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ORIGINAL RESEARCH

The Association Between Periodontitis and the Prevalence and Prognosis of Metabolic Syndrome

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Objective: Periodontitis and metabolic syndrome (MetS) are both linked to inflammation, but their association remains unclear. This study aimed to explore the association between periodontitis and MetS prevalence and evaluate its impact on the prognosis of all-cause and cardiovascular mortality in MetS.

Methods: Data were obtained from the National Health and Nutrition Examination Survey (NHANES) database. Logistic regression analysis was used to investigate the association between periodontitis and the prevalence of MetS, while Cox regression analysis was applied to assess the association between periodontal status and the poor prognosis in individuals with MetS. Furthermore, restricted cubic spline (RCS) analysis was performed to evaluate the linear and nonlinear associations between periodontal parameters, including attachment loss (AL) and probing depth (PD), and the prevalence and mortality of MetS.

Results: A total of 9,270 individuals were included in the analysis. Individuals with periodontitis had a higher prevalence of MetS compared to those without periodontitis (OR=1.24, 95% CI: 1.08–1.43). Cox regression analysis revealed that periodontitis was associated with an increased risk of all-cause mortality (HR=2.03, 95% CI:1.40–2.92) and cardiovascular mortality (HR=2.32, 95% CI:1.05–5.10) among individuals with MetS. Furthermore, the RCS analysis demonstrated that AL had a nonlinear association with the risk of prevalence, all-cause mortality and cardiovascular mortality in MetS (P for nonlinearity < 0.05). However, PD was linearly associated with the increased risks of these outcomes (P overall < 0.05).

Conclusion: Periodontitis is associated with an increased risk of MetS, as well as higher risks of all-cause and cardiovascular mortality.

Keywords: MetS, periodontitis, NHANES

Introduction

Metabolic syndrome (MetS) comprises a cluster of risk factors such as obesity, dyslipidemia, hypertension, insulin resistance, and hyperglycemia.[1] It is estimated around 40% of people over 60 years old meet the diagnostic criteria of MetS in the United States.[2] There are several studies have reported that MetS is related to a higher risk of cardiovascular disease, cerebrovascular disease, and diabetes.[2–5] Given the substantial influence of MetS on human health, early detection and intervention strategies for MetS are key topics of discussion among researchers in related fields.

People with oral diseases are prone to metabolic disorders.[6] Periodontitis, a common oral disease, is typically triggered by ecologically dysfunctional changes in the microbiota, eventually resulting in the loss of periodontal attachments.[7,8] According to large-scale epidemiological studies, as many as half of the world's adults suffer from periodontal disease, with 10.5–12.0% at risk of severe periodontitis.[9] In addition, individuals with periodontitis have higher serum levels of proinflammatory cytokines than non-periodontitis. Consequently, periodontitis is related to several chronic diseases, including aspiration pneumonia and cardiovascular disease.[10]

Periodontal disease and MetS exhibit pro-inflammatory and immune response effects, with shared inflammatory mediators such as C-reactive protein, prostaglandin E2, interleukin-1β, and tumor necrosis factor-α. Studies have indicated that the pathological processes of these two conditions involve common inflammatory signaling pathways,

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dysregulated adipokine production, exacerbated oxidative stress, and disrupted matrix remodeling. These interconnected mechanisms link localized periodontal inflammation to systemic metabolic dysregulation and adverse cardiovascular outcomes.[11] Furthermore, a bidirectional relationship has been observed between periodontal disease and metabolic syndrome (MetS), potentially linked to systemic inflammation triggered by periodontal infections. Persistent chronic inflammation may contribute to the development of insulin resistance, disrupt lipid metabolism, and accelerate the progression of MetS.[12]

Although previous research has evaluated the impact of periodontitis on MetS. However, the definitions for periodontitis and MetS varied significantly, resulting in considerable heterogeneity in these studies. Furthermore, there have been no studies on the association between periodontitis and MetS mortality. The National Health and Nutrition Examination Survey (NHANES) database is an invaluable resource that not only provides detailed information on the diagnosis of periodontitis and metabolic syndrome but also includes follow-up survival data for each participant. Therefore, we investigated the impact of periodontitis on prognosis and the prevalence of MetS in individuals through NHANES.

