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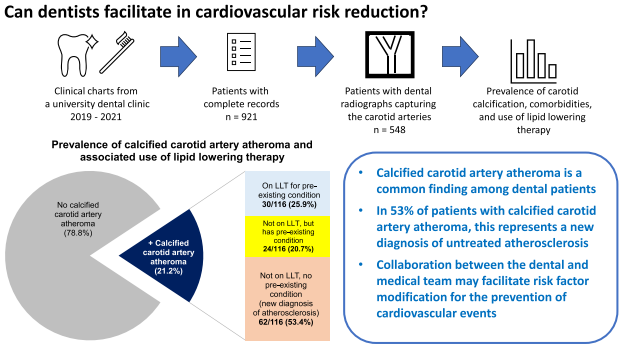
Original Research

Calcified carotid artery atheroma on standard dental radiographs: A public health opportunity for cardiovascular risk reduction

Vicky Mai [a,1], Aneesha Taneja [b,1], Hannu Larjava [b], Babak Chehroudi [b], David MacDonald [c,2], Christina Luong [d,2,*]

[a] University of British Columbia, Faculty of Medicine, Vancouver, BC, Canada
[b] University of British Columbia, Division of Periodontics, Vancouver, BC, Canada
[c] University of British Columbia, Division of Oral & Maxillofacial Radiology, Vancouver, BC, Canada
[d] University of British Columbia, Division of Cardiology, Vancouver, BC, Canada

GRAPHICAL ABSTRACT



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ABSTRACT

Objective: Calcified carotid artery atheroma (CCAA) can be identified incidentally on standard dental panoramic radiographs (DPRs). We sought to (1) determine the prevalence of CCAA on DPRs in a general dental population and (2) establish the proportion of patients in whom this would represent a new statin-indicated condition.
Methods: We identified patients aged ≥30 with DPRs from 2019 to 2021 from the University of British Columbia Dental Clinic. Patient charts were reviewed for use of lipid-lowering therapies (LLT) and existing statin-indicated conditions. DPRs for each patient were evaluated for the presence and characteristics of CCAA.
Results: Of 921 patients with a DPR and documented medical history, 548 (59.5 %) were diagnostic for evaluation of CCAA. Although 116/548 (21.2 %) of these patients had evidence of CCAA, only 25.9 % (30/116) were already on LLT; another 20.7 % (24/116) of patients with CCAA had a pre-existing statin-indicated condition but were not on LLT. Therefore, in 53.4 % (62/116) of patients with CCAA-positive DPRs, this constituted a new diagnosis of atherosclerosis not yet treated with LLT, representing 6.7 % (62/921) of the clinic population and

* Corresponding author at: University of British Columbia; Diamond Health Care Centre 9th Floor Cardiology, 2775 Laurel Street, Vancouver, British Columbia V5Z 1M9, Canada.
E-mail address: christina.luong@ubc.ca (C. Luong).
[1] Joint first authors.
[2] Joint senior authors.

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11.3 % of individuals with DPRs of diagnostic quality (62/548). Dyslipidemia, hypertension, coronary artery disease, diabetes, atrial fibrillation, stroke/transient ischemic attack, older age, and male sex were all found to be significant predictors of CCAA.
Conclusion: CCAA is a common finding among patients with DPRs and in over half of cases, the presence of CCAA represents a new diagnosis of atherosclerosis. The high prevalence of new, untreated atherosclerosis in this population indicates an opportunity for risk factor modification and collaboration between dentists and physicians to optimize patient care.

1. Introduction

Coronary artery disease is one of the leading causes of morbidity and mortality in Canada. In 2020, 17.5 % of Canadians died of heart disease and 4.5 % died of cerebrovascular disease [1]. Atherosclerosis is a multifocal disease resulting from deposition of plaques across the arterial vasculature. Due to the systemic nature of atherosclerosis, detection of calcifications in the carotid arteries (also known as calcified carotid artery atheroma, or CCAA) can serve as a marker of advanced plaque deposition in other vascular territories such as the coronary arteries [2-7].

The most common location for CCAA is in the common carotid artery or the bifurcation of the internal and external carotid arteries. Angiography is considered the "gold standard" for diagnosing CCAA [8]. While duplex ultrasound is commonly used for the initial diagnosis of CCAA, the ability to identify CCAA incidentally on dental radiographs has been well-documented since 1981 [9-10]. The reported prevalence of CCAA on DPR has ranged from 2 to 4.5 % in asymptomatic patients to as high as 22–37 % in patients with specific medical comorbidities and risk factors [11]. As a part of routine care, dentists often take a standard dental panoramic radiograph (DPR) of the teeth to evaluate oral health. These radiographs often capture a satisfactory view of the carotid arteries in the C3-C5 region. DPRs can detect carotid calcifications with a sensitivity of 80 % [12] and specificity of up to 98 % [13]. While patients may not seek medical care until symptomatic, many will routinely visit a dentist for check-ups and teeth cleaning.

