD (OR=3.34; 95 % CI [1.11–10.00]; $p=0.027$) (Table 4). There was no association between periodontitis and osteoporosis considering the 26 women with vitamin D sufficiency ($p=0.473$). A univariate and multivariate regression analysis was performed in the 113 participants who had serum dosages of 25(OH)D. The regression analysis confirmed that the chance for presenting periodontitis increased in osteoporosis without medication, while in treated osteoporosis, this chance decreased. However, vitamin D levels (low/sufficient) were not associated to periodontitis in the regression analysis and did not show interaction with osteoporosis, losing statistical significance (Table 5).

Discussion

Based on the evaluation of 134 postmenopausal women who had similar clinical and demographic characteristics, we found that chronic periodontitis was more prevalent and severe in women with osteoporosis as compared to those with normal BMD. Moreover, normal levels of vitamin D and the use of anti-osteoporosis drugs clearly improved the periodontal *status* of women. Among the studies involving periodontitis and osteoporosis, the present study was the first one to simultaneously investigate the influence of osteoporosis medication and 25(OH)D levels.

There is enough biological plausibility to support that osteoporosis and periodontal disease may be related [3, 8, 32]. The effects of osteoporosis, which accumulated over the years in the periodontium, may be more remarkable in advanced

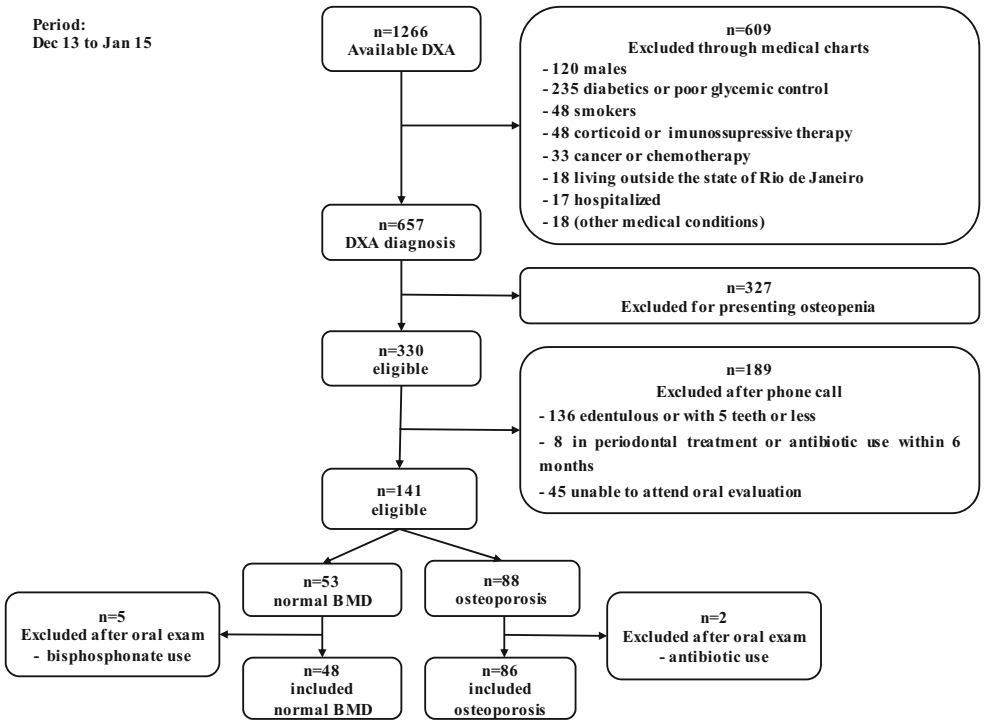

Fig. 1 Flow chart of the sample selection. *BMD* bone mineral density, *DXA* dual-energy X-ray absorptiometry

ages. In order to verify the potential effects of osteoporosis in the periodontium, only patients older than 65 years were evaluated in the present study.

The CAL and GR parameters were worse in women affected by osteoporosis than in those with normal BMD, in the studied population. Worse periodontal parameters have been associated to osteoporosis in studies from different countries [12, 13, 17]. However, other authors reported controversial results [9–11]. Studies assessing the association between osteoporosis and periodontal disease differ widely in their methodology, using samples with different selection criteria, social and demographic characteristics, different methods to measure periodontal disease, and BMD assessment. The present study used a full-mouth examination methodology, performed at six sites per tooth, which accurately reflects the prevalence and the severity of periodontal disease. In addition, very strict inclusion criteria were used, and many conditions that could potentially confound these results were excluded.

