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ORIGINAL ARTICLE

Calcified carotid artery atheromas in individuals with cognitive dysfunction

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ABSTRACT

Objective: The aim of this case-control study was to investigate whether cognitively impaired individuals have a higher burden of calcified carotid artery atheroma (CCAA) than controls without cognitive impairment.

Material and methods: The study included 154 cases with Alzheimer's disease ($n = 52$), mild cognitive impairment ($n = 51$), or subjective cognitive decline ($n = 51$) diagnosed at a university memory clinic. Seventy-six cognitively healthy controls were sampled through the Swedish population register. All participants underwent clinical oral and panoramic radiographic examinations. Two oral and maxillofacial radiologists performed blinded analyses of the panoramic radiographs for signs of CCAA, which was registered as absent or present and, if present, unilateral or bilateral. Consensus assessment was used for all statistical analyses.

Results: CCAA was common (40%) in this middle-aged and older Swedish population. We found no differences in the prevalence of CCAA between cases and controls (40% vs. 42%).

Conclusion: Cognitively impaired patients do not have a higher burden of CCAA than matched controls without cognitive impairment.

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Introduction

There is growing interest in potential associations between systemic and oral diseases, and diagnostic data from a dental examination may be important in a broader medical context. The mechanism underlying the development of cerebral vascular disease, coronary artery disease and peripheral vascular disease is atherosclerosis [1]. Rupture of the atherosclerotic plaque may lead to serious complications, such as myocardial infarction, stroke or acute coronary syndrome [2]. The use of dental panoramic radiographs is widespread in dental practice, and these radiographs often include information with diagnostic potential for systemic diseases [3–6]. Panoramic radiographs often include not only the maxillary and mandibular regions, but also parts of the neck, including the area of the bifurcation of the carotid arteries, a frequent site for the development of atherosclerotic plaques. On the panoramic radiograph, a calcified atheroma in the carotid artery may be detectable as a radiopacity, referred to as a calcified carotid artery atheroma (CCAA) [6].

Dementia is a broad term for several neurological disorders characterized mainly by memory loss and cognitive impairment. Alzheimer's disease (AD) accounts for 50–70% of all dementia cases. Typical signs of AD are short-term memory loss, disorientation, irritability and behavioural changes. One of several hypotheses proposed for the aetiology of AD is the inflammatory hypothesis [7]. Other cognitive disorders are also recognized, including subjective cognitive decline (SCD) and mild cognitive impairment (MCI). SCD includes a history of symptoms of cognitive dysfunction but with no objective signs, whereas MCI has objective symptoms with minor cognitive failure on memory tests [8].

The relationship between dementia and cardiovascular disease (CVD) is not fully understood. A large cohort study from the Swedish Dementia Registry reported an association between all types of CVD and a greater risk of mortality among patients diagnosed with cognitive disorders [9]. Links between CVD, cognitive impairment and dementia have recently been described [10–12].

The aim of this study was to investigate whether individuals with cognitive dysfunction have a higher burden of CCAA detected on panoramic radiographs than cognitively healthy controls. A subanalysis was also carried out to investigate CCAA in different oral health conditions.

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Materials and methods

Study design

All participants were recruited as part of a recently published case-control study conducted between 2013 and 2017 to investigate the association between periodontitis and cognitive dysfunction [13]. A description of the study population and the clinical and radiographic examination, except for the analysis of CCAA in panoramic radiographs, were presented in the previous paper. Critical features relevant to the current investigation are outlined below.

