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ORIGINAL ARTICLE

Association of carotid intima-media thickness with periodontitis may depend on glycemic control

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Abstract

Background: There is evidence indicating that atherosclerosis is associated with periodontitis, especially in those with diabetes. The purpose of the present study was to determine whether glycemic control influences such association.

Methods: Cross-sectional data on 214 patients diagnosed with type 2 diabetes mellitus were obtained including results of basic laboratory tests, a periodontal examination, and carotid measurements. The association of periodontal parameters and carotid intima-media thickness (cIMT) or carotid plaque (CP) was evaluated in subgroups.

Results: Mean cIMT was significantly correlated with mean PLI, mean BI or number of PD ≥4 mm in the whole sample and the group with poor glycemic control. In the group with good glycemic control, however, only the number of PD ≥4 mm was associated with mean cIMT. A multiple logistic regression analysis also revealed that each 1 increase in mean PLI, mean BI or number of PD ≥4 mm was correlated with an increased cIMT in the whole sample.

Conclusions: In addition to confirming the relationship between periodontitis and atherosclerosis, our study found a stronger association in groups with poor glycemic control compared to those with good glycemic control, suggesting that blood glucose modifies the association between periodontitis and arterial injury.

KEYWORDS
carotid arterial injury, diabetes, oral hygiene, periodontal disease, periodontal medicine, systemic health/disease

1 | INTRODUCTION

Atherosclerotic diseases, including coronary heart disease, cerebrovascular disease and peripheral vascular disease, account for the majority of deaths from a global perspective (Libby et al., 2019). Increasing evidence points to a role of inflammation in the development of atherosclerotic lesions (Libby et al., 2019). Periodontitis is a chronic multifactorial inflammatory disease resulting in progressive destruction of the tooth-supporting apparatus (Papapanou et al., 2018), which is associated with dysbiotic plaque biofilms and may lead to the entry of bacteria or their products into the bloodstream and activation of the host inflammatory response by multiple mechanisms (Schenkein et al., 2020).

Accumulating epidemiological evidence suggests that periodontitis is associated with atherosclerotic disease (Herrera et al., 2020; Jönsson et al., 2020; Sanz et al., 2020), but this association seems to necessarily involve diabetes mellitus, which was not only proved to be bidirectionally linked to periodontitis (Genco et al., 2020; Graves

Hong Yang and Pei Cao co–first authors contributing equally to this work.

et al., 2020) but also showed to confer a twofold excess risk of vascular outcomes (Cosentino et al., 2020). Southerland et al found that only those with both diabetes and severe periodontitis were significantly more likely to have increased IMT (defined as more than 1 mm) and CHD (Southerland et al., 2012). In a Chinese population, the dose-dependent association between periodontal status and cIMT in hyperglycemic participants was not found in overall study or in euglycemic participants (Yu et al., 2014). However, groups of diabetes mellitus in studies above included participants ever diagnosed even with normal fasting glucose level. The purpose of the present study was to determine whether glycemic control influences the association between periodontitis and atherosclerotic disease in a population diagnosed with type 2 diabetes mellitus (T2DM).

2 | MATERIALS AND METHODS

The participants were obtained in collaboration with an epidemiologic investigation of T2DM in Chinese population, which enrolled 700 participants from seven community clinics in Beijing using stratified random sampling method with Inclusion criteria of (a) diagnosed with T2DM, (b) at least four times diabetes revisit records in a year, and (c) without malignant tumor, severe renal or liver diseases or acute cardiovascular events in 3 months. A total of 352 individuals volunteered to participate in our study and signed informed written consent. All participants are required to complete a questionnaire and then receive biochemical test and physical, carotid ultrasonographic and periodontal examinations, although 104 of the participants quit halfway complaining about endless examinations. Out of the 248 participants with complete data, 34 were excluded due to having less than 10 remaining teeth or use of antibiotics for more than 1 week in the past 3 months. A total of 214 individuals were included in the final analysis (Figure 1). This study conformed to the ethical guidelines of the 1975 Declaration of Helsinki and was priorly approved by the Ethics Committee of Beijing Hospital (Approval no. 2019BJYYEC-074-02).