Materials and Methods

Research Design and Data Sources

The NHANES database is a publicly available database reviewed and approved by the National Center for Health Statistics (NCHS). As displayed in Figure 1, 30468 individuals were included from the NHANES 2009–2014 cycles. Among these individuals, those with missing variable data were excluded, and 9,270 individuals to assess the impact of

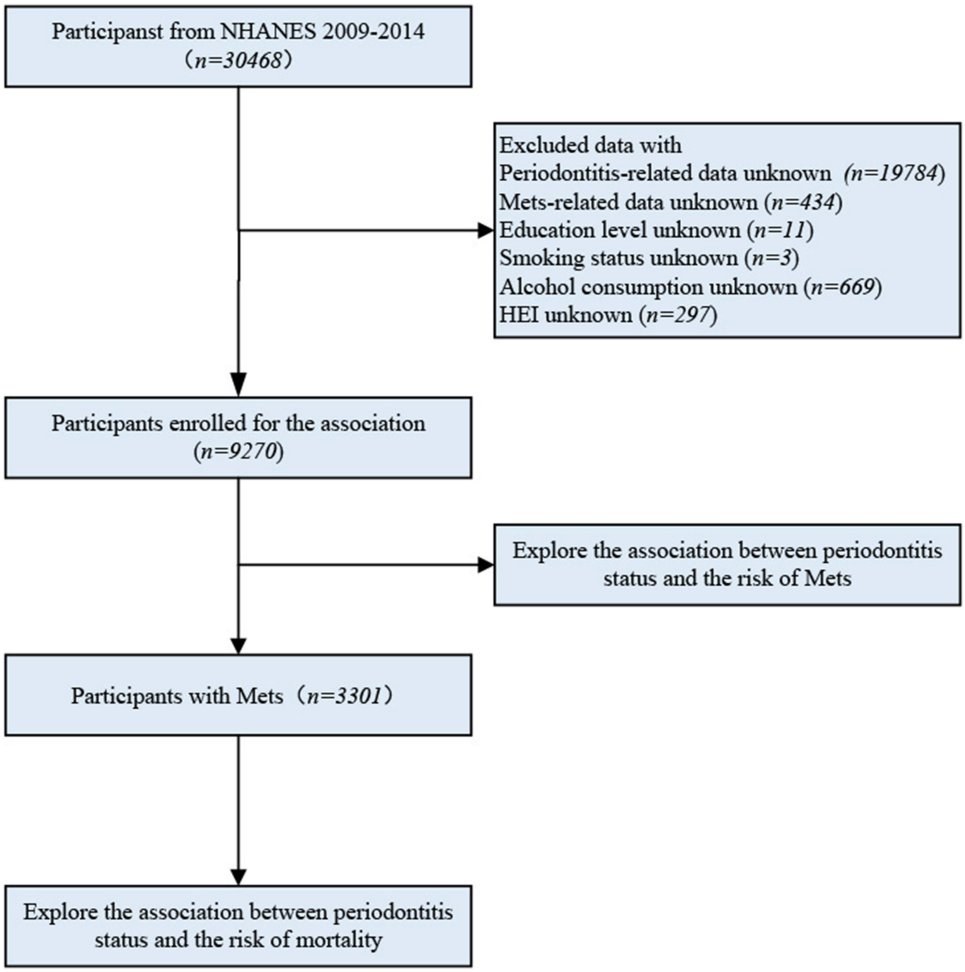

Figure 1 The flowchart of this study.
Abbreviations: NHANES, the National Health and Nutrition Examination Survey; MetS, metabolic syndrome.

periodontitis on the prevalence of MetS. Meanwhile, 3,301 were included in the investigation of the impact of periodontitis on its mortality.