Study population

A total of 230 individuals were enrolled in this study. The cases comprised 154 individuals recently diagnosed with AD, MCI, or SCD who were enrolled from the Karolinska Memory Clinic at Karolinska University Hospital in Huddinge, Sweden. Inclusion criteria were age 50–80 years; newly diagnosed AD, MCI, or SCD; and informed consent prior to donation of cerebrospinal fluid and plasma for research purposes. Eligible dementia cases were identified for participation in the current study by a senior medical consultant specializing in geriatric medicine (ME) at the Karolinska Memory Clinic. Seventy-six cognitively healthy individuals matched for age and gender served as controls. The controls were eligible if they had not experienced severe memory loss or disrupted daily life, had not sought medical attention for memory loss and were residents of the municipality of Huddinge, Stockholm county, Sweden, during the study period. The following exclusion criteria applied to all participants: severe medical conditions, such as brain tumours, clinically significant liver, kidney, or lung dysfunction and endocrine disease. Among cases, persons with vascular dementia were excluded. Before the oral examination, data on socioeconomic status, education and medical history were collected using a standardized questionnaire for cases and controls. All participants underwent clinical and radiological dental examinations. Panoramic radiographs covered both jaws and the neck area, including the carotid arteries. The radiographs were acquired with a ProMax® (Planmeca Oy/Ab, Helsinki, Finland) using a CCD detector (pixel size 33 μm) according to a standard exposure protocol: 68 kV, 7.0 mA and 16.4 s. The panoramic radiographs were anonymized and coded before being downloaded in both JPEG and DICOM formats for assessment. The radiographic examinations were performed to assess marginal alveolar bone loss with a low dose of radiation compared to full mouth intraoral radiographic examination (i.e. the primary reason for the panoramic examinations was not to assess CCAA).

Data collection

Two specialists in oral and maxillofacial radiology (JA and ELJ) who were blinded to information about the participants independently assessed the panoramic radiographs for CCAAs. Other structures in the same area of interest (e.g. the hyoid bone, calcified triticeal cartilage, lymph nodes, or thyroid cartilage) were differentiated from CCAA. The radiographs were analysed in a room with dim lighting using Preview software (Apple Inc., Cupertino, CA, USA) and high-resolution screens (Retina Display, 15-inch IPS-display with LED-backlight, 2880×1800 pixels, 220 ppi, maximum brightness 300 cd/m^2, contrast ratio 900:1, colour depth 8 bits, 100% sRGB; Apple Inc., Cupertino, CA, USA). Settings, such as contrast and brightness, were adjusted to optimize the conditions for detecting calcifications in the neck region. All CCAAs were registered for each side of the neck (left and right). In case of disagreement, the presence or absence of a CCAA was determined by consensus. The findings were then summarized as unilateral or bilateral presence and included in the statistical analyses.

Data on marginal alveolar bone loss and tooth loss were retrieved from our previous study [13]. The severity of marginal alveolar bone loss was assessed as mild or none (loss of supporting bone less than one-third the root length), localized (loss of supporting bone more than one-third the root length in $<30\%$ of teeth), or generalized (loss of supporting bone more than one-third the root length in $\geq 30\%$ of teeth). Tooth loss was defined as having fewer than 20 remaining teeth in the dentition.

Inter-observer agreement

Inter-observer agreement between the examiners was assessed using Cohen's Kappa (κ). For detection of CCAA, the inter-observer agreement between the two radiologists was $\kappa = 0.71$. The inter-observer agreement between JH and KB, who assessed marginal alveolar bone loss on the panoramic radiographs, was $\kappa = 0.8$. Both κ-values were considered to represent 'substantial agreement' [14].

Ethical approval

This study was carried out in accordance with the Declaration of Helsinki. Ethical approval was granted by the Regional Ethical Review Board in Stockholm (2012/652-31/1). All participants provided written informed consent.

Statistical analysis

Sample size calculations were performed prior to the previous study [13]. The aim was to detect a 30% difference in marginal alveolar bone loss assuming 80% power and 5% alpha error for all cases combined vs. controls, as well as each subgroup vs. controls. The estimated number of required participants was 42 per group (AD, MCI, SCD and controls). To increase the statistical power, the minimum number of participants was set to 50 for each subgroup and 75 for controls.

Differences in the presence of CCAA among controls and cognitively impaired cases and the oral status in relation to CCAA were assessed by χ^2 based on a four-group comparison (AD, MCI, SCD and controls). Intergroup differences between the three subgroups (AD, MCI and SCD) and the control group were analysed using χ^2 and Fisher's exact test for categorical variables and analysis of variance for continuous variables. Analysis of differences between those with or without CCAA within the three subgroups (AD, MCI and SCD) and controls was performed using χ^2 and Fisher's exact test for categorical variables and analysis of variance for

continuous variables. Odds ratios (ORs) with 95% confidence intervals (CIs) were estimated using either binary logistic regression analyses (dichotomous outcome) or multinominal logistic regression analyses (nominal outcome). Logistic regression was used for the analysis of oral health conditions and the analysis of CCAA and dementia for both the combined all cases group and the independent diagnostic groups (AD, MCI, SCD). ORs were estimated for the combined all cases group using binary logistic regression modelling. For the independent diagnostic subgroups (AD, MCI, SCD and controls), multinominal logistic regression was used. Both crude and adjusted point estimates were fitted with corresponding 95% CIs.