Although CCAA is readily detected on standard dental imaging, little is known about the relationship of DPR detected CCAA and a patient's associated cardiovascular risk factors and treatment. Dentist detected CCAA in a patient with no known cardiovascular disease may represent a new diagnosis of atherosclerosis. Contemporary guidelines specify that carotid atherosclerosis is a condition that should prompt risk factor modification through both non-pharmacologic and pharmacologic means [14]. Robust evidence exists for the use of lipid-lowering therapies (LLT) such as statins in the prevention of major adverse cardiac events (MACE), including myocardial infarction, stroke, cardiovascular death, as well as all-cause mortality. Treatment with LLT can result in a 20–22 % relative risk reduction of MACE per 1 mmol/L reduction in LDL-C [15]. Earlier medical treatment of these patients to an LDL-C of $\leq$1.8 mmol/L would slow the progression of atherosclerosis and potentially lead to a greater reduction of MACE compared to a similar reduction in LDL-C at a later stage in life [16].

With this in mind we sought to 1) establish the prevalence of carotid calcifications on DPRs, 2) determine the proportion of patients with CCAA who represent a new diagnosis of atherosclerosis, and 3) ascertain the proportion of patients with carotid calcifications who are not on LLT. Unlike previous studies, our goal is to integrate the detection of DPR CCAA with a comprehensive medical and pharmacologic history. This approach aims to identify a population of patients who are presumed healthy at baseline but may benefit from earlier atherosclerosis treatment to prevent future cardiovascular events.

2. Methods

2.1. Study population

Consecutive patients aged $\geq$30 with DPRs enrolled at the University of British Columbia Dental Clinic from 2019 to 2021 were included in this study. Unique features of this clinic include discounted fees and its status as a referral center for specialty care, including endodontics, orthodontics, periodontics, and prosthodontics. As per standard practice within the clinic, there was electronic documentation of patients' self-reported medical conditions and medications, with changes over time. Patients who did not have a documented medical history or did not have a DPR were excluded. Access and use of the data in this project was approved by the University of British Columbia Clinical Research Ethics Board.

2.2. Clinical data

In this retrospective chart review, electronic records and imaging were reviewed by qualified research personnel to identify data elements for this study. These clinical parameters included documented existing statin-indicated conditions as outlined by the 2021 Canadian Cardiovascular Society Guidelines for the Management of Dyslipidemia [14], cardiovascular risk factors, and the use of LLT (see Table 1 for the list of parameters collected).

2.3. Imaging data

Standardized digital DPRs are performed on new patients after a full dental examination and repeated as clinically indicated in accordance with 2012 American Dental Association/Food and Drug Administration recommendations in conjunction with guidelines produced by Canada's provincial dental regulatory bodies [17]. The most recent DPR for each patient was reviewed by a board-certified dentist (Rater 1, AT) on bright monitors under reduced ambient lighting to assess for evidence and location (unilateral or bilateral) of CCAA. CCAA were defined as radiopacities adjacent to the cervical vertebrae in the region of the C3–C4 intervertebral disc level or near the retromolar level, independent of the hyoid bone; see Fig. 1 for example and Supplementary Figure 1 for diagnostic approach. At 70 % of total data accrual, a second reader (Rater 2, DM), a board-certified dentist and oral and maxillofacial radiologist overread a proportion of the scans. Rater 2 was blinded to clinical data and Rater 1 score, overread all positive CCAA cases (at 70 % of data collection) and a random sample of negative cases utilizing a computer-generated list (www.randomiser.org) to assess for agreement and assure accuracy. Interobserver agreement between the two raters was examined using Cohen's kappa.

2.4. Measurements and outcomes

The primary analyses for this study were 1) determining the prevalence of CCAA in an unselected population of patients with DPRs, 2) the proportion of patients for whom CCAA on DPR constituted a new diagnosis of atherosclerosis, and 3) the proportion of patients with CCAA who were not on LLT. Subgroup analysis was performed based on clinical factors with stratification by age ($<$50, 50–79, $\geq$80) and sex.

Table 1
Clinical characteristics and dental panoramic radiograph findings.

Patient characteristics	Total (n = 921)	CCAA- (n = 432)	CCAA+ (n = 116)	Non-diagnostic DPR (n = 373)	No DPR present (n = 10)
Age ± SD (mean, years)	60.4 ± 16.7	59.4 ± 16.5	65.5 ± 14.4	60.0 ± 17.1	68.0 ± 6.7
Sex					
Male	485	155	59	271	4
Female	436	277	57	102	6
Past medical history					
Carotid atherosclerosis	1	0	1	0	0
Hypertension	274	104	49	121	1
Diabetes	146	52	25	69	1
Chronic kidney disease	14	9	2	3	0
Dyslipidemia	85	30	17	38	0
Coronary artery disease	84	25	18	41	2
Heart failure	9	1	2	6	0
Atrial fibrillation	32	7	8	17	0
Peripheral artery disease	3	2	0	1	0
Stroke/Transient ischemic attack	42	14	11	17	0
Abdominal aortic aneurysm (or prior surgery)	1	0	1	0	0
Smoking history					
Current smoker	162	56	19	87	0
Ex-smoker	98	35	16	47	2
Non-smoker	661	341	81	239	8
Marijuana smoking history					
Current smoker	70	25	6	39	0
Ex-smoker	4	1	0	3	0
Non-smoker	847	406	110	331	10
Lipid-lowering therapy					
HMG-CoA reductase inhibitor (statin)	180	69	28	83	2
Ezetimibe	2	1	0	1	0
Statin/ezetimibe	6	4	1	1	0
PCSK9 inhibitor/ ezetimibe	1	0	0	1	0
Unknown	3	1	0	2	0

CCAA, calcified carotid artery atheroma; DPR, dental panoramic radiograph; SD, standard deviation.

