Acta Odontologica Scandinavica. 2014; 72: 401–412

informa
healthcare

REVIEW ARTICLE

Assessment of carotid calcifications on panoramic radiographs in relation to other used methods and relationship to periodontitis and stroke: a literature review

VIVECA WALLIN BENGTSSON[1], G. RUTGER PERSSON[1,2,3] & STEFAN RENVERT[1,4,5]

[1]*Department of Oral Sciences, Kristianstad University, Kristianstad, Sweden,* [2]*Departments of Periodontics and Oral Medicine, University of Washington, Seattle WA, USA,* [3]*Department of Periodontology University of Bern, Switzerland,* [4]*School of Dental Scences, Trinity Collage, Dublin, Ireland, and* [5]*Blekinge Institute of Technology, Karlskrona, Sweden*

Abstract

Objectives. To assess the literature on carotid calcifications defined from panoramic radiographs (PMX) and concurrent diagnosis of stroke and periodontitis. ***Materials and methods.*** A literature search screening for publications using search terms such as PMX and carotid calcification, stroke and periodontitis was performed in November 2012. ***Results.*** A total of 189 articles were retrieved, among which 30 were included in the review. The sensitivity for PMX findings of carotid calcifications (CC) compared to a diagnosis by Doppler sonography varied between 31.1–100%. The specificity for PMX findings of carotid calcifications compared to a diagnosis by Doppler sonography varied between 21.4–87.5%. Individuals with CC findings from PMX have more periodontitis and risk for stroke. ***Conclusions.*** There is a shortage of well-designed studies in older dentate individuals assessing the associations between periodontitis and radiographic evidence of CC and in relation to stroke or other cardiovascular diseases. ***Statement of Clinical Relevance.*** Carotid calcifications are prevalent in patients with periodontitis and such individuals may have an increased risk for stroke. The absence of signs of carotid calcification on panoramic radiographs is indicative of no calcification of carotid arteries.

Key Words: *panoramic radiograph, carotid calcification, periodontitis, review*

Introduction

Atherosclerosis is a chronic inflammatory disease with a multifactorial nature, characterized by thickening and the loss of elasticity of the arterial walls. Arterial calcification in major vessel beds outside the brain have been associated with vascular brain disease and linked to future risk of dementia and stroke [1]. Atherosclerosis is a systemic vascular process and a major cause of cardiovascular and cerebrovascular disease. In the US, stroke is the third leading cause of death [2].

Approximately 85% of all of stroke events are ischemic in nature and are caused by atheroma in the internal carotid artery [3]. Carotid artery sclerosis accounts for 20–30% of ischemic stroke events. Data have shown that neurologically asymptomatic individuals with more than 50% stenosis of the internal carotid artery have an elevated risk of developing stroke [4]. An accumulation of low-density lipoproteins (LDL) occurs in the intimate layer of the endothelium, culminating in the formation of atheromatous plaque, with superimposition of calcium deposits. Atheromas are composed of lipids and fibrous tissue, deposited on blood vessel cell walls [5]. Many factors pre-dispose to carotid atherosclerosis including: advancing age [6,7], male gender, hypertension [7], serum levels of low-density lipoprotein (LDL) [8], smoking habits [9], diabetes mellitus [7,10] and heavy alcohol intake [11].

Data also suggest that chronic infections attribute to the pathogenesis of atherosclerosis [12]. Periodontitis is a destructive inflammatory process of periodontal tissues initiated by primarily gram-negative bacteria [13]. Periodontitis has been associated with coronary heart disease and stroke [14–22]. Periodontitis has also been associated with endothelial dysfunction and sub-clinical carotid atherosclerosis intima media thickness [18,19,21,23,24]. Thickening of the intima media has been strongly associated with risk factors for stroke and with prevalent stroke [25].

Correspondence: Stefan Renvert, Health Science, University of Kristianstad, SE 29188 Kristianstad, Sweden. Tel: +46 44204090. E-mail: stefan.renvert@hkr.se

(Received 14 June 2013; accepted 16 September 2013)

ISSN 0001-6357 print/ISSN 1502-3850 online
DOI: 10.3109/00016357.2013.847489

Data also suggest that evidence of carotid calcification may be related to periodontitis [20,26–28]. There is currently no scientific evidence explaining the association between periodontitis and vascular diseases, i.e. stroke and acute coronary syndrome [29].

Several methods are used to assess arterial calcification. Plain radiographs, ultrasound-based carotid intimal-media-thickness assessment, brain magnetic resonance imaging (MRI) and computer tomography (CT) are methods that are being used to assess vascular pathology including calcifications of blood vessels associated with pathophysiology of vascular brain disease. Studies have shown that, compared with ultrasound plaque imaging, quantification of CT calcification provides additional information in regard to the ability to detect complex brain vascular conditions [1]. Angiography is considered the most accurate method to diagnose atherosclerotic diseases. While this procedure is invasive, complications may occur [30–32]. In other medical diagnostics, Doppler sonography (ultrasonography) methods have been used as a surrogate gold standard while the results obtained with this non-invasive imagining method are similar to those obtained with angiography [33].

Panoramic radiography is a frequently performed diagnostic tool used in the dental practice. Atheromatous plaques, even in the case of partial calcifications, resulting from the deposition of calcium salts, can be observed on panoramic radiographs. Calcifications in the area of the carotid artery bifurcation can be detected on panoramic radiographs in the range of 2–5% of the population [34–41]. Such uni- or bilateral calcifications can present as one or more irregular radio-opacities eventually punctuated by vertical–linear radiolucent areas. The calcification is usually localized ~25 mm posterior and inferior to the mandibular angle and adjacent to the space between vertebrae C3 and C4. Panoramic radiographs may, therefore, be suitable for the detection of such atheromatous calcifications [20,34–36,41].

The aim of the present review was to evaluate the use and value of panoramic radiographs in assessing carotid calcifications in relation to other used methods (gold standards). A second aim was to assess the literature on carotid calcifications defined from panoramic radiographs and concurrent diagnosis of stroke and periodontitis.

