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ORIGINAL ARTICLE

An investigation of the bidirectional link between osteoporosis and periodontitis

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Abstract

Summary This study investigated whether periodontitis affects systemic bone status and whether FRAX® is a screening tool for periodontal disease in elderly women. The findings showed that bone density was not influenced by periodontitis and highlighted that women with FRAX® score above the intervention threshold had greater chance to present severe periodontitis.

Purpose This study investigated whether periodontal disease is a predictor for systemic bone loss among elderly women. The utilization of FRAX® as a screening tool for severe periodontitis was also evaluated in this population.

Methods Current bone mineral density (BMD) for lumbar spine and proximal femur was used as an indicator of "bone status." Number of interdental sites with severe clinical attachment loss, frequency of bleeding on probing, and percentage of tooth loss due to periodontitis represented "periodontal disease" that was tested as a predictor of bone loss in a structural equation modeling analysis involving 110 participants. The intake of antiosteoporosis medication was considered in the analysis. Four other different criteria for periodontitis classification were also tested. FRAX® for major fracture was calculated without BMD, and with intervention threshold set by age. Longitudinally, BMD changes up to 10 years were also obtained and checked for possible association with periodontitis.

Results Periodontal disease was not a predictor for worse systemic bone status according to the different periodontal disease classifications, and was not associated with BMD changes. Antiosteoporosis medication directly predicted periodontal disease and systemic bone status. Women with FRAX® score above the intervention threshold had higher chance for periodontitis in more advanced stages: III/IV (OR = 1.13, 95% CI [1.04 to 1.22], $p = 0.03$).

Conclusion Periodontal disease did not constitute a predictor for reduced systemic bone density in the studied population of elderly women. On the other hand, FRAX® demonstrated to be a useful tool to suggest periodontal evaluation. Antiresorptive medication showed benefits on periodontal and bone status.

Keywords Bone density · FRAX · Osteoporosis · Periodontitis · Tooth loss · Elderly

Introduction

Periodontitis and osteoporosis are multifactorial chronic-inflammatory health disorders involving bone resorption [1]. Osteoporosis is a systemic skeletal disease characterized by loss of bone mass and increase of bone fragility [2, 3]. Hormonal changes, like the abrupt decline of estrogen levels during menopause, besides oxidative stress, result in bone loss

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which in turn contribute for the development of osteoporosis [4]. Even though the association of osteoporosis and periodontal disease has been thoroughly studied over the last decades, it remains unclear whether the relationship between the two conditions exists [5].

Periodontitis is characterized by a progressive destruction of the tooth-supporting apparatus, which includes the alveolar bone. The disease results from the interactions between the host inflammatory and immune systems, dysbiotic subgingival biofilms, and modifying environmental factors [6, 7]. Severe periodontitis affects 11% of the global population [8]. Factors like genetic contribution, micronutrient deficiencies such as vitamin D, hormonal changes, rheumatoid arthritis, smoking/tobacco use, and undiagnosed or sub-optimally controlled diabetes mellitus may be related to the periodontal disease development and progression. Glycemia drives oxidative stress and advanced glycation end products may also trigger a hyper inflammatory response to periodontal pathogens [9]. These clinical risk factors are also related to bone fragility and are taken into consideration to calculate the 10-year probability of fragility fractures according to the "fracture risk assessment tool" (FRAX®) [10]. Higher FRAX® scores have been associated with impaired periodontal status [11]. The association between FRAX® and periodontitis should be further investigated, since the National Osteoporosis Guideline Group (NOGG) has architected different intervention thresholds for FRAX®, specific for country and age [12].

Recent studies have suggested a bidirectional relationship between periodontal disease and systemic bone loss [13–15]. The potential explanation for the influence of periodontitis on systemic bone density is that periodontitis, although a localized chronic infection around the teeth, may cause systemic inflammatory burden, which may affect other organs [16]. There is a lack of studies that investigate the impact of periodontal disease on skeletal status and what is the magnitude of this relationship, if it exists.

The setting of this study has been described previously in a cross-sectional study that showed that elderly women with osteoporosis had greater chance of severe periodontitis, which was exacerbated among those who were not treated with antiresorptive drugs [17]. Moreover, a retrospective study explored the possible influence of bone fragility on the severity of periodontal clinical attachment loss (CAL) among 134 elderly women aged 65 to 80 years. The role of bone medication was also investigated over the periods of 6 and 10 years [18]. That longitudinal study has shown that bone fragility, in the absence of bone medication, was a relevant predictor for severe periodontal disease and tooth loss.

