SUMMARY

Tooth loss and osteoporosis may share common etiologic agents which may either directly influence or modulate the process of both diseases. The purpose of this study was to evaluate the relationship between systemic bone mineral density and tooth loss, controlling the known confounding factors. Among all inhabitants aged 70 years old in Niigata City in Japan, 600 people were selected randomly in order to have approximately the same number of each gender. 466 subjects were examined in this study. We evaluated the data on bone mineral density of the heel by using an Ultra-Sound Bone Densitometer and the number of missing teeth. The comparison of the number of missing teeth and 9 other variables between osteopenia (OG) and no osteopenia groups (NOG) was investigated by two-way ANOVA. The mean number of missing teeth for OG and NOG, respectively was 12.03±9.98 and 9.69±8.06 in females, 11.68±9.93 and 9.88±9.33 in males (OG vs. NOG, $p=0.047$). In addition, the number of missing teeth (coef.=-0.157, $p=0.005$) were significantly associated with stiffness (R2=0.318, $p<0.001$) by linear multiple regression analysis. This study might suggest that there was a significant relationship between the number of missing teeth and general bone mineral density.

Introduction

Osteoporosis is the most common metabolic bone disease among the elderly (65 years and older), and the incidence of osteoporotic fractures obviously increases with aging. Tooth loss also occurs frequently in an elderly population, and osteoporosis has long been suspected as a risk factor for oral bone loss. Tooth loss and osteoporosis may share common etiologic agents which may either directly influence or modulate the process of both diseases. There were some reports which showed a significant relationship between the number of missing teeth and osteoporosis. Among post-menopausal women, those with very low bone mineral density (BMD) scores had fewer teeth remaining than those who had normal BMD scores (Inagaki *et al.*, 2001). Furthermore, Krall *et al.* (1994, 1996) suggested that the greater rate of BMD loss at multiple skeletal sites was associated with the loss of one or more teeth in healthy post-menopausal women. However, several large studies failed to find significant associations between tooth status and bone mineral density (Elders *et al.*, 1992, Klemetti & Vaino, 1993).

Dental caries and periodontal disease are the main reasons for tooth loss. Especially, periodontal disease influences tooth loss in the elderly. The results of some previous studies have indicated a relationship between periodontal disease and osteoporosis or BMD (Von Wowern *et al.*, 1994; Mohammad *et al.*, 1997; Tezal *et al.*, 2000). The presence of skeletal osteoporosis strongly affects the alveolar bone resorption in edentulous patients (Hirai *et al.*, 1993). However, there were some reports which did not show any significant relationship

(Elders *et al.*, 1992; Klemetti *et al.*, 1994; Lundstrom *et al.*, 2001). Using periodontal attachment loss as an indicator of mandibular bone loss, no difference between the osteoporotic and the non-osteoporotic group was found (Kribbs, 1990). According to theses reports, the relationship between tooth loss and osteoporosis remains unclear. In addition, all of theses studies examined bone loss and periodontal condition or tooth loss in females. Even if the loss of bone mineral density is more significant in females than in males, the role of factors involved in the regulation of bone mineral density in males as well as in post-menopausal females needs to be evaluated further.

Furthermore, study-designs to examine the relationship between tooth loss or oral bone loss and osteoporosis were scarce in the previous reports. Many of the studies conducted to date have been plagued by relatively small sample sizes and have selected subjects with a wide range of ages (more than 20 years). A relationship is difficult to establish, as the results may easily be confounded by other factors such as gender, smoking, race and age, etc. in a small sample study.

The purpose of this study was to evaluate the relationship between systemic bone mineral density and tooth loss, controlling the known confounding factors.

Materials and methods

Subjects and Clinical Assessment

Initially, questionnaires were sent to all 4,542 inhabitants aged 70 years old according to a registry of residents in Niigata City in Japan, and they were informed of the purpose of this survey. The response rate was 81.4% (N=3,695). After dividing into groups of males and females, 600 people (screened population) were selected randomly in order to have approximately the same number of each gender for the study. The subjects for the study agreed to undergo medical and dental examinations, and signed informed consent forms regarding the protocol, which was reviewed and approved by the Ethics Committee of the Faculty of Dentistry, Niigata University.

Among the screened population, 466 subjects were examined in this study. The examinations were performed at local community centers in Niigata City. We utilized the data on bone mineral density (BMD) of the heel, which we measured using an Ultra-Sound Bone Densitometer (Lunar, Achilles ™). The ultrasound signal is sent to os calcis. Ultrasound densitometry enables the measurement of the physical properties of bone, specifically BMD. The ultrasound measurement contains two criteria, the velocity (speed of sound (sec); SOS) and frequency attenuation (broadband ultrasound attenuation (dB/MHZ); BUA) of a sound wave as it travels through a bone (Rossman *et al.*, 1989; Langton *et al.*, 1984). The stiffness is a clinical index combining SOS and BUA, which is calculated by the spread speed of supersonic waves. The formula is (BUA-50) $\times$0.67+(SOS-1380) $\times$0.28.

