Original Article

Are dental and periapical status related to incidental findings of calcifications along the course of the internal carotid artery in cone-beam computed tomography?

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ABSTRACT

Context: Given that tooth loss, periapical lesion, and manifestations of periodontal disease are generally related to previous inflammatory events and that a linear relationship exists between tooth loss and degree of arterial stiffness, reasonable ground exists to investigate whether there is an association with presence of calcifications along the course of the internal carotid artery (ICA). **Aims:** This study aims to determine whether an association exists between the extra- and intracranial calcifications of the internal carotid artery (ExCICA and InCICA, respectively) and missing teeth (MT) as well as the periapical index (PAI), in cone-beam computed tomography (CBCT) scans. **Settings and Design:** A retrospective study with CBCT examinations obtained from a database of a dental imaging center. **Materials and Methods:** A number of 174 adults' CBCT examinations of both genders were evaluated on the presence of calcifications along the course of the ICA and the number of MT as well as the PAI score. **Statistical Analysis Used:** The interobserver agreement was assessed by Cohen's kappa. The *t*-test for independent samples was used to compare the groups presented with or without calcifications. Furthermore, the Pearson's test was used to evaluate whether an association exists between variables that had a statistical difference. **Results:** The *t*-test showed a significant difference in the mean age (MA) and the number of MT between patients with and without presence of calcifications along the course of ICA, in both extra- and intracranial segments. The Pearson's correlation test showed a positive correlation between MA, MT, and both ExCICAs' presence and InCICAs' presence. Although the number of MT increases with age, this increment is high in the presence of ExCICA and even higher in the presence of InCICA. **Conclusion:** We support that not only patients' age but also the number of MT can be predictive for atherosclerosis "signs" presence.

Key words: Atherosclerosis, carotid artery plaque, cone-beam computed tomography, tooth loss

Introduction

Compelling evidence supports that the calcification's presence in atherosclerotic plaques may be used as a marker of atherosclerosis and is also related to cardiovascular diseases.[1-3] Its formation is attributed to the inflammatory process that occurred within the artery

Access this article online	
Quick Response Code:	Website: www.joomr.org
	DOI: 10.4103/jomr.jomr_30_17

Cite this article as: Da Silveira HL, Busanello FH, Nedel C, Vizzotto MB, Damaskos S. Are dental and periapical status related to incidental findings of calcifications along the course of the internal carotid artery in cone-beam computed tomography?. J Oral Maxillofac Radiol 2017;5:74-80.

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walls in all the developmental stages of the disease[4] and promoted by the low-density lipoproteins.[5] It is showed that the presence of atherosclerotic plaques is also independently related to well-known risk factors such as diabetes, dyslipoproteinemia, smoking, dietary habits, and elevated serum concentrations of the C-reactive protein.[6-8]

As it found, mural calcifications can be easily detected in nonenhanced computed tomography (CT) images.[9-11] Furthermore, the image quality of the carotids atherosclerosis' visualization – by CT – do not differ than those of cone-beam CT (CBCT), as the overall subjective images' quality is considered higher.[12,13]

Furthermore, recent CBCT studies showed that the incidence of these calcifications' presence in the course of the internal carotid artery (ICA), as incidental findings, and its association with age are in line with those of CT.[14-16]

Moreover, studies support that systemic inflammation may be, at least partly, both the cause and the predictor of progression of the endothelial dysfunction.[17,18] Based on this perspective, periodontitis as a chronic multifactorial infectious disease also affects the supporting structures of the teeth (root, periodontal ligament, and alveolar bone) and has also been considered as a major cause of tooth loss.[19]

Given that tooth loss, periapical lesion, and manifestations of periodontal disease are generally related to previous inflammatory events[20] and that a linear relationship exists between tooth loss and degree of arterial stiffness,[21] reasonable ground exists to investigate whether there is an association between the presence of incidentally found soft-tissue calcifications along the course of the ICA and both the tooth loss and the periapical status.