An important aspect found in the present study was the higher extension of the GR in patients with osteoporosis, when compared to women with normal BMD. Other researchers have previously reported these findings in patients with low BMD [2, 18, 33]. Pain from exposed dentine, root caries, abrasion, and aesthetic concerns may represent clinical complications of GR [34]. In addition, exposed root areas are more susceptible to biofilm accumulation and represent a challenge in cleaning, which in turn can perpetuate the clinical attachment loss. Periodontal management should be directed at prevention of further progression of the condition and the control of the symptoms [34].

The chance for having severe periodontitis was 2.49 higher in subjects with osteoporosis versus those with normal BMD. Other authors also found positive associations between osteoporosis and periodontitis, reporting similar odds ratios [14–17]. Furthermore, the lack of osteoporosis treatment contributed to a higher risk for having periodontal disease (OR 3.16) in the studied population. In the osteoporotic group, a positive effect of osteoporosis treatment was observed in the periodontal condition, when compared to untreated women. These results are in accordance with findings from other authors [15, 17]. Bisphosphonates (BP) are antiresorptive drugs used in osteoporosis treatment. It has been reported that oral BP therapy may also protect individuals against periodontal bone loss [25]. This effect on the alveolar bone was expected, and it has been demonstrated in other studies [24, 25, 35].

Although the sample size was not calculated for the subgroups of osteoporosis, we could observe that the negative effects of osteoporosis were reduced in the *periodontium* when patients had a history of osteoporosis treatment. The most widely accepted mechanism of action of BP is to inhibit osteoclast activity by promoting osteoclast apoptosis, and these compounds have also shown to act as anti-inflammatory agents [27].

BPs are highly concentrated in the jaws, because jaws have a faster bone turnover rate than other bones, which is related to the jaw activity and the bone remodeling on the periodontal ligament around the teeth [36]. Periodontal disease increases the demand for bone turnover/renewal in the jaws, being one of the conditions that may trigger osteonecrosis of the jaw [36]. Dental care is recommended for patients taking BP, in

Table 1 Sociodemographic and clinical data of the 134 study participants according to groups

Characteristics	Total (n=134)	Normal BMD (n=48)	Osteoporosis (n=86)	p value*
Age (years)	69.84±3.90	69.31±3.71	70.13±3.99	0.266
Ethnicity				
White	75 (56.0)	23 (47.9)	52 (60.5)	0.161
Nonwhite	59 (44.0)	25 (52.1)	34 (39.5)	
Education				
Incomplete primary education	63 (47.0)	24 (50.0)	39 (45.4)	0.943
Elementary school	35 (26.1)	12 (25.0)	23 (26.7)	
High school	31 (23.1)	10 (20.8)	21 (24.4)	
Higher education	5 (3.8)	2 (4.2)	3 (3.5)	
Family income				
<4 minimum wage per month	32 (23.9)	10 (20.8)	22 (25.6)	0.537
≥4 minimum month salary	102 (76.1)	38 (79.2)	64 (74.4)	
Number of dependents				
≤2	95 (70.9)	33 (68.7)	62 (72.1)	0.683
≥3	39 (29.1)	15 (31.3)	24 (27.9)	
Age at menopause(years)	48.19±5.73	48.85±6.49	47.81±5.26	0.161
Type of menopause				
Physiological	106 (79.1)	36 (75.0)	70 (81.4)	0.383
Surgical	28 (20.9)	12 (25.0)	16 (18.6)	
Body mass index (kg/m^2)	28.22±5.07	31.14±5.57	26.58±3.95	≤0.01*
Physical activity	54 (40.3)	21 (43.7)	33 (38.4)	0.543
Number of teeth	14.54±6.46	14.23±6.79	14.72±6.31	0.562
Toothbrushing frequency/day				
≤2	43 (32.1)	17 (35.4)	26 (30.2)	0.538
≥3	91 (67.9)	31 (64.6)	60 (69.8)	
Last visit to dentist				
≤2 years	67 (50.0)	22 (45.9)	45 (52.3)	0.471
>2 years	67 (50.0)	26 (54.1)	41 (47.7)	
Osteoporotic fracture(self-related)	11 (8.2)	0 (0)	11 (12.8)	0.010*