To identify studies included in the present review, a literature search was conducted in November 2012. The following phrases were used for screening and selection of studies: (I) (panoramic radiography and carotid calcification) OR (panoramic radiography and carotid calcifications) OR (panoramic radiography and carotid artery atheroma); (II) (carotid calcifications and stroke and panoramic radiography) OR (carotid calcification and dental) OR (carotid calcification and stroke and panoramic radiography) OR (carotid calcifications and dental); and (III) (carotid calcifications and periodontitis and panoramic radiography) OR (carotid calcification and periodontitis and panoramic radiography) OR (carotid calcifications and periodontal disease and panoramic radiography) OR (carotid calcification and periodontal disease and panoramic radiography) OR (periodontitis and carotid calcification) OR (periodontitis and carotid calcifications). Additional references were found in the literature lists of selected papers.

Papers not written in the English language, case reports and animal research were excluded. The abstracts of the publications obtained from the searches were screened. Searching for articles comparing panoramic radiography to other diagnostic methods resulted in 116 potential publications, among which 16 reported on the relationship between carotid calcifications identified from panoramic radiographs and other methods of assessments. When searching for publications on the association between carotid calcification and stroke, 65 potential publications were retrieved. From these publications 10 studies reported on the associations between carotid calcifications and stroke. When searching for publications on the association between carotid calcification and periodontitis, eight potential publications were retrieved. After reading the full text of these publications, four were included in this review.

A summery of findings on the ability to assess carotid calcifications on panoramic radiographs in comparison to other standard procedures to diagnose carotid calcifications is reported in Table I. Doppler sonography is often used as the 'gold standard' for diagnosing carotid calcifications and was compared to diagnosis made on panoramic radiographs in 12 out of the 16 selected studies.

Two studies compared carotid calcifications diagnosed on panoramic radiography to anterior posterior projection radiography [36,42]. According to these two studies [36,42], carotid calcifications and anterior posterior radiography were in concordance in all cases.

Yoon et al. [43] reported that 15% of carotid arteries were interpreted as calcified on panoramic radiography vs 41% on computer tomography. This indicates that the sensitivity to assess carotid calcification on panoramic radiographs is rather low when compared to computer tomography. Damaskos et al. [44] compared digital subtraction angiography to PMX on carotid level and showed a sensitivity of 60% and a specificity of 48%.

Sensitivity and specificity calculations, on a patient level, were reported in nine of the 17 studies. Thus, the sensitivity for panoramic radiography findings of carotid calcifications compared to a diagnosis by Doppler sonography varied, on a patient level from 31.1–100% [28,45–51,44]. A limitation for the identification of calcifications on panoramic radiographs is that the area of interest may not be included on the radiographic image or not detectable due to a low

Table I. Carotid calcifications diagnosed on PMX compared to other methods.

Reference, year	Patient selection and gender	Methods	Results	Comments
Friedlander [36], 1995	134 consecutive cases ≥65 years from a clinic in the US Men = 132 (91%) Women = 13 (9 %) Mean age = 68.2 years	Case series PMX were evaluated for presence or absence of CC by one clinician and compared to anterior posterior cervical spine radiographs CC was defined as: radio-opacities within the soft tissues of the neck at the level of the lower margin of the third cervical vertebra	6 patients had CC on PMX 6/6 in agreement with diagnosis on posterior cervical spine radiographs (100%)	Only 6 cases examined 100% agreement
Friedlander and Altman [42], 2001	52 female patients, with a history of amenorrhea > 12 months ago were recruited from 567 screened cases treated at a clinic in the US Women = 52 Mean age = 70 years Range = 55–90 years	Case series PMX were evaluated for presence or absence of CC by one clinician and compared to anterior posterior cervical spine radiographs CC was defined as: calcification in the area of the carotid bifurcation then underwent radiographic examination of the anterior posterior view of the cervical spine	16/52 patients (31%) had CC on PMX 16/16 in agreement with a diagnosis on posterior cervical spine radiographs (100%)	Only female pat Few cases 100% agreement
Almog et al. [53], 2002	778 consecutive patients, ≥55 years at a University in the US	Case series PMX were retrospectively evaluated for presence or absence of CC by an oral radiologist A vascular surgeon interpreted DS CC was defined as; heterogeneous radio opacities in a vertico-linear orientation adjacent to the hyoid bone, epiglottis and the cervical vertebrae at or above or below intervertebral space C3–4 on PMX	20 patients with PMX findings of CC were evaluated against DS Of the 40 sides with diagnosed CC on PMX, 26/40 had carotid artery stenosis 14/40 did not have carotid artery stenosis on DS	Subject characteristics unknown Site-based analysis on few subjects was performed
Ravon et al. [28], 2003	83 patients who had received a DS and periodontal assessment within 36 months at a University clinic in the US Men = 40 Mean age = 60 years Women = 43 Mean age = 64 years	Blinded case control study PMX were evaluated for presence or absence and size of CC by a periodontist and an oral radiologist CC was defined as; a radiographic agreement of radio opacities in the area of C3–C4	29/83 patients had CC on DS and 32/83 pat had CC on PMX Odds ratio of agreement CC on PMX and DS 32.4 Predictive value positive: 83% Predictive value negative: 74% Sensitivity: 80% Specificity: 83%	High level of accuracy between CC on PMX and DS
Friedlander et al. [45], 2005	1548 patients > 50 years attending oral surgery in the US Men = 1487 (96%) Women = 61 (3.9%) Range = 50–79 years	Case series PMX were analyzed by the authors A radiologist reviewed the DS sonograms CC was defined as: a radio opaque nodular mass adjacent to the cervical vertebra at or below the intervertebral disc level C3–C4 Those with presumptive atheroma's underwent DS	65 patients had CC on PMX DS confirmed all 65 cases 15/65 patients had stenosis > 50%	100% agreement between PMX and DS

Table I. (*Continued*).

