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Diagonal Earlobe Creases Associated with Dental Cone Beam CT Imaged Calcified Cervical Carotid Artery Atheromas: Risk Indicators of Myocardial Infarction

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Abstract

Aims: Older men harboring occult coronary artery atherosclerosis frequently succumb to myocardial infarctions (MI). Diagonal earlobe creases (DELC) and panoramic images (PIs) demonstrating calcified cervical carotid artery atheromas (CCCAA) have been shown to be independent “risk indicators” of future MI. Previously we had demonstrated a positive association between DELC and CCCAA on PIs. However, cone beam CT (CBCT) has replaced PIs for certain procedures therefore, we determined if there’s an association between DELC and CCCAA on CBCT.

Material and MEthods: In a prospective study of consecutive older (³ 55 years) male dental patients (N=104) two oral medicine specialists evaluated each for DELC. Two masked maxillofacial radiologists evaluated their CBCTs for CCCAA.

Results: Among the DELC+ cohort (N=50; mean age 68.8 ± 7.6 years), 29 patients (58%) evidenced CCCAA. Among the DELC- cohort (N=54; mean age 64.7 ± 7.0 years), 14 patients (26%) demonstrated CCCAA. Prevalence of CCCAA among the DELC+ cohort was significantly greater (p=0.0009) and after adjustment for age, 3.95 times more likely (OR 3.95; 95% CI: 1.71-9.02, p=0.001) than among the DELC- group. The DELC+ cohort was also more often hypertensive (p=0.036).

Conclusions: DELCs are positively associated with CBCT imaged CCCAA, an acknowledged “risk indicator” of future MI.

Key Points

1) Dentists can potentially identify clinically asymptomatic older male patients at risk of fatal cardiac arrest when performing a comprehensive maxillofacial clinical examination and reviewing their cone beam CT images.

2) Dentists when performing the extra oral component of a clinical examination should examine the patient’s earlobes for diagonal creases; an acknowledged “risk-indicator” of stenotic coronary artery atherosclerotic lesions.

3) Dentists must also carefully review their patients maxillofacial cone beam CT images for presence of cervical calcified carotid artery plaques; acknowledged “risk indicators” of stenotic coronary artery atherosclerotic lesions.

Introduction

Myocardial infarction (MI) arising from atherosclerosis of the coronary arteries (termed coronary artery disease; CAD) is the leading cause of death among older males residing in England and Wales, as well as in Brazil[1,2] However, approximately half of these men died of sudden cardiac arrest without ever having evidenced prior clinical symptoms or known classic risk factors.[3] Therefore, most physicians attempting

to identify which of their clinically asymptomatic male patients have occult atherosclerotic disease utilize prediction models (e.g., the Framingham Risk Score[4]) which quantify known risk factors (such as, systolic blood pressure, smoking status, cholesterol levels, and diabetes mellitus) but underestimation is often common with cardiovascular mortality ensuing.[5]

Augmentation of this medical screening process also frequently involves visual examination of the maxillofacial complex for the presence of clinical signs such as xanthelasmata (yellowish, cholesterol rich plaques seen most frequently on the upper eyelid) associated with occult croonary artery atherosclerosis.[6] Epidemiologic studies conducted in England have documented that there is an even higher incidence of coronary artery atherosclerosis with another maxillofacial sign, namely, a diagonal earlobe crease (DELC). On clinical examination the DELC appears as a deep grove in the lobe extending from the intertragal notch (incisure) to the inferior-posterior edge of auricle.[7] Furthermore, ear, nose, and throat surgeons from the Royal Force Hospital in London and Northwick Park Hospital, Harrow Middlesex have documented among their mixed gender cohort (n = 1200) of clinic and hospitalized patientes that 52 (4.3%) individuals provided a positive history of CAD and of these, 25 (48%) were noted to have DELC on examination.[8] This association being highly significant (chi-square = 59.13, p = < 0.001) and using the Mantel-Haenszel test it was confirmed that those results were not associated with cofounders such as age (chi-square = 33.59, p = < 0.001) or sex (chi-square = 54.61; p < 0.001). Post-mortem studies conducted by pathologists from the Royal Sussex County Hospital, Brighton confirmed the relationship between the presence of a DELC and the ratio of risk (RR) of cardiovascular disease (CAD) among a cohort of males (N = 171; mean age 70.3).[9] Study results revealing that the presence of a crease was associated with a 1.49 (RR 95%; 1.13–1.96) increased risk of death from CAD.

