The association between periodontal disease, tooth loss and bone mineral density in a Korean population


Abstract

Objective: We aimed to evaluate whether clinical attachment loss (CAL), a measure of the severity of periodontal disease or number of teeth present is associated with bone mineral density (BMD).

Methods: The study population consisted of 5383 people aged 50 years and older who participated in the Dong-gu Study. BMD at the lumbar spine and femoral neck was measured by dual-energy X-ray absorptiometry. Oral examination included assessments of the number of teeth present and CAL. Number of teeth present was categorized into three equal categories. CAL values were divided into tertiles in terms of the percentage of sites with CAL ≥ 4 mm. Analysis of covariance was used to compare the adjusted means of BMD according to the tooth number and the tertiles of CAL.

Results: There was a significant association between the number of teeth present and BMD in men. Compared with men with 22 or more teeth, men with 10 and less teeth had lower BMD. CAL was significantly associated with lower BMD at the lumbar spine in women.

Conclusion: Our data indicate that tooth loss and CAL were associated with low BMD. However, the magnitude of these associations was relatively small and the clinical significance was unclear.

Osteoporosis is a systemic skeletal disease that is characterized by the loss of bone mass and weakened bone microarchitecture, which results in increased susceptibility to fracture (Kuo et al. 2008). Periodontitis is an inflammatory disease characterized by the loss of both connective tissue and alveolar bone of the periodontium. Both diseases share some common features; both are bone resorptive diseases involving damage to the bone tissue; both are a silent disease where the symptoms do not manifest themselves until the later stages of the disease; and both are common in middle-aged and older women, and have common risk factors such as age, smoking, cardiovascular disease and dietary factors (Kuo et al. 2008).

The association between osteoporosis and periodontitis has been evaluated since the 1960s (Groen et al. 1968). Some authors (Weyant et al. 1999, Tezal et al. 2000, Famili et al. 2005, Hattatoglu-Sonmez et al. 2008, Sultan & Rao 2011) reported no relationship...

Several studies have investigated the relationship between osteoporosis and tooth loss (Mohammad et al. 1997, Inagaki et al. 2001, Gur et al. 2003, Taguchi et al. 2004). Some investigators have reported that tooth loss is related to low BMD and accelerated oral bone loss has been reported in women with osteoporosis (Kribbs 1990, Inagaki et al. 2001, Taguchi et al. 2004, Lamonte et al. 2012). However, others failed to find an association between tooth loss and skeletal BMD in post-menopausal women (Klemetti et al. 1994, May et al. 1995, Mohammad et al. 1997, Earnshaw et al. 1998). To date, the evidence for an association between tooth loss and BMD remains unclear, and the reported results are contradictory.

Due to the ageing populations of both men and women in many parts of the world, osteoporosis is becoming an enormous public health problem (Phipps et al. 2007). However, most of the published studies have focused on post-menopausal women; whereas for men, there has been only one longitudinal study performed by Phipps et al. (2007), and only two studies targeted both men and women (Ronderos et al. 2000, Yoshihara et al. 2004). Therefore, the purpose of this study was to evaluate whether clinical attachment loss (CAL), a measure of the severity of periodontal disease or the number of teeth present is associated with BMD at the lumbar spine and femoral neck in a large-scale population-based study in Korea comprising of male and female community dwellers who were 50 years of age and older.

Materials and Methods

Study population

The Dong-gu study is an ongoing prospective study that is designed to investigate the prevalence, incidence and risk factors of chronic diseases in urban population. We used the national resident registration records to identify potential participants. From 2007 to 2010, 34,040 eligible participants aged 50 years and older, who resided in the Dong-gu district of Gwangju Metropolitan City in South Korea, were invited to participate in the project via telephone. A total of 9260 participants were enrolled and the response rate for this study was 27.2% (3711 men and 5549 women). Periodontal examination was carried out in 5621 participants among 7577 participants who participated in the study from 2008 to 2010. Among these, 109 participants were excluded because the BMD measurements were not available, and 129 additional participants were excluded because of missing data on smoking status, diabetes status, and education, osteoporosis medication, hormone replacement therapy and oral contraceptive use. Analyses were confined to the remaining 5383 participants (2272 men, 3111 women). This study was conducted in accordance with the Declaration of Helsinki guidelines. The study protocol was approved by the institutional review board of Chonnam National University Hospital, and informed consent was obtained from each participant.

