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Unravelling the link between periodontitis and abdominal aortic calcification in the US adult population: a cross-sectional study based on the NHANES 2013–2014

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ABSTRACT

Objective We aimed to explore the association between periodontitis and abdominal aortic calcification (AAC) among a nationally representative sample of US adults.

Design Cross- sectional study.

Setting The National Health and Nutrition Examination Survey (2013–2014).

Participants A total of 2149 participants aged 40 years or older who have complete information for periodontitis and AAC assessment test were included in this study.

Primary and secondary outcome measures AAC scores can be accurately identified on lateral spine images obtained by dual-energy X-ray absorptiometry, and both the AAC-24 and AAC-8 semiquantitative scoring tools were used for AAC evaluation. Linear regression analysis was used to investigate the relationship between periodontitis and the AAC-8 and AAC-24 scores. Multivariate logistic regression models and reported ORs were used to examine the relationship between periodontitis and AAC.

Results The prevalence of severe periodontitis combined with severe AAC was 8.49%–8.54%. According to the AAC-8 and AAC-24 score classifications, patients with severe periodontitis had higher odds of severe AAC (AAC-8 score ≥3: (OR: 2.53; 95% CI 1.04 to 6.17) and AAC-24 score >6: (OR: 3.60; 95% CI 1.48 to 8.78)). A positive association between mild–moderate periodontitis and severe AAC was found only when the AAC-24 score was applied (OR: 2.25; 95% CI 1.24 to 4.06). In the subgroup analyses, the likelihood ratio test showed no multiplicative interaction (all p value for interaction >0.05).

Conclusions The findings showed that periodontitis is associated with an increased risk of severe AAC in the US population aged 40 years and older; this requires further large-scale prospective studies for confirmation.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ A complex, multistage probability sampling approach was used to obtain a representative sample of individual composition to investigate the total national population.
⇒ Our study fully considered socioeconomic status, behavioural factors and medical history of the participants and controlled for a wide range of confounders.
⇒ Periodontitis and abdominal aortic calcification were defined based on objective clinical data collected by calibrated professionals.
⇒ Given the cross-sectional design of the National Health and Nutrition Examination Survey, it is difficult for us to determine causality, and further large-scale prospective studies are needed.
⇒ Because of the sample size, we were not able to include the new periodontal profile class system to precisely classify periodontal disease.

INTRODUCTION

Periodontitis has become a global public health challenge and imposes serious burdens on society and health services. There have been approximately 1.1 billion prevalent cases of severe periodontitis worldwide over the past 30 years, an increase of 8.44% in age-standardised prevalence.[1] Forty-six per cent of American adults aged 30 years and older have periodontitis, 8.9% of whom have severe periodontitis, which is positively associated with increasing age.[2] Periodontitis can affect the risk of systemic diseases, including cardiovascular disease (CVD),[3 4] diabetes[5] and chronic kidney disease (CKD),[6] through mechanisms such as periodontal microbial damage and inflammatory cascades, and this relationship may be causal and bidirectional. Deaths due to all causes and cause-specific causes are associated with periodontitis and its sequelae.[7] As part of its strategy, the Centers for Disease Control and Prevention (CDC) is supporting and improving periodontal disease surveillance.[8]

The abdominal aorta is considered to be valuable in observing early atherosclerotic calcification,[9] and its degree of calcification

is closely related to the prevalence of and the mortality due to CVD.[10] Abdominal aortic calcification (AAC) is characterised by metabolic disorders involving minerals, such as calcium and phosphorus, and abnormal deposition in the vascular wall, which is common in patients with chronic disease.[11 12] Some epidemiological evidence suggests that periodontitis is associated with arterial calcification at multiple sites. A Chinese cohort study showed that periodontitis increased the risk of aortic calcification and was more pronounced in men and younger participants than in women and older participants.[13] In addition, a cross-sectional study and meta-analysis suggested that periodontitis was associated with carotid calcification,[14 15] and there was radiographic evidence suggesting the possible involvement of intracranial carotid calcification.[16] However, other cohort studies reported inconsistent conclusions.[17 18] In recent years, vascular calcification, including soft tissue calcification, has been recognised as an active process regulated by multiple molecular signalling pathways in response to chronic inflammatory stimuli.[19] Previous animal studies demonstrated that periodontitis and vascular calcification promoted each other,[20] and the mechanisms involved were gradually revealed in subsequent studies.[21–24]

An assessment of the utility of the AAC score in a 25-year cohort study of 617 Framingham Heart Study participants was conducted by Kauppila *et al* using lateral lumbar radiography as the AAC grading tool (AAC score).[25] Based on the AAC score, it is possible to assess subclinical vascular disease at a low cost, with predictive value for cardiovascular events and mortality independent of coronary calcification.[26] Therefore, using AAC data obtained from dual-energy X-ray absorptiometry (DXA) in the 2013–2014 National Health and Nutrition Examination Survey (NHANES), the aim of this study was to investigate the relationship between periodontitis and AAC and propose new ideas for the prevention and management of AAC in clinical practice. We hypothesised that periodontitis would be associated with an increased prevalence of AAC.

MATERIALS AND METHODS

Data source

The current cross-sectional study analysed data from individuals who participated in the 2013–2014 NHANES, which was performed by the National Center for Health Statistics at the CDC. The NHANES 2013–2014 was a cross-sectional, nationally representative survey of the US non-institutionalised civilian population designed to examine demographic, socioeconomic, health and nutritional information. To ensure a representative sample, complex multistage sampling was used to collect data, and strata were determined based on geographical location and population proportions.[27]

The NHANES 2013–2014 was the only cycle that also performed examinations for periodontitis and AAC. Participants ≥40 years of age who received a full-mouth periodontal examination and participated in lateral

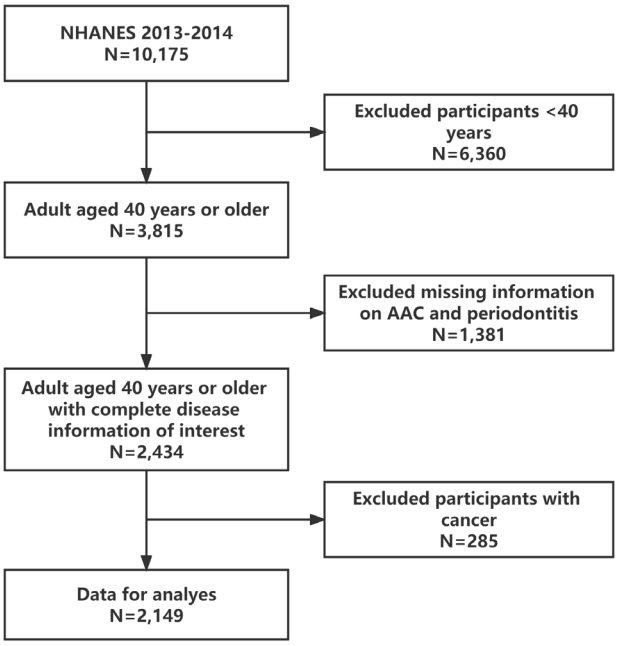

Figure 1 Flow chart of eligible National Health and Nutrition Examination Survey (NHANES) participants included in this study. AAC, abdominal aortic calcification.