Furthermore, Japanese[10] and Brazilian[11] medical imaging studies have bolstered the validity of the DELC as a “risk indicator”/surrogate marker of future MI. Specifically, these clinician scientists have respectively documented an association between DELC and cervical carotid artery ultrasound studies which demonstrate calcified plaque and between DELC and angiography studies which evidence coronary artery stenotic lesions in 1 or more vessels. Dental scientists in Brazil and the United States have likewise confirmed this association by demonstrating that patients harboring DELC are more likely to have a PI which displays CCCAA.[12] This latter finding is critically important because American and Swedish maxillofacial radiologists have previously observed that patients having PIs demonstrating CCCAA, are at heightened risk of a future MI.[13,14] Irrespective of these findings demonstrating that DELC is related to atherosclerotic lesions and adverse clinical outcomes only a very small minority of researchers have been able to demonstrate and association between DELC and specific atherogenic risk factors.

Cone beam computed tomography (CBCT), of the maxillofacial complex is increasingly replacing PI in the oral surgery setting. The system’s high spatial resolution allows for detailed imaging of the bifurcation region of the cervical carotid artery including the identification of calcifications within plaques.[15] This is a critically important attribute given that the presence of ultrasound confirmed

calcified carotid artery bifurcation lesions is strongly associated with coronary artery calcium scoring (OR 4.39; $p < 0.001$, 95% CI: 3.72–5.18) an acknowledged risk factor for future MI.[16] Therefore, the purpose of this study was to determine if there is an association between an ear crease (DELC) and a CBCT imaging series which demonstrates CCCAA. The investigators hypothesized that patients who were DELC+ would signifcantly more often have CBCT images which displayed CCCAA. The specific aims of the study were to compare the prevalence rates of CCCAA between groups of patients with (DELC+) and without (DELC-) creases on clinical examination as well as to measure the prevalence of associated classical atherogenic risk factors and age.

However, a prospective study attempting to discern if there is an association between an ear crease (DELC) and a CBCT imaging series demonstrating CCCAA + has not been previously reported. Therefore, we designed a project to determine if older Brazilian men who had a DELC evidenced CCCAA on CBCT more often than individuals devoid of such a crease. The authors hypothesized that patients who were DELC+ (predictor variable) would significantly more often have CBCT images which display CCCAA+ (outcome variable). The specific aim of the study was to compare the prevalence rates of CCCAA between groups of patients with and without DELC on clinical examination.

Material and Methods

This prospective population-based observational study was approved by the Ethics Committee of the XXXXXXXXXXXXXXXXXXXX, and by the National Council of Ethics in Research, XXXXXXXX under protocol number 6.839.057. The study population was comprised of consecutive male patients (aged ≥ 55 year) registered at the dental school and in need of dental cone beam CT Imaging for implant placement. Study exclusion criteria consisted of all females and male patients younger than age 55 as well as those having an ear piercing, a history of stroke, neck surgery or therapeutic regional irradiation.

After signing an informed consent an abbreviated medical history relative to atherogenic risk factors was obtained from each patient. They were specifically queried as follows: “Have you ever been diagnosed with or provided medication to treat ischemic cardiovascular disease [that is myocardial infarction (heart attack) or stroke], hypertension, diabetes mellitus, or hyperlipidemia?” Each patient was then examined by 2 oral medicine specialists (ACS and GFC) for the presence of DELC after positioning the dental chair at an angle of 45^0 to avoid artifact. The DELC (predictor variable) was considered present if there was a crease (≥ 1mm in depth running from the intertragal notch diagonally backward to the inferior-posterior edge of the lobule at approximately 45^0. (Fig. 1). Individuals diagnosed with either unilateral or bilateral DELC by consensus between the examiners were assigned a designation of DELC+.