Reference, year	Patient selection and gender	Methods	Results	Comments
Bayram et al. [46], 2006	4106 patients ≥40 years randomly chosen from the computer database at a University clinic in Turkey Men = 1678 (41%) Women = 2428 (59%)	Case series PMX were retrospectively evaluated for presence or absence of CC by a radiologist CC was defined as: one or more radio opaque mass adjacent to the cervical vertebrae at or below the intervertebral space between C3 and C4 on PMX 88 patients had CC on PMX 23 patients with CC on PMX consented to DS	DS confirmed in 8/23 patients a CC finding on PMX	Low prevalence of CC Few patients analyzed with DS Mean age and range unclear Low sensitivity
Madden et al. [47], 2007	52 patients ≥18 years who recently had carotid DS examination at a University clinic in the US Men = 32 (61.5%) Women = 20 (38.5%) Mean age = 66.6 years ± 11.6 years Range = 29–88 years	Case series PMX were evaluated for the presence or absence of CC and interpreted by a trained oral radiologist (Cohen $\kappa = 0.73$ between repeated PMX assessments) DS analysis was performed by a cardiologist defining stenosis by a 5 graded scale CC was defined as: any detectable calcifications on PMX.	22/52 had CC on PMX 14/52 had CC on DS PMX specificity = 87.5% PMX sensitivity = 31.1% Negative predictive value = 42.5% (95%CI: 31–55%) Positive predictive value = 78.7% (95% CI: 61–90%)	PMX is not reliable in identifying carotid artery calcification or stenosis when compared to DS
Romano-Sousa et al. [48], 2009	16 patients from the archives of the Health Department in Brazil	Case series 2 oral radiologists interpreted the PMX images The DS images were analyzed by a medical ultrasound specialist CC was defined as: calcifications in the cervical region The radiographic findings of calcifications were compared to the results of color DS	True Positive = 59.4% True Negative = 28.1% False Positive = 9.4% False Negative = 3.1 %	Few patients evaluated Selection criteria unclear Fair agreement between PMX and DS
Damaskos et al. [44], 2008	40 patients with confirmed CC at a University clinic in Greece Men = 31 (77.5%) Women = 9 (22.5%) Mean age men = 69 years Mean age women = 71 years	Case series Digital subtraction angiography confirmed diagnosis and the degree of stenosis. Two radiologists evaluated the PMX images CC was defined as: radio opaque nodular heterogeneous radio opacities in a vertico-linear orientation, adjacent to the cervical vertebra at, above or below the C3–C4 intervertebral disc level or at an angle of 45° from the mid angle and present on PMX	In all cases, histology confirmed the presence of calcium depositions 28/40 patients had CC on PMX PMX sensitivity 70% on a patient level and 60% on carotid level Specificity 48% (on carotid level) Predictive value positive: 62% Predictive value negative: 46%	Low sensitivity Low specificity Low amounts of calcifications may explain the difficulties in finding lesions in PMX
Gouvea et al. [49], 2009	1000 patients ≥50 years at a dental school in Brazil	Case series PMX were reviewed retrospectively and evaluated for calcifications in the carotid region CC was defined as: radio opaque alterations in a vertico-linear orientation or below intervertebral space C3–4.	35 patients had CC on PMX 10/35 patients underwent DS DS detected calcifications 7/10 patients True positive: 70%	Mean age, gender, range and case selection unclear Unclear who interpreted DS Few patients included

Table I. (*Continued*).

Reference, year	Patient selection and gender	Methods	Results	Comments
Yoon et al. [43], 2008	110 patients at a University Clinic in Korea Men = 66 (60%) Women = 44 (40%) Mean age = 65.2 years Range = 50–82 years	Case series 220 carotid arteries were evaluated CC was defined as: heterogeneous radio opacities in a vertico-linear orientation adjacent to the hyoid bone, epiglottis and the cervical vertebrae either above or below the intervertebral space between C3 and C4 CT scans were interpreted by a neuro-radiologist	33/220 carotid arteries had CC on PMX and 90/220 on CT scans Sensitivity = 22% Specificity = 90% Positive predictive value: 61% Negative predictive value: 63%	Unclear patient selection Low sensitivity High specificity
Christou et al. [27], 2010	14 ischemic stroke patients at a University hospital in Switzerland Men = 7 (50%) Women = 7 (50%) Mean age = 71 years ± 10 months	Case series PMX were taken and evaluated for presence or absence of CC by two dentists CC was defined as: an area that extended 1.5 cm inferior and 2.5 cm posterior of the cortical rim of the mid-point of the md angle on PMX DS was taken from all patients	Using DS 21 arteries were diagnosed with CC 15/21 were diagnosed on PMX	Few patients Unclear who interpreted DS Fair sensitivity All 14 stroke patients had CC on PMX
Hoke et al. [57], 2010	411 patients randomly selected with pre-existing cardiovascular disease in Austria Men = 271 (66%) Women = 140 (34%) Mean age = 69 years Range = 62–76 years	Case series PMX were taken and evaluated for the presence or absence of CC The degree of carotid stenosis was measured by DS	226 patients had CC on PMX No statistically significant association between CC detected on PMX and the presence of a significant carotid stenosis (> 25%) or the degree of carotid stenosis on DS (kappa analysis) (κ = 0.08)	Patients with pre-existing cardiovascular disease Sensitivity and specificity not reported PMX findings on CC have no clinical consequence
Ertas and Sisman [50], 2011	105 patients > 40 years University clinic in Turkey Men = 38 (36.2%) Women = 67 (63.8%)	Case control study PMX were evaluated for the presence or absence of CC studied by 2 oral radiologists Patients whose PMX showed CC were included in the study group 70/105 Patients without CC 35/105 were included in the control group CC was defined as: a single discrete radio opaque nodular mass within the soft tissues of the neck located 1.5 cm inferior and 2.5 cm posterior to the cortical rim of the mid-point of the md angle Those with CC on PMX were referred to DS	70/105 patients had CC on PMX in 103/210 arteries 64/105 patients had CC by DS and in 104/210 arteries PMX sensitivity = 80% PMX specificity = 81%	All arteries showing clinically significant stenosis in DS were also diagnosed by PMX as having CC High level of sensitivity and specificity
Johansson et al. [58], 2011	117 patients without previous cerebrovascular event at a University Clinic, Sweden Age range: 18–74 years	Case series PMX were interpreted for calcifications in the area of the carotid arteries by two oral radiologists DS examinations were performed by experienced vascular sonographers	117 patients with evidence of CC on PMX and on anterior–posterior projections were identified DS confirmed calcified atherosclerotic lesion in 108/109 of the patients	Information on gender not reported DS calcified atherosclerotic lesion was found in 99% of the patients with

Table I. (*Continued*).