The aim of the present study was to contribute with data to answer the following research questions: Is periodontitis a predictor for reduced systemic bone density in elderly women? And is FRAX® a useful screening tool for periodontitis in elderly women?

Materials and methods

Study design

This was a study that used current BMD, 10-year changes in BMD, FRAX® score, and periodontal data to verify the relationship between the systemic and local bone status, in a population of elderly women.

This study used both cross-sectional and longitudinal data. The cross-sectional data were current BMD, FRAX score, and periodontal clinical parameters, whereas the longitudinal data were changes in BMD in the last 10 years. This study evaluated the relationship between systemic BMD and periodontal status.

Participants

In the present study, the eligible participants were those women with at least two densitometric reports between January 2004 and January 2015, assessed at the Hospital Naval Marcilio Dias (HNMD), Rio de Janeiro, Brazil. Smokers, former smokers, those with diabetes mellitus and bone diseases other than osteoporosis, or those who used medications that affect the bone, with the exception of antiosteoporosis drugs, were excluded. All participants signed an informed consent form. The present study was approved by the Research Ethics Committees of the Hospital Clementino Fraga Filho at the Universidade Federal do Rio de Janeiro and the HNMD, registering 1,142,247 and 1,152,782, respectively.

Bone mineral density, trends, and annual percent changes

Cross-sectional BMD was measured by dual-energy X-ray absorptiometry (DXA) at the lumbar spine (L1 to L4), femoral neck, and total hip, using the densitometer GE Lunar DPX-NT (GE Health Care Clinical Systems Medical Equipment). The equipment was calibrated and operated according to the manufacturer's standards. The coefficient of variation remained at 1.5% for lumbar spine and 2.0% for femur. The DXA scannings were performed in a standardized way by trained technologists.

In order to obtain longitudinal changes in BMD, the participants were followed up for BMD since their first assessment of DXA, up to 10 years. All the densitometric reports were performed by the same trained physician, since 2004. Trends are the longitudinal percent changes between BMD measurements. These values can be positive, when the patient presented a gain in bone density, or negative, when presented loss. The variable "lowest trend BMD" for each participant, regarding the three skeletal sites (lumbar spine, femoral neck, and total hip), was considered as the greatest decrease in bone loss between DXA assessments, up to 10 years. The "annual

percent change in BMD" was calculated for each participant, as the sum of the rates divided by exact elapsed time in years since baseline, that is, up to 10 years, with positive values indicating a yearly gain, and negative values indicating a yearly loss.

Medical history included type and duration of antiresorptive drugs, when prescribed for osteoporosis management.

Ten-year probability for fracture: FRAX®

The Fracture Risk Assessment (FRAX®) was calculated for hip and major fractures using the online form of the FRAX® calculation tool (www.shef.ac.uk/frax) which included the femoral neck BMD [10]. Then, the 10-year fracture probabilities for Brazil were adopted using the country-specific FRAX® models, without BMD measure [19, 20]. The setting of intervention thresholds with FRAX® followed the methodology described by NOGG [21]. For each participant, it was considered (0) when FRAX® score was below the intervention threshold at the age-specific fracture probability, or (1) when it was above the intervention threshold [20].

Oral data periodontal evaluation and tooth loss

As a cross-sectional data, a full-mouth periodontal examination was performed by one examiner at the Brazilian's Naval Dental Center (OCM), in Rio de Janeiro, using a North Caroline periodontal probe (Hu-Friedy®, USA). The probing depth (PD) was measured as the distance from the gingival margin to the deepest point of the periodontal pocket reached by the probe. The CAL measures were taken as the distance from the cement-enamel junction to the base of the periodontal pocket. Both PD and CAL were registered at six sites on each tooth (interproximal and middle sites, on buccal and lingual sites). Gingival recession (GR) was obtained by the difference between CAL and PD measures. Bleeding on probing (BOP) was assessed after periodontal probing, at the same sites, to evaluate the absence (0) or presence (1) of periodontal inflammation. Third molars were excluded from the examinations. Periodontal examinations were performed by one calibrated and blinded experienced dentist. Intra-examiner reliability for PD and CAL measurements were, respectively, 0.82 and 0.83, as determined by intra-class correlation.

Periodontitis case was defined as interdental CAL ≥ 5 mm at two non-adjacent teeth, used as the thresholds to define periodontitis stages III and IV [7]. Stages I and II represent the earlier stages of attachment loss. Stage III means that periodontitis has produced significant damage to the periodontal attachment apparatus and, in the absence of advanced treatment, tooth loss may occur. At the more advanced stage IV, periodontitis may culminate with loss of masticatory function. In the absence of proper control of the periodontitis and adequate rehabilitation, the dentition is at risk of being lost [22].