DXA scans of the thoracolumbar spine were included in this study. In the 2013–2014 cycle of the NHANES, 10 175 participants completed the survey. However, in this study, individuals aged <40 years without complete information about periodontitis and AAC were excluded (N=7741). Additionally, participants with cancer (N=285) were excluded from the analysis. Ultimately, 2149 participants were included in the analysis (figure 1). All participants provided written informed consent to participate in NHANES. The study was designed according to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines for reporting cross-sectional studies,[28] and all procedures were performed in accordance with the principles of the Helsinki Declaration of 1975.

Definitions of periodontitis

Oral health examinations were performed by dental examiners who were licensed dentists in at least one state in the USA. During oral health assessments, a portable dental chair, lights and compressed air were provided in a mobile examination centre (MEC). All dental examiners received standardised training and collected reliable statistical data to objectively assess examiner agreement.[29]

Six measurement points were selected for periodontal examinations (mesiobuccal, midbuccal, distobuccal, mesiolingual, midlingual and distolingual) for all teeth, with the exception of third molars. Indicators of periodontitis included probing depth and clinical attachment loss, which are important bases for the CDC/American Academy of Periodontology(AAP) classification/case definition.[30] Accordingly, periodontitis was divided into

mild periodontitis, moderate periodontitis and severe periodontitis, No periodontitis was defined as no evidence of mild, moderate or severe periodontitis. Because there were few data from those with mild periodontitis, mild periodontitis and moderate periodontitis were combined for analysis in our study.

AAC outcomes

AAC can be accurately identified on lateral spine images obtained by DXA and shows good sensitivity and specificity at lower radiation doses.[31 32] Those <40 years old, pregnant, weighing over 450 pounds or ingesting barium within the last week were ineligible for DXA scans in this study. Both the AAC-24 and AAC-8 semiquantitative scoring tools were used for AAC evaluation.[25] An assessment of the length of anterior and posterior aortic wall calcification anterior to the L1–L4 vertebral bodies was made using the AAC-8 score, and participants with a score of 3 or more were considered to be at high risk for AAC. Using the L1–L4 region as a reference, the anterior and posterior aortic walls are divided into four segments to calculate the AAC-24 score. Depending on the degree of calcification, each vertebral body can receive a score from 0 to 6, with a total possible score of 0 to 24; this allows a more precise assessment of AAC. We categorised AAC-24 scores into three groups: no calcification (AAC-24 score=0), mild-to-moderate calcification (6≥AAC-24 score>0) and severe calcification (AAC-24 score>6).

Covariates

Based on previous studies, we considered some confounding factors potentially associated with periodontitis and AAC in our analysis, including socioeconomic factors, behavioural factors, body mass index (BMI), medical history and laboratory measurements.[33 34]

Information about socioeconomic factors was obtained during the home interview. The poverty income ratio (PIR) was stratified into <1.3, 1.3–3.5 and >3.5, as recorded in the original survey. Behavioural factors were obtained from self-reports. A never smoker is an individual who has never smoked more than 100 cigarettes in their lifetime. Former smokers were defined as those who smoked more than 100 cigarettes in their lifetime and had quit smoking, and smokers have to smoke at least 100 cigarettes in their lifetime and smoke some days or every day to qualify as current smokers. The status of alcohol consumption was categorised as never (never drank greater than or equal to 12 drinks in their lifetime), former (greater than or equal to 12 drinks in 1 year and did not drink last year, or did not drink last year but drank ≥12 drinks in their lifetime), current mild (≤1 drink per day for women or ≤2 drinks per day for men on average over the past year), current moderate (2 drinks per day for women or 3 drinks per day for men on average over the past year), current heavy drinkers (≥3 drinks per day for women or ≥4 drinks per day for men on average over the past year). BMI was measured at an MEC using standard protocols and stratified into≥30 and <30.

Those participants who self-reported heart failure, angina, coronary heart disease, heart attack or stroke diagnosed by a physician were classified as having CVD. The definition of hypertension was a diagnosis by a healthcare professional, an average blood pressure of ≥130/80 mm Hg or using hypertension medications.[35] Diabetes was defined as a diagnosis made by a physician or other healthcare professional, glycated haemoglobin (%) >6.5, random blood glucose (mmol/L) ≥11.1 or use of diabetes medication or insulin. As defined by the International Renal Association, chronic kidney disease is characterised by an estimated glomerular filtration rate <60 mL/min/1.73 m^2 or a urine albumin–creatinine ratio of at least 30.[36] Based on serum creatinine, the Chronic Kidney Disease Epidemiology Collaboration equation was used to estimate the glomerular filtration rate.[37] Laboratory data were obtained from participant serum samples that were processed in the Collaborative Laboratory Services, Ottumwa, Iowa, USA, for analysis. Detailed instructions regarding specimen collection and processing are documented in the NHANES Laboratory Procedures Manual, and quality control was in accordance with standard procedures.

Statistical analysis

A weight is assigned to the NHANES to compensate for the complex survey design, survey non-responses and poststratification adjustment to match the total US population. All results of this study were weighted by 2-year MEC weights. In accordance with the CDC/AAP classification of periodontitis, descriptive statistics were calculated to describe the characteristics of the participants. Continuous variables are presented as the weighted mean±SD and were compared using a one-way analysis of variance, while categorical variables were compared using the Rao-Scott χ^2 test and are presented as weighted percentages (95% CI). Linear regression was used to evaluate the association of the AAC-8 score and AAC-24 score as dependent variables with periodontitis with varying degrees of severity as independent variables. Beta coefficients and 95% CIs were calculated. Multivariate logistic regression analysis was performed to evaluate the correlation between periodontitis with varying degrees of severity and AAC with varying degrees of severity using ORs and 95% CIs. Model 1 was adjusted for age, sex and race; Model 2 was adjusted for the parameters in Model 1 plus insurance, education level, smoking status, alcohol consumption status, PIR, BMI, diabetes, hypertension, CVD and CKD; and Model 3 was adjusted for the parameters in Model 2 plus albumin, serum calcium, serum phosphorus, uric acid, total 25-hydroxyvitamin D, haemoglobin, total cholesterol, high-density lipoprotein cholesterol (HDL-C) and triglycerides (TGs). Subgroup analysis stratified by age, sex, CVD, hypertension, diabetes and CKD was also conducted using stratified multivariate regression analysis, and multiplicative interactions were assessed using likelihood ratio tests.

In this study, we used the MissForest[38] package in R software to address missing covariates. The algorithm can address categorical and continuous variables and shows superior performance. The numbers and percentages of missing covariate data are shown in online supplemental table 1. Sensitivity analyses were performed as followed: (1) only participants with complete data were included, and participants with missing covariates were excluded; (2) mild and moderate periodontitis were not combined for analysis, and mild periodontitis was excluded; and (3) participants with CVD were excluded. R software (V.4.1.3) was used for all statistical analyses. It was considered statistically significant if the p value was less than 0.05 for all statistical tests of two-tailed.