Reference, year	Patient selection and gender	Methods	Results	Comments
				calcifications of the carotid arteries
Imanimoghaddam et al. [51], 2012	960 patients > 40 years at a University Clinic in Iran Men = 436 (45.4%) Women = 524 (54.6%) Mean age = 55.5 ± 10.6 years	Case series PMX were evaluated by an oral radiologist for the presence or absence of CC CC was defined as: one or more heterogeneous radio opacities in a vertico-linear orientation adjacent to the cervical vertebrae at or below the intervertebral space C3–C4	15/960 patients had CC on PMX 12/15 patients had CC identified by DS Sensitivity: 80%	Large number of patients were screened but few cases studies due to exclusion criteria CC on PMX confirmed in 80% of the cases

CC, Carotid calcification; DS, Doppler sonography; PMX, Panoramic Radiograph; TIA, Transient Ischemic Attack.

degree of calcification [52]. Thus, it is critical that the area of interest is properly projected.

The specificity for panoramic radiography findings of carotid calcifications compared to a diagnosis by Doppler sonography varied from 21.4–87.5% [28,47,50]. Thus, the specificity is higher than the sensitivity, indicating that a negative diagnostic finding on a routine panoramic radiograph should be considered as an indication of no carotid stenosis, assuming the area of interest is available for analysis. A positive finding should be viewed with scrutiny to prevent false interpretations. If warranted, further medical attention is needed. It should also be pointed out that not all calcifications imply significant stenosis and not all atherosclerotic lesions are calcified [53].

The associations between carotid calcifications as defined from panoramic radiographs and stroke are reported from 10 studies (Table II). In a majority of the studies, carotid calcifications were detected in a few cases, limiting the power of the studies. For example, in the study by Kumagai et al. [54] with 2374 individuals, only 95 of these individuals had evidence of carotid calcification on PMX. Among these individuals, only eight of them had a history of stroke. Similarly, in the publication by Lewis and Brooks [55] only 9/1156 individuals had evidence of carotid calcification on PMX. None of these individuals had a history of stroke. In contrast, in the publication by Persson et al. [20], 198/1064 patients had evidence of carotid calcification on PMX. The study population included study individuals ≥60 years and the authors reported a high level of association between carotid calcification on PMX and a history of stroke [20]. In contrast, only 15% were ≥55 years in the previously reported study [55]. In seven of the studies selected fewer than 10 individuals with stroke were identified. In two studies [38,55] the mean age of the patients was lower than age 50, limiting the possibilities of detecting carotid calcification on PMX and that the patients should have a history of stroke at that age. In the study by Christou et al. [27] based on a limited number of individuals with a history of stroke ($n = 14$) all of them demonstrated evidence of carotid calcification on PMX. Based on a limited number of studies with sufficient number of study individuals at potential risk for stroke, radiographic evidence of carotid calcification may indicate individuals at risk for stroke. Thus, studies to assess the presence of carotid calcification on panoramic radiographs and how such findings are related to cerebrovascular events should primarily be performed, including individuals at risk for such events. If studies are performed in populations with a low likelihood of carotid calcification the diagnostic specificity of panoramic radiography to detect such calcifications would approach 100% and with the reverse for test sensitivity.

Studies on the association between carotid calcifications defined from panoramic radiographs and a diagnosis of periodontitis are presented in Table III.

Table II. Carotid calcifications on PMX and stroke.

Reference, year	Patient selection and gender	Methods	Results	Comments
Friedlander et al. [35], 1994	19 patients, Veterans Administration, US Treatment for a cerebrovascular accident Men only Mean age = 66 years Range= 51–78 years	Case series PMX were evaluated for presence or absence of CC by one clinician CC was defined as a radio-opaque nodular mass adjacent to the cervical vertebra at or below the intervertebral disc level C3–C4 Medical charts were reviewed	7/19 patients had CC on PMX Sensitivity: 36.8 In patients with CC on PMX: 5/7 had a history of TIA 2/7 had a history of stroke	Patients with cerebrovascular accidents Few patients Only male patients PMX evaluation with low sensitivity
Carter et al. [38], 1997	Consecutive patients attending a University Clinic, US 1175 patients Men = 573 (45.7%) Women = 602 (54.3%) Mean age = 40.1 years	Case series PMX were evaluated for the presence or absence of CC by an oral radiologist CC was defined as: radio-opacities inferior to the angle of the mandible across from the superior border of the thyroid cartilage opposite the C3 or C4 vertebral bodies All patients were interviewed about their medical history in regards to stroke	42/1175 patients had CC on PMX In patients with CC on PMX: 1/42 of the patients with CC on PMX had a history of TIA:s or prior cerebrovascular accident	Even gender distribution low mean age One case identified among PMX CC positive cases No data on stroke among PMX negative patients identified
Cohen et al. [59], 2002	Random sample of PMX collected Veterans Administration, US 1879 PMX Only men > 55 years of age	Longitudinal case series (follow-up 3.6 years) CC identified on PMX CC was identified as: an area of interest that extended 1.5 cm inferior and 2.5 cm posterior to the cortical rim of the mid-point of the mandibular angle, using a viewing box Charts were reviewed for pre-existing vascular events	71/1879 patients had CC on PMX In patients with CC on PMX: 29/71 had cerebrovascular events during follow-up Stroke 5/29 TIA 2/29	Only male patients Unclear who evaluated PMX 7% (5) patients with CC on PMX developed stroke Most patients with CC had multiple risk factors
Friedlander and Cohen [60], 2007	1409 patients with PMX, Veterans Administration, US Mean age = 66 years Male patients	Longitudinal case-series CC evaluated from PMX CC was defined as: an area of interest extending 2.5 cm inferior and 2.5 cm posterior to the cortical rim of the mid-point of the mandibular angle Medical chart review for TIA/strokes	46/1409 patients had CC on PMX In patients with CC on PMX: 5/46 patients had a history of stroke/TIA. At a later time another 5 patients had a stroke/TIA for a total of 10/46 patients Mean time to an adverse event 2.9 years	Approximately 20% with CC finding on PMX have or will experience TIA
Kumagai et al. [54], 2007	2374 patients receiving treatment in an oral surgery clinic, Japan Men = 915 (38.5%) Women = 1459 (61.4%) Range = 2–92 years	Case series CC evaluated from PMX by two examiners CC was defined as: a radio opaque nodular mass independent of the hyoid bone, adjacent to the cervical vertebra at or below the C3–C4 intervertebral disc level The medical history was reviewed	95/2374 patients had CC on PMX 40/2374 had a history of stroke 8/40 had CC and stroke The relationship between CC and history of stroke ($p < 0.001$)	There is a relationship between PMX evidence of CC and a history of stroke
Lewis and Brooks [40], 1999	1156 patients admitted to Emergency University Clinic with PMX, US Men = 554 Women = 602 Mean age = 32 years	Case report PMX were evaluated for the presence or absence of CC by one author CC was defined as: visualization of cervical spine presence of radiographic artifacts and abnormal radio opacity in the region of the right and left common carotid artery Medical chart review	9/1156 patients had CC on PMX None of the patients had a history of stroke	Large study population, case series, few cases identified with CC. None of these patients had a history of stroke