Definition for Periodontitis

Periodontitis was diagnosed based on the categorization system developed by the American Academy of Periodontology and the Centers for Disease Control and Prevention (CDC-AAP).[13] Individuals identified with mild, moderate, or severe periodontitis were categorized into the periodontitis group, whereas those without a periodontitis diagnosis were placed in the non-periodontitis group in this study. In addition, we calculated the attachment loss (AL) and probing depth (PD) for each participant, which were used to further explore the relationships between periodontal parameters and the prevalence and prognosis of MetS.

Diagnostic Definitions for MetS

MetS is defined using harmonized criteria proposed by the International Diabetes Federation (IDF) and the American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI) in 2009.[2] When at least three of the following five elements are present, MetS is diagnosed. (1): waist circumference (WC) not less than 102 cm for men and not less than 88 cm for women; (2) triglycerides (TG) not less than 150 mg/dL; (3) blood pressure (BP) ≥130 mmHg or diastolic BP ≥85 mmHg, or the use of antihypertensive medication; (4) fasting blood glucose (FBG) not less than 100 mg/dL, or the use of medication to control blood glucose levels; (5) high-density lipoprotein cholesterol (HDL) less than 50 mg/dL for women and less than 40 mg/dL for men, or the use of medication to manage lipid levels.

Mortality Data and Definition

Following the International Classification of Diseases (ICD-10), which is employed to identify potential causes of death, the NCHS categorizes cardiovascular mortality as death due to heart disease, denoted by the ICD-10 codes I00-I09, I11, I13, and I20-I51.[14]

Definition of Covariables

The demographic characteristics included age, gender, race, and education. Education was categorized into three groups: less than high school, high school, and more than high school. Using 100 cigarettes as nodes, smoking status was defined as follows: "never" for those who had smoked fewer than 100 cigarettes in their lifetime, "former" for those who had smoked more than 100 cigarettes but were not currently smoking, and "now" for those who had smoked more than 100 cigarettes and were currently smoking either occasionally or regularly.[15] The categorization of alcohol consumption status was defined as follows: "never" (fewer than 12 drinks in a lifetime), "former" (at least 12 drinks in one year but none in the past year, or no drinks in the past year but at least 12 drinks in a lifetime), "mild" (an average of up to 1 drink per day for women or up to 2 drinks per day for men over the past 12 months), "moderate" (1 to 3 drinks per day for women or 2 to 4 drinks per day for men), and "heavy" (an average of 4 or more drinks per day for women or 5 or more drinks per day for men in the past 12 months).[16] The Healthy Eating Index-2015 (HEI-2015) is a dietary quality metric devised by the Center for Nutrition Policy and Promotion at the United States Department of Agriculture (USDA). If the two-day average HEI-2015 score was at or above the 60th percentile, individuals were considered to "healthy diet"; otherwise, they were classified as "unhealthy diet".[17,18] Physical activity (PA) data were collected through a questionnaire-based on the Global Physical Activity Questionnaire, which categorized respondents according to adherence to US PA guidelines (adults should perform moderate-intensity PA for at least 150 minutes per week, equivalent to 600 metabolic equivalent (MET) minutes per week). Based on PA recommendations, individuals were categorized as "physically inactive" (fewer than 600 MET minutes per week) or "physically active" (600 or more MET minutes per week).[18,19]

Statistical Analysis

Due to the intricate NHANES sampling design, all analyses accounted for sample weights to accurately analyze the NHANES data. Weighted means ± standard errors were applied to continuous data, whereas weighted frequency percentages represented categorical variables. Mann–Whitney *U*-test and Rao-Scott test were to examine the differences between the two groups.