The total number of interproximal sites with CAL ≥ 6 mm was also registered and used to increase the diagnostic specificity of periodontitis. The binary variables (0) "no periodontal disease" and (1) "presence of periodontal disease" were created. Besides the recent classification of periodontal disease, four other criteria were also used to define periodontal disease, as follows:

1. Severe periodontitis: a case was based in two or more interproximal sites with a CAL greater than or equal to 6 mm (not in the same tooth) and one or more interproximal sites with a PD greater than or equal to 5 mm [23];
2. Established periodontitis: a case was based in any site (buccal/lingual and interproximal sites), with a CAL greater than or equal to 6 mm in two or more teeth and one or more sites with a PD greater than or equal to 5 mm [24];
3. Periodontitis: a case was based in one or more sites with a CAL greater than or equal to 4 mm and one or more sites with a PD greater than or equal to 4 mm [25];
4. Severe destructive periodontitis: a case was based in four or more sites with a CAL greater than or equal to 5 mm and one or more of the same sites with a PD greater than or equal to 4 mm [26].

The number of natural teeth was counted for each participant and confirmed using digital panoramic radiographs. Reasons of tooth loss were obtained through structured interviews and checked by digital data records of the OCM. The variable "percentage of tooth loss" was the percentage of missing teeth after menopause due to periodontal disease.

Dental attendance was considered as (1) for women who reported regular dental visits, or (0) for those with irregular or no dental care attendance.

Statistical analysis

Descriptive analyses were performed for sociodemographic, clinical, densitometry, and oral health data. The participants were separated into two groups, according to the stage of periodontitis: severity stages I/II or III/IV. Data were presented as means and standard deviation (SD) and proportions. Differences between groups were assessed through chi-square test, Fisher's exact test, and Mann–Whitney *U* test.

A hypothesized model encompassing periodontal disease as a predictor for a worse systemic bone status was developed and tested using a structural equation modeling (SEM) (Fig. 1). Confirmatory factor analysis (CFA) assessed the latent variables concerning systemic "Bone Status" and "Periodontal Disease." The former was composed of BMD at the femoral neck, BMD at the total hip, and BMD at the

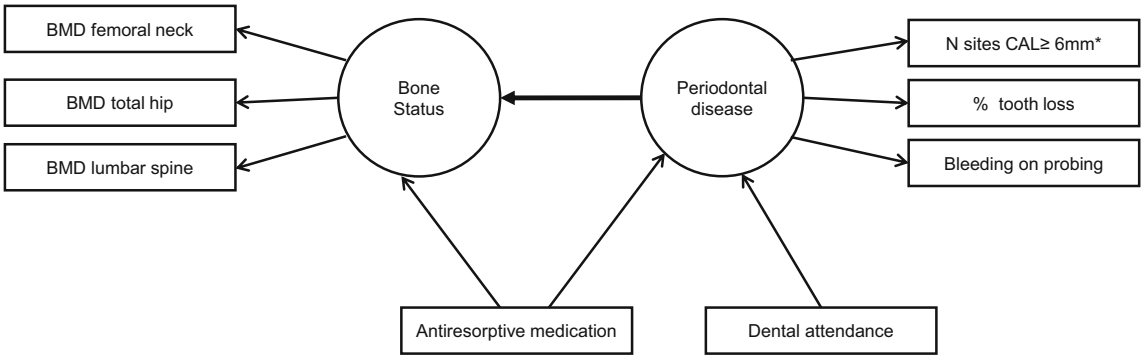

Fig. 1 Full theoretical model on the relationship between periodontal disease and systemic bone status, according to "number of interproximal sites with CAL ≥ 6mm" and to four criteria for periodontitis classification. BMD: bone mineral density; CAL: clinical attachment loss; N: number. *The model was also tested using the periodontitis classification, replacing the variable "number of interproximal sites with CAL ≥ 6mm" by the four references of periodontitis: severe periodontitis (≥ 2 interproximal sites with CAL ≥ 6 mm, not on the same tooth, and ≥ 1 interproximal site(s) with probing depth (PD) ≥ 5 mm); established periodontitis (≥ 2 teeth with CAL ≥ 6 mm and ≥ 1 site with PD ≥ 5 mm); periodontitis (≥ 1 site with CAL ≥ 4 mm and PD ≥ 4 mm); and severe destructive periodontitis (≥ 4 sites with CAL ≥ 5 mm and ≥ 1 same sites PD ≥ 4 mm). % tooth loss: percentage of postmenopausal tooth loss attributed to periodontal disease. Antiresorptive medication: corresponds to the number of years using antiosteoporosis medication

lumbar spine. The latter latent variable included the number of interproximal sites with CAL ≥ 6 mm, percentage of postmenopausal tooth loss attributed to periodontitis, and frequency of BOP. The indicator "number of interproximal sites with CAL ≥ 6mm" was replaced by the four other stages of periodontitis classification to evaluate the variation in the hypothesized model. "Dental attendance" and "antiresorptive medication" were observed variables in the SEM analysis. The model was also tested after removing "antiresorptive medication."