Mann-Whitney for continuous variables and chi-square for categorical variables. Data expressed as mean±SD or absolute number (%)

SD standard-deviation

*Significance level≤0.05

order to maintain a healthy periodontal status. No osteonecrosis of the jaw was noted in this study sample, possibly because its risk is very low, and a much greater sample size and longer periods of BP therapy would be necessary to detect this complication [37]. Fortunately, osteonecrosis of the jaw related to osteoporosis treatment is uncommon. Dentists need to properly manage patients who use BP and those who develop osteonecrosis of the jaw.

Vitamin D reduces the risk of osteoporotic fractures, and low vitamin D levels might have deleterious consequences to health outcomes [38]. We found that the frequency and the severity of chronic periodontitis were significantly associated with vitamin D insufficiency/deficiency in elderly women with osteoporosis. Awareness of the dental patient's systemic bone health status, as well as their vitamin D intake, may be important to understand their periodontal status and indicate directions for dealing with these patients [32].

In the studied population, there was a high prevalence of vitamin D inadequacy (77 %). Women with low vitamin D levels affected by osteoporosis exhibited higher chance to present periodontitis than those with normal BMD. Reports from other authors corroborate these findings [3, 29, 39]. However, performing a logistic regression analysis in a sample of 113 participants that had available serum 25(OH)D results, the association between periodontitis and vitamin D levels was not significant. Studies with larger samples could clarify whether, in cases of osteoporosis and vitamin D insufficiency/deficiency, supplementation with vitamin D could be a protective factor to periodontal tissues. A consensus about targets for bone health recommends that osteoporotic

Table 2 Clinical periodontal parameters of the 134 elderly women in the study, according to bone mineral density status, including the subgroups of treated and nontreated women with osteoporosis

Clinical parameters	Normal BMD (n=48)	Osteoporosis			p value[a]	p value[b]
		Total (n=86)	No medication (n=39)	With medication (n=47)		
% of sites with:						
Probing depth≥4 mm (%)						
Mean±SD	8.03±9.25	9.08±11.25	10.93±13.47	7.54±8.87	0.597	0.306
Median	3.87	6.20	7.14	5.83		
Range	0.00–38.67	0.00–73.73	0.00–73.33	0.00–35.19		
Probing depth≥6 mm (%)						
Mean±SD	0.92±1.90	1.48±3.11	2.03±3.94	1.02±2.15	0.331	0.116
Median	0.00	0.00	0.00	0.00		
Range	0.00–7.69	0.00–16.67	0.00–16.67	0.00–9.26		
Clinical attachment level≥4 mm (%)						
Mean±SD	21.32±15.68	26.88±20.85	29.63±23.81	24.60±17.98	0.215	0.344
Median	17.84	23.57	26.28	19.44		
Range	0.00–56.25	2.08–95.24	2.08–95.24	2.08–74.07		
Clinical attachment level≥6 mm (%)						
Mean±SD	2.61±4.24	7.08±10.17	8.70±12.26	5.73±7.94	0.003*	0.010*
Median	0.89	3.18	4.17	2.94		
Range	0.00–21.43	0.00–50.00	0.00–50.00	0.00–37.04		
Gingival recession≥3 mm (%)						
Mean±SD	4.53±5.32	9.34±10.23	9.82±11.04	8.94±9.60	0.002*	0.007*
Median	3.12	6.20	6.35	6.06		
Range	0.00–22.92	0.00–54.76	0.00–54.76	0.00–45.24		
Plaque index (%)						
Mean±SD	25.10±16.77	22.43±13.99	24.96±15.69	20.33±12.18	0.567	0.446
Median	20.29	19.29	19.84	18.89		
Range	0.00–69.44	0.00–52.94	1.19–52.94	0.00–46.97		
Bleeding on probing index (%)						
Mean±SD	15.19±12.55	16.15±13.04	18.56±15.23	14.15±10.67	0.624	0.443
Median	11.63	11.62	12.50	11.11		
Range	0.00–60.42	0.00–73.33	0.88–73.33	0.00–44.74		