To account for confounders in the analysis of CCAA and dementia in the subanalysis of oral health variables (marginal alveolar bone loss and tooth loss), the models were adjusted for age, gender, education, diabetes, body mass index and smoking. Covariate selection was based on knowledge of the subject matter and theoretical reasoning. In the analyses of oral status and CCAA, one edentulous case from the MCI subgroup was excluded from the analysis of marginal alveolar bone loss. Statistical analyses were performed using IBM SPSS® Statistics v. 23 (IBM Corp., Armonk, NY, USA) and Stata Statistical Software (Release16, StataCorp LP, College Station, TX, USA).

Results

Study population

A total 154 cases evenly distributed among the three diagnostic subgroups (AD: $n = 52$, MCI: $n = 51$, SCD: $n = 51$) and 76 controls were enrolled in the study. Descriptive background variables, such as age, gender, comorbidities, body mass index, smoking habits, education and income, are presented in Table 1. The combined cases and control group were well matched for age (mean ± standard deviation: 67 ± 8 vs. 69 ± 6 years). However, for logical reasons, the SCD group had a lower mean age (analysis of variance based on a four-group comparison, $p = .001$, Table 1). The mean ages for cases with dementia were 71 ± 6 (AD), 69 ± 7 (MCI) and 62 ± 6 (SCD) years. In addition, the difference in gender distribution between case subgroups and controls was not significant (male: AD 46% vs. MCI 50% vs. SCD 43% vs. controls 44%; χ^2: $p = .83$, Table 1).

CCAA and cognitive dysfunction

Descriptive characteristics stratified according to the presence or absence of CCAA are presented in Table 2. The prevalence of CCAA among cases and controls is presented in Table 3. Unilateral or bilateral CCAAs were registered in 42% of controls, 44% of the AD subgroup, 39% of the MCI subgroup and 35% of the SCD subgroup. The presence of bilateral CCAAs was found more often in cases with AD (21%) than in controls (20%), MCI (4%) and SCD (14%) ($p = .05$; analysis of variance based on a four-group comparison). Unilateral CCAA was present in 23% of the AD subgroup, 35% of the MCI subgroup and 22% of the SCD subgroup compared to 22% of controls.

As shown in Table 4, cases with AD, MCI, or SCD were not at higher risk of CCAA than the controls (adjusted OR 1.0, 95% CI 0.6–1.9; $p = .96$). The OR for CCAA was also assessed for the separate subgroups compared to controls. No significant associations were found when analysing subgroups and the ORs ranged from 1.0 to 1.1 (95% CIs: AD 0.5 to 2.3, MCI 0.4 to 2.1 and SCD 0.4 to 2.3).

Subanalysis of oral conditions and CCAA

The subanalysis of dental conditions included tooth loss and marginal alveolar bone loss (Table 5). ORs were 1.5 (95% CI 0.6

Table 1. Socioeconomic and clinical characteristics of all participants with or without cognitive disorders.

	All cases $n = 154$	AD $n = 52$	MCI $n = 51$	SCD $n = 51$	Control $n = 76$	
Variable						[a]*p* value
Mean age ± SD, years	67 ± 8	71 ± 6	69 ± 7	62 ± 6	69 ± 6	*.001*
Gender						.83
Male	72 (46.8)	24 (46.2)	26 (50.1)	22 (43.1)	33 (43.4)	
Female	82 (53.2)	28 (53.8)	25 (49.0)	29 (56.9)	43 (56.6)	
CVD	70 (45.5)	24 (46.2)	24 (47.1)	22 (43.1)	36 (47.4)	.98
BMI ≥25 kg/m^2	66 (42.9)	15 (28.9)	24 (47.1)	27 (52.9)	50 (65.8)	.41
Diabetes	17 (11.0)	7 (13.5)	4 (7.8)	6 (11.8)	8 (10.5)	.84
Smoking status						.72
Current	10 (6.5)	6 (11.5)	2 (3.9)	2 (3.9)	6 (7.9)	
Previous	66 (42.9)	22 (52.3)	24 (47.1)	20 (39.2)	32 (42.1)	
Never	78 (50.6)	24 (46.2)	25 (49.0)	29 (56.9)	38 (50)	
Education						*.01*
1–12 years	88 (57.1)	30 (57.7)	38 (74.5)	20 (39.2)	52 (68.4)	
University	66 (42.9)	22 (42.3)	13 (25.5)	31 (60.8)	24 (31.6)	
Income						.11
<180,000 SEK/year	27 (17.5)	9 (13.7)	11 (21.2)	7 (13.7)	13 (17.1)	
180,000–300,000 SEK/year	62 (40.3)	25 (48.1)	20 (39.2)	17 (33.3)	37 (48.7)	
300,000–520,000 SEK/year	52 (33.8)	15 (28.8)	17 (33.3)	20 (39.2)	13 (17.1)	
>520,000 SEK/year	13 (8.4)	3 (5.8)	3 (5.9)	7 (13.7)	13 (17.1)	

