RESEARCH ARTICLE

Carotid calcification in panoramic radiographs: radiographic appearance and the degree of carotid stenosis

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Objectives: Approximately 7% of patients examined with panoramic radiographs (PRs) for odontological reasons, and with incidental findings of carotid artery calcification (CAC), have significant ($\geq 50\%$) carotid stenosis (SCS). The aim of this study was to determine if the radiographic appearance of CACs in PRs could be categorized such that we could improve the positive-predictive value (PPV) for SCS detection.

Methods: This cross-sectional study included 278 patients with CACs identified by PRs, 127 with SCS and 151 without SCS. CACs were categorized based on the following appearances: (1) single, (2) scattered or (3) vessel-outlining. Correlates were derived for each category according to positivity or not for SCS in the corresponding neck sides. For a representative adult population (in dentistry) presenting with CACs in PRs, PPVs for SCS prediction were then calculated for three subgroups based on different combinations of appearances (2) and/or (3).

Results: Vessel-outlining CACs corresponded to 65% of neck sides with SCS vs 47% without SCS ($p < 0.001$). Single CACs corresponded to 15% of neck sides with SCS vs 27% without SCS ($p = 0.006$). Scattered CACs corresponded to 20% of neck sides with SCS vs 26% without SCS ($p = 0.127$). In the representative population, the PPVs for SCS detection were comparable (7.2–7.8%) for all three subgroups and when the presence of a CAC is the sole criterion (7.4%).

Conclusions: Stratifying the radiographic appearance of CACs in PRs does not improve the PPV for SCS detection. Whether different radiographic appearances are associated with future risk of stroke, or other cardiovascular events, remains unknown.

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Introduction

Atherosclerosis is a multifactorial and progressive disease that affects almost all older/elderly individuals, although to varying degrees of severity.¹ Disease development is

preferred at sites located near arterial branches and curvatures, e.g. the carotid bifurcation.¹ Extensive atherosclerotic plaques that narrow the carotid lumen ($\geq 50\%$) lead to the pathology termed significant carotid stenosis (SCS).² SCS is a risk factor for future vascular events including stroke and myocardial infarction.³ The severity of carotid stenosis is usually diagnosed and measured with carotid ultrasound. Calcifications within atherosclerotic lesions, independent of

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size, are commonly found in adults of 40 years of age and older,⁴ although there seems to be no correlation between the degree of calcification and extent of stenosis.^{5,6}

Carotid artery calcification (CAC) identified in panoramic radiographs (PRs) have a prevalence of 3–15% in the general adult population, with 99% of extirpated carotid plaques found to be calcified.^{7–11} CAC detection in PRs have a positive-predictive value (PPV) of 7% for the detection of SCS for those individuals in the general adult population (in dental care) eligible for asymptomatic carotid endarterectomy (*i.e.* 7% of the patients with CACs detected in PRs have a SCS).⁷ PRs reveal CACs in 84% of patients with verified carotid stenosis $\geq 50\%$.¹² However, compared with carotid ultrasound, PRs have a low to moderate accuracy in diagnosing SCS and should not be used for population screening.¹³ It has been suggested that incidental findings of CACs in PRs can be used to identify a subpopulation that has an increased risk for stroke, since an increased prevalence of SCS ($>5\%$) was observed with carotid ultrasound in male patients presenting with CACs in PRs.⁷ Given that the PPV is used to establish the reliability of a test, it would be desirable from a clinical point of view to refine the test such that a higher PPV is achieved, inclusive of both male and female patients.⁷

Refining this methodology necessitates a working knowledge of the limitations of the projection and acquisition of a PR, as well as an appreciation of the challenges and expertise needed to interpret CAC positivity. For example, CACs have to be differentiated from other calcified anatomical or pathological conditions that can occur within the area of the carotid arteries.^{9,14,15} Absolute measurements of CACs in PRs are unreliable because of variations in magnification, depending on the position of the CAC in relation to the sharp image layer, and can be misleading as parts of the CAC may be below the lower border, or dorsal to the posterior border of the panoramic image, as well as superimposed on other anatomical or pathological structures.¹² CACs in PRs are described as nodular, verticolinear, irregular and heterogeneous radio-opacities at the level of the third/fourth cervical vertebra that sometimes appear as two parallel radio-opacities.^{9,15–18} To date there has been no attempt to categorize CACs in PRs based on radiographic appearance or to analyse whether a specific feature is more prevalent among individuals with SCS.