2.5. Statistical analysis

Chi-square analyses were performed between overall age groups, sex, and each risk factor collected. The analyses were performed using SAS v9.4 (SAS Institute, Cary, North Carolina). A p-value of less than 0.05 was considered statistically significant.

3. Results

A total of 1000 consecutive patients were sampled, 56 of whom did not have a DPR on record. Out of the remaining 944 unique patients with a DPR, 23 were excluded for a lack of documented medical history. The remaining 921 patients (436 female, 485 men) analyzed had a mean age of 60.4 ± 16.7 years (Table 1). There were 548 (59.5 %) DPRs which were of diagnostic quality for the evaluation of CCAA. Notably, there were more males excluded due to non-diagnostic DPRs than females (271 males compared to 102 females). Of the DPRs of diagnostic quality, 116/548 (21.2 %) had evidence of CCAA.

To evaluate inter-rater agreement, a proportion of cases at the 70 % data accrual mark were reviewed by 2 raters. There was a total of 92 cases that were reviewed by both raters; the first 82 cases designated as positive for CCAA by Rater 1 and a random sample of 10 negative cases. Rater 2, blinded to the clinical information and Rater 1 score, assessed the radiographs for the presence or absence of CCAA on DPRs. For the positive cases (by Rater 1), there was an agreement on 80 cases out of the 82. For the negative CCAA cases (by Rater 1), there was an agreement on 9 of the 10 cases. Based on these results, Cohen's kappa was calculated, and almost perfect agreement between the two raters was observed (kappa = 0.84).

In patients with evidence of CCAA on DPRs, 25.9 % (30/116) were on LLT for a pre-existing condition (Fig. 2). 20.7 % (24/116) of these patients were not on LLT despite a pre-existing indication for treatment. CCAA identified on DPR was found to be significantly associated with the presence of any pre-existing indication for treatment with LLT ($p \leq 0.001$). Overall, 53.4 % (62/116) of CCAA-positive DPRs constituted a new diagnosis of atherosclerosis not yet treated with LLT. This new diagnosis accounted for 6.7 % (62/548) of the overall clinic population and 11.3 % (62/921) of individuals with DPRs of diagnostic quality.

Age was a statistically significant predictor of the presence of CCAA on DPR under chi-squared analysis ($p = 0.002$). Out of the diagnostic-quality DPRs, 11.4 % (17/149) of patients under 50 years old had detectable CCAA their DPR, compared to 24.2 % (80/331) of patients aged 50 to 70 years old and 27.9 % (19/68) of patients aged 80 years old and older (Fig. 3). Overall, 85.3 % (99/116) of the CCAA-positive DPRs were from patients who were aged 50 years old and older, and 14.7 % (17/116) were from patients under 50 years old. Among patients with CCAA-positive DPR who were under 50 years old, none were receiving LLT. In contrast, 73.8 % (59/80) of patients 50 to 79 years old and 52.6 % (10/19) of patients ≥ 80 years old were not on LLT. Upon closer examination of the CCAA-positive patients not on LLT, a significant proportion had no previously known conditions warranting LLT (Fig. 4). This was the case for 88.2 % (15/17) of those less than 50, 53.8 % (43/

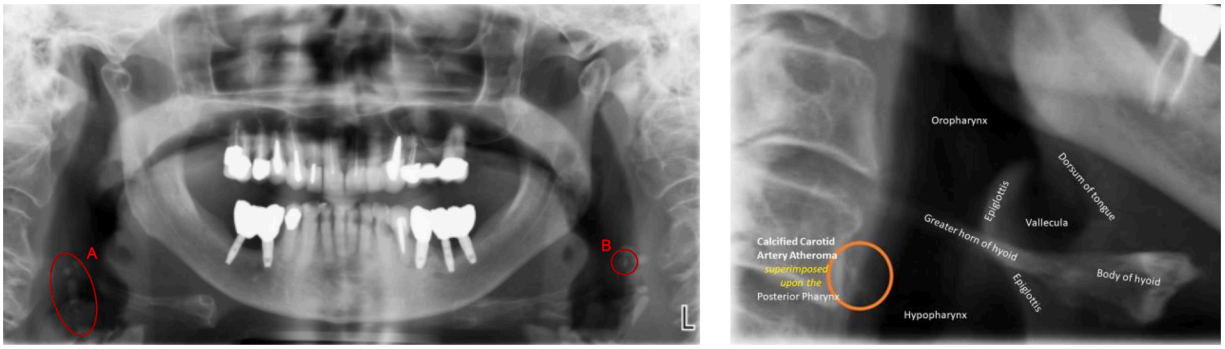

Fig. 1. CCAA found on DPR. A) general opacities showing evidence of atherosclerosis; B) crescent-shaped opacity specific to CCAA.: A section of a DPR with evidence of CCAA superimposed upon the posterior pharynx. The presence of CCAA lateral to the vertebral column confirms the diagnosis of CCAA, as opposed to other areas of calcification, which can also appear due to calcified cervical lymph nodes and calcified tristichous thyroid cartilage.