Notes: Values are given as *n* (%) unless noted. CVD: any type of ongoing clinically significant cardiovascular disease, including previous cardiovascular events; BMI: body mass index; AD: Alzheimer's disease; MCI: mild cognitive impairment; SCD: subjective cognitive decline. ALL CASES: AD, MCI and SCD groups combined. 1 SEK is approximately equal to 0.11 USD. P value italicized when P <0.05.
[a]Analysis of intergroup differences between the three subgroups (AD, MCI and SCD) and the control group was performed using χ^2 and Fisher's exact test for categorical variables and analysis of variance for continuous variables.

Table 2. Socioeconomic and clinical characteristics of all participants with or without cognitive disorders stratified according to the presence or absence of CCAA on panoramic radiographs.

	All cases $n=154$		AD $n=52$			MCI $n=51$			SCD $n=51$			Control $n=76$		
Variable	CCAA	No CCAA	CCAA	No CCAA	[a]*p*	CCAA	No CCAA	[a]*p*	CCAA	No CCAA	[a]*p*	CCAA	No CCAA	[a]*p*
Mean age ± SD, years	68 ± 8	67 ± 7	71 ± 7	70 ± 6	.94	71 ± 6	68 ± 7	.24	61 ± 5	62 ± 6	.53	70 ± 6	68 ± 6	.12
Gender					.48			.23			.56			.39
Male	30 (41.6)	42 (58.4)	10 (41.6)	14 (58.4)		12 (46.1)	14 (53.9)		8 (36.3)	14 (63.7)		15 (45.4)	18 (54.6)	
Female	31 (38.0)	51 (62.0)	13 (46.4)	15 (53.6)		8 (32)	17 (68)		10 (34.4)	19 (65.6)		17 (39.5)	26 (60.5)	
CVD	26 (37.1)	44 (62.9)	11 (45.8)	13 (54.2)	.53	8 (37.5)	16 (62.5)	.56	7 (31.8)	15 (68.2)	.44	20 (55.5)	16 (44.5)	*.02*
BMI ≥25 kg/m^2	27 (40.9)	39 (59.1)	8 (53.3)	7 (46.7)	.30	8 (33.3)	16 (66.7)	.30	11 (40.7)	16 (59.3)	.22	23 (46)	27 (54)	.14
Diabetes	10 (58.8)	7 (41.2)	4 (57.1)	3 (42.9)	.37	3 (75)	1 (25)	.16	3 (50)	3 (50)	.35	8 (100)	0 (0)	*.001*
Smoking status					.17			.58			.77			.25
Current	4 (40)	6 (60)	2 (33.3)	4 (66.7)		1 (50)	1 (50)		1 (50)	1 (50)		4 (66.6)	2 (33.4)	
Previous	24 (36.3)	42 (63.7)	7 (31.8)	15 (68.2)		11 (45.8)	13 (54.2)		6 (30)	14 (70)		15 (46.8)	17 (53.2)	
Never	33 (42.3)	45 (57.7)	14 (58.3)	10 (41.7)		8 (32)	17 (68)		11 (37.9)	18 (62.1)		13 (34.2)	25 (65.8)	
Education					.33			.61			.60			*.03*
1–12 years	34 (38.6)	54 (61.4)	12 (40)	18 (60)		15 (39.4)	23 (60.6)		7 (35)	13 (65)		26 (50)	26 (50)	
University	27 (40.9)	39 (59.1)	11 (50)	11 (50)		5 (38.4)	8 (61.6)		11 (35.4)	20 (64.6)		6 (25)	18 (75)	
Income					.47			.32			.61			.79
<180,000 SEK/year	9 (33.3)	18 (66.7)	2 (22.2)	7 (77.8)		3 (27.2)	8 (72.8)		4 (57.1)	3 (42.9)		5 (38.4)	8 (61,6)	
180,000–300,000 SEK/year	30 (48.3)	32 (51.7)	13 (52)	12 (48)		11 (55)	9 (45)		6 (35.2)	11 (64.8)		17 (45.9)	20 (54.1)	
300,000–520,000 SEK/year	18 (34.6)	34 (65.4)	7 (46.6)	8 (53.4)		5 (29.4)	12 (70.6)		6 (30)	14 (70)		6 (46.1)	7 (53.9)	
> 520,000 SEK/year	4 (30.7)	9 (69.3)	1 (33.3)	2 (66.7)		1 (33.3)	2 (66.7)		2 (28.5)	5 (71.5)		4 (30.7)	9 (69.3)	