The aims of this cross-sectional study were to determine the prevalence of various features of CACs in the neck sides of individuals with and without SCS and to establish if specific features of CACs, or subgroups of feature combinations, could improve the PPV of detecting asymptomatic SCS in a representative adult population in dentistry.

Methods and materials

Participants

The study recruited 316 consenting and consecutively sampled patients who were examined with PR from

August 2007 to January 2011 at the Department of Oral and Maxillofacial Radiology, Umeå University Hospital, Umeå, Sweden. The study group was created from two previously described groups: Group A consisted of patients who had undergone odontological examination ($n = 167$) and were subsequently referred for carotid ultrasound examination due to CACs in PRs and frontal radiographs.⁷ Group B consisted of patients with verified carotid stenosis ($n = 149$) referred from the Stroke Center, Umeå University Hospital, Umeå, Sweden, for PR.¹² At re-evaluation using PRs alone, 163 patients from Group A and 115 patients from Group B were found to present with CACs. These 278 patients (188 males and 90 females) comprised the patient cohort in this study. Their mean age was 68 years (standard deviation, 6.6; range 45–86 years). These patients were divided into two groups based on the presence or absence of SCS; 46% (127/278) of patients were SCS positive (88 males and 39 females). SCS was present in 29% (164/556) of neck sides, and 84% (138/164) of neck sides with SCS presented with ipsilateral CACs in PRs. CACs in PRs were observed in 85% (473/556) of neck sides (Figure 1). In Group A, 7% (12/163) of patients had SCS, all of whom were male (12/112 males and 0/51 female).

The Regional Ethical Board in Umeå approved this study (Dnr 07-004M), which complies with the Helsinki declaration.

Modalities

Carotid ultrasound examinations were performed with a Siemens Acuson Sequoia™ 512 (Siemens, Mountain View, CA) by experienced sonographers and atherosclerotic carotid plaques were graded by translating flow velocities into North American Symptomatic Carotid Endarterectomy Trial-type stenoses.¹⁹ An Orthopantomograph® OP100 (Tuusula, Finland) was used for the panoramic examinations according to standard protocols. Images were analysed during optimal dim light conditions. More detailed descriptions of these procedures have been published previously.^{7,12}

Categories of carotid calcification

A separate observer (MG) first re-evaluated all PRs with the intention of categorizing the different radiographic appearances of CACs. The chosen categories were: (1) single CACs or a tight conglomerate of several calcifications, (2) scattered CACs with at least two calcified nodules and (3) parallel and vertically aligned single or scattered CACs that give the impression of outlining the anterior and posterior contours of a vessel, *i.e.* vessel-outlining (Figure 2). After these categories were defined, the separate observer (MG) provided oral and written descriptors of category features to two specialists in oral and maxillofacial radiology (JA and ELJ). They were also provided with 30 PRs with the three categories represented for calibration purpose. All 278 PRs were then mixed and analysed by the two observers (JA and ELJ), who were blinded to the presence or absence of SCS and

Figure 1 Flow chart of our patient cohort, with and without significant carotid stenosis (SCS), for whom carotid artery calcifications (CAC) were identified (or not) during panoramic radiographic (PR) examinations.

were free to adjust brightness and contrast levels during analyses. Consensus was reached in case of disagreement. Values for subjective variability (interrater agreement) were then calculated.

Analyses of category occurrence

Correlates for the different PR categories (groups 1–3) in relation to SCS were derived in two separate analyses. The first was at the neck side level of all material (i) and the second analysis was at the patient level (ii), inclusive of all patients in Group A, to evaluate if any category or combination of categories, on either neck side, could identify a subpopulation with a PPV for SCS detection over and above that already reported. Participants of Group A were chosen for the second analysis since that group most represents the adult population within dentistry with CAC in PR.

In analysis (i), the prevalence of the defined categories was calculated and analysed for significant differences in neck sides, with or without SCS. In analysis (ii), PPVs were calculated for different combinations including 95% confidence interval. PPVs were also tested for statistical significance (*i.e.* PPV > 5%). The combinations tested were based on the results from the first analysis (i).