This charts the SOS and BUA into biological relevant ranges. Stiffness is indicated in the monitor of the bone densitometer as the percentage for the value of the normal younger generation. Osteopenia was defined as a stiffness ≤ 85 for 70-year-old males, and ≤ 69 for females (Lunar Corporation, 1991). To monitor the general health condition, serum levels of disease markers and smoking habits were also investigated. These markers of disease or smoking habits were immunoglobulin (serum IgG concentration), nutritional factors (serum albumin, total cholesterol, calcium, vitamin C, vitamin E (α) concentrations), and smoking habits (serum cotinine concentration). We counted the number of missing teeth and measured grip power/weight as physical strength. In addition, body fat rate was measured by bio-electrical impedance analysis (TANITA, Body composition analyzer/scales^{TM}). A personal interview was conducted to obtain information regarding taking medication for osteoporosis.

Statistical Analysis

Finally, 460 subjects were included in the analysis, after excluding six people who were taking estrogen or medication known to influence calcium metabolism. Mean and standard deviation (SD) were used for characterizing the continuous variables. We compared the percentage of stiffness, number of missing teeth, serum values, body fat rate and grip power/weight between males and females. The comparison of serum values, body fat rate, grip power/weight, and the number of missing teeth between the osteopenia and the no

osteopenia groups were investigated by two-way analysis of variance (ANOVA) for discriminating among the effects of gender and bone mineral density. Furthermore, multiple linear regression analysis was performed to evaluate the relationship between the number of missing teeth and bone mineral density. As a dependent variable, the percentage of stiffness was used. As independent variables, we selected the variables, which had p-values less than 0.1 according to the analysis for each variable in addition to the number of missing teeth.

Results

Table 1 shows the comparison by mean values of the percentage of stiffness, the number of missing teeth, serum albumin concentration, serum IgG concentration, serum vitamin C concentration, serum vitamin E (α) concentration, serum cotinine concentration, serum calcium concentration, serum total cholesterol concentration, body fat rate and grip power/weight between males and females. There were significant differences in all variables except the number of missing teeth per person.

After dividing the subjects into osteopenia group (stiffness ≤ 69 for females, ≤ 85 for males, OG) and no osteopenia group (NOG), we compared serum albumin concentration, serum IgG concentration, serum vitamin C concentration, serum vitamin E (α) concentration, serum cotinine concentration, serum calcium concentration, serum total cholesterol concentration, body fat rate and grip power/weight by mean values (Table 2). There were significant differences in serum vitamin E(α) concentration, and body fat rate between OG and NOG adjusted by gender (Two-way ANOVA). Both values were greater in NOG. In addition, we evaluated the number of missing teeth per person between OG and NOG. The mean number of missing teeth for OG and NOG, respectively was 12.03±9.98 and 9.69±8.06 in females, 11.68±9.93 and 9.88±9.33 in males (Fig). The number of missing teeth was significantly higher in OG. As shown in the table, significant effects of stiffness (OG vs. NOG, $p=0.047$) were observed by two-way ANOVA

To evaluate the relationship between bone mineral density (stiffness) and the number of

missing teeth, four other variables (body fat rate, serum IgG concentration, gender and serum vitamin E(α) concentration) were selected for the independent variables of the final model. The result of linear multiple regression analysis by the final model is presented in Table 3. The number of missing teeth (coef.=-0.157, $p=0.005$), body fat rate (coef.=0.396, $p<0.001$), gender (coef.=-18.169, $p<0.001$) and serum vitamin E (α) concentration (coef.=0.262, $p=0.048$) were significantly associated with stiffness (R2=0.318, $p<0.001$).

Discussion

The results showed that the subjects in the osteopenia group had a higher number of missing teeth than the subjects in the no osteopenia group. This study clearly demonstrated that bone mineral density (BMD) is a risk factor for tooth loss in an elderly population. BMD may influence the progression of alveolar bone loss, manifesting clinically as periodontal disease.

Some systemic factors have been identified which contribute to loss of bone mass (Cummings *et al.*, 1985; Genco *et al.*, 1993). There are some common factors between BMD and oral bone loss such as smoking, nutritional deficiencies, age, medication use and immune dysfunction (Wactawski-Wende *et al.*, 1996). Therefore, it is reasonable that this study showed a significant relationship between BMD and the number of missing teeth.