At the conclusion of the clinical examination patients were referred for a CBCT examination performed by the school’s maxillofacial radiologists. Masked as to the results of the clinical examination of the ear lobes, and the patient’s medical history, a staff maxillofacial radiologist (ACL) and the University’s thesis advisor also a maxillofacial radiologist (PCS) viewed the obtained images utiizing soft tissue windows to best visualize vessel anatomy and associated calcifications in all three orthogonal planes, i.e.; axial,

coronal, and sagittal for the presence of these entities. However, for study consistency the CCCAAs were diagnosed in the axial projection (Fig. 2) utilizing the criteria (i.e., outcome vaiable) established by University of Connecticut Maxillofacial Radiology Staging Method[21] that is: single or multiple rice grain appearing radiopacities or as homogeneous linear or curvilinear (semi lunar) opacities when located lateral to the anterior tubercle of the transverse processes and posterior lateral to the greater cornu of the hyoid bone and pharyngeal airway.[22–24] For study purposes, the diagnosis of CCCAA + was established by consensus between the two examiners after excluding other calcified pathological entities (such as, sialoliths, tonsilloliths, calcified lymph nodes) and anatomical structures (such as, triticeous cartilage, upper horns of the thyroid cartilage).

Secondary predictor variables collected for study were the patients' atherogenic risk factors (i.e., a prior MI or stroke, hypertension, diabetes mellitus and hyperlipidemia) and age. Data was subsequently entered into statistical package SPSS software version 24.0 and analyzed. The predictor variable was the presence or absence of DELC on clinical examination. The outcome variable were the prevalence rates of CCCAA visualized on imaging examination between these groups. A two-sided statistical test was employed to determine the significance of this finding and was set at $p = 0.05$. The two sided test was likewise employed to determine the influence of the above noted atherogenic risk factors. Additionaly, in order to ensure that these differing CCCAA prevalence rates were not due to diferences in the age of study's participants the odds ratio (OR) for revealing its impact was determined by age-adjusted binary logistic regression using SPSS software, version 25.0.

Results

The study population consisted of 118 consecutives male patients aged ≥55 years. Excluded were 8 patients because of earlobe earrings/piercings as well as 6 others because their CBCT examination did not meet diagnostic imaging quality criteria (e.g., there were artifacts caused by patient movement and metallic objects). The final population of 104 men was subdivided into a study group (N = 50; mean age 68.78 ± 7.61) composed of patients who were DELC + and a control group (N = 54; mean age 64.79 ± 6.96) comprised of patients who were DELC-

As can be seen in the Table 1, the study group of individuals (DELC+) were significantly ($p = 0.0009$) more likely (58% vs 26%) to evidence CCCAA on imaging examinations than members of the control (DELC-) group. Also this same cohort (DELC+) as noted in Table 2 was significantly more likely to evidence systolic hypertension ($p = 0.0336$) then were members of the control group. Furthermore, as determined by the age-adjusted binary logistic regression analysis the computed OR of a DELC+ study participant having CCCAA was 3.95 times more likely when compared to a similarly aged DELC- participant (OR 3.95; 95% CI:1.71–9.02, $p = 0.001$).

Table 1
Association Between Diagonal Earlobe Crease and Cervical Carotid Artery Atheromas Imaged on Cone Beam Computed Tomography

Men (N = 104)	**N (%)**	**CCCAA+**	**P value**
#DELC+	50 (48.07%)	29 (58.00%)	0.0009
*DELC-	54 (51.92%)	14 (25.92%)	
#Study group: DELC+: positive for diagonal earlobe crease.			
*Control group: DELC-: negative for diagonal earlobe crease.			

Table 2
Prevalence of Classic Atherogenic Risk Factors Concomitant with DELC

#DELC+	**ICVD**	**S. HTN**	**DM**	**HYP**
	17 (34.00%)	**31 (6.,00%)**	**13 (26.00%)**	**18 (36.00%)**
*DELC-	13 (24.00%)	24 (44.44%)	9 (16.66%)	16 (29.63%)
P-value	0.1320	0.0366¥¥	0.122	0.2445
¥¥ Significant				
#Study group: DELC+: positive for diagonal earlobe crease.				
*Control group: DELC-: negative for diagonal earlobe crease.				
ICVD = Ischemic Cardiovascular Disease				
S.HTN = Systolic Hypertension				
DM = Diabetes Mellitus				
HYP = Hyperlipidemia				