Patient and public involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

RESULTS

Descriptive statistics of our study participants by periodontitis status according to the CDC/AAP case definitions are presented in table 1. The study included 2149 participants, representing 86 199 511 non-institutionalised adults (40 years and older) in the USA. Overall, participants had a mean age±SD of 54.96±0.32 years; 50.46% (95% CI 44.32 to 56.60) were women, and 68.14% (95% CI 54.20 to 82.08) were non-Hispanic white. The prevalence of mild–moderate periodontitis was 29.93 (95% CI 25.36 to 34.51) and that of severe periodontitis was 6.77 (95% CI 5.40 to 8.13). Periodontitis was more prevalent in older individuals, men, those with a low educational level, those with a low PIR and those with low insurance coverage than in their counterparts and showed differences among races. The prevalence of mild-to-moderate AAC and severe AAC was significantly higher in participants with periodontitis than in those without. In addition, we also found significant differences in smoking status, alcohol consumption status, CVD, diabetes, hypertension, CKD, albumin, total 25-hydroxyvitamin D, TGs and HDL-C compared with participants without periodontitis (all p<0.05).

Table 2 shows the relationships between periodontitis and the AAC-8 score and AAC-24 score in the linear regression analysis. In Model 1, which was adjusted for age, sex and race, severe periodontitis showed a significant positive correlation with the AAC-8 (β: 0.29; 95% CI 0.08 to 0.50) and AAC-24 (β: 0.80; 95% CI 0.25 to 1.34) scores compared with no periodontitis. However, the association disappeared in the subsequent models adjusted for additional covariates. In addition, no correlation was found between mild–moderate periodontitis and the AAC-8 score or AAC-24 score.

Table 3 presents the association between periodontitis and AAC based on the multivariate logistic regression analysis. In fully adjusted Model 3, severe periodontitis was positively associated with AAC in the high-AAC risk group (AAC-8 score ≥3 points) (OR: 2.53; 95% CI 1.04 to 6.17) compared with the low-AAC risk group (AAC-8 score <3 points). The degree of periodontitis and AAC as defined by the more refined AAC-24 score were further analysed. Mild–moderate and severe periodontitis were associated with an increased prevalence of severe AAC (OR: 2.25; 95% CI 1.24 to 4.06 and OR: 3.60; 95% CI 1.48 to 8.78) relative to participants without AAC. Furthermore, this association remained when participants with mild–moderate AAC were replaced with a reference population; mild–moderate and severe periodontitis were associated with severe AAC (OR: 2.28; 95% CI 1.28 to 4.06 and OR: 2.93; 95% CI 1.28 to 6.69). In addition, no correlation was found between periodontitis and mild–moderate AAC.

In the subgroup analysis (table 4), we investigated the association between periodontitis and severe AAC based on an AAC-8 score ≥3. We found that the likelihood ratio test for multiplicative interactions was not statistically significant for age, sex, CVD, hypertension, diabetes or CKD after adjustment for potential confounders (p value for interaction >0.05). Thus, we did not find any substantial evidence to demonstrate systematic differences in associations between different subpopulations in the population, indicating that our main results were stable.

In the primary study, we imputed missing covariates (the proportions of all missing variables were less than 5.00% except for the PIR, at 8.19%) using the MissForest package. The random forest analysis had a seed number of 500 and completed data imputation after eight iterations. Model performance indicators normalised root mean squared error computed was 0.578 and proportion of falsely classified was 0.336. In the sensitivity analysis, we excluded participants with missing covariates, and we included 1818 individuals with complete data in the subsequent analyses. The baseline distribution of participant characteristics did not differ significantly from that in the previously included population, but it was worth mentioning that the prevalence of severe AAC with severe periodontitis have decreased by approximately 1% (online supplemental table 2). Further logistic regression analysis showed, our result regarding the association of periodontitis and AAC differed from that in the primary analysis. In Model 3, only mild–moderate periodontitis was associated with an increased risk of severe AAC (OR: 1.89; 95% CI 1.01 to 3.56), and the remaining associations were attenuated or had disappeared (online supplemental table 3). When we decoupled mild–moderate periodontitis and excluded participants with mild periodontitis, the results of the sensitivity analysis were similar to those of the main analysis (online supplemental table 4). It is worth mentioning that mild–moderate periodontitis was associated with a reduced prevalence of mild-to-moderate AAC in participants without CVD, and the association of severe periodontitis with AAC in the high-AAC risk group (AAC-8 scores ≥3 points) disappeared (online supplemental table 5).

Table 1 General characteristics of included participants (n=2149) according to the periodontal status in the NHANES 2013–2014