2.1 | General health measures

Information about medical history, lifestyle and oral hygiene was collected by a standardized questionnaire administered by trained interviewers. Physical examination included body weight, height and waist and hip circumference. Body mass index (BMI) and waist: hip ratio (WHR) were calculated. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured after at least 5 min of rest before the initial measurement in a seated position. The average of three measurements was used. Hypertension was defined as having an average SBP ≥135 mmHg or DBP ≥85 mmHg or ever diagnosed or medicated for hypertension based on the 2013 ESH/ESC guidelines (Mancia et al., 2013). Blood samples were collected after an overnight fast from each participant. Levels of biochemical markers were obtained by routine methods at Jinan KingMed Diagnostics Group Co., Ltd., including low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), total cholesterol (TC) and hemoglobin A1c (HbA1c), fasting plasma glucose (FPG). Good glycemic control was defined as FPG equal or less than 7 mmol/L and HbA1c less than 7% according to Guideline for the prevention and treatment of T2DM in China (2020 edition; Zhu, 2021).

2.2 | Periodontal examination

A group of professional dentists from Peking University School of Stomatology performed the periodontal examination in each

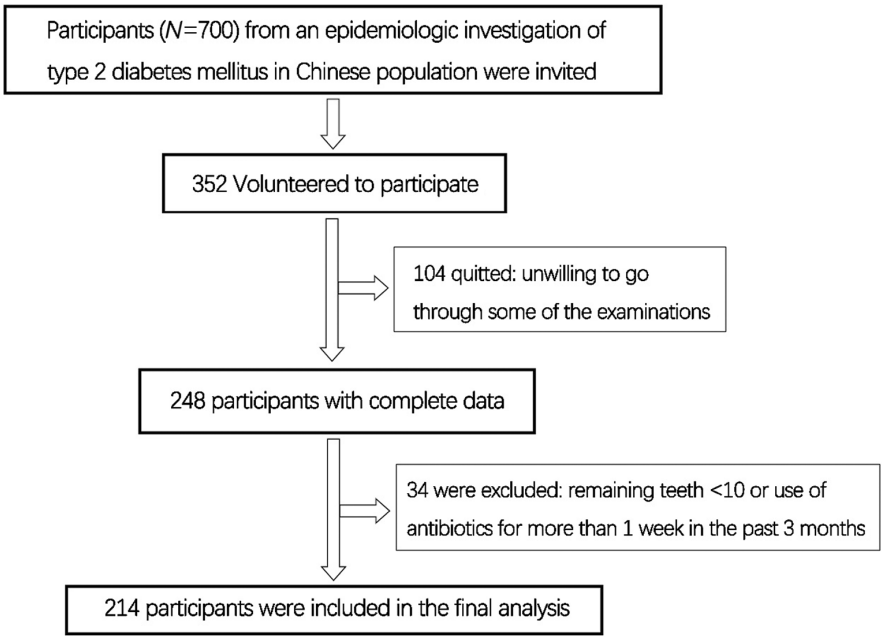

FIGURE 1 Flow chart comprising recruitment and exclusion.

patient, including data on plaque index (PLI), probing depth (PD), clinical attachment loss (CAL) and bleeding index (BI) measured at mesial-buccal and distal-lingual sites for all teeth with a Williams probe (Hu-Friedy, Chicago, IL, USA) excluding the third molars. All examiners were calibrated to a standard examiner, and the agreement of probing depth within 1 mm ranged from 82.14% to 95.37%. Kappa statistics ranged from 0.77 to 0.93. Mean value of PLI, PD, CAL, BI and number of pockets ≥4 mm, percentage of sites with CAL ≥5 mm (CAL ≥ 5 mm%) or BI >2 (BI > 2%) was calculated. Diagnosis of periodontitis and stages of the disease was defined based on The 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. More than 30% tooth with CAL ≥5 mm or PD ≥6 mm were classified as generalized stage III or stage IV periodontitis.