SD standard-deviation

*Significance level≤0.05

[a] Mann-Whitney (comparison between normal group and osteoporosis group)

[b] Kruskal-Wallis (comparison between normal group and the two osteoporosis subgroups)

Table 3 Odds ratio (OR) and confidence interval for the association between periodontitis and osteoporosis in the 134 studied elderly women, according to anti-osteoporosis treatment

	Normal BMD (n=48)	Osteoporosis		
		Total (n=86)	Without medication (n=39)	With medication (n=47)
Periodontitis: n (%)	12 (25.0)	39 (45.3)	20 (51.3)	19 (40.4)
Odds ratio (confidence interval)		2.49 (1.14–5.43)	3.16 (1.28–7.82)	2.04 (0.85–4.87)
p		0.020*	0.011*	0.109

*Significance level≤0.05

Table 4 Odds ratio (OR) and confidence interval for the association between periodontitis and osteoporosis in the 87 subjects who presented low levels of vitamin D

	Normal BMD $n=32$	Osteoporosis $n=55$
Periodontitis: *n* (%)	5 (15.6)	21 (38.2)
Odds ratio (confidence interval)	3.34 (1.11–10.00)	
p	0.027*	

*Significance level≤0.05

patients with serum 25(OH)D levels less than 20 ng/ml should receive vitamin D supplementation and fragile elderly at elevated risk for falls and fractures should maintain at least 24 ng/ml levels, ideally 30 ng/ml [38].

Low body mass index has been considered a condition that contributes to osteoporosis and fractures [40]. Higher values were found in the group of women with normal BMD, suggesting a protective effect of higher body mass index on bone for these women. Body mass index did not show association with periodontitis.

At menopause, women undergo an accelerated phase of trabecular bone loss. During this phase, the loss of trabecular bone is threefold to fivefold greater than the loss of cortical bone. Later, a slower phase of bone loss prevails with the loss of both cancellous and cortical bone, which continues throughout life. With aging, remodeling becomes unbalanced. Every time that bone matrix is remodeled, more bone is removed than it is replaced. The final product of this process is bone loss and structural decay, fragility, and bone fracture. In old ages, the bone fractures arise mainly at the cortical bone [41, 42]. Authors have demonstrated that, in bones of elderly humans, the intracortical remodeling thinned the cortex from within by cavitation, leaving cortical remnants that looked similar to trabeculae [43]. This may explain the high occurrence of fractures in cortical bones in advanced ages [43]. The process is probably the same in the alveolar bone. The alveolar bone crest is constantly exposed to remodeling, due to damage repair and/or adaptation to loading, as consequence of jaw functions, like mastication. Thus, in the alveolar crests of older individuals with osteoporosis, fractures may occur due to the fragility and porosity of cortical remnants.

Many authors have found association between higher CAL and low BMD in elderly [12, 13, 17, 33]. Clinical attachment level and gingival apical migration are often the result of bacterial infection [2]. However, there were no differences in the plaque index and bleeding on probing between the analyzed groups of the present study. These findings might suggest that, in elderly people with osteoporosis, the periodontal attachment loss and the GR may occur in conjunction with the circumferential loss of the supporting alveolar bone, independently of the presence of a periodontopathogenic biofilm. A possible explanation to this theory is the synergism between three factors: (1) the estrogen deficiency [33, 42], (2) the reduced healing quality of bones with low BMD [44], and (3) the age-dependent oxidative stress, which consequently impairs wound healing [45] after alveolar crest microfractures.

Methodological precautions were taken in the present study, like excluding smokers and diabetic women. Another precaution was the search for nonclinical vertebral fractures in patients with normal BMD, as these fractures would confirm impaired bone quality and strength, irrespective of bone density [40].