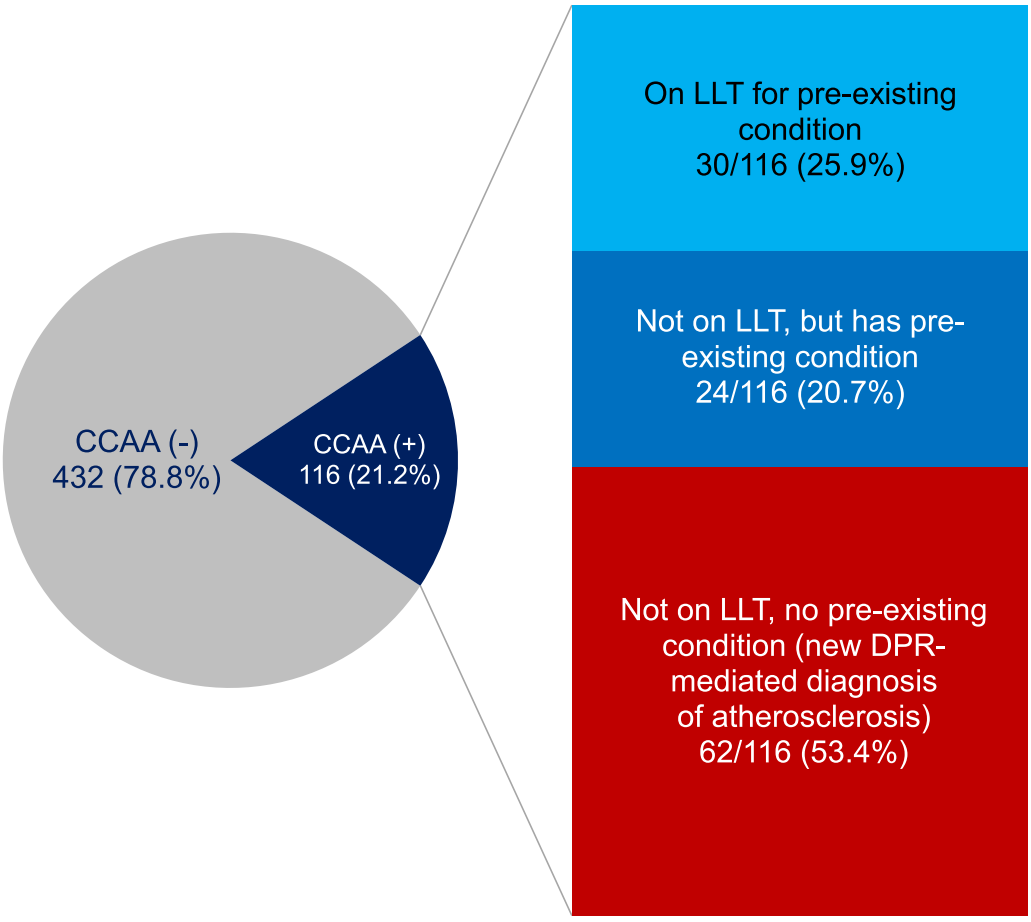

Fig. 2. Prevalence of calcified carotid artery atheroma and associated use of lipid lowering therapy. Over half of patients with calcified carotid artery atheroma on dental panoramic radiographs represent a new diagnosis of atherosclerosis. CCAA-positive patients were stratified by those taking LLT and those with pre-existing indications for treatment with LLT. CCAA, calcified carotid artery atheroma; DPR, dental panoramic radiograph; LLT, lipid-lowering therapy.