Thus, this study aims to determine whether an association exists between the incidental findings of calcifications along the extra- and intracranial course of the ICA in CBCT scans and tooth loss as well as the periapical status.

Materials and Methods

After a prior study published,[16] we decided follow a research line using a methodology partly similar. Thus, the CBCT scans were used to evaluate missing teeth (MT) and periapical status. A number of 174 adults' CBCT examinations of both genders is also defined our study's cohort. This study included 84 males (mean age [MA], 60.38 ± 12.06 years) and 90 females (MA, 62. 35 ± 12.93 years), which had age range of 40–89 years and MA of 61.4 years and interquartile range of 21. The scans enrolled in the current study were obtained from the database of a Brazilian dental imaging center and were acquired from October 2011 to March 2013. These were of patients who were referred either by dentists or oral and maxillofacial surgeons for (a) orthognathic surgery, (b) facial trauma, and (c) implants' placement (cases for both maxilla and mandible).

The inclusion criteria were as follows: (a) patients should be 40 years of age or older, (b) CBCT examinations were taken with the maxillofacial protocol mode (full or large field of view), and (c) scans should not present movement and/or stripe artifacts. Both the patients' age and gender were recorded. Next, the scans were codified.

The Ethical and Research Committees of the Federal University of Rio Grande do Sul approved our study protocol (Ref. 27417).

All the CBCT examinations were acquired with an i-CAT® CBCT scanner (Imaging Sciences International, PA, Hatfield, Pennsylvania, USA), in 120 kV/3.3 s, ranging from 3 to 8 mAs/patient. The volumetric reconstructions of these data sets (16 cm × 13 cm, voxel size 0.2 mm) were created using the i-CAT Vision® software (i-CAT vision Q, Imaging Sciences International, Hatfield, PA, USA).

Primarily, the CBCT volumetric data sets were evaluated retrospectively and independently by two oral and maxillofacial radiologists (SD and HLDS) on the presence of calcifications along the course of the ICA. The observers were blinded regarding the patients' medical and dental history (clinical, histological, and radiographic). In addition, no prior individual information (which might have biased the examiners' opinion) could be obtained by the observers, because of the applied codification.

The image analysis was standardized and performed in all the multiplanar reconstructions (axial, coronal, and sagittal) of each volume. The series of the CBCT images were displayed on a flat panel, 22 inch Philips Brilliance 200P TFT (Philips, Eindhoven, The Netherlands), at a resolution setting of 1600 × 1200 pixels. Calcification was recorded if it was present in a series of at least three sequential slices (axial, coronal, and/or sagittal), in order to avoid false-positive findings as a result of image noise or artifact.

Radio-opacities depicted within the cervical portion of the artery, from the carotid bifurcation area until its entrance into the carotid canal, were considered to be extracranial calcifications of the ICA (ExCICAs). Any similar radio-opacity depicted along the artery's intracranial course – from the ascending part of the petrous portion up to the cavernous portion – was recorded as an intracranial calcification of the ICA calcification (InCICA). The imaging criteria used for the identification of both the ExCICAs' presence and InCICAs' presence within the ICA's course have already presented in the literature[22] and also recently in our previous studies.[14-16,23]

Subsequently, to quantify the dental status, we choose the number of MT as parameter strongly related to atherosclerosis presence.[24-27] In addition, we retrospectively evaluated the periapical index (PAI) score as a measure of periapical status for each tooth separately. Thus, we included in our study the number of teeth with apical lesion (TAL), endodontically treated TAL (ETTAL), and endodontically treated teeth (ETT). In this manner, when an apical lesion was present in more than one root, the highest score was registered. PAI scores 1 and 2 signified a nondiseased apical periodontium, and PAI scores 3, 4, and 5 signified the presence of an apical radiolucency.[28]

Both the dental status and the periapical status were evaluated independently by two examiners (HLDS and FHB): one oral and maxillofacial radiologist and other an endodontist. For their calibration, 20 CBCT scans were used. These were not included in the main text. Furthermore, they were blind to data regarding the presence of calcifications along the ICA's course.