Notes: Values are given as *n* (%) unless otherwise noted. CCAA: calcified carotid artery atheroma; CVD: any type of ongoing clinically significant cardiovascular disease, including previous cardiovascular events; BMI: body mass index; AD: Alzheimer's disease; MCI: mild cognitive impairment; SCD: subjective cognitive decline. ALL CASES: AD, MCI and SCD groups combined. 1 SEK is approximately equal to 0.11 USD. P value italicized when P <0.05.
[a]Analysis of differences between those with or without CCAA within the three subgroups (AD, MCI and SCD) and controls was performed using χ^2 and Fisher's exact test for categorical variables and analysis of variance for continuous variables.

Table 3. Prevalence of CCAA among all cases, subgroups and controls.

CCAA localization	All cases $n=154$	AD $n=52$	MCI $n=51$	SCD $n=51$	Control $n=76$	*p* Value[a]
U/B	61 (39.6)	23 (44.2)	20 (39.2)	18 (35.2)	32 (42.1)	.80
R	42 (27.2)	16 (30.8)	12 (23.5)	14 (27.5)	22 (28.9)	.86
L	39 (25.3)	18 (34.5)	10 (19.6)	11 (21.6)	25 (32.9)	.18
Bilateral	20 (13.0)	11 (21.2)	2 (3.9)	7 (13.7)	15 (19.7)	.05
Unilateral	41 (26.6)	12 (23.1)	18 (35.3)	11 (21.6)	17 (22.4)	.31
Unilateral-R	22 (14.3)	5 (9.6)	10 (19.6)	7 (13.7)	7 (9.2)	.32
Unilateral-L	19 (12.3)	7 (13.5)	8 (15.7)	4 (7.8)	10 (13.2)	.67

Notes: Values are given as *n* (%). CCAA: calcified carotid artery atheroma; U/B: unilateral and bilateral; R: right side; L: left side. 'All cases' includes all patient subgroups. AD: Alzheimer's disease; MCI: mild cognitive impairment; SCD: subjective cognitive decline.
[a]Analysis of the difference in the presence of CCAA was assessed by χ^2 test based on a four-group comparison including the subgroups and controls.

Table 4. Odds ratios (ORs) for calcified carotid artery atheroma (CCAA) among all cases and subgroups compared to controls.

	Crude			Adjusted		
CCAA, *yes*	*OR*	95% CI	*p*	*OR*	95% CI	*p*
All cases, $n=61/154$	0.9	0.5–1.6	.72	1.0	0.6–1.9	.96
AD, $n=23/52$	1.1	0.5–2.2	.81	1.1	0.5–2.3	.86
MCI, $n=20/51$	0.9	0.4–1.8	.75	1.0	0.4–2.1	.91
SCD, $n=18/51$	0.8	0.4–1.6	.44	1.0	0.4–2.3	.10

Notes: AD: Alzheimer's disease; MCI: mild cognitive impairment; SCD: subjective cognitive decline. Point estimates are given for both crude and adjusted ORs with 95% confidence intervals (CIs).

to 3.8) for tooth loss, and the relationship between marginal alveolar bone loss and the presence of CCAA varied among the patient groups (Table 5). A subanalysis performed to investigate a possible association between marginal bone loss (mild or no bone loss vs. localized and generalized bone loss) and CCAA among all cases and controls found that marginal alveolar bone loss was associated with CCAA (Table 5; OR 2.1, 95% CI 1.1 to 3.7).