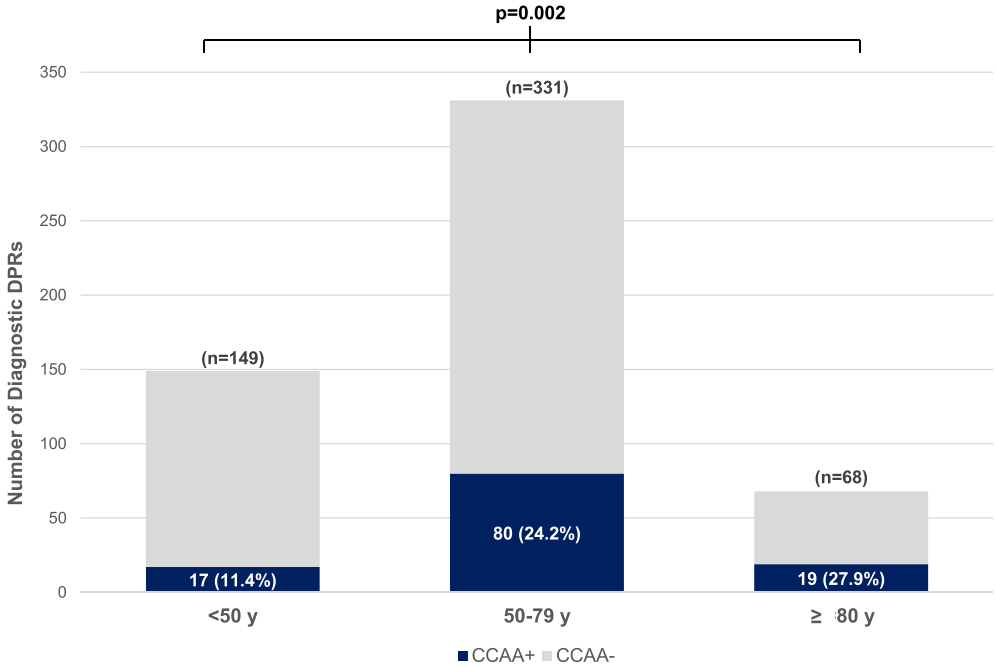

Fig. 3. Distribution of calcified carotid artery atheroma by age (<50 y, 50–79 y, and >80). There was a significant difference in the prevalence of CCAA between age groups; $p = 0.002$. CCAA, calcified carotid artery atheroma; DPR, dental panoramic radiograph.

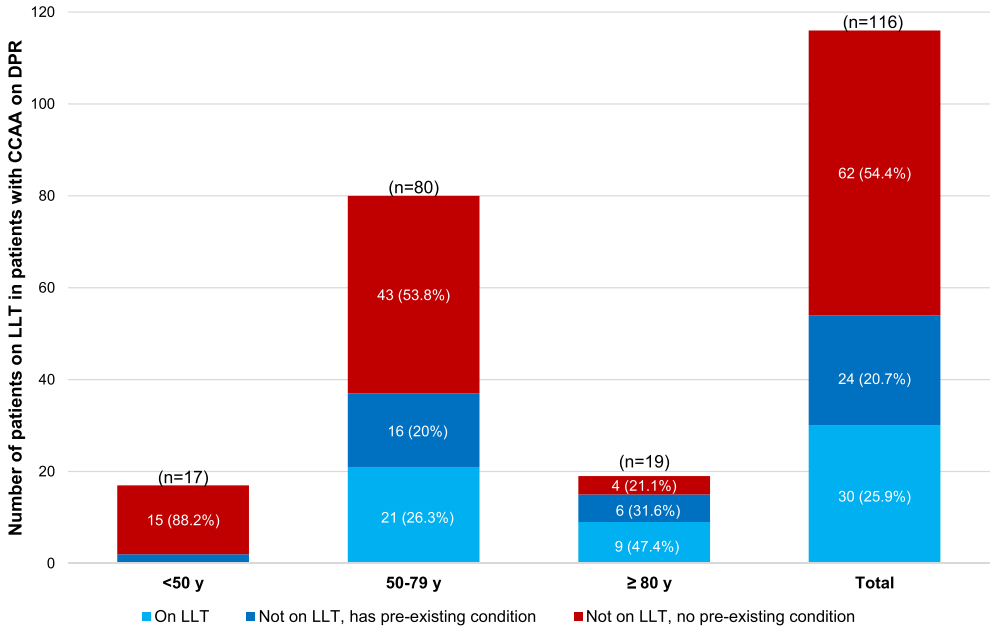

Fig. 4. Prevalence of lipid lowering therapy in patients with calcified carotid artery atheroma on dental panoramic radiograph by age group; age stratified <50 y, 50–79 y, and >80 y. CCAA, calcified carotid artery atheroma; DPR, dental panoramic radiograph; LLT, lipid-lowering therapy.

80) for patients 50 to 79, and 21.1 % (4/19) for those 80 and over.

A larger proportion of males were excluded from analysis due to non-diagnostic DPRs than females (271 males compared to 102 females). Despite this, sex was also a statistically significant predictor for the presence of CCAA on DPRs under chi-squared analysis ($p = 0.004$). Males had a greater prevalence of CCAAs identified on DPRs in comparison to females (27.6 %, 59/214 in males, 17.1 %, 57/334 in females) (Fig. 5). Of the males with CCAAs, 67.8 % (40/59) were not on LLT in comparison to 80.7 % (46/57) of females (Fig. 6).

The results of multiple chi-squared analyses are shown in Table 2. Several statistically significant predictors of CCAA were identified, including presence of hypertension ($p \leq 0.001$), dyslipidemia ($p = 0.011$), coronary artery disease ($p = 0.001$), diabetes mellitus ($p = 0.011$), atrial fibrillation ($p = 0.005$), and stroke/transient ischemic attack ($p = 0.007$). Chronic kidney disease, heart failure, peripheral artery disease, and a history of abdominal aortic aneurysm was not statistically significant as a predictor of CCAA on DPR. The three strongest predictors of CCAA identified on DPRs were a combination of male sex, presence of any pre-existing indication for treatment with LLT, and hypertension.