Table II. (*Continued*).

Reference, year	Patient selection and gender	Methods	Results	Comments
Ravon et al. [28], 2003	83 patients with a DS assessment with or without positive results were identified from clinical records at a University clinic, US	Blinded case control study PMX were evaluated for presence or absence and size of CC by a periodontist and an oral radiologist CC was defined as; a radiographic agreement of radio opacities in the area of C3–C4	5/29 patients with CC had a history of stroke None of the 54 patients without CC had a history of stroke	Absence of CC on PMX had a high likelihood of no history of stroke
Tamura et al. [61], 2005	2568 patients at an oral surgery University clinic, Japan Men = 1221 (47.5%) Women = 1347 (52.5%) Mean age = 62.2 years Range = 50–70 years	Case series PMXs were retrospectively evaluated for the presence or absence of CC by three clinicians CC was defined as: a radio-opaque nodular mass adjacent to the cervical vertebrae at or below the intervertebral space C3 and C4 Medical records and follow-up interviews with patients having CC	106/2568 patients had CC on PMX In patients with CC on PMX: 2 patients died within 3.5 years from cerebrovascular disease	Large number of individuals studied, few cases with CC and very few reported with cerebrovascular complications
Tanaka et al. [62], 2006	659 patients 80-year old residents, Japan Men = 262 (39.7%) Women = 397 (60.3%)	Case series PMXs were retrospectively evaluated for the presence or absence of CC by one expert radiologist CC was defined as: a radio opaque nodular mass adjacent to the cervical vertebrae at or below the intervertebral space between C3 and C4 Baseline and 5-year follow-up examination Second examination years 5: occurrence of the same vascular events were collected from 191 of the individuals Causes of death were evaluated in 108 individuals who had died within 5 years after baseline examination	33/657 individuals had CC on PMX. In patients with CC, 3/33 had a history of cerebrovascular disease. In patients without CC, 10/626 had cerebrovascular diseases ($p < 0.05$) 191 individuals completed a second examination 8/191 had CC at baseline None of the 8 individuals with CC experienced a cerebrovascular incidence during follow-up, whereas 10/183 without CC had such events	Old individuals were studied CC on PMX had a low predictive value in identifying those at risk for cerebrovascular disease.
Christou et al. [27], 2010	14 patients with Ischemic stroke University Hospital Switzerland and with DS recordings Men = 7 (50%) Women = 7 (50%) Mean age = 71	Case series PMX were evaluated for the presence or absence of CC by two dentists CC was defined as: an area that extended 1.5 cm inferior and 2.5 cm posterior of the cortical rim of the mid-point of the md angle	All 14 stroke cases had PMX evidence of CC Sensitivity: 100% 15/21 CC on individual left/right sides detected on DS and also found on PMX Sensitivity: 71.4%	Few individuals High degree of PMX detection on a subject-based level in those with a history of stroke

CC, Carotid calcifications; PMX, Panoramic Radiograph; TIA, Transient Ischemic Attack.

Table III. Carotid calcifications on panoramic radiographs and periodontitis.