Discussion

This study did not find any clear association between CCAAs detected on panoramic radiographs and cognitive dysfunction. The prevalence of unilateral or bilateral CCAA was 40% and 42% for cases and controls, respectively. Somewhat lower frequencies (28–39%) have been reported in recent studies for cases with relatively high mean age [6,15]. In contrast, clearly lower frequencies (4–5%) have been reported among younger cases with a mean age between 54 ± 13 and 58.6 ± 10.3 years [16,17]. As age is an independent risk factor for the progression of atherosclerosis [18], the age-dependent differences in CCAA frequencies are in line with previous research [19] and a major contributor in this study.

Accurate detection of CCAAs requires knowledge of other calcified structures found on panoramic radiographs in the area of the carotid arteries. Earlier research suggested that acceptable inter-observer agreement can be achieved by a general dental practitioner after some training [20]. The calcified carotid stenosis detectable on panoramic images can be asymptomatic or symptomatic. Symptomatic carotid stenosis requires medical, and sometimes surgical, treatment to prevent additional events [3,21]. When suspected CCAAs are detected on panoramic radiographs, general dental practitioners who have been educated in the detection of CCAAs should inform the patients and, if they are not already on medication to prevent CVD, recommend they seek medical advice. By carefully assessing the evidence for CCAA on all panoramic radiographs taken in dental practice, the dentist may facilitate early diagnosis of a medical condition, as detection of CCAAs on a panoramic radiograph would allow early intervention to prevent severe cardiovascular events. The cost-efficiency is high and no extra dose of radiation is involved.

Table 5. Oral disease stratified by subject group and CCAA prevalence and odds ratios (ORs) for oral disease exposure and calcified carotid artery atheroma among AD, MCI, SCD and controls.

Subject group	All cases (AD, MCI, SCD) $n = 154$		AD $n = 52$		MCI $n = 51$		SCD $n = 51$		Controls $n = 76$		Odds ratios[a]			
CCAA presence	Yes *n* (%)	No *n*	Yes *n* (%)	No *n*	Yes *n* (%)	No *n*	Yes *n* (%)	No *n*	Yes *n* (%)	No *n*	*p* Value[b]	Crude OR (95% CI)	*p* Value	Adjusted OR (95% CI)	*p* Value
Variable															
Tooth loss											.55				
No (20–32 remaining teeth)	56 (39.7)	85	21 (45.5)	25	18 (39.1)	28	17 (34.6)	32	27 (39.1)	42		Ref		Ref	
Yes (0–19 remaining teeth)	5 (38.4)	8	2 (33.3)	4	2 (40)	3	1 (50)	1	5 (71.4)	2		1.5 (0.6–3.8)	.36	0.9 (0.3–2.6)	.86
Marginal alveolar bone loss											.14				
None or mild	29 (32.9)	59	11 (40.7)	16	9 (31)	20	9 (28.1)	23	16 (32)	34		Ref		Ref	
Localized	27 (52.9)	24	8 (47)	9	10 (52.6)	9	9 (60)	6	14 (58.3)	10		2.3 (1.3–4.0)	.01	2.1 (1.1–3.7)	.02
Generalized	5 (35.7)	9	4 (50)	4	1 (50)	1	0 (0)	4	2 (100)	0					

Notes: CCAA: calcified carotid artery atheroma; AD: Alzheimer's disease; MCI: mild cognitive impairment; SCD: subjective cognitive decline. Marginal alveolar bone loss was defined as follows: mild or none, loss of supporting bone less than one-third of the root length; localized, loss of supporting bone more than one-third of the root length in $<30\%$ of teeth; generalized, loss of supporting bone more than one-third of the root length in $\geq 30\%$ of teeth. P value italicized when $P < 0.05$.

[a]Estimated using logistic regression. Adjustments were made for age, gender, education, smoking, body mass index and diabetes mellitus.

