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Research Article

Association of Carotid Artery Calcification Detected on Dental Panoramic Radiographs with a History of Osteoporosis Diagnosis without Prevalent Fractures

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Abstract

Introduction: Aortic calcification seen on lateral radiographs might be an independent predictor of osteoporosis in the elderly. It is not clear whether the presence of carotid artery calcification (CAC) on dental panoramic radiographs (DPRs) is associated with osteoporosis. We examined the association between CAC on DPRs and a history of osteoporosis diagnosis without prevalent fractures.

Methods: Of 1132 Japanese patients (432 males, 700 females) age ≥ 50 years who underwent digital DPR to diagnose dental disease at our university hospital between 2007 and 2012, 542 (237 males, 305 females) participated in this study. The mean±SD age of the subjects was 68.4±7.7 years. One experienced oral and maxillofacial radiologist identified the presence of CAC. Information on subject lifestyles and disease histories was obtained using a structured questionnaire and confirmed in a telephone interview and from medical records. An independent *t*-test, chi square test, or Fisher's exact test was used to compare differences in osteoporosis diagnosis without prevalent fractures, age, gender, body mass index, history of smoking, diabetes mellitus, and rheumatoid arthritis between subjects with and without CAC. Logistic regression analysis was used to calculate the odds ratio of having a history of osteoporosis diagnosis without prevalent fractures in subjects with CAC after adjusting for the covariates.

Results: Subjects with CAC had a significantly higher risk of being diagnosed with osteoporosis without prevalent fractures than did subjects without CAC ($P = 0.03$). The crude odds ratio of having a history of an osteoporosis diagnosis without prevalent fractures in subjects with CAC was 2.45 (95% confidence interval [CI] 1.06–5.62). The odds ratio after adjusting for covariates was 2.31 (95% CI 0.91–5.90).

Conclusions: The CAC incidentally detected on DPRs might be useful for identifying elderly males and females who should be referred for further examinations regarding osteoporosis.

INTRODUCTION

The occurrence of osteoporotic fractures contributes to re-fractures, decreases the quality of life, and increases mortality risk and medical costs. In Japan, the number of patients with hip fractures in 2005 was approximately thrice that in 1987 [1]. Mortality after hip or spine fractures is relatively high (10–20%), especially in males. In community-dwelling participants age ≥ 60 years from the Dubbo Osteoporosis Epidemiology Study with incident fractures, Bliuc *et al.* . reported that the 5-year mortality after re-fracture was 39% in females and 51% in males [2]. The estimated number of osteoporotic patients age ≥ 40 years in Japan is 12.8 million, based on a survey of the prevalence of osteoporosis diagnosed using bone mineral density (BMD) in the lumbar vertebrae or proximal femur [3]. Only about 20% of these patients receive treatment for osteoporosis [4]. Many patients with osteoporosis who are at risk of fracture are under-diagnosed in Japan. Asymptomatic patients with a low skeletal BMD or a high risk of fractures are unlikely to visit medical professionals to undergo BMD assessment. Several screening tools are available, such as those based on questionnaires, but, again, asymptomatic patients with low skeletal BMD are unlikely

to visit medical professionals for further examination, even if such screening tools indicate a possible risk of fracture [5].

Recent studies have demonstrated an association between cardiovascular disease and osteoporosis [6-9]. Previously, we showed that postmenopausal females with low skeletal BMD had endothelial dysfunction, the first stage of atherosclerosis [10]. Research suggests common etiological mechanisms for these diseases [11]. Several shared factors regulated bone and the vasculature and calcification of the vascular walls in many ways resembles the bone-formation process. Since vascular calcification is the final stage of atherosclerosis [12], it is reasonable that elderly males and females with vascular calcification might have a high risk of osteoporosis or fractures. From the perspective of an association between atherosclerosis and osteoporosis, several investigators have demonstrated the usefulness of aortic calcification detected on lateral radiographs for identifying elderly males and females at risk of having a low skeletal BMD or fracture [13,14]. Bagger *et al.* . reported that age, body mass index (BMI), and the severity of aortic calcification were independent predictors of hip fractures in 2662 generally healthy postmenopausal females with a mean age of 65.0±7.1 years at baseline [13]. El Maghraoui *et al.* . reported that an extended abdominal aortic calcification was independently associated with prevalent vertebral fractures regardless of age, BMI, history of fractures, or skeletal BMD in 908 postmenopausal females with a mean age of 60.9±7.7 (range 50–91) years [14].