Initially, the consistency of the interobserver agreement was assessed by Cohen's kappa. Inconsistencies were solved by consensus resulting in the data set that was finally used for the statistical analysis. Thereafter, the frequencies of the recorded presence or absence of the calcifications and its relation with the MA (in years), MT, TAL, ETTAL, and ETT were analyzed.

The *t*-test for independent samples was used to compare the groups presented with or without calcifications and the different variables (MA, MT, TAL, ETTAL, and ETT). Furthermore, the Pearson's test was used to evaluate whether an association exists between variables that had a statistical difference. Statistical analyses were performed using the IBM-SPSS (Statistics for Windows, Version 21.0 software package [Armonk, NY: IBM Corp.]). $P < 0.05$ was considered statistically significant.

Results

The reproducibility between the two examiners who evaluated the CBCT data sets on the presence of calcifications within the ICAs course was excellent (Cohen's Kappa = 0.85). Likewise, the examiners who evaluated the CBCT data sets for dental and periapical status obtained excellent values for the interexaminer agreement. (Cohen's Kappa values were 0.99 and 0.87 for tooth loss and periapical status, respectively). The MA, MT, TAL, ETTAL, and ETT, in the presence of ExCICAs or InCICAs, for both genders, are presented in Table 1.

The group with ExCICAs presents higher MA than that of the group without (68.84 years and 57.68 years, respectively). Furthermore, the group with InCICAs presents higher MA than that the group without (68.20 years and 53.96 years, respectively). The same applies for MT and TAL [Table 1].

The *t*-test for equality of means showed a significant difference in the MA and the number of MT between patients with and without presence of calcifications along the course of ICA in both segments, extra- and intracranial. There were not differences for the other variables as the number of TAL, ETTAL, and ETT [Table 2].

Subsequently, data were submitted to the Pearson's correlation test to evaluate whether an association exists between MA, MT, and both ExCICAs' presence and InCICAs' presence. The results showed a positive correlation between these variables [Table 3]. This result translates to the fact that the greater the number of MT, the greater the possibility of the calcifications to be depicted within the course of the ICA [Figure 1]. The results also showed that in the presence of ExCICA, the probability of InCICA's depiction is greater and vice-versa [Table 3].

The number of MT increases with age, as it expected. However, this increment is high in the presence of ExCICA and even higher in the presence of InCICA [Figure 2]. The

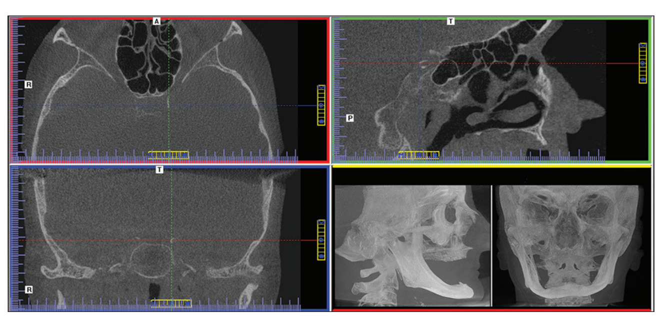

Figure 1: Patient with presence of InCICA and 32 missing teeth

Table 1: Mean age (years), missing teeth, teeth with apical lesion, endodontically treated teeth with apical lesion, and endodontically treated teeth from patients of both genders with or without extracranial calcification of the internal carotid arteries and intracranial calcification of the internal carotid arteries