2.3 | Measures of carotid atherosclerosis

The carotid arteries were evaluated by two experienced physicians from Beijing Hospital with high-resolution B-mode ultrasonography (model Aplio i800; CANON Medical Systems Corporation, Tochigi, Japan). Carotid intima-media thickness (cIMT) was measured bilaterally along the 10 mm plaque-free segment in both far wall and near wall of the Common carotid artery, internal carotid artery and carotid bifurcation. The maximum of cIMT values along each segment was recorded. Increased cIMT was defined as any cIMT measurement ≥1 mm for an individual (Hayashida et al., 2013). Mean values of the cIMT measurements were also calculated for analyse. A plaque was defined as high echogenicity or cIMT more than 1.5 mm.

2.4 | Statistical analysis

Analyses were done with the use of STATA, version 15.1 (College Station, TX). Quantitative variables were expressed as mean and standard deviations were calculated. Frequency and percentage were calculated for qualitative variables. Differences between groups (non-plaque vs. carotid plaque and normal cIMT vs. increased cIMT), were assessed by Student's *t*-test or Pearson's chi-squared test for quantitative variables and categorical variables, respectively. For multivariate analysis, multiple linear regression was used to evaluate the linear associations between periodontal parameters and mean cIMT while adjusting for potential confounders, including age, gender, educational level, family income, BMI, WHR, blood lipid level, glycemic control, hypertension, smoking and alcohol consumption. To evaluate effect modification by glycemic control condition, separate regressions were performed for both good glycemic control group and poor glycemic control group. Multivariate logistic regression was also applied to evaluate the adjusted odds ratios (aOR) of the association of periodontitis with increased cIMT and carotid plaque while considering same confounders above. Values of $p < 0.05$ were considered statistically significant.

3 | RESULTS

A total of 214 patients (95 men and 125 women) diagnosed with T2DM were included, the mean age was 60.46 ± 7.69 years, 106 (49.5%) of them were considered to control blood glucose well. Eighty-four (39.3%) were classified as stage III or stage IV periodontitis.

The prevalence of carotid plaque and increased cIMT was 58.4% ($N = 125$) and 52.3% ($N = 112$). Age, sex and hypertension ratio differed significantly between the carotid plaque group and non-plaque group; on the other hand, age, WHR and prevalence of uncontrolled diabetes were significantly higher among those with increased cIMT compared to those with normal cIMT. Mean PLI, mean CAL, mean PD, CAL ≥5 mm% and prevalence of class III&IV periodontitis were considered significantly different between those with and without carotid plaque. Individuals with increased cIMT had significantly higher Mean PLI, mean PD, mean BI, BI >2% and number of pockets ≥4 mm (Table 1).

The results of the multiple linear regression models for mean cIMT are shown in Table 2. Over the whole sample, mean cIMT was significantly correlated with mean PLI or BI after adjusting for age, gender, educational level, family income, BMI, WHR, blood lipid level, diabetes, hypertension, smoking and alcohol consumption with a coefficient of 0.064 ($p < 0.05$, 95% CI: 0.008, 0.120) and 0.058 ($p < 0.05$, 95% CI: 0.005, 0.110), respectively. A similar correlation was found in uncontrolled diabetes patients with a larger coefficient of 0.091 ($p < 0.05$, 95% CI: 0.005, 0.178) and 0.080 ($p < 0.05$, 95% CI: 0.004, 0.156), but not in well controlled diabetes patients. Only number of pockets ≥4 mm was found to correlated with mean cIMT significantly in the whole sample and both groups (poor or good glycemic control).

The results of the multiple logistic regression model for carotid plaque or increased cIMT are shown in Tables 3 and 4. Confounding factors were adjusted, including age, gender, educational level, family income, BMI, WHR, blood lipid level, diabetes, hypertension, smoking and alcohol consumption. Each 1 increase in mean PLI was the only periodontal parameter correlated with carotid plaque with an aOR of 3.37 ($p < 0.05$, 95% CI: 1.58, 7.02). Mean PLI, mean BI, BI >2% and number of pockets ≥4 mm was corelated with increased cIMT, the aORs were 2.51 ($p < 0.05$, 95% CI: 1.22, 5.18), 3.18 ($p < 0.05$, 95% CI: 1.48, 6.84), 9.67 ($p < 0.05$, 95% CI: 2.26, 41.28) and 1.04 ($p < 0.05$, 95% CI: 1.02, 1.07), respectively. Such correlation was not found for other periodontal parameters in our study.