After estimating the full SEM model, non-significant paths were removed to generate a statistically parsimonious model. Nine hundred bootstrap samples were resampled from the original data set to derive less biased standard errors and 95% confidence interval (CI) bootstrap percentiles. Chi-square test was used to assess the adequacy of overall model fit. A chi-square and degrees of freedom (X^2/df ratio) < 3.0, comparative fit index (CFI) and goodness-of-fit (GFI) statistics of 0.90 or above, and a standardized root-mean-squared (SRMR) residual < 0.08 indicated an acceptable model fit.

The sample size of 110 participants was based on posteriori analysis, in which the difference of FRAX® major fracture was 30% higher in subjects with periodontitis III/IV than those with periodontitis I/II. The sample size was determined as 108 participants ($N = 72$ for periodontitis III/IV; $N = 36$ for the other group) (http://statpages.info/proppowr.html). For the other aim of the study, the sample size of 110 participants was also adequate, considering a structural equation model directed toward a hypothesis testing for complex models with two latent variables and the respective two observed variables in each model, with a *beta* estimated as 0.27. The confidence interval (CI) used was 95% with a power study of 80% for each sample size calculation.

The association between periodontitis and FRAX® major fracture, without BMD, according to NOGG, was evaluated using odds ratios (ORs) and their respective 95% CIs. The mean frequency of sites of GR ≥ 3 mm was calculated for each participant. Spearman coefficient tested the correlation between FRAX® and frequency of GR ≥ 3 mm.

Two-sided p values of 0.05 or less were considered to indicate statistical significance in all statistical analyses that were performed using the SPSS software version 24.0 (IBM) and SPPS AMOS version 24.0 (IBM, Armonk, NY, USA).

Results

Characteristics of the study population

After applying the study criteria, the analysis was undertaken on the basis of data for 110 elderly women of the original 1266 patient files with DXA assessment (Fig. 2) [17].

DXA dual-energy X-ray absorptiometry

The characteristics of the participants according to periodontitis severity groups are described in Table 1. Women with periodontitis in the severity stages III/IV presented lower BMD and higher FRAX® scores than women with periodontitis in the stages "I/II." Periodontitis stages III/IV were significantly associated with higher prevalence of osteoporosis. The greatest trends in proximal femur and lumbar spine, as well as annual percent changes in BMD, did not differ between groups. The same was observed for pattern of medical and number of DXA and dental attendance. The mean number of tooth loss caused by periodontal disease, frequency of BOP,

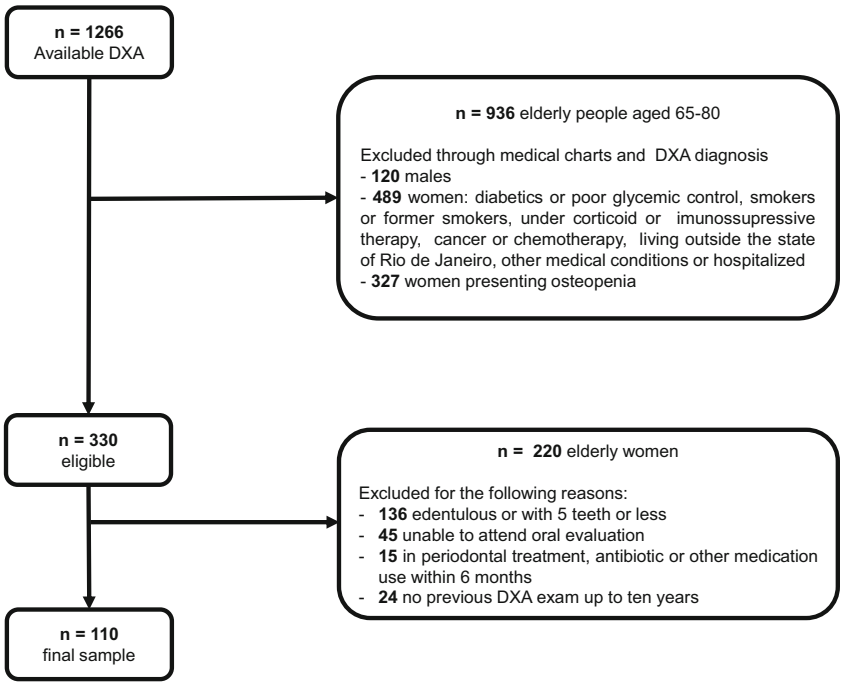

Fig. 2 Flow chart of the sample selection

and number of interdental sites with CAL ≥ 6 mm were higher in the "stage III/IV" group.