Reference, year	Patient selection and gender	Definition of periodontitis	Methods	Results	Comments
Beckström et al. [26], 2007	201 pre-treatment cancer patients Men = 63 (31.3%) Women = 138 (68.6%) Mean ag e= 52.1 years Range = 11–87 years	> 1 mm bone loss on PMX	CC on PMX were evaluated by an oral radiologist CC was defined as: measures of soft tissue triangles anterior to the third and fourth cervical vertebrae. Carotid regions of interest were zoomed Alveolar bone loss was measured on Digital PMX as root length from CEJ-root tip. Distance from CEJ-alveolar crest minus 1 was divided by the root length and multiplied by 100 (PRI index)	23/47 patients had unilateral CC from PMX and with 24.2% alveolar bone level. 24/47 patients had bilateral CC from PMX and with 25.7% alveolar bone level Patients with no CC – 10.4% alveolar bone level and significantly different from those with uni or bilateral CC	Pre-treatment cancer patients Significant correlation CC - ABL loss
Persson et al. [20], 2002	1064 patients from Seattle, US and Vancouver, Canada Men = 485 (45.6%) Women = 579 (54.4%) Mean age = 67.2 ± 4.7 years Range = 60–75 years	Pocket depth ≥5 mm Clinical attachment level ≥4 mm Bone loss on PMX = the distance between the bone level and the CEJ ≥4 mm	CC on PMX was evaluated by two examiners CC was defined as: a vertically aligned radiopaque nodular structure appearing adjacent to the cervical vertebral space C3–C4 The extent of alveolar horizontal bone height was assessed using an index system 0–3	181/1064 patients had CC on PMX Alveolar bone loss in 516/1064 patients Odds ratio association periodontitis and CC was 2.1 (95% CI: 1.3–3.2, $p < 0.001$)	Significant association between periodontitis and CC
Ravon et al. [28], 2003	83 patients who had received a DS and periodontal assessment within 36 months at a University clinic in the US Men = 40 Mean age = 60 years Women = 43 Mean age = 64 years	If ≥30% of the teeth had a distance cement–enamel junction to bone level ≥4 mm	CC on PMX were evaluated by a periodontist and an oral radiologist CC was defined as: a radiographic agreement of radio opacities in the area of C3–C4	32/83 patients had CC on PMX 29/32 patients had CC on DS 24/29 of the DS positive subjects had periodontitis 6/54 of DS negative subjects had periodontitis The odds ratio that patients with periodontitis had CC was 38.4 (95% CI: 10.6–138.7, $p < 0.001$)	A dose–response relationship between the size of CC and the severity of periodontitis was identified on PMX
Tiller et al. [56], 2011	824 patients from a dental practice in Germany Men = 349 (42%) Women = 475 (58%) Mean age= 48.32 ± 16.52 years	Periodontal risk according to: distance CEJ–bone, in relation to patient age including a bone loss factor for missing teeth (low, moderate, high)	CC on PMX were examined by a calibrated investigator Bone loss level = dividing the maximum bone loss by root length Bone loss/Age Index = Dividing the bone loss value by patient age	74/824 patients had CC on PMX In patients with low risk of periodontitis 9/282 had CC In patients with moderate periodontitis risk 33/335 had CC In patients with high periodontitis risk 32/107 had CC	Statistical analysis failed to show a significant association between periodontitis risk and CC

CC, Carotid calcifications; DS, Doppler sonography; PMX, Panoramic radiography.

Four studies were retrieved. When periodontitis was defined as alveolar bone loss > 4 mm between the cement–enamel junction and bone level at ≥30% of sites, a dose–response relationship between the size of the carotid calcification and the severity of periodontitis on panoramic radiographs was reported [28]. Using the same definition of periodontitis, Persson et al. [20] also reported an association between carotid calcification on panoramic radiographs and periodontitis. In individuals with periodontitis, defined as > 1 mm bone loss on a panoramic radiograph, 25.7% of individuals with bilateral carotid calcifications had periodontitis compared to 10.4% among those without carotid calcifications [26]. In contrast, Tiller et al. [56] failed to show a significant periodontitis risk and radiographic evidence of carotid calcification on PMX when multivariate regression analysis was performed. It should also be recognized that the study by Tiller et al. [56] studied the risk of periodontitis and not a diagnosis of periodontitis.

Although it requires training to detect calcifications on panoramic radiographs, analysis of panoramic radiographs for carotid calcification made under optimal conditions with the help of view boxes and magnifying lenses could be a useful tool in assessing individuals at risk for stroke. The use of digital images could also enhance the ability to detect carotid calcifications. A shortcoming with digital panoramic images is the reduced dimensions resulting in that such images often do not include the area of interest for detection of carotid calcifications. On the other hand, digital radiographs can be adjusted for contrast. Color enhancement through computer programs may also facilitate the detection of radio-opacities, suggesting calcified carotid arteries.

Conclusions

The study designs, selection and number of study individuals and the age of the included individuals differed among the studies, making it difficult to draw any definite conclusions. The results of the present literature review indicate, though, that carotid calcifications are more frequently found in panoramic radiographs from older individuals and that periodontitis as evidence of alveolar bone loss was more often identified among individuals with radiographic evidence of carotid calcifications. The sensitivity of panoramic radiographs to identify carotid calcifications against Doppler sonography is in most studies low. The absence of radiographic evidence of carotid calcification on PMX is consistent with negative findings using Doppler sonography and, thus, the specificity is high. A positive diagnostic finding on a routine panoramic radiograph suggests further medical attention.

There is a shortage of well-designed studies in older dentate individuals assessing the associations between periodontitis and radiographic evidence of carotid calcification on panoramic radiographs and with a further relationship to a history of stroke or other cardiovascular diseases. The majority of the studies available for review can be considered as case series and there are few, if any, published longitudinal data or clinical follow-up studies beyond assessments with Doppler sonography and angiography.

***Declaration of interest*:** The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

References

[1] Bos D, Ikram MA, Elias-Smale SE, Krestin GP, Hofman A, Witteman JC, et al. Calcification in major vessel beds relates to vascular brain disease. Arterioscler Thromb Vasc Biol 2011; 31:2331–7.

[2] American Heart Association. Heart disease and stroke statistics: 2008 update. American Heart Association. Circulation 2008;117:e25–146.

[3] Hubar JS. Carotid artery calcification in the black population: a retrospective study on panoramic radiographs. Dentomaxillofac Radiol 1999;28:348–50.

[4] Nadareishvili ZG, Rothwell PM, Beletsky V, Pagniello A, Norris JW. Long term risk of stroke and other vascular events in patients with asymptomatic carotid artery stenosis. Arch Neurol 2002;59:1162–6.

[5] Zhadanov VS, Sternby NH. Monitoring of atherosclerosis. Int J Cardiol 2004;95:39–42.

[6] Madhuri V, Chandra S, Jabbar A. Age associated increase in intima media thickness in adults. Indian J Physiol Pharmacol 2010;54:371–5.

[7] Schneer S, Bachar GN, Atar E, Koronowski R, Dicker D. Evaluation of Framingham and systematic coronary risk evaluation scores by coronary computed tomographic angiography in asymptomatic adults. Am J Cardiol 2013;111:700–4.

[8] Shah S, Casas JP, Drenos F, Whittaker J, Deanfield J, Swerdlow DI, et al. Causal relevance of blood lipid fractions in the development of carotid atherosclerosis Mendelian randomization analysis. Circ Cardiovasc Genet 2013;6:63–72.