In a previous report, a significant correlation between several skeletal bone mass measurements and the number of remaining mandibular teeth in 85 osteoporotic women between 50 to 80 years of age was observed (Kribs *et al.*, 1990). Some other reports showed that mandibular bone mass was significantly correlated with skeletal bone mass as well (Klemetti *et al.*, 1993; Von Wowern *et al.*, 1994). In addition, the BMD of the mandible is affected by the mineral status of the skeleton and also by general diseases that cause generalized bone loss (Klemetti *et al.*, 1993). However, there was a report which showed no correlation between skeletal and mandibular bone measurements (Mohajery & Brooks, 1992; Southard *et al.*, 2000). According to these conflicting results, general bone mineral density

might not influence the alveolar bone loss directly in some cases. The skeleton is heterogenic, and bone density, bone turnover rate and bone remodeling ability differ in each part of the skeleton, suggesting that those regions, although related to each other, have some degree of independence. However, the results of these studies should be interpreted with caution since the number of subjects might be small, the age of subjects might not have been restricted, and the oral or skeletal bone loss might have been measured in a variety of ways, only in females.

In addition, we found a significant relationship between stiffness and serum vitamin E (α) concentration or body fat rate. Vitamin E deficiency was found to cause loss of bone calcium and this could be due to increased free radical activity or decreased calcium availability for bone deposition (Ima-Nirwana *et al.*, 1999; Mohamen *et al.*, 2002). Body composition characteristics are associated with the BMD. An association between low amounts of fat tissue and decreased BMD was found in some reports (Gillette-Guyonnet *et al.*, 2000; Kirchengast *et al.*, 2001). Body fat rate might influence BMD.

In this study, we chose to restrict the age of subjects to 70 years old. Therefore, we could remove the influence of aging for BMD and tooth loss. In addition, ultrasonic bone density measurements were checked to evaluate BMD in this study. Ultrasound densitometry of the os calcis was highly reproducible and had a high correlation with BMD measured by dual energy x-ray absorptiometry (DEXA) in different parts of the skeleton (Heaney *et al.*, 1989; Resch *et al.*, 1990; Yamazaki *et al.*, 1994).

In conclusion, this study might suggest that there is a significant relationship between the number of missing teeth and general bone mineral density in a well-designed, large-scale study.

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Table 1. Comparison of bone mineral density, missing teeth, serum values, body fat rate, grip power/weight between males and females.

Variables	Subjects		*p* value
	Males (n=248)	Females (n=212)	
Stiffness (%, mean±SD)	76.57±12.85	62.53±10.10	<0.001
No. of missing teeth (mean±SD)	11.23±9.79	11.43±9.56	0.813
Albumin (g/dl, mean±SD)	4.07±0.24	4.14±0.23	0.001
IgG (mg/dl, mean±SD)	1269.52±267.62	1322.92±274.88	0.037
Vitamin C (mcg/dl, mean±SD)	6.21±2.92	8.32±3.24	<0.001
Vitamin E (α) (mcg/dl, mean±SD)	11.12±3.41	13.08±4.76	<0.001
Cotinine (mg/dl, mean±SD)	85.81±168.18	11.17±36.40	<0.001
Calcium (mg/dl, mean±SD)	4.42±0.19	4.49±0.35	0.007
Total cholesterol (mg/dl, mean±SD)	184.11±26.34	210.34±30.42	<0.001
Body fat rate (%, mean±SD)	19.87±5.00	28.58±6.43	<0.001
Grip power/weight (Kg/Kg, mean±SD)	0.68±0.11	0.49±0.09	<0.001

Table 2. Comparison of serum values, body fat rate, grip power between osteopenia and no osteopenia.

Variables	Subjects		p value[a]
	Osteopenia (n=342)	No osteopenia (n=118)	
Albumin (g/dl, mean±SD)	4.10±0.24	4.10±0.22	0.895
IgG (mg/dl, mean±SD)	1280.58±254.67	1333.60±314.94	0.068
Vitamin C (mcg/dl, mean±SD)	7.13±3.15	7.38±3.50	0.470
Vitamin E (α) (mcg/dl, mean±SD)	11.70±3.82	13.05±5.07	0.002
Cotinine (mg/dl, mean±SD)	54.35±141.23	41.90±95.04	0.315
Calcium (mg/dl, mean±SD)	4.45±0.29	4.47±0.21	0.416
Total cholesterol (mg/dl, mean±SD)	195.49±32.26	198.32±27.66	0.325
Body fat rate (%, mean±SD)	23.30±7.11	25.60±7.09	<0.001
Grip power/weight (Kg/Kg, mean±SD)	0.60±0.14	0.58±0.14	0.682

[a] p value by an analysis of two-way variance adjusted by gender and bone mineral density.

Figure Yoshihara *et al*.