4 | DISCUSSION

To the best of our knowledge, this is the first study to concentrate on the modification effect of glycemic condition within a group of patients ever diagnosed with T2DM when evaluating the association between periodontitis and atherosclerotic disease. Diabetes mellitus was tightly linked with periodontitis and identified as an independent risk factor for atherosclerotic disease (Pirih et al., 2021). Several

TABLE 1 Characteristics of the total sample.

	Total sample ($n=214$)			Total sample ($n=214$)		
	Non-plaque ($n=89$)	Carotid plaque ($n=125$)	p	Normal cIMT ($n=102$)	Increased cIMT ($n=112$)	p
Age, year	58.0±8.6	62.0±6.6	<0.01**	58.8±8.5	61.7±6.7	<0.01**
Gender						
Male	31	61	0.04*	40	52	0.29
Female	58	64		62	60	
Education						
≤9 years	23	44	0.15	31	36	0.78
>9 years	66	81		71	76	
Family income						
Low	15	35	0.15	22	28	0.42
Average	28	37		28	37	
High	46	53		52	47	
BMI	25.6±3.9	25.5±3.4	0.78	25.3±3.4	25.7±3.9	0.41
WHR	89.0±5.3	90.4±6.3	0.09	88.8±4.5	90.7±7.0	0.03*
LDL-C	2.60±0.73	2.45±0.80	0.15	2.50±0.80	2.51±0.75	0.85
HDL-C	1.49±0.49	1.40±0.32	0.12	1.38±0.31	1.48±0.47	0.06
TC	4.99±1.17	4.75±1.24	0.17	4.71±1.11	4.97±1.29	0.12
TG	1.85±2.24	1.65±1.32	0.41	1.59±0.83	1.86±2.30	0.26
Glycemic control						
Good	48	58	0.29	58	48	0.04*
Poor	41	67		44	64	
Hypertension						
No	37	27		36	28	
Yes	52	98	<0.01**	66	84	0.10
Smoke						
Never	81	102	0.15	91	92	0.18
Occasionally	1	2		2	1	
Everyday	7	21		9	19	
Alcohol consumption						
No	70	92	0.62	81	81	0.35
Occasionally	4	9		4	9	
Regular	15	24		17	22	
Periodontitis						
Class I and II	61	69	0.049*	62	68	0.992
Class III and IV	28	56		40	44	
Number of present teeth	24.7±3.9	24.1±4.5	0.25	23.8±4.5	24.9±3.9	0.07
Mean PLI	1.53±0.47	1.77±0.46	<0.01**	1.57±0.49	1.77±0.45	<0.01**
Mean CAL	2.67±1.44	3.26±1.61	<0.01**	2.92±1.76	3.09±1.38	0.47
Mean PD	3.26±0.67	3.47±0.80	0.04*	3.27±0.81	3.48±0.69	0.04**
Number of pockets ≥4 mm	35.7±13.1	37.1±11.2	0.41	33.2±11.9	39.5±11.3	<0.01**
Mean BI	1.61±0.47	1.69±0.52	0.20	1.56±0.41	1.76±0.56	<0.01**
CAL ≥5 mm%	31.1±30.9	42.4±32.6	0.01*	34.5±32.3	40.6±32.2	0.17
BI >2%	42.0±22.8	47.8±25.0	0.09	39.9±22.0	50.4±25.1	<0.01**

Note: Values in *n* or mean±SD.

Abbreviations: BI, bleeding index; BMI, body mass index; CAL, clinical attachment loss; cIMT, carotid intima–media wall thickness; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; PD, probing depth; PLI, plaque index; TC, total cholesterol; TG, triglycerides; WHR, waist: hip ratio.

*$p<0.05$; **$p<0.01$.

TABLE 2 Results of periodontal parameters in multiple linear regression models for mean cIMT.