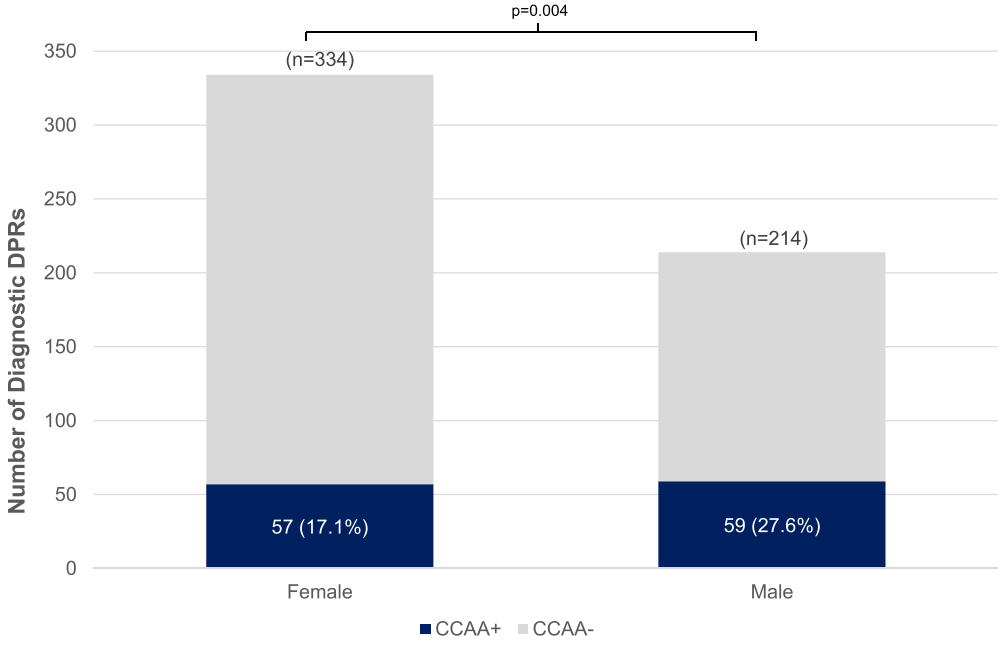

Fig. 5. Prevalence of calcified carotid artery atheroma on dental panoramic radiograph by sex. A greater proportion of male patients had CCAA on DPR compared to females; $p = 0.004$. CCAA, calcified carotid artery atheroma; DPR, dental panoramic radiograph; LLT, lipid-lowering therapy.

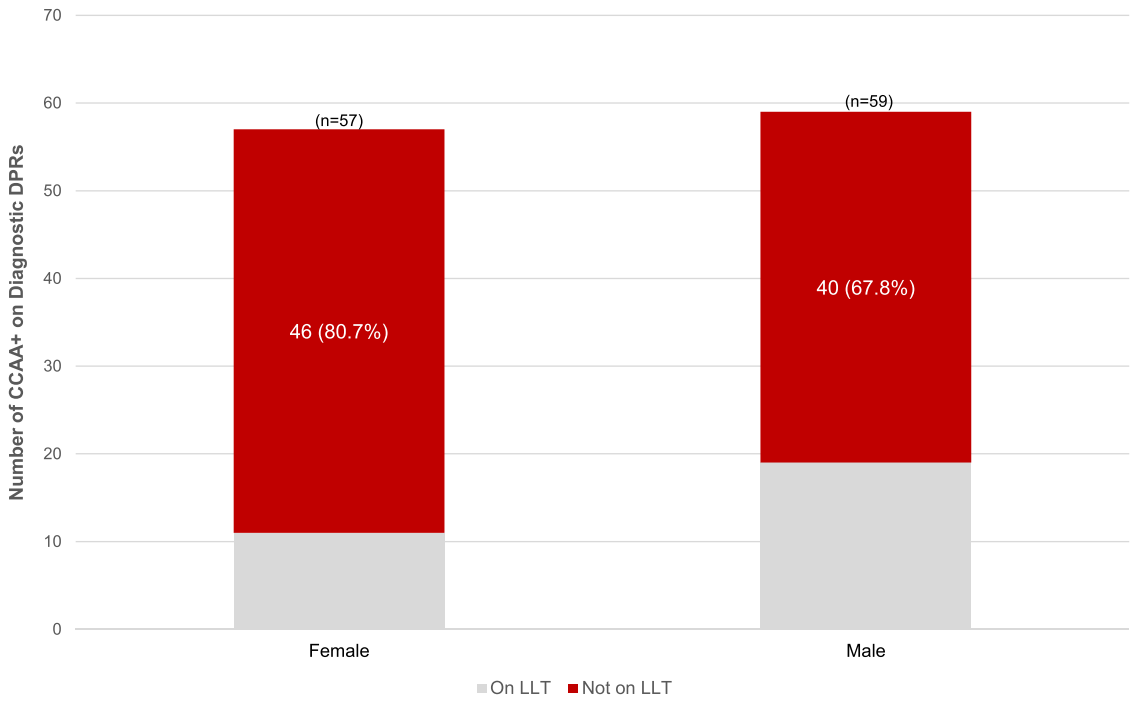

Fig. 6. Prevalence of lipid lowering therapy in patients with calcified carotid artery atheroma on dental panoramic radiograph by sex. CCAA calcified carotid artery atheroma; DPR dental panoramic radiograph.