Statistics

Statistical analyses were performed with the IBM SPSS® Statistics v. 22 package (IBM Corp., New York, NY; formerly SPSS Inc., Chicago, IL). Significant differences between groups were evaluated using the χ^2 (exact two sided) or binary logistic interaction test. A 95% confidence interval was calculated for all PPVs. The non-parametric binomial test was used to test for a statistically significant PPV (*i.e.* >5%). The level of

Figure 2 Examples of the radiographic appearance of carotid artery calcifications (CAC) in panoramic images according to the three evaluated categories: (a) single CAC or a tight conglomerate of several CACs, (b) scattered CACs with at least two calcified nodules, and (c, d) parallel and vertically aligned single or scattered CACs that give the impression of outlining the anterior and posterior contours of a vessel, *i.e.* vessel-outlining.

significance was set at $p < 0.05$. Interrater agreement was evaluated by calculating κ values.

Results

Radiographic appearance and degree of stenosis at the neck side level
CACs in PRs characterized as vessel-outlining were seen in 65% (90/138) of neck sides with SCS compared with 47% (156/335) without SCS, $p < 0.001$ (χ^2 test). This distribution was similar for males (64% of neck sides with SCS *vs* 45% without) and for females (68% of neck sides with SCS *vs* 50% of neck sides without), $p = 0.93$ (binary logistic interaction test). Single CACs were observed in 15% (21/138) of neck sides with SCS and in 27% (91/335) without SCS, $p = 0.006$ (χ^2 test). The final category, scattered CACs, were observed in 20% (27/

138) of neck sides with SCS and in 26% (88/335) of neck sides without SCS, $p = 0.127$ (χ^2 test; [Table 1](#)).

The interrater agreement between the two observers (JA and ELJ) for each category (including neck sides with no CAC) was moderate (κ value 0.68). However, interrater agreement of a vessel-outlining feature was substantial (κ value 0.78), then fell to moderate for single features (κ value 0.61).

Radiographic appearance and degree of stenosis at the patient level
In a representative adult population (in dentistry) presenting with CACs in PRs (Group A, $n = 163$), the outcome regarding PPV in subgroups of patients with the following inclusion criteria based on two different radiographic appearances of CAC were analysed: (Subgroup I) patients with vessel-outlining CACs on any side; (Subgroup II) patients with vessel-outlining CACs on any side and patients with bilateral scattered CACs;

Table 1 Distribution of the radiographic appearance of carotid calcifications in panoramic radiographs in patient neck sides with or without significant carotid stenosis

Radiographic appearance of carotid calcification in panoramic radiographs	Neck sides		p-value ^a
	Significant carotid stenosis (%) (n = 138)	No significant carotid stenosis (%) (n = 335)	
Single	21 (15)	91 (27)	0.006 ^b
Scattered	27 (20)	88 (26)	0.127
Vessel-outlining	90 (65)	156 (47)	<0.001 ^c

^a χ^2 test (exact two sided).
^bA statistically significant reduction in the correlate between a single carotid calcification and significant carotid stenosis was identified.
^cA statistically significant increase in the correlate between a vessel-outlining carotid calcification and significant carotid stenosis was identified.

and (Subgroup III) patients with vessel-outlining CACs on any side and patients with scattered CACs on any side. Patients only presenting a single CAC were not included in the analysis. The resulting PPVs were very similar in the three subgroups, ranging from 7.2% to 7.8%. When comparing 95% confidence intervals, there were no discernible improvements in PPV compared with the conventional method (7.4%), where CAC positivity, regardless of appearance, is the sole criterion (Table 2). The binomial test revealed no significant differences for PPV compared with the conventional method ($p = 0.12$), even when considering Subgroup I ($p = 0.14$), in which the highest PPV was achieved.

Of concern was that some patients with SCS and CAC were missed in the different subgroups. Missed SCS cases amounted to 33% (4/12), 25% (3/12) and 17% (2/12) in Subgroup I, II and III, respectively. On the other hand, false positives were reduced by 37% (56/151), 26% (40/151) and 25% (38/151) in Subgroup I, II and III, respectively.

Discussion

The hypothesis in the present study was that an enhanced selection process based on the radiographic appearance of CACs found in PRs could lead to an improved PPV for SCS detection. Although there was a clear association between vessel-outlining calcifications and SCS, it did not result in a higher PPV when applied to a representative adult population in dentistry, nor did any other subgroup with the defined combinations of radiographic appearances.