Periodontal assessment

Three certified dental hygienists performed the clinical examination using a dental mirror and Williams probe (Hu-Friedy, Chicago, IL, USA). Full-mouth records were made for the number of teeth present and dental caries, whereas a periodontal examination was limited to a random half-mouth. The distance from the gingival margin to the base of the pocket (pocket depth) and gingival recession were measured at six sites per tooth (mesio-buccal, mid-buccal, disto-buccal, mesio-lingual, mid-lingual and disto-lingual). The distance from the cemento-enamel junction to the base of the pocket (clinical attachment loss) was calculated as the sum of pocket depth and gingival recession. Also, bleeding on probing (BOP) was measured. Among these parameters, CAL was chosen as the criterion for classifying the severity of periodontal disease. The percentage of the sites in oral cavity with CAL of 4 mm or greater was analysed, which was for the participants with one or more teeth (2175 men and 2990 women). When counting the number of teeth, the third molars were included, and only the teeth with complete erosions into oral cavity were counted. In the inter-examiner reliability test, the percent agreement was 83.3% (Kappa = 0.60) for CAL.

Bone mineral density measurements

Participants had their lumbar spine and femoral neck BMD measured by Lunar Prodigy (GE, Madison, WI, USA). Lumbar spine BMD was measured from L1 to L4. The machine was calibrated daily using the physical phantom. All BMD scans were conducted by certified examiners using standardized procedures following the protocols recommended by the manufacturer. Any images with metal or other attenuating material in the region of interest, as well as any images of poor quality, were deleted. Intra-scanner reproducibility of repeated measurements, expressed as coefficient of variation, was less than 1%.

Other measurements

Trained examiners interviewed the participants using a questionnaire that included items on cigarette use, use of antidiabetic medication, use of antihypertensive medication and menopausal status. Education was categorized as middle school or less, high school or higher. Smoking status was measured as never smokers (smoked <100 cigarettes in their lifetime and not currently smoking), former smokers (smoked ≥100 cigarettes in their lifetime and currently a non-smoker) and current smokers (smoked ≥100 cigarettes in their lifetime and currently a smoker) and categorized for analysis as current smokers or non-smokers (excluding never smokers and former smokers). Body weight was measured to the nearest 0.1 kg, whereas the participants were dressed in light clothing. Height was measured to the nearest 0.1 cm with the participant in stocking feet. Venous blood samples were collected from participants following an overnight fast. Serum was separated on site and stored at © 2014 John Wiley & Sons A/S. Published by John Wiley & Sons Ltd
−70°C until required. Fasting blood glucose was measured using a model 7600 automatic analyser (Hitachi, Tokyo, Japan). We defined diabetes (DM) as fasting serum glucose ≥126 mg/dL or use of insulin or oral antidiabetic medication.

Statistical analysis

Data are presented as mean ± standard deviation (SD) or percentage for categorical variables. We used t-tests to determine statistically significant differences between the continuous variables and chi-square tests to determine statistically significant differences in the categorical variables. Mann–Whitney U-test was used to compare data for tooth number and CAL. All analyses were stratified by gender. The participants were classified into subgroups based on both CAL and the number of teeth present, and the BMD at the lumbar spine and femoral neck was compared between the different subgroups. The number of teeth present was categorized into three equal categories (22–32, 11–21 and 0–10 teeth). The CAL values were divided into tertiles (0–10.9, 11.0–27.3, 27.4–100) in terms of the percentage of the sites with CAL equal to or greater than 4 mm. Analysis of covariance (ANCOVA) was used to compare the adjusted means of BMD at the lumbar spine and right femoral neck according to the tooth number and the tertiles of CAL, after adjusting for age, height, weight, current smoking status, education, DM status and osteoporosis medication in men and women, and further adjusting for menopausal status, hormone replacement therapy and oral contraceptive use in women. Bonferroni correction was applied for multiple comparisons. We added an interaction term between sex and CAL and the number of teeth present to explore whether sex modified the association of CAL and the number of teeth present with BMD in model adjusting for age, height, weight, current smoking, education and DM status. Statistical analyses were performed using the spss version 15.0 software package (SPSS, Chicago, IL, USA). Statistical significance was set at p < 0.05.