	Total sample ($n=214$)		Good glycemic control ($n=106$)		Poor glycemic control ($n=108$)	
	Coef	*p*	Coef	*p*	Coef	*p*
Mean PLI	0.064 (0.008, 0.12)	0.02*	0.062 (−0.15, 0.14)	0.11	0.091 (0.005, 0.18)	0.04*
Mean BI	0.057 (0.004, 0.11)	0.03*	0.048 (−0.03, 0.12)	0.22	0.080 (0.004, 0.16)	0.04*
Mean PD	0.015 (−0.02, 0.05)	0.41	0.010 (−0.04, 0.06)	0.69	0.030 (−0.02, 0.08)	0.26
Number of pockets ≥4 mm	0.0037 (0.002, 0.006)	<0.01**	0.0037 (0.001, 0.007)	0.01*	0.0039 (0.001, 0.007)	0.03*
Mean CAL	−0.011 (−0.03, 0.01)	0.10	−0.018 (−0.04, 0.007)	0.15	−0.005 (−0.03, 0.02)	0.73
CAL ≥5 mm%	−0.076 (−0.18, 0.03)	0.16	−0.135 (−0.29, 0.02)	0.08	−0.021 (−0.18, 0.13)	0.78
BI >2%	0.104 (−0.008, 0.21)	0.06	0.109 (−0.05, 0.27)	0.18	0.129 (−0.33, 0.29)	0.12

Note: For the whole sample, multiple linear regression was adjusted for age, gender, educational level, family income, BMI, WHR, blood lipid level, glycemic control, hypertension, smoking and alcohol consumption. In the subgroup analysis, same confounders were adjusted except for glycemic control.

Abbreviations: BI, bleeding index; CAL, clinical attachment loss; cIMT, carotid intima–media wall thickness; PD, probing depth.

*$p<0.05$; **$p<0.01$.

TABLE 3 Results of mean-PLI in multiple logistic regression models for carotid plaque or increased cIMT.

	Carotid plaque (OR, 95% CI)	*p*	Increased cIMT (OR, 95% CI)	*p*
Mean-PLI	3.37 (1.58–7.2)	<0.01**	2.52 (1.22–5.18)	0.01*
Age	1.08 (1.03–1.14)	<0.01**	1.06 (1.01–1.11)	0.02*
Gender	1.35 (0.54–3.41)			
Female	1		1	
Male	1.35 (0.54–3.41)	0.52	1.01 (0.41–2.46)	0.99
Education				
≤9 years	1		1	
>9 years	0.94 (0.85–1.04)	0.89	1.36 (0.66–2.80)	0.40
Family income	0.79 (0.52–1.20)	0.27	0.87 (0.58–1.30)	0.49
BMI	0.94 (0.85–1.04)	0.22	1.03 (0.93–1.13)	0.574
WHR	1.07 (1.00–1.14)	0.06	1.09 (1.02–1.16)	0.01*
LDL-C	0.05 (0.01–0.46)	<0.01**	0.02 (0–0.17)	<0.01**
HDL-C	0.03 (0–0.32)	<0.01**	0.06 (0.01–0.63)	0.02*
TC	13.2 (2.03–85.3)	<0.01**	30.8 (4.72–200.2)	<0.01**
TG	0.70 (0.49–1.01)	0.06	0.59 (0.41–0.85)	<0.01**
Glycemic control				
Good	1		1	
Poor	1.10 (0.56–2.13)	0.79	1.58 (0.84–2.97)	0.16
Hypertension				
No	1		1	
Yes	2.65 (1.29–5.46)	<0.01**	1.38 (0.68–2.81)	0.37
Smoke				
Never	1		1	
Occasionally	1.24 (0.09–16.5)	0.87	0.52 (0.04–7.10)	0.62
Everyday	2.22 (0.71–6.91)	0.17	2.12 (0.74–6.05)	0.16
Alcohol consumption	1.23 (0.73–2.06)	0.43	1.09 (0.66–1.79)	0.74

Abbreviations: BMI, body mass index; cIMT, carotid intima–media wall thickness; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; OR, odds ratio; PLI, plaque index; TC, total cholesterol; TG, triglycerides; WHR, waist: hip ratio.