	Gender	MA (years)	MT	TAL	ETTAL	ETT
ExCICA						
Absent	Male					
	Mean	56.759	10.690	0.207	0.621	2.879
	n	58	58	58	58	58
	SD	11.299	7.002	0.522	0.791	2.136
	Female					
	Mean	58.603	14.103	0.414	1.017	3.897
	n	58	58	58	58	58
	SD	12.327	9.348	1.556	1.177	3.172
	Total					
	Mean	57.681	12.397	0.310	0.819	3.388
	n	116	116	116	116	116
	SD	11.809	8.400	1.160	1.018	2.740
Present	Male					
	Mean	68.462	15.308	0.500	1.115	2.769
	n	26	26	26	26	26
	SD	9.696	9.895	0.707	2.233	3.626
	Female					
	Mean	69.156	17.594	0.594	0.844	2.688
	n	32	32	32	32	32
	SD	11.271	10.506	1.012	0.847	2.558
	Total					
	Mean	68.845	16.569	0.552	0.966	2.724
	n	58	58	58	58	58
	SD	10.509	10.212	0.882	1.611	3.054
InCICA						
Absent	Male					
	Mean	53.600	9.333	0.267	0.800	2.933
	n	45	45	45	45	45
	SD	9.884	6.474	0.580	1.254	2.082
	Female					
	Mean	54.368	10.763	0.263	1.211	4.105
	n	38	38	38	38	38
	SD	9.963	7.879	1.032	1.212	2.902
	Total					
	Mean	53.952	9.988	0.265	0.988	3.470
	n	83	83	83	83	83
	SD	9.867	7.142	0.813	1.244	2.544
Present	Male					
	Mean	68.205	15.333	0.333	0.744	2.744
	n	39	39	39	39	39
	SD	9.362	8.928	0.621	1.585	3.234
	Female					
	Mean	68.192	18.692	0.635	0.769	3.000
	n	52	52	52	52	52
	SD	11.739	9.879	1.585	0.921	3.029
	Total					
	Mean	68.198	17.253	0.505	0.758	2.890
	n	91	91	91	91	91
	SD	10.728	9.578	1.268	1.241	3.104

SD: Standard deviation; InCICA: Intracranial calcification of the internal carotid artery; ExCICA: Extracranial calcification of the internal carotid artery; MA: Mean age; MT: Missing teeth; TAL: Teeth with apical lesion; ETTAL: Endodontically treated teeth with apical lesion; ETT: Endodontically treated teeth

t-test for equality of means does not show a significant difference in the MA, in the number of TAL, ETTAL, and ETT between males and females. Interestingly, there was difference in the number of MT [Table 4]. One of the most probable explanations is that females' MA was higher than that of men.

Discussion

In this retrospective cohort study of a Brazilian population-based sample, we investigated whether an association exists between both the MT and PAI, considered as the perspective of previous inflammatory events,[29] and the presence of calcifications along the course of ICA, considered as atherosclerosis "signs" presence, that incidentally found in CBCT scans.

We found that a significant positive correlation exists between MT and the presence of calcifications within the course of ICA, either extra- or intracranially, also related to age. Our findings corroborate those of other studies providing strong evidence on the relation of MT and the atherosclerosis presence.[27,29]

To our knowledge, most of the studies in the literature have focused primarily on the risk of arterial stiffness, prevalent coronary heart disease, myocardial infarction and stroke in relation to tooth loss, and periodontal disease, whereas we have used the incidentally found atherosclerosis "signs" presence as the primary outcome from a cohort of Brazilian dental patients. Reasonably, our findings will shed light on the influence of the patients' oral status – by means of MT and periodontal disease presence – on the depiction of atherosclerosis "signs" in the imaging modalities commonly used in dental praxis (panoramic radiographs and CBCTs). Given that tooth loss is mainly attributed to periodontal disease, owing to its' inflammatory background,[29] we believe that the number of MT as a covariant in our study was pertinent. Notably, we found association only between tooth loss with atherosclerosis "sings" presence, regardless of gender, and not with TAL, ETTAL, and ETT. This event is probably due to the lack of the long-term cumulative inflammatory effects in those cases.[24] Furthermore, the imaging modality used (CBCT) is sufficient to depict accurately all the examined parameters of our study.[30,31] Interestingly, the increasing number of MT with age is high in the presence of ExCICA and even higher in the presence of InCICA. Because both ExCICA's presence and/or InCICA's presence are indicative of increased risk of myocardial infraction and stroke[32,33] and dental status, oral hygiene, and particularly tooth loss are associated with the degree of carotid stenosis and predict future progression of the disease,[34] we believe that our findings contribute to the identification of patients at risk of atherosclerosis using MT as a surrogate marker.