Table 2
Predictors of Calcified carotid artery atheroma.

Variable	*p-value*	Variable	*p-value*
Age (50–79, >80 vs. <50)	0.002*	Past medical history	
Sex (male vs. female)	0.004*	Carotid atherosclerosis (present vs. absent)	0.212
Pre-existing indication for treatment with LLT (present vs. absent)	<0.001*	Hypertension (present vs. absent)	<0.001*
Smoking history (Current, Ex-smoker, Non-smoker)	0.084	Diabetes (present vs. absent)	0.011*
Marijuana smoking history (Current, Ex-smoker, Non-smoker)	0.865	Chronic kidney disease (present vs. absent)	1.000
* Significance of 0.05 by exact Chi-square test		Dyslipidemia (present vs. absent)	0.011*
		Coronary artery disease (present vs. absent)	0.001*
		Heart failure (present vs. absent)	0.115
		Atrial fibrillation (present vs. absent)	0.005*
		Peripheral artery disease (present vs. absent)	1.000
		Stroke/TIA (present vs. absent)	0.007*
		Abdominal aortic aneurysm or prior surgery (present vs. absent)	0.212

LLT, lipid-lowering therapy; CAD, coronary artery disease; DM, diabetes mellitus; AF, atrial fibrillation; TIA, transient ischemic attack; HTN, hypertension.

4. Discussion

Our study is a large cohort investigating the prevalence of CCAA and its relation to existing diagnoses of atherosclerosis and use of lipid-lowering therapy. We found that CCAA is a relatively common finding among patients with DPRs (21.2 % of DPRs of adequate quality), and that in 53.4 % of these cases, the presence of CCAA represented a new diagnosis of atherosclerosis. We demonstrated that systematic reporting of CCAA on DPRs can identify a new statin-indicated condition in a significant proportion of dental patients (6.7 % of the total clinic sample). Existing literature has mainly focused on the prevalence of CCAA in the setting of specific medical conditions such as type 2 diabetes, stroke, sleep apnea, chronic kidney disease, metabolic syndrome, or following head and neck radiation therapy. These studies have been limited by relatively small sample sizes and did not examine the frequency of baseline treatment for atherosclerosis with lipid-lowering therapy, an important distinction in our project [11].

Friedlander et al. in 1994 found that in 19 male patients with a recent cerebrovascular accident, subsequent DPRs taken found 37 % of these patients had radiographic evidence of CCAA [18]. Additionally, in 2000, Friedlander found that 49 patients with type 2 diabetes mellitus had a 20.4 % prevalence of CCAAs on DPRs compared to 4 % in non-diabetics [19], and Uthman et al. in 2007 reported a 38.8 % prevalence of CCAAs in 157 Iraqi patients with 'stroke-related' disease compared to a healthy control group [20]. These studies did not investigate the prevalence of CCAA in a general population, where the proportion of these patients would be diluted into a healthy patient pool. Notably, a 2003 study in Japan aimed at 80-year-olds reviewed 659 patients and found a 5 % prevalence of CCAAs, though the medical histories of these patients were not collected to provide context for these findings [21].

A study by Friedlander et al. in 2005 compared a presumptive diagnosis of CCAA on DPR from 1548 patients with Doppler ultrasonography to determine the prevalence of large occlusive lesions in neurologically asymptomatic dental patients [22]. They found that 79 % of these patients had mild (< 50 %) stenosis, 17 % had moderate (50–69 %) stenosis, and 4 % had severe (≥ 70 %) stenosis. This indicates that a large subset of the population with CCAA can be detected with DPR, even if they have mild stenosis.

While the traditional concern regarding carotid atherosclerosis has been the risk of ischemic stroke, the presence of carotid atherosclerosis is an indicator of advanced plaque deposition in other vascular territories, such as the coronary arteries [2-7]. A meta-analysis revealed that the detection of carotid plaque via ultrasound demonstrates an 80 %

sensitivity and a 67 % specificity for identifying coronary stenosis of ≥50 %, underscoring the significant correlation between these conditions [23]. Oftentimes, a patient can be asymptomatic until there is over 50 % or even over 70 % occlusion of the carotid arteries. A 2006 study by Goessens et al. reported a 10 % prevalence of asymptomatic carotid artery stenosis of ≥ 50 % in a cohort of patients who had clinical evidence of atherosclerosis in other vascular territories [24]. In fact, the SMART Study in 2007 demonstrated that asymptomatic carotid artery stenosis was an independent predictor of vascular events (hazard ratio 1.5) and vascular death (hazard ratio 1.8) in patients with clinical manifestations of arterial disease or type 2 diabetes mellitus [25]. Carotid artery stenosis has also been noted as a predictor of myocardial infarction and mortality [26,27]. This underscores the importance of early initiation of LLT in this patient population.