Results

Table 1 shows the general characteristics of the study population by gender. The mean age was 66.1 ± 7.9 in men and 64.0 ± 8.0 in women, the median percentage of sites with CAL≥4 mm was 25.0 in men and 14.3 in women and the median number of teeth present was 25 in men and 25 in women.

Table 2 presents adjusted means of BMD at the lumbar spine and femoral neck according to CAL and number of teeth present by sex. There was a significant association between the number of teeth present and BMD at the lumbar spine (p = 0.004) and femoral neck (p = 0.020) in men, but not in women. Compared with participants with 22 or more teeth, participants with 10 and less teeth had a lower BMD at lumbar spine (1.162 ± 0.005 versus 1.125 ± 0.012, p = 0.016) and femoral neck (0.882 ± 0.003 versus 0.859 ± 0.007, p = 0.019). Periodontal disease as measured by CAL was significantly associated with a lower BMD at the lumbar spine in women (p = 0.014), but not with BMD at lumbar spine in men and the femoral neck in both sexes. Compared with the lowest tertile, the second tertile of percentage of sites with CAL≥4 mm had a lower lumbar spine BMD in women (1.003 ± 0.004 versus 0.987 ± 0.004 versus 0.987 ± 0.004, p = 0.022). To test the robustness of our results, we performed additional sensitivity analysis including only participants with 12 or more teeth. We found similar findings (data not shown).

Discussion

In this study, we found that the number of teeth present was associated with more BMD at the lumbar spine and femoral neck in men, but not in women. We also found that periodontal disease as measured by CAL was significantly associated with a lower BMD at the lumbar spine in women, but not with BMD at lumbar spine in men and the femoral neck in both sexes.

Several previous studies reported that osteoporotic conditions contribute to tooth loss (Kribbs 1990, Krall et al. 1996, Inagaki et al. 2001, Krall 2001, Taguchi et al. 2004, Nicopoulou-Karayianni et al. 2009). In a longitudinal study, the higher rates of loss of BMD at multiple skeletal sites were associated with the loss of one or more teeth in healthy white post-menopausal women (Krall et al. 1996). Two previous studies also reported that tooth loss was statistically significantly increased in women with a lower BMD (Kribbs 1990, Inagaki et al. 2001). On the

| Table 1. General characteristics of the study population by gender |
|------------------------|------------------------|------------------------|------------------------|
|                        | Men (N = 2272)         | Women (N = 3111)       | p value                |
| Age, years             | 66.1 ± 7.9             | 64.0 ± 8.0             | <0.001                 |
| Weight, kg             | 65.8 ± 9.0             | 57.8 ± 7.9             | <0.001                 |
| Height, cm             | 165.9 ± 5.6            | 153.4 ± 5.5            | <0.001                 |
| BMI, kg/m²             | 23.9 ± 2.8             | 24.6 ± 2.9             | <0.001                 |
| Education              |                        |                        |                        |
|                       | Middle school or less  | 1029 (45.3)            | 2306 (74.1)            | <0.001                 |
|                       | High school or higher  | 1243 (54.7)            | 805 (25.9)             |                        |
| Current smoker (%)     | 551 (24.3)             | 51 (1.6)               | <0.001                 |
| Diabetes mellitus (%)  | 525 (23.1)             | 499 (16.0)             | <0.001                 |
| Osteoporosis medication (%) | 43 (1.9)       | 601 (19.3)             |                        |
| Menopause (%)          | –                      | 2994 (96.2)            |                        |
| Hormone replacement therapy (%) | –                  | 581 (18.7)             |                        |
| Oral contraceptive (%) | –                      | 654 (21.0)             |                        |
| Lumbar spine BMD, g/cm² | 1.160 ± 0.204        | 0.990 ± 0.166          | <0.001                 |
| Femoral neck BMD, g/cm² | 0.879 ± 0.129        | 0.792 ± 0.120          | <0.001                 |
| Tooth number           | 25 (19–28)             | 25 (20–28)             | 0.736                  |
| Percentage of sites with CAL≥4 mm* | 25.0 (12.2–42.3) | 14.3 (6.4–26.9) | <0.001                 |