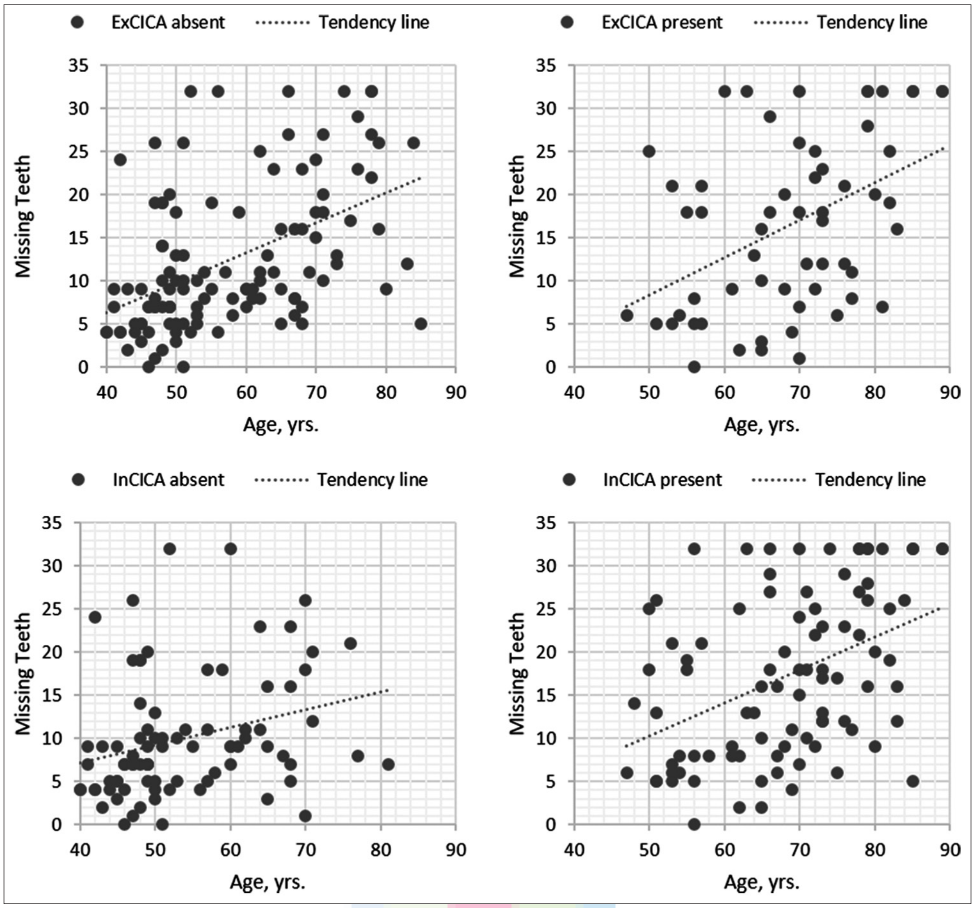

Figure 2: The distribution of the number of missing teeth in the presence or absence of ExCICA and InCICA, according to age (in years)

Table 2: *t*-test for equality of means between patients with and without calcifications presence along the course of internal carotid artery in both segments, extra- and intracranial

	t	Significant (two-tailed)	Mean difference	SE difference	95% CI of the difference	
					Lower	Upper
ExCICA						
MA	−6.092	0.000	−11.164	1.832	−14.781	−7.547
MT	−2.870	0.005	−4.172	1.454	−7.042	−1.303
TAL	−1.395	0.165	−0.241	0.173	−0.583	0.100
ETTAL	−.731	0.466	−0.147	0.200	−0.542	0.249
ETT	1.449	0.149	0.664	0.458	−0.240	1.568
InCICA						
MA	−9.089	0.000	−14.246	1.567	−17.340	−11.152
MT	−5.628	0.000	−7.265	1.291	−9.813	−4.717
TAL	−1.473	0.143	−0.240	0.163	−0.563	0.082
ETTAL	1.218	0.225	0.230	0.189	−0.143	0.602
ETT	1.340	0.182	0.580	0.433	−0.274	1.434