*$p<0.05$; **$p<0.01$.

TABLE 4 Results of periodontal parameters in multiple logistic regression models for carotid plaque or increased cIMT.

	Carotid plaque (aOR)	*p*	Increased cIMT (aOR)	*p*
Mean PD	1.32 (0.84–2.07)	0.24	1.46 (0.95–2.26)	0.09
Number of pockets ≥4 mm	1.01 (0.98–1.03)	0.50	1.04 (1.02–1.07)	<0.01**
Mean CAL	1.17 (0.93–1.46)	0.18	0.94 (0.76–1.15)	0.53
Mean BI	1.60 (0.80–3.20)	0.19	3.18 (1.48–6.84)	<0.01**
Class III and IV Periodontitis	1.66 (0.85–3.26)	0.67	0.87 (0.46–1.65)	0.07
CAL ≥5 mm%	3.31 (0.81–13.6)	0.10	0.70 (0.20–2.49)	0.58
BI >2%	3.53 (0.86–14.5)	0.08	9.67 (2.26–41.3)	<0.01**

Note: Multiple logistic regression was adjusted for age, gender, educational level, family income, BMI, WHR, blood lipid level, glycemic control, hypertension, smoking and alcohol consumption.
Abbreviations: aOR, adjusted odds ratio; BI, bleeding index; CAL, clinical attachment loss; cIMT, carotid intima–media wall thickness; PD, probing depth.
*$p < 0.05$; **$p < 0.01$.

previous studies noticed the role of T2DM when they explored this issue. Southerland et al. found that individuals with diabetes and severe periodontitis were significantly more likely to have IMT >1 mm (OR = 2.2, 95% CI:1.4–3.5) compared to those without diabetes or periodontal disease (Southerland et al., 2012). The cross-sectional data gather from 847 residents in Beijing indicated that associations between mean CAL, percentage of sites with CAL ≥5 mm with cIMT and atherosclerotic plaque were only found in those with hyperglycemia (defined as fasting plasma glucose ≥6.1 mmol/L and/or ever diagnosed with diabetes). A retrospective cohort study included 17,009 patients with diabetes showed presence of periodontitis was an independent risk factor for either cerebral or myocardial infarction (HR: 1.17, 95% CI: 1.02–1.34) and fine oral hygiene instruction was negatively associated with risk of cerebral or myocardial infarction (Song et al., 2021; HR: 0.79, 95% CI: 0.70–0.90). None of these studies compared the hyperglycemic patients with those control glucose well. Our investigation provided the evidence that glycemic control modifies the association between periodontitis and atherosclerosis in T2DM patients, for several periodontal parameters were linearly and dose-dependently associated with mean cIMT in our multiple linear regression models in patients with poor glycemic control but not in patients with good glycemic control.