The distribution of periodontitis in the sample was as follows: (a) severe periodontitis, 43 women (39.1% of the sample); established periodontitis, 56 women (50.9% of the sample); severe destructive periodontitis, 65 women (59.1% of the sample); periodontitis, 84 women (76.4% of the sample).

Among the 110 participants, 40 women were receiving oral antiresorptive drugs. The mean period under medication treatment was 4.43 ± 2.72 years. The antiresorptive medications taken by these 40 women were the following: alendronate 70 mg/weekly ($n = 27$), risedronate 35 mg/weekly ($n = 9$); and ibandronate 150 mg/monthly ($n = 1$); two women had changed medications to strontium ranelate 60 mg/daily, and one to teriparatide 20 mcg/daily in the previous year. The adherence to the treatment was checked by self-reported data and by digital medical records at the hospital, which were considered adequate.

Structural equation modeling

Measurement model

Standardized loadings obtained using CFA provide the magnitude of the correlation between the indicators (observed variables) and the latent variable. All the loadings for "Bone Status" were statistically significant and substantially high, indicating the appropriateness of the latent variable to represent the "Bone Status" (standardized regression weights ≥ 0.73; $p = 0.003$). The loadings for the "Periodontal Disease" latent variable were also statistically significant (standardized regression weights ≥ 0.31; $p = 0.01$) (Online Resource 1). The measurement model showed adequate fit (X^2/df ratio = 1.40, SRMR = 0.06, GFI = 0.97, CFI = 0.99).

Theoretical models: bone status with periodontal disease

The higher the score for each one of the three indicators of the latent "Periodontal Disease," the worse the periodontal status was. The opposite is observed with the other latent: the higher the scores for each one of the BMD sites, the better "Bone Status."

"Periodontal Disease" according to the "number of interproximal sites with CAL ≥ 6mm," "frequency of postmenopausal tooth loss," and "BOP frequency" was not associated with "Bone Status" in the unadjusted and adjusted analysis for "antiresorptive medication." Although the results have shown an inverse effect of periodontal disease on "Bone Status" (beta direction was negative), it was non-significant, neither for "number of interproximal sites with CAL ≥ 6mm" nor when it was replaced by the four other criteria of periodontitis—"severe periodontitis," "established periodontitis," "periodontitis," and "severe destructive periodontitis." These results remained similar even when the analysis included "antiresorptive medication" (Table 2).

Otherwise, "antiresorptive medication" exhibited significant effects on "Periodontal Disease" ($\beta = -0.239$; $p = 0.04$) and on "Bone Status" ($\beta = 0.645$; $p = 0.003$; respectively). These results mean that more years of medication intake imply in better "Bone Status" and lower severity in "Periodontal

Table 1 Descriptive clinical characteristics of the 110 study participants, according to the periodontitis severity

Characteristics	Severity of periodontitis		
	Stages I/II ($n = 38$)	Stages III/IV ($n = 72$)	p
Age (years)	69.00 ± 3.53	69.69 ± 3.66	0.31
Medical variables			
BMD femoral neck (g/cm^2)	0.896 ± 0.134	0.823 ± 0.121	0.009*
BMD total hip (g/cm^2)	0.914 ± 0.136	0.845 ± 0.128	0.01*
BMD lumbar spine (g/cm^2)	1.000 ± 0.187	0.941 ± 0.161	0.12
FRAX® major fracture[a]	3.99 ± 1.77	5.20 ± 2.72	0.01*
FRAX® hip fracture[a]	0.92 ± 0.88	1.58 ± 1.57	0.01*
Lowest trend femoral neck (%)[b]	− 2.57 ± 3.65	− 3.47 ± 3.55	0.09
Lowest trend total hip (%)[b]	− 2.03 ± 2.79	− 2.68 ± 2.11	0.08
Lowest trend lumbar spine (%)[b]	− 2.52 ± 4.77	− 2.51 ± 4.41	0.92
Annual change femoral neck (%)[c]	0.18 ± 1.07	− 0.19 ± 1.65	0.24
Annual change total hip (%)[c]	− 0.06 ± 0.72	− 0.25 ± 1.16	0.23
Annual change lumbar spine (%)[c]	0.64 ± 1.17	0.56 ± 1.6	0.45
Years of medical monitoring[d]	5.79 ± 2.93	6.26 ± 3.33	0.33
N DXA assessments[d]	3.97 ± 1.73	4.53 ± 2.38	0.46
Osteoporosis, N (%)[e]	19 (50)	53 (73.6)	0.02*
Antiresorptive drugs use (in years)	4.15 ± 3.05	4.56 ± 2.59	0.55
Body mass index (kg/m^2)[f]	27.68 ± 3.75	27.19 ± 4.54	0.29
Age at menopause (years)	47.34 ± 7.60	47.25 ± 5.50	0.47
Oral outcomes			
Tooth loss (%)[g]	0.28 ± 1.28	2.38 ± 3.79	< 0.001*
Bleeding on probing (%)[h]	10.46 ± 8.62	18.76 ± 14.54	0.001*
N interdental CAL ≥6 mm[i]	0.11 ± 0.31	4.40 ± 4.45	< 0.001*
Dental attendance, N (%)[j]	38 (100)	65 (90.3)	0.09