InCICA: Intracranial calcification of the internal carotid artery; ExCICA: Extracranial calcification of the internal carotid artery; MA: Mean age; MT: Missing teeth; TAL: Teeth with apical lesion; ETTAL: Endodontically treated teeth with apical lesion; ETT: Endodontically treated teeth; SE: Standard error; CI: Confidence interval

Liljestrand *et al.* and Oluwagbemigun *et al.*also supported that the number of MT, "may indicate an increased risk for cardiovascular disease, and it could be added into existing cardiovascular risk profiles as an additional risk factor".

Moreover, the gender difference that found in predisposition of MT is attributed to several reasons, such as treatment bias, dental practice differences, sociocultural determinants, and increasing age. Given that the MA of the female population of our study was higher than that of males (62.35 ± 12.93 years and 60.38 ± 12.06 years, respectively), and that the prevalence of both genders of having calcium deposition in the arterial wall increases significantly until the 8th decade,[9] we believe that the influence of "gender", as a variable, in our study results does not affect the outcomes, because of the elderly population studied.

One of the limitations of the current study is that it does not provide clear evidence regarding the patients' medical history on the presence of atherosclerosis. This is due to the retrospective nature of the study. Thus, we aimed to solely correlate easily available clinical parameters, as those described previously, and their relation to atherosclerosis "signs" presence. This is to be mentioned; despite the limitations of this retrospective study, and the absences of any similar information regarding medical, socioeconomic, and racial status, our study results based on incidental

Table 3: Pearson correlations coefficient

	ExCICA	InCICA	Age (years)	MT
ExCICA				
Pearson correlation	1	0.431**	0.421**	0.214**
Significant (two-tailed)		0.000	0.000	0.005
InCICA				
Pearson correlation	0.431**	1	0.570**	0.394**
Significant (two-tailed)	0.000		0.000	0.000
MA (years)				
Pearson correlation	0.421**	0.570**	1	0.506**
Significant (two-tailed)	0.000	0.000		0.000
MT				
Pearson correlation	0.214**	0.394**	0.506**	1
Significant (two-tailed)	0.005	0.000	0.000	

**Correlation is significant at the 0.01 level (two-tailed). InCICA: Intracranial calcification of the internal carotid artery; ExCICA: Extracranial calcification of the internal carotid artery; MA: Mean age; MT: Missing teeth

Table 4: *T*-test for equality of means between genders

	t	Significant (two-tailed)	Mean difference	SE difference	95% CI of the difference	
					Lower	Upper
MA	−1.039	0.300	−1.975	1.900	−5.725	1.776
MT	−2.333	0.021	−3.225	1.382	−5.954	−0.497
TAL	−1.101	0.272	−0.180	0.164	−0.503	0.143
ETTAL	−0.962	0.337	−0.182	0.189	−0.555	0.191
ETT	−1.438	0.152	−0.621	0.432	−1.474	0.231

MA: Mean age; MT: Missing teeth; TAL: Teeth with apical lesion; ETTAL: Endodontically treated teeth with apical lesion; ETT: Endodontically treated teeth; SE: Standard error; CI: Confidence interval

findings corroborate those of similar studies.[26,27,29] This strengthens the suggestion that "the progression of atherosclerosis is linearly related to increased tooth loss".[21] Future prospective clinical trials may provide more evidence on the significance of both the MT and PAI to the atherosclerosis presence also using either CBCT or panoramic radiographs.

Conclusion

Our study, using CBCT data sets, documents that the greater the number of MT, the greater the possibility of the calcifications to be detected within the course of the extra- and intracranial segments of ICA as incidental finding. As we found that a significant correlation exists between the MA and the number of MT between patients with and without calcifications presence along the course of ICA in both segments, we support that not only patients' age but also the number of MT can be predictive for atherosclerosis "signs" presence.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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