Characters	Overall (n=2149)	No periodontitis (n=1142)	Mild–moderate periodontitis (n=787)	Severe periodontitis (n=220)	P value
Age, year	54.96±0.32	53.84±0.47	57.13±0.52	55.78±0.73	0.001
Gender					<0.001
Male	49.54 (42.66 to 56.42)	44.26 (40.95 to 47.57)	56.17 (52.43 to 59.91)	69.60 (62.25 to 76.96)	
Female	50.46 (44.32 to 56.60)	55.74 (52.43 to 59.05)	43.83 (40.09 to 47.57)	30.40 (23.04 to 37.75)	
Race					<0.001
Mexican American	7.98 (4.63 to 11.32)	5.51 (2.88 to 8.15)	12.60 (6.75 to 18.46)	10.53 (4.02 to 17.05)	
Non-Hispanic black	10.53 (8.69 to 12.36)	7.38 (5.67 to 9.09)	14.16 (9.15 to 19.17)	23.88 (15.54 to 32.23)	
Non-Hispanic white	68.14 (54.20 to 82.08)	74.71 (69.73 to 79.70)	57.60 (46.77 to 68.43)	53.28 (42.62 to 63.94)	
Other Hispanic	5.22 (3.48 to 6.95)	4.38 (2.56 to 6.20)	6.79 (4.13 to 9.44)	6.09 (2.77 to 9.41)	
Other race or multiracial	8.14 (6.55 to 9.74)	8.02 (6.44 to 9.60)	8.85 (6.07 to 11.63)	6.21 (4.11 to 8.31)	
Education					<0.001
Less than high school	14.88 (12.36 to 17.39)	9.09 (6.59 to 11.59)	22.21 (17.08 to 27.35)	36.60 (27.56 to 45.64)	
High school	20.80 (17.18 to 24.43)	16.38 (13.54 to 19.21)	27.28 (22.81 to 31.75)	33.56 (26.94 to 40.19)	
Above high school	64.32 (52.71 to 75.93)	74.54 (70.84 to 78.23)	50.51 (44.66 to 56.35)	29.84 (20.31 to 39.37)	
Poverty-income ratio					<0.001
<1.3	16.84 (12.82 to 20.86)	10.14 (7.11 to 13.16)	27.38 (21.64 to 33.13)	32.91 (20.83 to 44.99)	
1.3–3.5	34.58 (30.67 to 38.50)	29.18 (25.57 to 32.80)	43.20 (38.79 to 47.62)	46.98 (36.21 to 57.75)	
>3.5	48.58 (38.30 to 58.85)	60.68 (55.49 to 65.87)	29.41 (23.79 to 35.03)	20.11 (10.19 to 30.04)	
Insurance coverage	84.99 (72.54 to 97.45)	91.46 (88.41 to 94.50)	76.37 (72.89 to 79.85)	62.68 (55.51 to 69.85)	<0.001
Body mass index (kg/m^2)					0.053
<30	64.10 (54.77 to 73.44)	66.54 (63.36 to 69.72)	59.50 (53.18 to 65.82)	61.67 (53.95 to 69.39)	
≥30	35.90 (31.24 to 40.56)	33.46 (30.28 to 36.64)	40.50 (34.18 to 46.82)	38.33 (30.61 to 46.05)	
Smoking status					<0.001
Now	16.07 (13.82 to 18.31)	10.48 (8.12 to 12.83)	21.91 (18.01 to 25.81)	42.48 (33.91 to 51.05)	
Former	25.38 (20.70 to 30.06)	23.00 (20.09 to 25.92)	31.13 (25.05 to 37.20)	22.22 (13.02 to 31.43)	
Never	58.55 (50.16 to 66.94)	66.52 (62.55 to 70.48)	46.96 (42.06 to 51.87)	35.30 (25.73 to 44.86)	
Alcohol consumption status					0.004
Never	11.48 (8.45 to 14.51)	11.22 (7.14 to 15.29)	12.77 (10.23 to 15.30)	8.23 (4.19 to 12.27)	
Former	14.23 (11.41 to 17.06)	11.54 (9.13 to 13.95)	18.94 (15.82 to 22.05)	18.63 (12.99 to 24.26)	
Mild	40.28 (33.73 to 46.83)	43.77 (39.36 to 48.18)	34.64 (29.89 to 39.39)	32.56 (24.85 to 40.26)	
Moderate	18.10 (14.08 to 22.11)	18.98 (16.05 to 21.92)	16.60 (11.73 to 21.47)	16.44 (9.60 to 23.28)	
Heavy	15.91 (13.83 to 18.00)	14.49 (12.30 to 16.68)	17.06 (13.06 to 21.06)	24.15 (16.68 to 31.61)	

Continued

Table 1 Continued

Characters	Overall (n=2149)	No periodontitis (n=1142)	Mild–moderate periodontitis (n=787)	Severe periodontitis (n=220)	P value
Cardiovascular diseases	7.43 (5.89 to 8.97)	5.95 (4.53 to 7.38)	10.68 (7.93 to 13.43)	6.88 (3.11 to 10.65)	0.004
Hypertension	56.64 (50.33 to 62.94)	52.31 (48.43 to 56.19)	63.24 (59.08 to 67.39)	67.92 (61.80 to 74.05)	<0.001
Diabetes	14.06 (12.22 to 15.91)	10.83 (8.78 to 12.87)	21.13 (18.83 to 23.43)	13.04 (7.94 to 18.15)	<0.001
Chronic kidney disease	14.66 (12.77 to 16.55)	12.21 (10.24 to 14.19)	19.73 (17.14 to 22.31)	15.13 (10.15 to 20.11)	<0.001
AAC-8 score					0.001
<3	94.86 (83.16 to 100.00)	96.68 (95.23 to 98.13)	91.78 (89.31 to 94.25)	91.51 (86.26 to 96.76)	
≥3	5.14 (3.60 to 6.68)	3.32 (1.87 to 4.77)	8.22 (5.75 to 10.69)	8.49 (3.24 to 13.74)	
AAC-24 score					<0.001
0	75.67 (64.85 to 86.49)	77.77 (74.00 to 81.53)	73.24 (67.18 to 79.30)	66.81 (59.03 to 74.58)	
1–6	19.55 (15.84 to 23.26)	19.38 (15.83 to 22.93)	18.75 (14.07 to 23.43)	24.65 (17.37 to 31.93)	
>6	4.78 (3.66 to 5.90)	2.85 (1.95 to 3.76)	8.01 (5.59 to 10.42)	8.54 (4.04 to 13.04)	
Laboratory measurements					
Albumin (g/dL)	4.27±0.01	4.30±0.01	4.21±0.02	4.20±0.02	<0.001
Serum calcium (mg/dL)	9.45±0.01	9.45±0.01	9.43±0.02	9.45±0.03	0.414
Serum phosphorus (mg/dL)	3.79±0.02	3.81±0.03	3.75±0.02	3.78±0.04	0.083
Uric acid (mg/dL)	5.37±0.03	5.29±0.03	5.53±0.08	5.42±0.13	0.063
Total 25-hydroxyvitamin D (nmol/L)	73.44±1.18	76.90±1.44	68.78±1.58	61.71±2.42	<0.001
Haemoglobin (g/dL)	14.19±0.04	14.15±0.04	14.20±0.08	14.42±0.11	0.097
Total cholesterol (mg/dL)	196.56±0.99	195.79±1.15	197.98±2.45	197.48±3.31	0.722
High-density lipoprotein cholesterol (mg/dL)	54.67±0.60	56.42±0.73	51.79±0.70	50.99±1.19	<0.001
Triglycerides (mg/dL)	162.83±3.69	152.54±3.39	182.64±9.60	171.49±13.54	0.015

Note: Values indicate the weighted mean±SD or weighted % (95% CI). P values are weighted.
AAC, abdominal aortic calcification; NHANES, National Health and Nutrition Examination Survey.

Table 2 Weighted linear regression coefficients (β) and 95% CIs for periodontal status and AAC score: The United States, 2013–2014

	Case/participants	Model 1 β (95% CI), Pp value	Model 2 β (95% CI), Pp value	Model 3 β (95% CI), p value
AAC-8 score				
No periodontitis	1142/2149	Reference	Reference	Reference
Mild–moderate periodontitis	787/2149	0.11 (–0.05 to 0.28) P=0.149	0.03 (–0.11 to 0.17) P=0.643	0.02 (–0.12 to 0.17) P=0.740
Severe periodontitis	220/2149	**0.29 (0.08 to 0.50) P=0.015**	0.17 (–0.07 to 0.41) P=0.159	0.17 (–0.08 to 0.41) P=0.173
AAC-24 score				
No periodontitis	1142/2149	Reference	Reference	Reference
Mild–moderate periodontitis	787/2149	0.34 (–0.10 to 0.78) P=0.110	0.15 (–0.22 to 0.52) P=0.393	0.14 (–0.26 to 0.54) P=0.472
Severe periodontitis	220/2149	**0.80 (0.25 to 1.34) P=0.011**	0.57 (–0.01 to 1.14) P=0.052	0.58 (–0.02 to 1.17) P=0.056

Note: Model 1 was adjusted for age, sex and race; Model 2 was adjusted for the parameters in Model 1 plus insurance, education level, smoking status, alcohol consumption status, poverty income ratio, body mass index, diabetes, hypertension, cardiovascular disease and chronic kidney disease; and Model 3 was adjusted for the parameters in Model 2 plus albumin, serum calcium, serum phosphorus, uric acid, total 25-hydroxyvitamin D, haemoglobin, total cholesterol, high-density lipoprotein cholesterol and triglycerides. Bold fonts indicate P value < 0.05.
AAC, abdominal aortic calcification.