BMD, bone mineral density; CAL, clinical attachment loss.

Values are expressed as mean ± SD or number (percentage). Tooth number and CAL values are expressed as median and inter-quartile ranges.

*The percentage of the site with CAL of 4 mm or greater was calculated for the participants with one or more teeth (2175 men and 2990 women).
other hand, other researchers failed to find a significant association between the number of teeth present and BMD (Mohammad et al. 1997, Earnshaw et al. 1998, Taguchi et al. 2005, Yoshihara et al. 2004, Yoshikawa-Bielaczyc et al. 2006, Phillips et al. 2007). For example, in a longitudinal study of men, they found no association between the number of teeth present and BMD at any anatomical site (Phillips et al. 2007). A previous study found that there was no significant association between the number of teeth present and BMD at any skeletal site in a cohort of 1365 early post-menopausal Caucasian women (Earnshaw et al. 1998). Possible explanations for these discrepancies may include the differences in the study participants in terms of race, age and sample size. In addition, BMD measurements at different skeletal sites might have also contributed to the discrepancy. Tooth loss in elderly is partly related to periodontitis. Caries, dentist’s decisions and prosthetic treatments inherently contribute to tooth loss. Even though the reasons of extraction were not identified in this study, fewer the number of teeth present showed low skeletal BMD in men. We hypothesize that other mechanisms besides periodontal infection may be the link between the number of teeth present and BMD.

Among the published studies, some studies (Weyant et al. 1999, Tezal et al. 2000, Famili et al. 2005, Hattatoglu-Sonmez et al. 2008, Sultan & Rao 2011) reported that there was no relationship between BMD and periodontal disease, whereas others (Whalen & Krook 1996, Mohammad et al. 1997, Yoshihara et al. 2004, Brennan et al. 2007, Miki et al. 2008, Al Habashneh et al. 2010, Suressh et al. 2010) found significant associations between BMD and periodontal disease (i.e. ABL, CAL). Ronderos et al. (2000) and Tezal et al. (2000) showed significant association between CAL and femoral neck BMD. And, recently, a study has reported that severe CAL was associated with low femoral neck BMD in Brazilian post-menopausal females (Gondim et al. 2012). On the other hand, Taguchi et al. (2005) reported that self-reported periodontal status was related to lumbar spine BMD, but was not significantly associated with femoral neck BMD in post-menopausal women, and this result is in agreement with this study. Our data suggest that the effect of the number of teeth present and CAL made a stronger contribution to BMD at the lumbar spine than at the femoral neck in men and women. This may suggest that BMD of a certain skeletal site is more associated with CAL than those of other skeletal sites. There are several possible explanations for this skeletal site-specific difference in terms of association between BMD and CAL. The skeleton is heterogeneous, and bone density, bone turnover rate and bone remodelling ability differ in some parts of the skeleton. In addition, compared to the femoral neck, the lumbar spine is mainly composed of trabecular bone and BMD loss in the lumbar spine is greater than that in the femoral neck after menopause (Taguchi et al. 2005). Alveolar bone is also composed of trabecular bone. This structural similarity may explain why tooth loss and CAL, the important clinical indicator of periodontal diseases, were significantly associated with BMD at the lumbar spine.