We stratified our patients by age to further assess the population in which this new diagnosis of carotid atherosclerosis was being found; these age ranges were chosen as thresholds that would most likely affect a clinical decision to begin LLT in a new diagnosis of atherosclerosis. While 85.3 % of the CCAA-positive DPRs were from patients who were ≥ 50 years old, 14.7 % were from patients < 50 years old. The majority of CCAA-positive patients (73.8 %) between 50 and 79 were not on LLT, whereas 100 % of the patients < 50 years old were not on LLT. The high prevalence of new and untreated atherosclerosis in the dental population, especially in patients <50 years old, indicates an opportunity for intervention with LLT for primary prevention of MACE. While there was a smaller subset of patients > 80 years old not on LLT, it is possible that these patients may not warrant starting LLT due to other factors, such as cardiovascular benefit in the context of life expectancy, concerns for polypharmacy, and other reasons that would be best discussed with a patient's primary care provider or cardiologist.

Dentist reporting of CCAA found on DPRs to a patient's primary care provider can result in earlier recognition of individuals at higher risk of MACE in the population. Identification of CCAA in the dentist's office can represent a new and effective way of utilizing routine imaging in the community to classify high-risk individuals in the population without additional imaging and potential radiation exposure. Our research establishes the foundation for future studies aimed at investigating how communication between dental professionals and the medical team can influence changes in patient management, particularly in the context of preventing cardiovascular events. We propose a potential workflow for CCAA detected in the dental office. When CCAA is found chair-side, the treating dentist should ask about recent uninvestigated/untreated stroke-like symptoms that would warrant referral to urgent care for management. In the absence of symptoms of carotid stenosis, a letter could be generated for the primary care physician that indicates: 1. that the patient has been found to have CCAA on DPR, 2. outlines the sensitivity and specificity of CCAA on DPR for carotid atherosclerosis, and 3. suggests cardiovascular risk review, lipid panel, and consideration for lipid-lowering therapy.

4.1. Limitations

While DPRs demonstrate a sensitivity of 80 % in detecting carotid calcifications [11], it is essential to acknowledge potential false negatives. Our image analysis was conducted under optimal conditions, utilizing bright monitors and reduced ambient lighting, circumstances that may not be readily available or feasible in a typical dental practice setting. Moreover, DPRs are primarily intended for assessing oral structures, and as such, the region of CCAA may not be consistently captured in routine imaging. In a study by Khambete et al., which compared DPRs with Doppler ultrasonography, they reported a sensitivity of 76 % and specificity of 98.3 % in a small sample of patients over 50 years old ($n = 50$) [13]. Additionally, Friedland et al. (2005) conducted a comparative analysis of CCAA on DPRs and Doppler ultrasonography ($n = 65$), confirming the presence of carotid atherosclerosis in all subjects [21]. These findings highlight the variability in sensitivity and specificity across studies.

A notable gender disparity emerged In the exclusion of participants with non-diagnostic DPRs, with a higher count observed among males (271) compared to females (102). We hypothesize that this may be due to an increased skull size, as previous anthropologic studies on skulls have reported larger skull sizes in males in all dimensions [28]. This larger skull size may contribute to the radiographic unit's inability, in certain cases, to fully capture the inferolateral neck portion during DPRs. Most current models of DPRs use shorter vertical collimators in order to reduce the height of the irradiated area solely to the bony jaws [29]. As a result the upper neck, may be excluded from the image of the larger patient, more frequently male. Nevertheless, such DPRs are deemed dentally diagnostic if they display the area of the dental complaint that induced the DPR's prescription. Despite this, there was still a significant association found between males and CCAA found on DPRs, likely indicating that our study is underestimating the prevalence in males.

Another important consideration in our study is pertains to the risk of inaccuracies in the reported data. We utilized self-reported medical and medication histories which is at risk of errors related to omissions or inaccurate reporting by patients. However, these errors would be expected to occur across the comparison groups so we would not anticipate a systematic bias that would impact the study result.

5. Conclusion

This study demonstrates that systematic reporting of CCAA on DPRs can identify a new diagnosis of atherosclerosis in a significant proportion of dental patients. The high prevalence of new, untreated atherosclerosis in this dental population indicates an opportunity for non-pharmacologic and pharmacologic interventions and highlights the importance of collaboration between dentists and physicians to optimize patient care.

CRediT authorship contribution statement

Vicky Mai: Writing – original draft, Visualization, Formal analysis, Data curation. **Aneesha Taneja:** Writing – review & editing, Formal analysis, Data curation. **Hannu Larjava:** Writing – review & editing, Supervision. **Babak Chehroudi:** Writing – review & editing, Supervision. **David MacDonald:** Writing – review & editing, Validation, Supervision, Resources. **Christina Luong:** Writing – review & editing, Validation, Supervision, Methodology, Funding acquisition, Formal analysis, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Christina Luong reports financial support was provided by Vancouver Coastal Health Research Institute. Christina Luong reports a relationship with Vancouver Coastal Health Research Institute that includes: funding grants. Christina Luong reports a relationship with Canadian Cardiovascular Society that includes: funding grants. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ajpc.2024.100714.

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