We also provided additional epidemiological evidence about the associations between periodontitis and atherosclerotic disease in T2DM patients. In particular, each one increase in mean PLI was associated with increased prevalence of carotid plaque and thickened cIMT, while the latter was further associated with mean BI and number of pockets ≥4 mm after adjusting for known risk factors of atherosclerosis. In addition, periodontal parameters such as mean PLI, mean BI, and number of pockets ≥4 mm were linearly and dose-dependently associated with mean cIMT. After controlling the confounding factors, each 1 increase in mean PLI, mean BI and each 10 more pockets ≥4 mm were associated with 0.064, 0.058 and 0.037 mm increase in mean cIMT, respectively. As a recent meta-analysis concluded, each 0.010 mm/year reduction of cIMT progression resulted in a relative risk for cardiovascular disease (CVD) of 0.91 (Willeit et al., 2020), indicating the linear association found in our study had clinical significance. These results are consistent with previous studies. The data obtained from 6017 persons from the Atherosclerosis Risk in Communities (ARIC) found severe periodontitis (OR 1.31, 95% CI 1.03–1.66) was associated with IMT ≥1 mm while adjusting for the other factors (Beck et al., 2001). A cross-sectional study in 1343 Korean adults showed individuals with severe periodontitis were at high risk of subclinical atherosclerosis (defined as cIMT ≥0.754 mm) with an aOR of 1.55 (95% CI: 1.07–2.24; Ahn et al., 2016). A meta-analysis carried out by Orlandi et al. (2014) demonstrated that the diagnosis of PD was associated with a mean increase in c-IMT of 0.08 mm (95% CI: 0.07–0.09). Jönsson et al. (2020) gathered data of 495 participants showing the OR for having carotid plaque in subjects with versus without periodontal disease was 1.75 (95% CI: 1.11–2.78). Together with the studies above, it is suggested that periodontitis is associated with atherosclerotic disease in T2DM patients. In the population of the present study, we found higher prevalence of carotid plaque in group of class III/IV periodontitis with odds ratio of 1.77, although the multiple logistic regression showed the difference between groups lack statistical significance. The 4th National Oral Health Survey reported very high prevalence of periodontitis in Chinese population (Jiao et al., 2021), leaving large amount of adults lacking professional periodontal therapy. Consequently, several patients with several untreated periodontitis showed probing depth of seven to nine millimeters generally, which was more severe than class III/IV periodontitis defined by the 2018 classification. Namely, the 2018 classification could not distinguish those with the most severe periodontitis in Chinese population, and it is rational to use periodontal parameters to assess the severity of periodontitis within the limitation of current classification. The difference in measurement of cIMT as well as threshold used for abnormal cIMT and carotid plaque may also account for the heterogeneity.

The relationship between CVD and diabetes is well known as a specific form of coexistence of these problems which is the so-called metabolic syndrome. As summarized in a recent review, metabolic syndrome, diabetes, and CVDs are associated with periodontitis (Pirih et al., 2021), potential underlying mechanisms

predominately focus on systemic vascular inflammation caused by periodontitis with several different inflammatory pathways including increased systemic inflammatory mediators and production of extracellular reactive oxygen species, endothelial dysfunction, and common genetic risk factors (Herrera et al., 2020). Yet available evidence confirms the association between every two of diabetes, atherosclerosis and periodontitis, it is not easy to assess the interactions of these diseases in the presence of them all simultaneously.

One weakness of our study was the limited sample size only allowed multiple logistic regression in the whole sample, which was not sufficient when divided into subgroups.

Based on the result of the present study, it is rational to assume that a T2DM patient might get a double bonus if they control glucose and periodontitis well from the perspective of prevention of CVD rather than they are doomed to high risk for CVD once diagnosed with DM and periodontitis, so as to provide stronger motivations for these patients to manage these NCDs. Although it has not been yet clarified whether periodontal therapy can reduce the risk of cardiovascular events, the available evidence suggests that periodontal therapy has an impact on cardiovascular events, reducing multiple cardiovascular risk factors (Orlandi et al., 2020), which is greater in those individuals suffering from both periodontitis and comorbidities like CVD and/or diabetes mellitus (Teeuw et al., 2014).

In conclusion, the present study indicates a linear and dose-dependent association between periodontitis and atherosclerotic disease in a T2DM population, which was stronger in those with poor glycemic control.

AUTHOR CONTRIBUTIONS

Pei Cao: Conceptualization; methodology; software; data curation; investigation; writing – original draft; validation; formal analysis; supervision. **Hong Yang:** Conceptualization; methodology; data curation; formal analysis; validation; investigation; funding acquisition; writing – original draft; supervision. **Xiaoxia Wang:** Conceptualization; methodology; data curation; supervision. **Xiao Xu:** Supervision; conceptualization; methodology; data curation. **Yifan Yang:** Supervision; conceptualization; methodology; data curation. **Fei Xue:** Supervision; conceptualization; methodology; data curation. **Qingxian Luan:** Supervision; project administration; resources; data curation; writing – review and editing; conceptualization; methodology; funding acquisition. **Lixin Guo:** Supervision; project administration; resources; data curation; conceptualization; methodology; funding acquisition.

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CONFLICT OF INTEREST STATEMENT

No potential conflicts of interest with respect to the authorship and/or publication of this article.

DATA AVAILABILITY STATEMENT

Research data are not shared.

PEER REVIEW

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