DISCUSSION

To our knowledge, this is the first population-based cross-sectional epidemiological study to explore the link between periodontitis and AAC in a nationally representative sample of US adults (40 years and older). Our study fully considered socioeconomic status, behavioural factors and medical history of the participants and controlled for a wide range of confounders. Severe periodontitis was positively associated with severe AAC, defined by either the AAC-8 score or AAC-24 score. A positive association between mild-to-moderate periodontitis and severe AAC was found only when AAC was classified by the AAC-24 score. In the subgroups stratified by age; sex; and CVD, hypertension, diabetes and CKD status, this association and the main results were generally consistent; the only difference was associated with the different severities of periodontitis, which differed in their associations with severe AAC in the stratified population. Linear regression evaluation of the AAC-8 score and AAC-24 score as dependent variables and the different severities of periodontitis as independent variables showed no linear correlation. In the sensitivity analysis, the association remained significant after excluding participants with mild periodontitis and CVD. However, the association was no longer significant after excluding participants with missing covariates.

To date, some epidemiological studies have suggested a close relationship between periodontitis and vascular calcification or CVD. A consensus report on periodontitis and CVD states that periodontitis is broadly associated with CVD and that the link is bidirectional; CVD drives the progression of periodontitis and vice versa.[39] NHANES-based cross-sectional studies have shown an association between periodontitis severity and cardiovascular risk,[4] as demonstrated by the results of a 13-year cohort study, and further studies suggest that periodontitis may be an independent risk factor for CVD.[40] Paul *et al* reviewed the pathophysiology of periodontitis and showed that inflammation associated with periodontitis may be the main mechanism affecting CVD and could be facilitated by common risk factors.[41] Vascular calcification has been shown to involve soft tissue calcification also caused by chronic inflammatory stimuli[19] and is closely related to the prevalence and prognosis of CVD. This may suggest that the association between periodontitis and CVD may depend on the severity of vascular calcification. The results of a cross-sectional Japanese population-based study suggest that measuring alveolar bone loss on panoramic radiographs may be an effective method to identify an increased risk of carotid artery calcification.[14] Imaging studies using cone-beam CT have further confirmed that the development of periodontitis may cause calcification involving the intracranial carotid arteries.[16] The results from a meta-analysis that included 12 studies also revealed a significant relationship between periodontitis and carotid artery calcification.[15] Similar to our findings, a cohort study in Chinese populations suggested that periodontitis was also positively associated with aortic calcification, and this association was more pronounced in men and in participants younger than 65 years.[13]

The exact mechanism of the link between periodontitis and AAC remains unclear and needs to be further explored. Existing mainstream views suggest that *Porphyromonas gingivalis* (*P. gingivalis*) infection and chronic inflammation are important bridges between periodontitis and vascular calcification.[19 41 42] Recent studies have shown that periodontal pathogens can be detected in

Table 3 Weighted multiple logistic regression coefficients (ORs) and 95% CIs for the association between periodontal status with AAC group: The United States, 2013–2014

	Case/participants	Model 1 OR (95% CI), p value	Model 2 OR (95% CI), p value	Model 3 OR (95% CI), p value
AAC-8 score ≥3 points versus AAC-8 score <3 points				
No periodontitis	46/1142	Reference	Reference	Reference
Mild–moderate periodontitis	66/787	**2.07 (1.01 to 4.22) P=0.047**	1.79 (0.95 to 3.38) P=0.069	1.84 (1.00 to 3.40) P=0.051
Severe periodontitis	**19/220**	**3.20 (1.22 to 8.40) P=0.025**	**2.53 (1.05 to 6.11) P=0.040**	**2.53 (1.04 to 6.17) P=0.043**
Mild–moderate AAC versus no AAC				
No periodontitis	224/1102	Reference	Reference	Reference
Mild–moderate periodontitis	144/723	0.89 (0.58 to 1.38) P=0.561	0.76 (0.53 to 1.08) P=0.113	0.72 (0.51 to 1.02) P=0.061
Severe periodontitis	50/200	1.46 (0.79 to 2.68) P=0.185	1.05 (0.52 to 2.10) P=0.886	0.96 (0.48 to 1.93) P=0.914
Severe AAC versus no AAC				
No periodontitis	40/918	Reference	Reference	Reference
Mild–moderate periodontitis	64/643	**2.57 (1.35 to 4.89) P=0.010**	**2.19 (1.23 to 3.89) P=0.011**	**2.25 (1.24 to 4.06) P=0.011**
Severe periodontitis	20/170	**6.13 (2.55 to 14.72) P=0.002**	**3.62 (1.63 to 8.06) P=0.004**	**3.60 (1.48 to 8.78) P=0.008**
Severe AAC versus mild–moderate AAC				
No periodontitis	40/264	Reference	Reference	Reference
Mild–moderate periodontitis	64/208	**2.59 (1.49 to 4.52) P=0.005**	**2.20 (1.27 to 3.80) P=0.008**	**2.28 (1.28 to 4.06) p=0.008**
Severe periodontitis	20/70	**3.16 (1.21 to 8.22) P=0.025**	**2.89 (1.27 to 6.60) P=0.015**	**2.93 (1.28 to 6.69) P=0.014**

Note: Model 1 was adjusted for age, sex and race; Model 2 was adjusted for the parameters in Model 1 plus insurance, education level, smoking status, alcohol consumption status, poverty income ratio, body mass index, diabetes, hypertension, cardiovascular disease and chronic kidney disease; and Model 3 was adjusted for the parameters in Model 2 plus albumin, serum calcium, serum phosphorus, uric acid, total 25-hydroxyvitamin D, haemoglobin, total cholesterol, high-density lipoprotein cholesterol and triglycerides. No AAC, mild–moderate AAC and severe AAC were defined by AAC-24 score. Bold fonts indicate P value < 0.05.
AAC, abdominal aortic calcification.