Logistic regression models were performed to examine the associations between periodontitis and the prevalence of MetS prevalence. Cox regression models were used to analyze the effect of periodontitis on all-cause and cardiovascular mortality in MetS individuals. We constructed three models to control for the influence of potential confounding variables. Model 1: Unadjusted model; Model 2: Adjusted for age, gender, race; Model 3: Adjusted for age, gender, race, smoking status, alcohol consumption, education, physical activity, and HEI-2015. The restricted cubic spline (RCS) analysis was conducted to explore the dose-response associations of AL and PD with the prevalence, all-cause mortality, and cardiovascular mortality in MetS. R software (version 4.3.1) was used for all analyses in this study.

Results

Baseline Characteristics

Table 1 indicates that 9,270 individuals in all were enrolled in the research, comprising 3303 individuals with MetS and 5967 without MetS. MetS individuals were more highly distributed among those ≥ 60 years, unhealthy diets, physical activity inactive, and periodontitis. Furthermore, there were differences between all variables except gender.

Table 1 The Baseline Characteristics of Individuals in This Study

Variable	Overall	Non-MetS	MetS	*P*-value
	(*N*=9270)	(*N*=5967)	(*N*=3303)	
Age (years)				< 0.001
<60	6225 (72.75)	4300 (76.72)	1925 (64.92)	
≥60	3045 (27.25)	1667 (23.28)	1378 (35.08)	
Gender				0.477
Female	4572 (49.74)	2848 (49.37)	1724 (50.46)	
Male	4698 (50.26)	3119 (50.63)	1579 (49.54)	
Race				0.005
Non-Hispanic Black	1900 (10.25)	1225 (10.24)	675 (10.27)	
Non-Hispanic White	4146 (70.17)	2660 (69.90)	1486 (70.71)	
Other Hispanic	932 (5.26)	587 (5.34)	345 (5.10)	
Other races	969 (6.51)	716 (7.22)	253 (5.09)	
Mexican American	1323 (7.81)	779 (7.29)	544 (8.82)	
Education				< 0.001
Less than high school	2076 (14.58)	1230 (13.37)	846 (16.95)	
High school	2022 (21.10)	1215 (19.00)	807 (25.25)	
More than high school	5172 (64.32)	3522 (67.63)	1650 (57.80)	
Smoking Status				0.014
Never	5136 (55.95)	3379 (57.42)	1757 (53.05)	
Former	2382 (26.85)	1465 (25.66)	917 (29.18)	
Now	1752 (17.21)	1123 (16.92)	629 (17.77)	
Alcohol consumption				< 0.001
Never	1201 (9.89)	698 (9.24)	503 (11.18)	
Former	1612 (14.54)	899 (12.28)	713 (19.01)	
Mild	3346 (39.67)	2282 (41.45)	1064 (36.18)	
Moderate	1423 (17.90)	979 (18.70)	444 (16.31)	
Heavy	1688 (17.99)	1109 (18.33)	579 (17.32)	
Physical activity				0.005
Inactive	3615 (35.79)	2060 (31.26)	1555 (44.72)	
Active	5655 (64.21)	3907 (68.74)	1748 (55.28)	

(*Continued*)

Table 1 (Continued).

Variable	Overall (*N*=9270)	Non-MetS (*N*=5967)	MetS (*N*=3303)	*P*-value
HEI-2015				< 0.001
Unhealthy diets	5958 (63.82)	3735 (60.70)	2223 (69.97)	
Healthy diets	3312 (36.18)	2232 (39.30)	1080 (30.03)	
Periodontitis				< 0.001
No	4596 (58.65)	3151 (61.88)	1445 (52.28)	
Yes	4674 (41.35)	2816 (38.12)	1858 (47.72)	
AL	1.64 (0.03)	1.59 (0.03)	1.75 (0.04)	< 0.001
PD	1.44 (0.02)	1.42 (0.02)	1.49 (0.02)	< 0.001

Abbreviations: MetS, metabolic syndrome; HEI-2015, The Healthy Eating Index-2015; AL, attachment loss; PD, probing depth.