Mann–Whitney for continuous variables and chi-square or Fisher's exact test for categorical variables. Data expressed as mean ± standard deviation or absolute number (%). *N*, number; *BMD*, bone mineral density measured by dual-energy X-ray absorptiometry (DXA); *CAL*, clinical attachment loss

*Significance level ≤ 0.05

[a] FRAX®: Fracture Risk Assessment tool obtained for hip and major fractures. FRAX® calculation used data on age, sex, body mass index, prior fragility fracture, parental history of hip fracture, current tobacco smoking, long-term use of oral glucocorticoids, rheumatoid arthritis, other causes of secondary osteoporosis, alcohol consumption, and BMD femoral neck

[b] Trend: represents the rates of BMD variation; the lowest trend registered in the densitometer data storage, up to 10 years

[c] Annual percent change in BMD: the sum of the rates divided by exact elapsed time in years since baseline, that is, up to 10 years, with positive values indicating a yearly gain, and negative values indicating a yearly loss

[d] Years of medical monitoring and N DXA assessments: between 2004 and 2014

[e] Osteoporosis: diagnosis based on *T* score ≤ -2.5 in one or more of the following sites: lumbar spine, hip and total femur, in the last DXA assessment

[f] Body mass index (BMI): defined as the weight in kilograms divided by the square of the height in meters

[g] Tooth loss (due periodontitis): represents the percentage of postmenopausal tooth loss caused by periodontal disease (and not for any other reasons) in dental history

[h] Bleeding on probing: determined by a dichotomous way, as absent or present, and considered present if bleeding occurred up to 15 s after removing the periodontal probe of the periodontal site

[i] CAL: measured as the distance from the cement-enamel junction (CEJ) to the base of the periodontal pocket

[j] Dental attendance: determined by a dichotomous way, considered as "yes" for woman who reported regular dental visits or "no" for irregular or no dental care attendance

Disease." There was a direct effect of "dental attendance" on "Periodontal Disease" ($\beta = -0.523$; $p = 0.02$), which means that a regular dental care attendance is associated to a lower severity in "Periodontal Disease." The parsimonious model was not tested since "Periodontal Disease" did not predict "Bone Status" in the full model.

The full models exhibited good fit indices (Online Resource 2). A sample size of 110 participants has lent a

Table 2 Direct effects of the full structural equation models on the relationships between periodontal disease, systemic bone status, and bone medication

	Model with medication β (SE) p	Model without medication β (SE) p
Periodontal disease (N CAL ≥ 6 mm), bone status	− 0.064 (0.11) 0.51	− 0.232 (0.11) 0.07
Dental attendance, periodontal disease	− 0.473 (0.21) 0.01	− 0.523 (0.19) 0.02
Medication, periodontal disease	− 0.239 (0.11) 0.04	–
Medication, bone status	0.645 (0.06) 0.003	–
Other criteria for "Periodontal Disease"		
Severe periodontitis, bone status	− 0.098 (0.10) 0.31	− 0.235 (0.12) 0.07
Established periodontitis, bone status	− 0.042 (0.11) 0.66	− 0.223 (0.12) 0.09
Periodontitis, bone status	− 0.080 (0.11) 0.39	− 0.175 (0.15) 0.15
Severe destructive periodontitis, bone status	− 0.093 (0.09) 0.32	− 0.199 (0.11) 0.11