the blood of patients with coronary heart disease, and it is hypothesised that periodontal pathogens can spread through the blood to other parts of the body, where they may enhance inflammatory processes, leading to the development or aggravation of atherosclerosis.[43] Evidence from in vitro cell culture studies suggests that *P. gingivalis* infection accelerates phosphate-induced calcification of vascular smooth muscle cells[22] and that *P. gingivalis* lipopolysaccharide increases alkaline phosphatase activity and upregulates the expression of genes involved in calcification to stimulate calcification.[44] In addition, it has been shown that *P. gingivalis* invasiveness is enhanced after high-glucose treatment, and vascular calcification can be initiated by stimulating autocrine regulation of bone morphogenetic protein 4 in aortic smooth muscle cells.[21] *P. gingivalis* infection elicits an inflammatory response in the host, which is in line with the definition of periodontitis as a chronic inflammatory disease. A meta-analysis suggested that the diagnosis of chronic aggressive periodontitis was consistently associated with higher C-reactive protein and high-sensitivity C-reactive protein levels, and treatment reduced serum C-reactive protein levels.[45] In addition, studies have observed an association between periodontitis and systemic inflammation, which increases with the severity of periodontal disease.[46] Notably, there are studies revealing other possible mechanisms involved in the link between periodontitis and vascular calcification, including the activation of osteoprotegerin/receptor activator of nuclear factor-κB ligand and endoplasmic reticulum stress-induced apoptosis.[23 24]

Our study has several important strengths. Our findings were derived from a large nationwide random sample survey and can be generalised to the adult non-institutionalised population in the USA. Periodontitis and AAC were defined based on objective clinical data collected by calibrated professionals. In addition, this study addressed a number of known potential confounders, and sample weights were applied in each analysis following the NHANES guidelines

Table 4 Subgroup analysis for the association between periodontal status and risk of severe AAC (AAC-8 score ≥3 points)

	Periodontal status OR (95% CI), p value			
	No periodontitis	Mild–moderate periodontitis	Severe periodontitis	P value for interaction
Age				0.212
≥60 years	Reference	1.90 (0.88 to 4.11) P=0.096	**5.66 (1.15 to 27.92) P=0.035**	
<60 years	Reference	3.44 (0.83 to 14.15) P=0.083	1.58 (0.24 to 10.43) P=0.611	
Gender				0.207
Male	Reference	1.90 (0.55 to 6.56) P=0.285	**4.40 (1.09 to 17.85) P=0.039**	
Female	Reference	**2.37 (1.42 to 3.93) P=0.003**	0.92 (0.29 to 2.94) P=0.876	
Cardiovascular diseases				0.381
Yes	Reference	1.61 (0.31 to 8.35) P=0.548	NA*	
No	Reference	**1.95 (1.02 to 3.73) P=0.044**	2.14 (0.86 to 5.35) P=0.096	
Diabetes				0.837
Yes	Reference	**4.00 (1.49 to 10.69) P=0.009**	**9.64 (1.45 to 64.16)* P=0.022**	
No	Reference	1.51 (0.67 to 3.40) P=0.293	2.21 (0.76 to 6.44) P=0.136	
Hypertension				0.085
Yes	Reference	1.81 (0.88 to 3.74) P=0.099	**3.39 (1.35 to 8.56) P=0.013**	
No	Reference	**3.27 (1.08 to 9.91) P=0.037**	0.73 (0.08 to 6.72) P=0.767	
Chronic kidney disease				0.501
Yes	Reference	**2.20 (1.15 to 4.21) P=0.021**	1.57 (0.22 to 11.17) P=0.630	
No	Reference	1.81 (0.79 to 4.12) P=0.147	**2.98 (1.21 to 7.34) P=0.020**	

Note: All presented covariates were adjusted (as Model 3) except the corresponding stratification variable. *Wide CI and no production OR are due to the small sample size for this comparison. Bold fonts indicate P value < 0.05.
AAC, abdominal aortic calcification.

to account for the complex survey design. However, several limitations of this study warrant attention. Given the cross-sectional design of the NHANES, it is difficult for us to determine causality, and further large-scale prospective studies are needed. In addition, we cannot exclude the possibility of residual confounding by other confounding factors related to oral health, which could have influenced the observed results. It is worth noting that only a small proportion of patients with severe periodontitis in our study had severe AAC; perhaps because of this, the results of the sensitivity analysis excluding patients with missing covariates were not robust. This also suggests that the conclusions of this study should be interpreted with caution. An explanation for this phenomenon is the possibility of selection bias.[47] In addition, tooth loss is not considered in the CDC/AAP case definition of periodontitis; therefore, the prevalence of the disease may be underestimated.[30] Because of the sample size, we were not able to include the new periodontal profile class (PPC) system to precisely classify periodontal disease because this classification method classifies periodontitis into seven categories: PPC-A to PPC-G.[48]

CONCLUSION

Our study suggests that periodontitis is associated with an increased risk of severe AAC in the US population aged 40 years and older. The associations investigated in this study are credible due to their cross-sectional nature, but these findings require further large-scale prospective studies to confirm.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

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Supplementary Material

TABLE 1 The numbers and percentages of missing covariate data

Covariate	Numbers	Percentages (%)
Education	1	0.05
Poverty-income ratio	176	8.19
Body mass index	6	0.28
Smoking status	2	0.09
Alcohol consumption status	97	4.51
Cardiovascular diseases	1	0.05
Chronic kidney disease	52	2.42
Albumin	58	2.70
Serum calcium	72	3.35
Serum phosphorus	59	2.75
Uric acid	60	2.79
Total 25-hydroxyvitamin D	49	2.28
Hemoglobin	38	1.77
Total cholesterol	53	2.47
High-density lipoprotein cholesterol	53	2.47
Triglycerides	60	2.79

TABLE 2 General characteristics of included participants (n = 1,818) according to the periodontal status in the NHANES 2013–2014 (excluded participants with missing covariates).