Discussion

The purpose of this study was to determine if a cohort of community-residing older Brazilian male dental patients with DELC + on clinical examination were significantly more likely to concurrently evidence CCCAA + on CBCT than those whose clinical examination was devoid of an ear crease. The authors hypothesized that patients with DELC+ would be more likely to evidence CCCAA. The specific aim of the study was to compare the prevalence rates of CCCAA on imaging between DELC + and DELC- groups. In this study we report that patients who were DELC+ evidenced a significantly greater prevalence (58% vs 25.9%; p = 0.0009) of CCCAA than those without a crease. Furthermore we also discerned that the DELC+ cohort was significantly more likely to evidence systolic hypertension (p = 0.036) than those

without a crease. Lastly, we determined that the OR of a DELC+ study subject having such a lesion was 3.95 times more likely in comparison to a similarly aged DELC- participant.

The results of our project are in accord with those of the only other previously published (i.e., in abstract form) study which evaluated the concomitant presence of a DELC and calcific carotid artery atherosclerotic disease utilizing two different dental imaging systems.[17] In a small (N = 20 patients) retrospective cohort study conducted in a dental school, 6 of the 10 study group patients (mean age 58 years) with a DELC evidenced cervical atherosclerotic disease on either CBCT or a PI where as none of the 10 control patients (mean age 43 years) who were devoid of a DELC demonstrated any imaging evidence of calcific vascular disease. Furthermore, the results of this current study also mirror those of an earlier study (conducted by us) in which we demonstrated that among community-dwelling older Brazilian male dental patients those with DELC were significantly more likely to evidence CCCAA on a PI than those without a crease.[12]

Early research findings originally published in this journal by the senior author (AHF) demonstrated that panoramic dental radiographs, on occasion, reveal calcified atherosclerotic lesions in the cervical component of the carotid vasculature.[18] The author at that time emphasizing that these lesions have the potential to embolize and block cerebral blood supply causing approximately 25% of all future ischemic stroke. This publication however elicited a critically important and far ranging Commentary in Lancet. The author denoting that these panoramic imaged lesions were in fact “risk indicators” of the systemic nature of atherosclerotic disease and that more advanced disease was more likely in the coronary vessels placing such patients at an even higher risk of a future myocardial infarction because when these plaques rupture they trigger thrombus formation (clot) which blocks blood flow to heart muscle.[19]

Thus germane to the results of this present study are those of the Copenhagen City Heart Study, a population-based prospective project of 35 years duration involving almost 11,000 Danes who were initially free of ischemic heart diseases. Upon conclusion of the study it was determined that patients (N = 1,465), with a DELC were at significantly greater risk of developing ischemic heart disease (that is; fatal/nonfatal MI, angina pectoris, and need for revascularization procedures) after multifactorial adjustment for chronological age and classic cardiovascular risk factors (i.e., hyperlipidemia, hypertension, diabetes mellitus, body mass index, and smoking history).[20] The results of this Danish observational study are also consistent with one recently conducted in China where men (mean age 64) with known or suspected coronary artery atherosclerotic lesions and having a DELC in comparison those without a crease were significantly more likely on coronary angiography to evidence severe stenotic disease.[21]

The pathophysiologic mechanism linking DELC to the etiology of atherosclerosis remains unsettled since first observed in 1973 by Sanders T. Frank, M.D., an American pulmonologist who noted the presence of “a prominent crease in a lobule portion of auricle” [DELC (Frank’s Sign)] among a cohort of relatively young (≤ age 60) men evidencing angina resulting from ischemic heart diseases.[22] Numerous hypothesis have been offered for this association with the most convincing arising from histopathologic

findings diagnosed by biopsies of the skin encompassing the DELC from a cohort of patients suffering a fatal MI.[23] Specifically noted was the loss and degeneration of elastin and elastic fibers as well as thickening of the pre-arterioles reflecting microvascular disease also found present in the coronary bed. These histopathologic findings were absent in autopsy specimens of the control cohort who had neither suffered an MI nor had a DELC. It has also been suggested that the earlobe and the myocardium have anatomical similarities because both are supplied by an end-artery type of microcirculation without collaterals thereby having a propensity to rapidly become anoxic, if end arteries are occluded.[24] These investigators concluded that DELC is an acquired physical sign resulting from vascular disease.