Data expressed in β bootstrapped standardized estimate (SE standard error), and p values. *BMD*, bone mineral density; *BOP*, bleeding on probing; *CAL*, clinical attachment loss; *N*, number. Besides BOP and percentage of postmenopausal tooth loss, the following classification for periodontitis constructed the latent "Periodontal Disease" in model 1: number of interproximal sites with CAL ≥ 6 mm; severe periodontitis (≥ 2 interproximal sites with CAL ≥ 6 mm, not on the same tooth, and ≥ 1 interproximal site(s) with probing depth (PD) ≥ 5 mm); established periodontitis (≥ 2 teeth with CAL ≥ 6 mm and ≥ 1 site with PD ≥ 5 mm); periodontitis (≥ 1 site with CAL ≥ 4 mm and PD ≥ 4 mm); and severe destructive periodontitis (≥ 4 sites with CAL ≥ 5 mm and ≥ 1 same sites PD ≥ 4 mm)

power of 80% in a structural equation model to detect an anticipated minimum effect size of 0.27, with a 0.05 level of significance, directed toward a hypothesis testing for complex models with two latent variables and the respective two observed variables in each model [27].

The intervention threshold of FRAX® with periodontal status and gingival recession

Among women with a FRAX® score of major fracture above the intervention threshold set by age, stablished by NOGG, without BMD, the odds of presenting periodontitis stages III/IV was higher than among women with the scores below the threshold (OR = 1.13; 95% CI [1.04–1.22]; $p = 0.03$).

A hundred percent of those women who presented a score above the NOGG threshold ($n = 8$) presented periodontitis III/IV. Then, this score reached a sensitivity of 100.0% (95% CI [63.1 to 100%]) and a specificity of 37.3% (95% CI [27.9 to 47.4%]). This means that women with scores above the NOGG threshold had 100% likelihood of presenting more sites exhibiting advanced periodontal attachment loss, while those who were below the threshold had a 37.3% chance of not presenting advanced CAL.

There was a significant positive correlation between FRAX® and frequency of GR ≥ 3 mm ($rho = 0.214$, $p = 0.02$).

Logistic regression analyses were performed considering the criteria for periodontitis as dependent variables, and independent variables were BMI, age, fragility fracture, and premature menopause. The results did not show statistical significance.

Discussion

This study provided important findings on the field of the bidirectional relationship between periodontal disease and systemic bone density. First, periodontitis did not influence the reduced systemic bone density. Periodontitis was not a predictor for impaired systemic bone density in elderly women even when different definitions of periodontitis were used, when the SEM was applied. Second, FRAX®, irrespective of BMD, has shown an association with advanced stages of periodontitis.

Currently, the assessment of BMD is the cornerstone for the operational description of osteoporosis and can be readily used in clinical practice [28]. Although the reduced bone mineral density may be clinically reflected on periodontal apparatus [17, 29–31], the bidirectional relationship—periodontitis impairing bone status—has also been investigated. The present findings differ from a previous study that reported that women with periodontitis were more likely to develop osteoporosis [14]. Different methodological aspects between the studies may explain the lack of agreement. The SEM is a powerful statistical technique that allows the testing of complex relationships between variables specified within a hypothesized model [32]. The theoretical model provided a framework which represents "Periodontal Disease" with "Bone Status," by combining data on BMD assessed by DXA from the three most important sites (femoral neck, total femur hip, and lumbar spine). The validity of the latent variables were supported by the estimates obtained through CFA [33]. Loss of periodontal tissue of support due to the inflammatory process is the primary clinical feature of periodontitis [7]. Among the indicators of "Periodontal Disease,"

interdental CAL ≥ 6 mm was set to increase specificity and accuracy in identifying a periodontitis case [22]. This way, as the severity of periodontal disease increases, the specificity increases and CAL is more firmly established. The other classifications of periodontal disease used to substitute CAL ≥ 6 mm did not show any differences in these results.

Another indicator of "Periodontal Disease" was the percentage of postmenopausal tooth loss attributed to periodontal disease. Tooth loss is a potential true endpoint for assessing the severity of periodontal disease [34]. Frequency of BOP was used in the SEM because it measures periodontal inflammation, which is also an important clinical parameter relative to assessment of periodontitis treatment outcomes and residual disease risk posttreatment [22]. The larger the amount of inflamed periodontal tissue, the larger the chances of periodontitis eliciting bacteremia, systemic inflammatory responses, or cross-reactivity [16].

Antiresorptive drugs exhibited significant effects on bone density as well as on periodontal status, which is in accordance with previous findings [17, 35]. The mean period of bisphosphonate use was 4.4 years, which was similar to the period reported by other authors who observed the benefits of this medication on the periodontal status in postmenopausal women [36]. Adjunctive bisphosphonate therapy appears to be effective in managing periodontitis [37].