Characters	Overall (n=1,818)	No Periodontitis (n=977)	Mild-Moderate periodontitisc (n=661)	Severe periodontitis (n=180)	P-value
Age, year	55.19±0.33	54.01±0.46	57.70±0.57	55.36±0.69	< 0.001
Gender					< 0.001
Male	50.34 (43.00-57.67)	45.25 (41.74-48.75)	57.01 (52.84-61.19)	69.00 (60.78-77.22)	
Female	49.66 (43.17-56.16)	54.75 (51.25-58.26)	42.99 (38.81-47.16)	31.00 (22.78-39.22)	
Race					< 0.001
Mexican American	7.64 (4.29-10.99)	5.37 (2.90- 7.83)	12.37 (6.12-18.62)	8.40 (2.34-14.45)	
Non-Hispanic Black	9.81 (8.10-11.53)	7.07 (5.36- 8.78)	12.69 (8.36-17.02)	23.04 (14.37-31.72)	
Non-Hispanic White	69.93 (55.21-84.66)	75.53 (70.47-80.58)	60.66 (49.90-71.41)	57.80 (45.71-69.90)	
Other Hispanic	4.87 (3.34- 6.40)	4.10 (2.37-5.83)	6.45 (3.97-8.92)	5.27 (1.70-8.84)	
Other race or multi-racial	7.74 (6.20- 9.28)	7.94 (6.34- 9.54)	7.83 (4.98-10.68)	5.48 (2.78- 8.18)	
Education					< 0.001
Less than hight school	13.49 (10.82-16.16)	7.91 (5.25-10.56)	20.34 (14.62-26.06)	36.09 (26.10-46.08)	
Hight school	21.25 (16.88-25.62)	16.12 (12.81-19.42)	29.19 (23.88-34.51)	34.89 (27.67-42.12)	
Above hight school	65.26 (52.75-77.76)	75.98 (71.61-80.34)	50.47 (44.14-56.80)	29.02 (17.31-40.72)	
Poverty-income ratio					< 0.001
< 1.3	17.53 (12.79-22.26)	10.69 (7.03-14.35)	28.23 (21.62-34.84)	35.11 (21.93-48.30)	
1.3-3.5	32.60 (28.53-36.67)	26.79 (22.77-30.80)	42.48 (37.54-47.42)	44.16 (33.74-54.59)	
> 3.5	49.88 (38.79-60.96)	62.52 (56.61-68.44)	29.29 (23.25-35.33)	20.73 (9.98-31.48)	
Insurance coverage	85.84 (72.59-99.10)	92.31 (89.14-95.48)	77.09 (73.42-80.77)	63.27 (55.48-71.07)	< 0.001
Body mass index (kg/m2)					0.051
< 30	63.56 (53.32-73.81)	66.24 (62.27-70.22)	58.38 (52.44-64.31)	60.96 (51.39-70.54)	
≥ 30	36.44 (31.69-41.18)	33.76 (29.78-37.73)	41.62 (35.69-47.56)	39.04 (29.46-48.61)	
Smoking status					< 0.001
Now	16.29 (13.83-18.75)	10.56 (7.95-13.16)	22.14 (18.08-26.19)	44.56 (34.80-54.33)	
Former	25.66 (20.34-30.98)	22.66 (19.38-25.94)	32.94 (26.12-39.75)	22.22 (12.52-31.92)	
Never	58.05 (49.27-66.83)	66.79 (62.21-71.36)	44.93 (39.88-49.98)	33.22 (22.02-44.41)	
Alcohol consumption status					0.018
Never	10.71 (7.52-13.90)	10.61 (6.27-14.94)	11.70 (9.07-14.33)	7.42 (3.00-11.83)	
Former	14.43 (11.55-17.31)	11.67 (9.23-14.11)	19.33 (16.24-22.41)	19.08 (13.23-24.92)	
Mild	40.15 (32.54-47.76)	43.22 (37.75-48.68)	35.28 (29.93-40.63)	32.53 (24.03-41.03)	
Moderate	18.73 (14.49-22.97)	19.72 (16.57-22.87)	17.18 (11.48-22.88)	16.25 (8.35-24.15)	
Heavy	15.98 (13.25-18.70)	14.79 (11.82-17.77)	16.51 (11.81-21.21)	24.73 (16.17-33.29)	
Cardiovascular diseases	7.82 (6.33- 9.32)	6.24 (5.05- 7.44)	11.38 (8.50-14.26)	7.24 (2.99-11.48)	0.003
Hypertension	56.45 (49.84-63.06)	52.01 (47.49-56.52)	63.21 (58.69-67.74)	68.69 (63.15-74.24)	< 0.001
Diabetes	14.17 (11.92-16.43)	10.97 (9.01-12.93)	21.37 (18.55-24.19)	12.97 (7.27-18.67)	< 0.001
Chronic kidney disease	14.93 (12.73-17.13)	12.57 (10.40-14.75)	19.74 (16.90-22.59)	16.15 (10.83-21.47)	< 0.001
AAC-8 score					0.005
< 3	94.75 (82.27-107.22)	96.32 (94.70-97.94)	91.82 (89.49-94.15)	92.69 (88.05-97.32)	
≥ 3	5.25 (3.65- 6.86)	3.68 (2.06- 5.30)	8.18 (5.85-10.51)	7.31 (2.68-11.95)	
AAC-24 score					0.004
0	75.38 (64.00-86.75)	77.23 (73.37-81.09)	73.27 (67.34-79.21)	67.15 (58.31-76.00)	
1-6	19.79 (15.77-23.82)	19.62 (15.94-23.31)	18.85 (14.06-23.64)	25.48 (17.29-33.67)	
> 6	4.83 (3.85- 5.81)	3.15 (2.14- 4.16)	7.88 (5.61-10.15)	7.37 (2.91-11.83)	
Laboratory measurements					
Albumin (g/dL)	4.27±0.01	4.29±0.02	4.22±0.02	4.20±0.03	0.001
Serum calcium (mg/dL)	9.45±0.01	9.45±0.01	9.43±0.02	9.47±0.03	0.573
Serum phosphorus (mg/dL)	3.79±0.02	3.81±0.03	3.74±0.02	3.77±0.03	0.096
Uric acid (mg/dL)	5.37±0.04	5.29±0.04	5.54±0.10	5.45±0.14	0.126
Total 25-hydroxyvitamin D (nmol/L)	73.21±1.48	76.57±1.85	68.88±1.87	60.62±2.46	< 0.001
Hemoglobin (g/dL)	14.21±0.04	14.17±0.04	14.23±0.09	14.44±0.12	0.114
Total cholesterol (mg/dL)	195.97±1.04	195.69±1.29	196.00±1.97	198.53±3.98	0.828
High-density lipoprotein cholesterol (mg/dL)	54.62±0.70	56.58±0.85	51.33±0.75	50.60±1.43	< 0.001
Triglycerides (mg/dL)	160.21±3.40	152.06± 4.25	174.33± 4.71	175.34±16.35	0.011

Values indicate the weighted mean ± SD or weighted % (95% confidence interval). P-values are weighted. AAC, abdominal aortic calcification

TABLE 3 Weighted multiple logistic regression coefficients (ORs) and 95% confidence intervals for the association between periodontal status with AAC group: The United States, 2013 to 2014 (exclude participants with missing covariates)

	Case/participants	Model 1 OR (95% CI), P- value	Model 2 OR (95% CI), P- value	Model 3 OR (95% CI), P- value
AAC-8 score ≥ 3 points versus AAC-8 score < 3 points				
No periodontitis	44/977	Reference	Reference	Reference
Mild–moderate periodontitis	57/661	1.72(0.84,3.54) p=0.116	1.53(0.81,2.88) p=0.171	1.56(0.83,2.92) p=0.153
Severe periodontitis	15/180	2.44(0.96,6.21) p=0.059	1.80(0.81,4.00) p=0.137	1.80(0.77,4.22) p=0.160
Mild–moderate AAC versus no AAC				
No periodontitis	224/939	Reference	Reference	Reference
Mild–moderate periodontitis	144/607	0.87(0.58,1.31) p=0.439	0.71(0.50,1.02) p=0.060	0.69(0.49,0.97) p=0.033
Severe periodontitis	50/164	1.52(0.78,2.96) p=0.181	1.06(0.49,2.30) p=0.869	0.99(0.46,2.10) p=0.972
Severe AAC versus no AAC				
No periodontitis	38/784	Reference	Reference	Reference
Mild–moderate periodontitis	54/538	**2.11(1.10, 4.05)** **p=0.030**	**1.89(1.02, 3.50)** **p=0.044**	**1.89(1.01, 3.56)** **p=0.048**
Severe periodontitis	16/139	**5.22(1.85,14.76)** **p=0.007**	**2.81(1.06, 7.42)** **p=0.038**	2.73(0.92, 8.13) p=0.068
Severe AAC versus mild–moderate AAC				
No periodontitis	38/231	Reference	Reference	Reference
Mild–moderate periodontitis	54/177	**2.20(1.20,4.04)** **p=0.018**	1.82(0.98,3.39) p=0.059	1.87(0.96, 3.66) p=0.065
Severe periodontitis	16/57	2.41(0.79,7.29) p=0.103	1.85(0.78,4.38) p=0.147	1.85(0.75, 4.60) p=0.168