In addition, the incidental finding of carotid artery calcification (CAC) on dental panoramic radiographs taken to diagnose dental disease suggests a high risk of osteoporosis, although this finding has been used to identify elderly people with a high risk of cardiovascular disease, such as coronary heart disease and ischemic stroke [15-17]. Recently, Friedlander *et al.* first demonstrated a significant inverse association between CAC detected on dental panoramic images and femoral neck BMD measured using dual x-ray absorptiometry (DXA) in postmenopausal white females [18]. The incidental CAC finding detected on dental panoramic radiographs might be a useful indicator to identify asymptomatic individuals who should be referred to medical professionals for further examinations regarding osteoporosis. Therefore, this study investigated the association between CAC detected on dental panoramic radiographs and a history of osteoporosis diagnosis without prevalent fractures.

MATERIALS AND METHODS

Subjects

Of 1132 Japanese patients (432 males, 700 females) age ≥ 50 years who visited our university hospital and underwent dental panoramic radiographs for the diagnosis of dental disease between 2007 and 2012, 542 (237 males, 305 females) responded to our invitation and participated in this study, after giving informed consent. On being enrolled, a structured questionnaire including a history of several diseases (osteoporosis, cardiovascular diseases, pneumonia, fracture, diabetes mellitus, hyperlipidemia, hypertension, rheumatoid arthritis, and cancer), lifestyle, and food consumption was mailed to all subjects. We followed up missing data in returned questionnaires by telephone. We also confirmed a history of osteoporosis diagnosis without prevalent fractures in both a telephone interview and the medical records. The ethics committee of our institution reviewed and approved the study protocol (no. 0152).

CAC determination on dental panoramic radiographs

Panoramic radiographs were obtained using an AZ-3000 dental x-ray instrument (Asahi, Kyoto, Japan). Two experienced radiological technologists took the radiographs. A digital radiography system (Regius Model 170; Konica Minolta Holdings, Tokyo, Japan) was used for all subjects. The panoramic radiographs were developed using a laser imager (Drypro SD-P; Konica Minolta Holdings). All panoramic radiographs used were satisfactory for evaluation.

An experienced oral and maxillofacial radiologist (AT) determined the presence of CAC on 1132 dental panoramic radiographs, which included those of both responders and non-responders to our study. He was trained by medical radiologists and had diagnosed oral and maxillofacial lesions by using several imaging modalities including conventional radiographies (26 years of experience) as well as computed tomography (CT) (24 years of experience) and ultrasonography (18 years of experience). He has had a large number of opportunities to compare CAC detected on dental panoramic radiographs with that detected on CT or ultrasonography. To evaluate inter-examiner reproducibility, another experienced oral and maxillofacial radiologist (KU) examined all 1132 dental panoramic radiographs. One or more heterogeneous radio-opacities in a verticolinear orientation adjacent or inferior to the hyoid bone, epiglottis, and cervical vertebrae at, above, or below the between C3-C4 intervertebral was diagnosed as CAC (Figure 1), after ruling out confounding radio-opacities in close proximity to the vessel, such as a calcified triticeous cartilage or calcified superior cornu of thyroid cartilage [15]. The number of remaining teeth was also recorded.

Statistical analysis

The data for continuous variables are expressed as the means±SD. The kappa statistic was used to assess the inter-examiner reproducibility between the two experienced radiologists. An independent *t*-test or chi-square test was used to evaluate differences in age, gender, number of teeth remaining, and presence of CAC between responders and non-responders to our study. Further, an independent *t*-test, chi square test, or Fisher's exact test was used to evaluate differences in osteoporosis

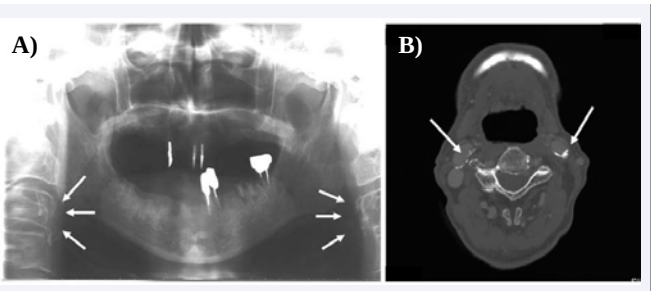

Figure 1 Carotid artery calcification (white arrows) on a dental panoramic radiograph (A) and computed tomography image (B).

diagnosis without prevalent fractures, age, gender, BMI, history of smoking, diabetes mellitus, and rheumatoid arthritis between subjects with and without CAC.