According to results from a previous study, screening with carotid ultrasound for SCS is indicated in males, eligible for asymptomatic carotid endarterectomy, when CACs are revealed by PRs. Indication for this method was based on the statistical significance of the relevant subpopulation in terms of the requisite 5% PPV threshold.⁷ However, recent studies suggest that indications for surgical intervention in patients with asymptomatic SCS will change in the near future and that factors (*e.g.* plaque morphology) other than the degree of carotid stenosis have been identified that also predispose to future cardiovascular events.^{20,21} The PPV threshold for carotid ultrasound examination might also be raised due to recent findings, but to what level remains uncertain. Therefore, if screening with carotid ultrasound of patients

with CACs in PRs is indicated in the future, it is of importance to identify methods that can improve PPV for SCS detection with carotid ultrasound.

Patients with CACs are at higher risk of future cardiovascular events than patients without CACs in PRs, and patients with CACs are recommended to have their cardiovascular risk factors checked.²² Whether the different radiographic appearances of CACs in PRs are associated with future risks of stroke or other cardiovascular events remains unknown.

Little information has been gleaned from medical studies regarding the relevance of features of calcification in atherosclerotic lesions. Progressing atherosclerotic lesions grow in a crescent shape within the intima, where calcification can develop at different locations within the lesion, which in turn is considered to be a sign of long standing, chronic pathology.⁴ PRs do not reveal the soft-tissue components that surround the observed CAC and most contribute to luminal reduction. However, it is reasonable to assume that two parallel CACs seen in PRs represent circumferential calcifications in the carotid artery and that these could be associated with a substantial volume of soft tissue. Under these circumstances, the scope for luminal reduction can be greater than other features of CACs in PRs. We found that this feature was very common (65%) in patients with SCS than features described as “single” or “scattered”. Furthermore, neck sides with single CACs were significantly less likely to be associated with SCS.

When analyses were performed regarding the radiographic appearance and degree of stenosis at the patient level, the degree of positive associations between vessel-outlining CACs and SCS on any neck side was established as our basis for further analyses. The analyses were performed solely for subgroups of patients in Group A, which best represents the general adult patient population in dentistry. CACs observed in PRs of patients in dental care gave rise to a previously reported PPV (for SCS) of 7%.⁷ In this study, the use of the vessel-outlining feature did not improve the PPV for SCS when used alone or in combination with the scattered feature. Compared with previous results, where only the presence or absence of CACs in PRs was considered,⁷ the method presently used yielded similar PPVs. The numbers of false positives were reduced by 25–37% in the various combinations but, contemporaneously, 17–33% of patients with SCS were missed. This implies that the radiographic descriptors

Table 2 Frequencies of patients with or without significant carotid stenosis (SCS) in different subgroups (I–III), presenting different combinations of radiographic appearances of carotid artery calcifications (CAC). The positive-predictive values (PPVs), with 95% confidence interval (CI) regarding SCS in the different subgroups are shown

Subgroups with combinations of radiographic appearances of CAC	SCS (%)		PPV (95% CI)
	Yes	No	
I	8 (67%)	95 (63%)	7.8% (2.5–13.0%)
II	9 (75%)	111 (74%)	7.5% (2.7–12.3%)
III	10 (83%)	128 (85%)	7.2% (2.9–11.6%)
All	12 (100%)	151 (100%)	7.4% (3.3–11.4%)

I, Patients with a vessel-outlining CAC on any side; II, patients with a vessel-outlining CAC on any side and patients with bilateral scattered CAC; III, patients with vessel-outlining CAC on any side and patients with scattered CAC on any side.

used in this study offer neither an advantageous, nor practicable option with which to usefully categorize CACs identified by PRs.

Even though the κ values were “moderate” to “substantial” between the two observers there is always some variability when multiple observers use a subjective scale. A potential risk for a lower PPV can be anticipated should the scale be implemented in general dental practice including many observers with varying experience. The ability to detect calcifications at all also varies in general practice.

A limitation of this study was that none of the female patients in Group A presented with SCS despite having CACs. Larger studies are now needed to test the accuracy of these findings.

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Conclusion

Stratifying the radiographic appearance of CACs captured in PRs, inclusive of the combinatorial criteria described, failed to improve the PPV with which SCS among patients with CACs can be detected. The trialled methodology provided no improvement over that used previously, in which only the presence or absence of carotid calcifications in PRs were considered.

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