Some limitations must be considered when interpreting our findings. Although the hospital where the study was placed attends more than 20,000 elderly in Rio de Janeiro and surrounding areas, the sample utilized in the study may not represent the general elderly population, because it is a selected population of dependents of the Brazilian Navy members. In addition, a strict inclusion and exclusion criteria were used in the study. Women with osteopenia were excluded from this study design for a better comparison of the clinical features of extreme measurements of BMD in the periodontium. This was a methodological precaution; however, it limits the possible conclusions that could be drawn for osteopenic women. Another limitation is that not all patients measured 25(OH)D. Finally, it may not be correct to state that osteoporosis can be a definite causal factor for periodontitis, because sectional studies do not show the development of events. Prospective studies would be more powerful in relating the sequence of

Table 5 Univariate and multivariate regression analysis for periodontitis in the 113 participants who had serum dosages of 25(OH)D

Independent variables	Univariate		Multivariate	
	Odds ratio	*p*	Odds ratio	*p*
Normal BMD	1		1	
Osteoporosis without medication	3.49	0.021*	3.38	0.026*
Osteoporosis with medication	2.83	0.048*	2.63	0.069
Low levels 25(OH)D	0.497	0.127	0.545	0.198
Adequate levels 25(OH)D	1		1	
Body mass index (kg/m^2)	0.973	0.483	1.034	0.469

*Significance level≤0.05

risk factors to periodontal disease in order to establish causal relations between osteoporosis and periodontal disease.

There are some clinical implications associated with the results of the present study. Medicine has enhanced the prevention and treatment of osteoporosis by informing women about risks to bone health after menopause. Dentists can provide the elderly the awareness of their oral health condition, preventing and treating possible negative effects related to osteoporosis, including low levels of vitamin D. Future longitudinal studies involving subjects with osteoporosis might verify the effect of the drugs used for the osteoporosis treatment in the periodontal condition, in a vitamin D-controlled setting.

Conclusions

Elderly women affected by osteoporosis presented higher prevalence and severity of periodontitis. These negative effects of osteoporosis on the periodontal status were minimized by osteoporosis treatment.

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Compliance with ethical standards

Conflicts of interest None.