Logistic regression analysis was used to calculate the odds ratio of having a history of osteoporosis diagnosis without prevalent fractures in subjects with CAC after adjusting for age, gender (binary parameter), BMI, history of smoking (binary), diabetes mellitus (binary), and rheumatoid arthritis (binary). Statistical significance was set at $P< 0.05$. All computations were conducted using SPSS (ver. 19.0; IBM, Chicago, IL, USA).

RESULTS

The kappa score for determining CAC on dental panoramic radiographs between the two experienced radiologists was 0.90. There were significant differences in gender and the presence of CAC between responders and non-responders to our study (Table 1). Males responded to and participated in our study significantly ($P < 0.001$) more often than did females. Non-responders had a significantly larger number of CAC detected on dental panoramic radiographs than responders ($P = 0.006$). No significant differences were observed in age and number of teeth remaining between groups.

Subjects with CAC had a significantly ($P = 0.03$) higher risk of receiving an osteoporosis diagnosis without prevalent fractures than did subjects without CAC (Table 2). After the diagnosis of osteoporosis, all were prescribed some medicine, such as bisphosphonate, hormone replacement therapy, selective estrogen receptor modulator, vitamin D, and parathyroid hormone. There were no significant differences in age, gender, BMI, history of smoking, and diabetes mellitus between subjects with and without CAC. Subjects with CAC tended ($P = 0.06$) to have rheumatoid arthritis more than those without CAC.

The crude odds ratio of having a history of receiving an osteoporosis diagnosis without prevalent fractures in subjects with CAC was 2.45 (95% confidence interval [CI] 1.06–5.62) (Table 3). The odds ratio after adjusting for age, gender, BMI, history of smoking, diabetes mellitus, and rheumatoid arthritis was 2.31 (95% CI 0.91–5.90).

DISCUSSION

This is the first study demonstrating an association between CAC detected on dental panoramic radiographs and a history of osteoporosis diagnosis without prevalent fractures, although Friedlander *et al.* . first observed a significant inverse association between CAC detected on dental panoramic images and femoral neck BMD measured using DXA in postmenopausal white females [18]. In our study, which included males and females age ≥ 50 years, subjects with CAC detected on dental panoramic radiographs tended to have a higher risk of receiving an osteoporosis diagnosis without prevalent fractures than did those without CAC. This suggests that CAC detected incidentally on dental panoramic radiographs is a useful indicator for identifying the elderly who should be referred to a medical professional for further investigations, such as DXA examination, before fractures occurrence.

In this study, non-responders had a significantly larger number of CAC (15.9%) than responders (10.3%). It is likely that a large number of non-responders with CAC will die because investigators have reported that dental patients with CAC detected on dental panoramic radiographs had a higher risk of cardiovascular disease, including myocardial infarction and ischemic stroke, resulting in death [15,19]. In addition, males responded to and participated in this study significantly more often than females, although the reason for this is not known. In this study, an invitation was mailed to dental patients who visited our university hospital and underwent dental panoramic radiographs. Perhaps an invitation by telephone would increase the response rate. Since significant differences in gender and the presence of CAC between responders and non-responders might produce selection bias, further investigations using other invitation methods are necessary to eliminate or minimize the selection bias in future studies.

Tanaka et al. . reported that the rate of CAC was 5.0% in 659 panoramic radiographs of 80-year-old residents of Fukuoka

Table 1: Differences in the characteristics of responders and non-responders to the invitation to participate in the study.

	Responders	Non-responders	*P-value*
Number of patients	542	580	
Gender (male)	237 (43.7)	195 (33.0)	< 0.001
Age (years)	68.4±7.7	67.7±9.2	0.14
Number of teeth remaining	21.6±6.4	21.0±6.8	0.19
Presence of CAC	56 (10.3)	94 (15.9)	0.006

Results are presented as the means±SD or numbers of subjects (%).
CAC: carotid artery calcification

Table 2: Differences in the characteristics of the subjects with and without carotid artery calcification (CAC).