Several risk factors that significantly contribute to fracture risk have been identified, giving rise to the development of FRAX®, a tool that integrates information derived from clinical risk factors [10]. A previous study encompassing the effects of bone fragility on periodontal attachment integrated BMD and FRAX® in a latent named "Bone Fragility" [18]. In the present methodology, FRAX® was not included as an indicator of the latent "Bone Status" due to obvious reasons: FRAX® scores are generated from data on age, gender, body mass index, prior fragility fracture, parental history of hip fracture, current tobacco smoking, long-term use of oral glucocorticoids, rheumatoid arthritis, other causes of secondary osteoporosis, and alcohol consumption. Therefore, periodontal disease is not supposed to influence FRAX®.

FRAX® scores for major fracture and hip fracture, calculated with femoral neck BMD, were positively associated with stage III/IV periodontitis. The NOGG sets the intervention threshold for FRAX® at the age-specific fracture probability equivalent to women with a prior fragility fracture [12]. Using the Brazilian FRAX® model, without BMD, the score obtained for major fracture higher than the intervention thresholds indicated a greater likelihood of diagnosing advanced stages of periodontitis [19, 20]. Accordingly, the algorithm, designed to support primary care physicians on identifying postmenopausal women who may be candidates for treatment based on the level of fracture risk, may also be a useful screening tool for periodontitis, reaching a sensibility of 100%.

Additionally, women with higher FRAX® scores presented greater frequency of more advanced GR. FRAX® was associated with frequency of sites with CAL ≥ 6 mm (rho = 0.676, $p \leq 0.001$), which was expected. Loss of attachment can be accompanied by GR, which is not necessarily linked to periodontal disease. Gingival recession facilitates dental plaque retention and increases the risk of root caries, which are considered common conditions in older adults.

While CAL measures the cumulative experience of destructive periodontal disease, reflecting a longitudinal history, trends and annual percent changes in BMD refer to longitudinal assessment of systemic bone mass. The estimated annual mean of periodontal attachment loss for postmenopausal women was reported as 0.052 mm, while for periodontitis, the progression was considerably higher: 0.57 mm [34]. While independent studies have shown evidence on periodontal disease predicting low bone mineral density, no studies using a comprehensive approach evaluated the direct effects and interactions between these components in the same sample of participants. Our theoretical model encompasses cross-sectional measures on oral health. However, clinical attachment loss and percentage of postmenopausal tooth loss represent, in fact, clinical results of the periodontal disease over time. As periodontal disease progresses, the CAL is higher and, consequently, tooth losses. It would be reasonable to think that, if the progression of periodontal disease impaired systemic bone status or caused loss of bone mass over time, then, periodontal disease should also have shown association with current BMD (not validated in the modeling analysis), and with the trends and the annual changes of BMD (no association with periodontitis III/IV).

The selection of periodontal disease classification may represent bias in the measurement association. This may jeopardize the comparison to other studies and consensual knowledge. From a methodologic point of view, using different criteria of classification is a strength characteristic of the present study [23–26]. The recent new classification of periodontal disease, which stages the disease in I to IV, was also used in the performed analyses [7, 22]. This new classification may be more successful in the standardizing methodologies involving periodontitis.

This study has some limitations that should be recognized. First, the sample of elderly women may not be representative of the general population, since it involves postmenopausal women who did not present diabetes or smokers, which are well-established predictors of periodontitis. The results for FRAX® would probably be higher, if the sample included smokers, diabetic patients, women with rheumatoid arthritis, or those under long-term use of oral glucocorticoids. Using the abovementioned exclusion criteria prevents confounding factors. Moreover, the oral and medical data of 110 participants was retrospectively obtained. A prospective research design would be more appropriate to explore and elucidate

the order of events. Future studies should include participants with severe and generalized periodontitis, as well as those with rapid progression rates (grade C), in order to investigate whether severe cases of periodontitis influence systemic bone status.

Once people are living longer, ideally, individuals should achieve maximal peak bone mass early in life, which reduces the risk of osteoporosis [38, 39]. The masticatory system should not be isolated from the other organs and systems in the body. Age and medical and dental status are important aspects when a clinician assesses a patient's status and treatment needs [40]. The implementation of FRAX® in primary dental care may be useful not only for identifying people at risk for fragility fractures but also as a screening tool for periodontitis, which may be helpful for controlling its progression and consequently reducing tooth loss and the negative impacts on quality of life.

Conclusion

The FRAX® may be a useful tool for the screening of periodontitis in this population, irrespective of BMD. Otherwise, periodontal disease was not a predictor for reduced systemic bone density nor for larger rates of bone loss in the studied population of elderly women.

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Compliance with ethical standards

Conflicts of interest None.

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