References

1. Martinez-Maestre MA, Gonzalez-Cejudo C, Machuca G, Torrejon R, Castelo-Branco C (2010) Periodontitis and osteoporosis: a systematic review. Climacteric 13:523–529
2. Reddy MS, Morgan SL (2013) Decreased bone mineral density and periodontal management. Periodontol 2000 61:195–218
3. Jabbar S, Drury J, Fordham J, Datta HK, Francis RM, Tuck SP (2011) Plasma vitamin d and cytokines in periodontal disease and postmenopausal osteoporosis. J Periodontal Res 46:97–104
4. Consensus development conference (1993) Diagnosis, prophylaxis, and treatment of osteoporosis. Am J Med 94:646–650
5. Looker AC, Borrud LG, Dawson-Hughes B, Shepherd JA, Wright NC (2012) Osteoporosis or low bone mass at the femur neck or lumbar spine in older adults: United States, 2005-2008. NCHS Data Brief 93:1–8
6. Hernlund E, Svedbom A, Ivergard M, Compston J, Cooper C, Stenmark J, McCloskey EV, Jonsson B, Kanis JA (2013) Osteoporosis in the European Union: medical management, epidemiology and economic burden. A report prepared in collaboration with the International Osteoporosis Foundation (IOF) and the European Federation of Pharmaceutical Industry Associations (EFPIA). Arch Osteoporos 8:136
7. Armitage GC, Robertson PB (2009) The biology, prevention, diagnosis and treatment of periodontal diseases: scientific advances in the United States. J Am Dent Assoc 140(Suppl 1):36s–43s
8. Tezal M, Wactawski-Wende J, Grossi SG, Ho AW, Dunford R, Genco RJ (2000) The relationship between bone mineral density and periodontitis in postmenopausal women. J Periodontol 71: 1492–1498
9. Weyant RJ, Pearlstein ME, Churak AP, Forrest K, Famili P, Cauley JA (1999) The association between osteopenia and periodontal attachment loss in older women. J Periodontol 70:982–991
10. Famili P, Cauley J, Suzuki JB, Weyant R (2005) Longitudinal study of periodontal disease and edentulism with rates of bone loss in older women. J Periodontol 76:11–15
11. Lundstrom A, Jendle J, Stenstrom B, Toss G, Ravald N (2001) Periodontal conditions in 70-year-old women with osteoporosis. Swed Dent J 25:89–96
12. Yoshihara A, Seida Y, Hanada N, Miyazaki H (2004) A longitudinal study of the relationship between periodontal disease and bone mineral density in community-dwelling older adults. J Clin Periodontol 31:680–684
13. Iwasaki M, Taylor GW, Nakamura K, Yoshihara A, Miyazaki H (2013) Association between low bone mineral density and clinical attachment loss in Japanese postmenopausal females. J Periodontol 84:1708–1716
14. Gomes-Filho IS, Passos Jde S, Cruz SS, Vianna MI, Cerqueira Ede M, Oliveira DC, dos Santos CA, Coelho JM, Sampaio FP, Freitas CO, de Oliveira NF (2007) The association between postmenopausal osteoporosis and periodontal disease. J Periodontol 78:1731–1740
15. Passos JS, Vianna MI, Gomes-Filho IS, Cruz SS, Barreto ML, Adan L, Rosing CK, Cerqueira EM, Trindade SC, Coelho JM (2013) Osteoporosis/osteopenia as an independent factor associated with periodontitis in postmenopausal women: a case-control study. Osteoporos Int 24:1275–1283
16. Al Habashneh R, Alchalabi H, Khader YS, Hazza'a AM, Odat Z, Johnson GK (2010) Association between periodontal disease and osteoporosis in postmenopausal women in Jordan. J Periodontol 81: 1613–1621
17. Moedano DE, Irigoyen ME, Borges-Yanez A, Flores-Sanchez I, Rotter RC (2011) Osteoporosis, the risk of vertebral fracture, and periodontal disease in an elderly group in Mexico city. Gerodontology 28:19–27
18. Pepelassi E, Nicopoulou-Karayianni K, Archontopoulou AD, Mitsea A, Kavadella A, Tsiklakis K, Vrotsos I, Devlin H, Horner K (2012) The relationship between osteoporosis and periodontitis in women aged 45-70 years. Oral Dis 18:353–359
19. Gondim V, Aun J, Fukuda CT, Takayama L, Latorre Mdo R, Pannuti CM, Rodrigues Pereira RM, Romito GA (2013) Severe loss of clinical attachment level: an independent association with low hip bone mineral density in postmenopausal females. J Periodontol 84:352–359
20. Marjanovic EJ, Southern HN, Coates P, Adams JE, Walsh T, Horner K, Devlin H (2013) Do patients with osteoporosis have an increased prevalence of periodontal disease? A cross-sectional study. Osteoporos Int 24:1973–1979
21. Tak IH, Shin MH, Kweon SS, Nam HS, Cauley JA, Kim OJ, Kim YJ, Chung HJ, Kim OS (2014) The association between periodontal disease, tooth loss and bone mineral density in a Korean population. J Clin Periodontol 41:1139–1144
22. Mohammad AR, Hooper DA, Vermilyea SG, Mariotti A, Preshaw PM (2003) An investigation of the relationship between systemic bone density and clinical periodontal status in post-menopausal Asian-American women. Int Dent J 53:121–125
23. Kanis JA, McCloskey EV, Johansson H, Cooper C, Rizzoli R, Reginster JY (2013) European guidance for the diagnosis and management of osteoporosis in postmenopausal women. Osteoporos Int 24:23–57
24. Rocha ML, Malacara JM, Sanchez-Marin FJ, Vazquez de la Torre CJ, Fajardo ME (2004) Effect of alendronate on periodontal disease