	Absence of CAC	Presence of CAC	*P*-value
Number of subjects	486	56	
Osteoporosis diagnosis (yes)	31 (6.3)	8 (14.2)	0.03
Age (years)	68.3±7.7	69.9±7.6	0.14
Gender (male)	210 (43.2)	27 (48.2)	0.48
Body mass index (kg/m^2)	22.1±3.1	21.4±2.7	0.15
History of smoking (yes)	123 (25.3)	18 (32.1)	0.27
Diabetes mellitus (yes)	48 (9.9)	3 (5.3)	0.27
Rheumatoid arthritis (yes)	8 (1.6)	3 (5.3)	0.06

Results are presented as the means±SD or numbers of subjects (%).

Table 3: Odds ratio of having a history of an osteoporosis diagnosis without prevalent fractures in subjects with carotid artery calcification.

Adjusted covariates	Odds ratio	95% CI	*P*-value
None	2.45	1.06 to 5.62	0.03
Age	2.25	0.97 to 5.24	0.06
Age, gender	2.58	1.04 to 6.39	0.04
Age, gender, BMI	2.50	1.00 to 6.24	0.05
Age, gender, BMI, smoking	2.50	1.00 to 6.24	0.05
Age, gender, BMI, smoking, DM	2.52	1.01 to 6.30	0.05
Age, gender, BMI, smoking, DM, RA	2.31	0.91 to 5.90	0.08

CI: Confidence Interval; BMI: Body Mass Index; DM: Diabetes Mellitus; RA: Rheumatoid Arthritis.

Prefecture [20]. Tamura et al. . found that 4.1% of patients had CAC detected on dental panoramic radiographs in 2568 patients with a mean age of 62.2 (range 50–70) years who visited a university hospital [19]. In comparison with these reports, the incidence of CAC (10.3%) in our study was relatively large. In contrast, Kumagai *et al.* . found a relatively higher rate of CAC in smokers (14.1% for males and 14.3% for females) in comparison with non-smokers (4.8% for males and 9.0% for females) in a hospital-based population age ≥ 50 years [21]. A large number of residents with CAC in Fukuoka Prefecture might have died from cardiovascular disease before reaching 80 years of age in Tanaka *et al.* [20]. . Tamura *et al.* . did not give the proportion of subjects with a history of smoking [19]. The combination of age and smoking status might influence the prevalence of CAC detected on dental panoramic radiographs. In addition, these previous studies did not use digital panoramic radiographic equipment, such as that used in our study. Horsley *et al.* . reported a relatively high rate of CAC (25%) on digital dental panoramic radiographs and hypothesized that the high rate of CAC compared to previous studies was due to the difference between film- and digital-based observations [22]. Beckstrom *et al.* . also reported a high rate of CAC (24%) on digital dental panoramic radiographs in 201 preradiation head and neck cancer patients compared with that (7%) of their previous similar study on film-based dental panoramic radiographs [23]. Regarding this disparity between the two studies, they explained that the images obtained from digital panoramic radiography could be enhanced to better visualize the carotid bifurcation region. We cannot detect hypocalcification of carotid artery in the carotid bifurcation region when we compare the presence of CAC detected by film-based panoramic radiographs with that detected by CT. A detectability of CAC on film-based dental panoramic radiographs depends on the degree of calcification. In our recent study regarding the development of computer based diagnosis system, a detectability of several degree of calcification of carotid artery on digitized dental panoramic radiographs was relatively low because the contrast of these CAC was basically low on film-based dental panoramic radiographs before digitization [24].

Our study had limitations. First, the study population consisted of patients who visited our university hospital. This implies that our subjects are not representative of Japanese adults in general. Second, the study had a cross-sectional, rather than longitudinal, design. Third, the diagnostic criteria for osteoporosis without prevalent fractures might differ among medical hospitals or clinics. The diagnostic criteria and treatment guidelines for osteoporosis used in Japan were revised recently [25,26]. It is important to confirm how osteoporosis was diagnosed in a future study, as the diagnostic criteria for osteoporosis depended on the individual medical doctors in our study.

CONCLUSIONS

The subjects with CAC detected on dental panoramic radiographs tended to have a high risk of receiving an osteoporosis diagnosis without prevalent fractures or medication for osteoporosis. Our study suggests that CAC detected incidentally on dental panoramic radiographs is useful for identifying elderly people who should be referred to medical professionals for further examination of osteoporosis before fractures occur.

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