Model 1 was adjusted for age, sex, and race; Model 2 was adjusted for the parameters in Model 1 plus insurance, education level, smoking status, alcohol consumption status, PIR, BMI, diabetes, hypertension, CVD and CKD; and Model 3 was adjusted for the parameters in Model 2 plus albumin, serum calcium, serum phosphorus, uric acid, total 25-hydroxyvitamin D, hemoglobin, TC, HDL-C, and TGs. No AAC, mild–moderate AAC and Severe AAC were defined by AAC-24 score. AAC: abdominal aortic calcification.

TABLE 4 Weighted multiple logistic regression coefficients (ORs) and 95% confidence intervals for the association between periodontal status (exclude participants with mild periodontitis) with AAC group: The United States, 2013 to 2014

	Case/participants	Model 1 OR (95% CI), P- value	Model 2 OR (95% CI), P- value	Model 3 OR (95% CI), P- value
AAC-8 score ≥ 3 points versus AAC-8 score < 3 points				
No periodontitis	34/1142	Reference	Reference	Reference
Moderate periodontitis	53/773	1.94(0.86,4.40) P=0.096	1.68(0.82,3.46) P=0.147	1.73(0.87,3.42) P=0.109
Severe periodontitis	14/220	**3.12(1.17,8.36)** **P=0.029**	**2.44(1.02,6.00)** **P=0.046**	**2.44(1.01,6.05)** **P=0.048**
Mild–moderate AAC versus no AAC				
No periodontitis	224/1102	Reference	Reference	Reference
Moderate periodontitis	141/711	0.90(0.57,1.41) P=0.587	0.75(0.52,1.09) P=0.121	0.72(0.50,1.03) P=0.069
Severe periodontitis	50/200	1.46(0.80,2.68) P=0.184	1.05(0.52,2.11) P=0.881	0.96(0.48,1.94) P=0.906
Severe AAC versus no AAC				
No periodontitis	40/918	Reference	Reference	Reference
Moderate periodontitis	62/632	**2.37(1.07, 5.22)** **P=0.036**	1.97(0.96,4.06) P=0.063	**2.03(1.02,4.03)** **P=0.044**
Severe periodontitis	20/170	**6.02(2.44,14.86)** **P=0.002**	**3.49(1.53,7.97)** **P=0.006**	**3.48(1.42,8.54)** **P=0.010**
Severe AAC versus mild–moderate AAC				
No periodontitis	40/264	Reference	Reference	Reference
Moderate periodontitis	62/203	**2.47(1.23,4.96)** **P=0.018**	**2.10(1.08,4.07)** **P=0.031**	**2.17(1.09, 4.32)** **P=0.030**
Severe periodontitis	20/70	**3.10(1.15,8.32)** **P=0.030**	**2.76(1.16,6.57)** **P=0.025**	**2.75(1.14, 6.63)** **P=0.027**

Model 1 was adjusted for age, sex, and race; Model 2 was adjusted for the parameters in Model 1 plus insurance, education level, smoking status, alcohol consumption status, PIR, BMI, diabetes, hypertension, CVD and CKD; and Model 3 was adjusted for the parameters in Model 2 plus albumin, serum calcium, serum phosphorus, uric acid, total 25-hydroxyvitamin D, hemoglobin, TC, HDL-C, and TGs. No AAC, mild–moderate AAC and Severe AAC were defined by AAC-24 score. AAC: abdominal aortic calcification.

TABLE 5 Weighted multiple logistic regression coefficients (ORs) and 95% confidence intervals for the association between periodontal status with AAC group: The United States, 2013 to 2014 (exclude participants with cardiovascular diseases)

	Case/participants	Model 1 OR (95% CI), P- value	Model 2 OR (95% CI), P- value	Model 3 OR (95% CI), P- value
AAC-8 score ≥ 3 points versus AAC-8 score < 3 points				
No periodontitis	34/1066	Reference	Reference	Reference
Mild–moderate periodontitis	53/692	2.25(0.98,5.17) P= 0.054	1.90(0.95,3.81) P=0.067	**1.95(1.02,3.73)** **P=0.044**
Severe periodontitis	14/202	**3.27(1.26,8.48)** **P=0.022**	2.18(0.88,5.45) P=0.088	2.14(0.86,5.35) P=0.096
Mild–moderate AAC versus no AAC				
No periodontitis	208/1038	Reference	Reference	Reference
Mild–moderate periodontitis	118/639	0.83(0.52,1.32) P=0.371	**0.68(0.47,0.99)** **P=0.049**	**0.65(0.45,0.94)** **P=0.026**
Severe periodontitis	44/187	1.33(0.70,2.51) P=0.330	0.90(0.41,1.95) P=0.774	0.83(0.38,1.81) P=0.618
Severe AAC versus no AAC				
No periodontitis	28/858	Reference	Reference	Reference
Mild–moderate periodontitis	53/574	**3.17(1.61, 6.26)** **P=0.005**	**2.62(1.44, 4.76)** **P=0.004**	**2.71(1.49, 4.93)** **P=0.003**
Severe periodontitis	15/158	**6.00(2.47,14.57)** **P=0.002**	**3.00(1.31, 6.87)** **P=0.013**	**2.89(1.13, 7.40)** **P=0.029**
Severe AAC versus mild–moderate AAC				
No periodontitis	28/236	Reference	Reference	Reference
Mild–moderate periodontitis	53/171	**3.17(1.73, 5.80)** **P=0.003**	**2.99(1.68, 5.32)** **P=0.001**	**3.16(1.75, 5.69)** **P<0.001**
Severe periodontitis	15/59	**3.79(1.38,10.43)** **P=0.017**	**3.82(1.42,10.27)** **P=0.011**	**3.75(1.32,10.60)** **P=0.016**

Model 1 was adjusted for age, sex, and race; Model 2 was adjusted for the parameters in Model 1 plus insurance, education level, smoking status, alcohol consumption status, PIR, BMI, diabetes, hypertension and CKD; and Model 3 was adjusted for the parameters in Model 2 plus albumin, serum calcium, serum phosphorus, uric acid, total 25-hydroxyvitamin D, hemoglobin, TC, HDL-C, and TGs. No AAC, mild–moderate AAC and Severe AAC were defined by AAC-24 score. AAC: abdominal aortic calcification.