[9] Giudice R, Izzo R, Manzi MV, Pagnano G, Santoro M, Rao MA, et al. Lifestyle-related risk factors, smoking status and cardiovascular disease. High Blood Press Cardiovasc Prev 2012;19:85–92.

[10] Reunanen A. Mortality in type 2 diabetes. Ann Clin Res 1983; 15:26–8.

[11] Tousoulis D, Ntarladimas I, Antoniades C, Vasiliadou C, Tentolouris C, Papageorgiou N, et al. Acute effects of different alcoholic beverages on vascular endothelium, inflammatory markers and thrombosis fibrinolysis system. Clin Nutr 2008;27:594–600.

[12] Lindsberg PJ, Grau AJ. Inflammation and infections as risk factors for ischemic stroke. Stroke 2003;34:2518–32.

[13] Carrion J, Scisci E, Miles B, Sabino GJ, Zeituni AE, Gu Y, et al. Microbial carriage state of peripheral blood dendritic cells (DCs) in chronic periodontitis influences DC differentiation, atherogenic potential. J Immunol 2012;189:3178–87.

[14] Beck J, Garcia R, Heiss G, Vokonas PS, Offenbacher S. Periodontal disease and cardiovascular disease. J Periodontol 1996;67:1123–37.

[15] Destefano F, Anda RF, Kahn HS, Williamson DF, Russel CM. Dental disease and risk of coronary heart disease and mortality. BMJ 1993;306:688–91.

[16] Dörfer CE, Becher H, Ziegler CM, Kaiser C, Lutz R, Jörss D, et al. The association of gingivitis and periodontitis with ischemic stroke. J Clin Periodontol 2004;31:396–401.
[17] Grau AJ, Buggle F, Ziegler C, Schwarz W, Meuser J, Tasman AJ, et al. Association between acute cerebrovascular ischemia and chronic and recurrent infection. Stroke 1997;28: 1724–9.
[18] Grau AJ, Becher H, Ziegler CM, Lichy C, Buggle F, Kaiser C, et al. Periodontal disease as a risk factor for ischemic stroke. Stroke 2004;35:496–501.
[19] Joshipura KJ, Hung HC, Rimm EB, Willett WC, Ascherio A. Periodontal disease, tooth loss, and incidence of ischemic stroke. Stroke 2003;34:47–52.
[20] Persson RE, Hollender LG, Powell VL, MacEntee M, Wyatt CC, Kiyak HA. Assessment of periodontal conditions and systemic disease in older subjects. II. Focus on cardiovascular diseases. J Clin Periodontol 2002;29:803–10.
[21] Kinane D, Bouchard P; Group E of European Workshop on Periodontology. Periodontal diseases and health. Consensus Report of the Sixth European Workshop on Periodontology. J Clin Periodontol 2008;35:333–7.
[22] Bouchard P, Boutouyrie P, Dáiuto F, Deanfield J, Deliargyris E, Fernandez- Avvilés F, et al. European workshop in periodontal health and cardiovascular disease-consensus report. Euro Heart J 2010;12:13–22.
[23] Desvarieux M, Demmer RT, Rundek T, Boden-Albala B, Jacobs DR Jr, Papapanou PN, et al. Relationship between periodontal disease, tooth loss, and carotid artery plaque: the Oral Infections and Vascular Disease Epidemiology Study (INVEST). Stroke 2003;34:2120–5.
[24] Söder PO, Söder B, Nowak J, Jogestrand T. Early carotid atherosclerosis in subjects with periodontal diseases. Stroke 2005;36:1195–2000.
[25] Ebrahim S, Papacosta O, Whincup P, Wannamethee G, Walker M, Nicolaides AN, et al. Carotid plaque, intima media thickness, cardiovascular risk factors, and prevalent cardiovascular disease in men and women: the British Regional Heart Study. Stroke 1999;30:841–50.
[26] Beckström BW, Horsley SH, Scheetz JP, Khan Z, Silveira AM, Clark SJ, et al. Correlation between carotid area calcifications and periodontitis: a retrospective study of digital panoramic radiographic finding in pre-treatment cancer patients. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2007;103:359–66.
[27] Christou P, Leemann B, Scimmel M, Kiliaridis S, Müller F. Carotid artery calcification in ischemic stroke patients detected in a standard dental panoramic radiographs a preliminary study. Adv Med Sci 2010;55:26–31.
[28] Ravon NA, Hollender LG, McDonald V, Persson GR. Signs of carotid calcification from dental panoramic radiographs are in agreement with Doppler sonography results. J Clin Periodontol 2003;35:277–90.
[29] Lockhart PB, Bolger AF, Papapanou PN, Osinbowale O, Trevisan M, Levison ME, et al. American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee of the Council on Cardiovascular Disease in the Young, Council on Epidemiology and Prevention, Council on Peripheral Vascular Disease, and Council on Clinical Cardiology. Periodontal disease and atherosclerotic vascular disease: does the evidence support an independent association?: a scientific statement from the American Heart Association. Circulation 2012;125:2520–44.
[30] Cinat M, Lane CT, Pham H, Lee A, Wilson SE, Gordon I. Helical CT angiography in the preoperative evaluation of carotid artery stenosis. J Vasc Surg 1998;28:290–300.
[31] Moneta GL, Edwards JM, Chitwood RW, Taylor LM Jr, Lee RW, Cummings CA, et al. Correlation of North American Symptomatic Carotid Endarterectomy Trial (NASCET) angiographic definition of 70% to 99% internal carotid artery stenosis with duplex scanning. J Vasc Surg 1993; 197:152–7.
[32] Rossouw JE. Lipid-lowering interventions in angiographic trials. Am J Cardiol 1995;28:76 86C–92C.
[33] Huber P. Cerebral angiography. 2nd ed. New York: Thieme; 1982. pp 290–3; 257–82.
[34] Friedlander AH, Lande A. Panoramic radiographic identification of carotid arterial plaques. Oral Surg Oral Med Oral Pathol 1981;52:102–4.
[35] Friedlander AH, Manesh F, Waster lain CG. Prevalence of detectable carotid artery calcifications on panoramic radiographs of recent stroke victims. Oral Surg Oral Med Oral Pathol 1994;77:669–73.
[36] Friedlander AH. Identification of stroke-prone patients by panoramic and cervical spine radiography. Dentomaxillofac Radiol 1995;24:160–4.
[37] Friedlander AH, Friedlander IK. Panoramic dental radiography: an aid in detecting individuals prone to stroke. Br Dent J 1996;181:23–6.
[38] Carter LC, Haller AD, Nadarajah V, Calamel AD, Aguirre A. Use of panoramic radiography among an ambulatory dental population to detect patients at risk of stroke. J Am Dent Assoc 1997;128:977–84.
[39] Friedlander AH, Friedlander IK, Yueh R, Littner MR. The prevalence of carotid atheromas seen on panoramic radiographs of patients with obstructive sleep apnea and their relation to risk factors for atherosclerosis. J Oral Maxillofac Surg 1999;57:516–21.
[40] Lewis DA, Brooks SL. Carotid artery calcification in a general dental population: a retrospective study of panoramic radiographs. Gen Dent 1999;47:98–103.
[41] Almog DM, Tsimidis K, Moss ME, Gottlieb RH, Carter LC. Evaluation of training program for detection of carotid artery calcifications on panoramic radiographs. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2000;90:111–17.
[42] Friedlander AH, Altman L. Carotid artery atheromas in postmenopausal women. Their prevalence on panoramic radiographs and their relationship to atherogenic risk factors. J Am Dent Assoc 2001;132:1130–6.
[43] Yoon SJ, Yoon W, Kim OS, Lee JS, Kang BC. Diagnostic accuracy of panoramic radiography in the detection of calcified carotid artery. Dentomaxillofac Radiol 2008;37:104–8.
[44] Damaskos S, Griniatsos J, Tsekouras N, Georgopoulos S, Klonaris C, Bastounis E, et al. Reliability of panoramic radiograph for carotid atheroma detection: a study in patients who fulfill the criteria for carotid endarterectomy. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2008;106: 736–42.
[45] Friedlander AH, Garrett NR, Chin EE, Baker JD. Ultrasonographic confirmation of carotid artery atheromas diagnosed via panoramic radiography. J Am Dent Assoc 2005;136: 635–40.
[46] Bayram B, Uckan S, Acikgoz A, Müderrisoglu H, Aydinalp A. Digital panoramic radiography: a reliable method to diagnose carotid artery atheromas? Dentomaxillofac Radiol 2006;35: 266–70.
[47] Madden RP, Hodges JS, Salmen CW, Rindal DB, Tunio J, Michalowicz BS, et al. Utility of panoramic radiographs in detecting cervical calcified carotid atheroma. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2007;103: 543–8.
[48] Romano-Sousa CM, Krejci L, Medeiros FM, Graciosa--Filho RG, Martins MF, Guedes VN, et al. Diagnostic agreement between panoramic radiographs and color Doppler images of carotid atheroma. J Appl Oral Sci 2009; 17:45–8.
[49] Gouvea AF, Vargas PA, Jorge J, Lopes MA. Using panoramic radiographs to detect carotid artery calcifications: are they a helpful diagnostic tool? Gen Dent 2009;57:480–4.