in postmenopausal women: a randomized placebo-controlled trial. J Periodontol 75:1579–1585
25. Jeffcoat MK (2006) Safety of oral bisphosphonates: controlled studies on alveolar bone. Int J Oral Maxillofac Implants 21:349–353
26. Lane N, Armitage GC, Loomer P, Hsieh S, Majumdar S, Wang HY, Jeffcoat M, Munoz T (2005) Bisphosphonate therapy improves the outcome of conventional periodontal treatment: results of a 12-month, randomized, placebo-controlled study. J Periodontol 76: 1113–1122
27. Valverde P (2008) Pharmacotherapies to manage bone loss-associated diseases: a quest for the perfect benefit-to-risk ratio. Curr Med Chem 15:284–304
28. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, Murad MH, Weaver CM (2011) Evaluation, treatment, and prevention of vitamin d deficiency: an endocrine society clinical practice guideline. J Clin Endocrinol Metab 96:1911–1930
29. Garcia MN, Hildebolt CF, Miley DD, Dixon DA, Couture RA, Spearie CL, Langenwalter EM, Shannon WD, Deych E, Mueller C, Civitelli R (2011) One-year effects of vitamin d and calcium supplementation on chronic periodontitis. J Periodontol 82:25–32
30. Kanis JA (1994) Assessment of fracture risk and its application to screening for postmenopausal osteoporosis: synopsis of a who report. Who study group. Osteoporos Int 4:368–381
31. Page RC, Eke PI (2007) Case definitions for use in population-based surveillance of periodontitis. J Periodontol 78:1387–1399
32. Genco RJ, Borgnakke WS (2013) Risk factors for periodontal disease. Periodontol 2000 62:59–94
33. Ronderos M, Jacobs DR, Himes JH, Pihlstrom BL (2000) Associations of periodontal disease with femoral bone mineral density and estrogen replacement therapy: cross-sectional evaluation of us adults from NHANES III. J Clin Periodontol 27:778–786
34. Tugnait A, Clerehugh V (2001) Gingival recession-its significance and management. J Dent England 29:381–394
35. Palomo L, Buencamino-Francisco MC, Carey JJ, Sivanandy M, Thacker H (2011) Is long-term bisphosphonate therapy associated with benefits to the periodontium in postmenopausal women? Menopause 18:164–170
36. Marx RE (2011) Oral and intravenous bisphosphonate-induced osteonecrosis of the jaws: history, etiology, prevention, and treatment, 3rd edn. Quintessence Books, Canada
37. Khan AA, Morrison A, Hanley DA, Felsenberg D, McCauley LK, O'Ryan F, Reid IR, Ruggiero SL, Taguchi A, Tetradis S, Watts NB, Brandi ML, Peters E, Guise T, Eastell R, Cheung AM, Morin SN, Masri B, Cooper C, Morgan SL, Obermayer-Pietsch B, Langdahl BL, Al Dabagh R, Davison KS, Kendler DL, Sandor GK, Josse RG, Bhandari M, El Rabbany M, Pierroz DD, Sulimani R, Saunders DP, Brown JP, Compston J (2015) Diagnosis and management of osteonecrosis of the jaw: a systematic review and international consensus. J Bone Miner Res 30:3–23
38. Rizzoli R, Boonen S, Brandi ML, Bruyere O, Cooper C, Kanis JA, Kaufman JM, Ringe JD, Weryha G, Reginster JY (2013) Vitamin d supplementation in elderly or postmenopausal women: a 2013 update of the 2008 recommendations from the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO). Curr Med Res Opin 29:305–313
39. Millen AE, Hovey KM, LaMonte MJ, Swanson M, Andrews CA, Kluczynski MA, Genco RJ, Wactawski-Wende J (2013) Plasma 25-hydroxyvitamin d concentrations and periodontal disease in postmenopausal women. J Periodontol 84:1243–1256
40. NOF (2013) Clinician's guide to prevention and treatment of osteoporosis. National Osteoporosis Foundation, Washington, DC
41. Riggs BL, Khosla S, Melton LJ 3rd (1998) A unitary model for involutional osteoporosis: estrogen deficiency causes both type I and type II osteoporosis in postmenopausal women and contributes to bone loss in aging men. J Bone Miner Res 13:763–773
42. Khosla S, Melton LJ 3rd, Riggs BL (2011) The unitary model for estrogen deficiency and the pathogenesis of osteoporosis: is a revision needed? J Bone Miner Res 26:441–451
43. Zebaze RM, Ghasem-Zadeh A, Bohte A, Iuliano-Burns S, Mirams M, Price RI, Mackie EJ, Seeman E (2010) Intracortical remodelling and porosity in the distal radius and post-mortem femurs of women: a cross-sectional study. Lancet 375:1729–1736
44. Wolfl C, Schweppenhauser D, Guhring T, Takur C, Honer B, Kneser U, Grutzner PA, Kolios L (2014) Characteristics of bone turnover in the long bone metaphysis fractured patients with normal or low bone mineral density (bmd). PLoS One 9:e96058
45. Smith PC, Caceres M, Martinez C, Oyarzun A, Martinez J (2015) Gingival wound healing: an essential response disturbed by aging? J Dent Res 94:395–402