Mechanisms explaining the relationship between periodontal disease including tooth loss and osteoporosis have been suggested in the review papers (Wactaski-Wende 2001, Kuo et al. 2008). The regional increase in cytokines due to periodontal diseases accelerates systemic bone resorption by modulating host responses (Reddy 2001). For example, it has been reported that cytokines such as interleukin-1α and β (IL-1), tumour necrosis factor-α (TNF-α) and interleukin-6 (IL-6) induce osteoclastic activity, increase bone turnover rate and act as major determinants of osteoporosis (Ralston 1994). In addition, it was reported that some genetic factors and certain lifestyle factors such as smoking, low calcium intake and socioeconomic status such as income and education might act as risk factors for both diseases (Payne et al. 2000). In this study, there was also significant association after full adjustments for confound-
ers. Furthermore, local factor, such as subgingival calculus, which is causally related to periodontal diseases, may obscure the association between low BMD and CAL. (Brennan et al. 2007).

In this study, there was sex difference in the effect of the number of remaining teeth on BMD, with a significant association in men but not in women. There were three studies that examined whether there exist a sex-related difference in the association between the number of teeth present and BMD (May et al. 1995, Taguchi et al. 2004, Yoshihara et al. 2005). May et al. (1995) demonstrated that self-reported tooth loss was associated with lower BMD at the lumbar spine and hip in men but not in women. However, other two studies reported a similar association between the number of teeth present and BMD in both men and women. Taguchi et al. (2004) shows that self-reported number of teeth present was significantly associated with the femoral neck BMD in both men and women but not with lumbar spine BMD. Retention of four teeth was significantly associated with a 0.004 g/cm² increase in the femoral neck BMD in both men and women. Yoshihara et al. (2005) demonstrated that there was a significant relationship between BMD of the os calcis and the number of teeth present in both men and women and there was no significant difference in gender. The mechanisms underlying this gender difference are not known. Women with a higher percentage of body fat have better oestrogen metabolism and thus have a smaller risk of osteoporosis than women with a lower percentage of body fat (Ribot et al. 1994). It is possible that this sex-related difference is due to the effect of sex hormone. Further studies are needed to determine the exact nature of this interaction.

The strength of this study compared to the previous studies is that, it included both sexes and a wide range of ages. Also, this is the first large-scale population-based study in a Korean cohort for measuring BMD and periodontal variables. However, this study has some limitations as well. First, even our best attempts with known factors associated with tooth loss, CAL and BMD in this analysis, residual confounding by calcium intake, income and unknown factors may exist. Second, our periodontal assessment (CAL) was restricted to half-mouth, and this partial mouth assessment may seem to be less accurate than whole-mouth assessment for studying periodontitis. However, Dowsett et al. (2002) proved that, in evaluating mean PI, GI, PD, and CAL, half-mouth assessment was an acceptable alternative to whole-mouth assessment (intra-class correlation coefficients, ICCs > 0.92). They also suggested that studies are confined to half-mouth because of examiner and participant fatigue, time consumption and cost cutting. Finally, as this was a cross-sectional study, it was not possible to draw a conclusion regarding causality between CAL, the number of teeth present and BMD. In conclusion, the results of this study suggest that tooth loss and CAL, the clinical indicator for the severity of periodontal disease, may be associated with low BMD. However, the magnitude of these associations was relatively small and the clinical significance was unclear.

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No specific.

References
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Scientific rationale for the study: Previous research has shown an inconsistent result of the association between osteoporosis and periodontitis. We used the first large-scale population-based study in a Korean cohort for measuring BMD and periodontal variables, taking into account a confounding factor such as for age, weight, height, education, current smoking, diabetes mellitus, medication for osteoporosis, menopausal status, hormone replacement therapy and oral contraceptive use.

Principal findings: The number of teeth present was positively associated with BMD at the lumbar spine and femoral neck in men, but not in women. Periodontal disease was significantly associated with a lower BMD at the lumbar spine in women, but not with BMD at lumbar spine in men and the femoral neck in both sexes.

Practical implications: The number of teeth present and CAL, the clinical indicator for the progression of periodontal disease, may be associated with BMD.