Given that DELC + is often observed alongside the presence of other classic atherogenic risk factors we also attempted to determine if this potential relationship existed among our cohorts. We tested for a prior history of ischemic cardiovascular disease [i.e.; myocardial infarction (heart attack), stroke], systolic hypertension, diabetes mellitus, and hyperlipidemia. Systolic hypertension was the only atherogenic “risk factor” identified in our results as being significantly associated with the appearance of CCCAA on the CBCT images of DELC+ subjects. Its denotation is in accord with the results of a number of other previously published studies. Most germane being evaluation of a population of medical clinic attendees (N = 150 males over age 50).[25] The researcher determined, like we, that a diagnosis of hypertension was significantly associated with DELC+. Furthermore, his study like ours discounted diabetes mellitus as being a significant risk component associated with DELC. However, his study (unlike ours) did demonstrate that having a prior history of both cardiovascular disease, and hyperlipidemia were associated with DELC. Thus, this issue of DELC’s relationship with a variety of atherogenic risk factors remains among researchers as a question in flux possibly indicating that this clinical finding results from its sharing of risk factors with aging, associated underlying medical conditions, and the specific populations analyzed.[26] Thus, we strongly advocate that the patient be informed both verbally and in writing (including providing them with copies of their dental images) as to the cardiovascular implications of the imaging and clinical findings so that upon consultation with their primary care (or medical specialist) physician a more comprehensive cardiovascular evaluation process may ensue.

Our study had both a number of strengths and limitations. As for strengths, this is the first study to be published in the dental/medical literature to demonstrate an association between CCCAA on CBCT and DELC on clinical examination of older male patients. This finding represents the linkage of what had historically been two independent “risk indicators” of a future MI and therefore has profound clinical implications. Specifically, it empowers dentists to join with their physician colleagues in the identification of a subgroup of men who although devoid of classical cardiac symptoms and established traditional atherogenic risk factors remain at significant MI risk because they harbor occult coronary artery disease. Our study also had a number of limitations. Firstly, although we demonstrated an association between DELC and CCCAA our study’s design did not permit definitive identification of the biological mechanisms linking these two risk indicators. Secondly, because we limited study enrollment to men aged 55 and over, we can not extend our results to younger men or to women of any age. Furthermore, the study’s lack of a longitudinal component only permits the authors to speculate as to the likelihood of future

adverse cardiovascular events befalling older males concomitantly having these two risk indicators. Lastly, while CBCT permits easy identification of calcified atheromas it unlike carotid Doppler ultrasonography is unable to assess the degree of vessel obstruction.

We conclude that our results confirm the ability of dental healthcare professionals to identify a subset of older men, who while appearing relatively healthy, harbor validated “risk indicators” (that is DELC and CCCAA) of future adverse cardiovascular events. The identification of this potentially vulnerable cohort enhances opportunities for early provision of preventive treatments likely to obviate morbidity and mortality. This assessment is easily accomplished in the dental office during initial patient evaluation by concurrently examining the ear lobes for DELC and interpreting the entire CBCT data set for CCCAA. However we do concede that further research in this área is indicated and thus are planning to replicate this study among post menopausal women, a cohort of individuals who like older men often sucumb to an unanticipated MI.

Declarations

Ethics declaration (competing interests)

The Declaration of Helsinki protocols were followed and the patients gave their written, informed consent to participate in this study. Furthermore, this prospective population-based observational study was approved by the Ethics Committee of the Pontifícia Universidade Católica do Paraná (PCPR) and Instituto Latino-Americano de Ensino e Pesquisa em Odontologia (ILAPEO), and by the National Council of Ethics in Research of Brazil under protocol number 6.839.057.

Competing Interests’ statement

The authors declare that they have no conflict of interest.

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Figures



Figure 1

A diagonal earlobe crease (DELC) on a patient's right side delineated by white arrows. Note the deep grove in the lobe extending from the intertragal notch (incisure) diagonally backward to the inferior-posterior edge of the lobule at 45 degrees.



Figure 2

Cervical calcified carotid artery atheromas (CCCAA) delineated by red circles in the axial plane of a dental cone beam computed tomography (CBCT) image. The atheromas appearing as straight and curvilinear opacities located lateral to the anterior tubercule of the tansverse process and posterior lateral to the pharyngueal airway.

Note: The numerous vertical white lines are artifacts arising from thyroid gland shield.

Supplementary Files

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- Table1.docx
- Table2.docx