[50] Ertas ET, Sisman Y. Detection of incidental carotid artery calcifications during dental examinations: panoramic radiography as an important aid in dentistry. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2011;112:e11–17.
[51] Imanimoghaddam M, Rah Rooh M, Mahmoudi Hashemi E, Javadzade Blouri A. Doppler sonography confirmation in patients showing calcified carotid artery atheroma in panoramic radiography and evaluation of related risk factors. J Dent Res Dent Clin Dent Prospects 2012;6:6–11.
[52] Friedlander AH. Odd practice. Br Dent J 2009;207:464–5.
[53] Almog DM, Horev T, Illig KA, Green RM, Carter LC. Correlating carotid artery stenosis detected by panoramic radiography with clinically relevant carotid artery stenosis determined by duplex ultrasound. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2002;94:768–73.
[54] Kumagai M, Yamagishi T, Fukui N, Chiba M. Carotid artery calcification seen on panoramic dental radiographs in the Asian population in Japan. Dentomaxillofac Radiol 2007;36:92–6.
[55] Lewis DA, Brooks SL. Carotid artery calcification in a general dental population: a retrospective study of panoramic radiographs. Gen Dent 1999;47:98–103.
[56] Tiller R, Bengel W, Rinke S, Ziebolz D. Association between carotid area calcifications and periodontal risk: a cross sectional study of panoramic radiographic findings. BMC Cardiovasc Disord 2011;11:67.
[57] Hoke M, Schmidt B, Schillinger T, Kluger W, Wiesbauer F, Mlekusch W, et al. Evidence of carotid atherosclerosis in orthopantomograms and the risk for future cardiovascular events. Vasa 2010;39:298–304.
[58] Johansson EP, Ahlqvist J, Garof MM, Karp K, Jäghagen EL, Wester P. Ultrasound screening for asymptomatic carotid stenosis in subjects with calcifications in the area of the carotid arteries on panoramic radiographs: a cross-sectional study. BMC Cardiovasc Disord 2011;11:44.
[59] Cohen SN, Friedlander AH, Jolly DA, Date L. Carotid calcification on panoramic radiographs: an important marker for vascular risk. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2002;94:510–14.
[60] Friedlander AH, Cohen SN. Panoramic radiographic atheromas portend adverse vascular events. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2007;103:830–5.
[61] Tamura T, Inui M, Nakase M, Nakamura S, Okumura K, Tagawa T. Clinico-statistical study of carotid calcification on panoramic radiographs. Oral Dis 2005;11:314–17.
[62] Tanaka T, Morimoto Y, Ansai T, Okabe S, Yamada K, Taguchi A, et al. Can the presence of carotid artery calcification on panoramic radiographs predict the risk of vascular diseases among 80-year-olds? Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2006;101: 777–83.