[b]Analysis of the difference in the presence of CCAAs based on a four-group comparison including AD, MCI, SCD and controls.

Previous research indicates a higher prevalence of CVD in patients with dementia than in cognitively healthy controls [9,22,23]. The present study did not find significant differences in the prevalence of CCAA among patients suffering from AD, the cognitive impairment subgroups and controls. There are several possible explanations for this observation. First, those diagnosed with AD, MCI and SCD had visited a memory clinic and undergone a thorough medical evaluation in which CVD may have been diagnosed and treated. Second, the cardiovascular health of the members in the control group was based on anamnestic data and they could potentially have undiagnosed CVD that manifested as CCAA. This self-reported health declaration by the controls is a limitation of this study. Furthermore, the studies referred to above included subjects with vascular dementia. In our study, patients suffering from vascular dementia were excluded because the aim was to investigate a possible association between non-vascular dementia and CCAA. It is likely that exclusion of these patients led to fewer participants with CCAA in our study population. In this context, the burden of CCAA is no greater in individuals with AD than in cognitively healthy subjects.

The association between the risk of cardiovascular events and CCAA on panoramic radiographs has been reported previously [4,6,24]. However, some studies have indicated that atheromas can be present but not detected on panoramic radiographs [25]. Compared to ultrasound examination, the method of choice for detection of carotid plaques [26], panoramic radiographs can depict carotid stenosis with $\geq$50% obstruction in up to 75% of cases [3]. The reason why all carotid plaques are not detectable may be a lack of calcification of the stenosis or because not all panoramic radiographs include the area of the carotid arteries. Therefore, a limitation of the present study is that whether all CCAAs were detected is unknown. However, the rate of undetected CCAAs can be expected to be similar across all groups.

Statistical analysis of bilateral CCAAs among the different patient groups indicated more serious carotid stenosis in patients with AD, with more cases of bilateral calcification (21% in AD vs. 4% in MCI and 14% in SCD). However, no conclusion can be drawn from this finding because the prevalence of CCAA in the control group was similar to the prevalence in the AD group (20% vs. 21%).

There is epidemiological evidence of an association between cardiovascular events and periodontitis [27,28]. The fact that periodontitis is related to cardiovascular disease is supported by the findings of the present study, as a higher prevalence of CCAA was observed among all participants, including the controls, with radiographically detected marginal alveolar bone loss. Recent research has also shown an association between CCAAs and periodontitis [15,29–32], which indicates that a greater burden of periodontal disease may contribute to CVD in general, including the formation of calcified plaque within the carotid arteries. In addition, CCAAs on panoramic radiographs can predict cardiovascular and all-cause mortality [29]. The presence of CCAAs on panoramic radiographs has also been associated with renal dysfunction, chronic kidney disease, chronic pancreatitis and comorbid diabetes [5,33,34].

The subanalyses have weaknesses. For example, there were few participants, resulting in statistical dilution and, therefore, the external validity is limited. Nonetheless, the suggested association between marginal alveolar bone loss and CCAA is notable and warrants further investigation. Importantly, although associations were found in the subanalysis of CCAA and signs of oral disease, the primary objective of this study was not to investigate a possible association between CCAA and oral health conditions. A larger population and different study design will be required to investigate such associations.

The present study has a number of strengths. Firstly, the study population is unique and no previous investigations of a similar study population have analysed the presence of CCAAs on panoramic radiographs. Secondly, patients with vascular dementia were excluded. Thus, the study explored whether AD, without the influence of vascular dementia, is associated with CCAA. Thus, the study design precluded investigation of the association between vascular dementia and the presence of CCAA. In future investigations of dementia and CVD, vascular dementia should be included as a separate dementia subgroup.

In conclusion, CCAA was a common finding on panoramic radiographs in this population consisting of older Swedish participants, regardless of cognitive status. However, the cases with cognitive impairment in this population did not exhibit a higher burden of CCAA than matched controls. This suggests that age and its medical consequences could be a more important factor in the prevalence of CCAA, indicating CVD. This implies that further investigation is warranted in larger populations.

Statement of clinical relevance

The links between cardiovascular disease and cognitive dysfunction are not entirely understood. This study explores the possible correlations between cognitive impairment, including Alzheimer's disease, and calcified carotid artery atheromas detected on dental panoramic radiographs.

Disclosure statement

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