Association Between Periodontitis and the Prevalence of MetS and Its Components

As displayed in Table 2, all three models demonstrated the increased risk of MetS in individuals with periodontitis compared to those without periodontitis (Model 1: OR=1.48, 95% CI 1.30–1.69; Model 2: OR=1.38, 95% CI:1.21–1.59; Model 3: OR=1.24, 95% CI: 1.08–1.43). Moreover, periodontitis was associated with an increased risk of elevated FBG ($P < 0.001$), WC ($P < 0.002$), and BP ($P < 0.001$), which are components of MetS. However, no association was found between periodontitis and elevated TG ($P = 0.238$) or decreased HDL levels ($P = 0.635$). Given the significance of periodontal parameters AL and PD in evaluating the severity of periodontitis, we conducted a further analysis to explore the impact of AL and PD on the prevalence of MetS and its components. It can be seen from Tables 3 and 4 that both AL and PD

Table 2 The Association Between Periodontitis and the Prevalence of MetS and Its Components

Variable	Non-periodontitis	Periodontitis	*P-value*
	OR (95% CI)		
MetS			
Model 1	1	1.48 (1.30,1.69)	<0.001
Model 2	1	1.38 (1.21,1.59)	<0.001
Model 3	1	1.24 (1.08,1.43)	0.003
Elevated FPG			
Model 1	1	1.71 (1.53,1.91)	<0.001
Model 2	1	1.40 (1.23,1.58)	<0.001
Model 3	1	1.34 (1.17,1.52)	<0.001
Reduced HDL			
Model 1	1	1.09 (0.96,1.23)	0.190
Model 2	1	1.20 (1.06,1.37)	0.007
Model 3	1	1.03 (0.91,1.17)	0.635
Elevated TG			
Model 1	1	1.29 (1.10,1.50)	0.002
Model 2	1	1.22 (1.03,1.45)	0.021
Model 3	1	1.10 (0.93,1.31)	0.238
Elevated WC			
Model 1	1	1.17 (1.04,1.32)	0.010
Model 2	1	1.29 (1.13,1.47)	<0.001
Model 3	1	1.24 (1.09,1.42)	0.002

(*Continued*)

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Table 2 (Continued).

Variable	Non-periodontitis	Periodontitis	*P-value*
	OR (95% CI)		
Elevated BP			
Model 1	1	1.68 (1.52,1.86)	<0.001
Model 2	1	1.38 (1.24,1.54)	<0.001
Model 3	1	1.34 (1.19,1.51)	<0.001

Notes: Model 1: Unadjusted model; Model 2: Adjusted for age, gender, race; Model 3: Adjusted for age, gender, race, smoking status, alcohol consumption, education, physical activity, and HEI-2015.
Abbreviations: OR, Odds Ratio; CI, Confidence Interval; MetS, metabolic syndrome; FPG, fasting blood glucose; HDL, high-density lipoprotein cholesterol; TG, triglycerides; WC, waist circumference; BP, blood pressure.

Table 3 The Association Between AL and the Prevalence of MetS and Its Components

Variable	Q1	Q2	Q3	Q4	*P* for trend
	OR (95% CI)				
MetS					
Model 1	1	1.25(1.03,1.51)	1.50(1.21,1.85)	1.70(1.42,2.03)	<0.001
Model 2	1	1.20(0.98,1.46)	1.36(1.10,1.68)	1.54(1.29,1.85)	<0.001
Model 3	1	1.19(0.97,1.45)	1.27(1.03,1.58)	1.31(1.06,1.61)	0.011
Elevated FPG					
Model 1	1	1.22(1.02,1.47)	1.69(1.41,2.02)	1.89(1.56,2.30)	<0.001
Model 2	1	1.06(0.88,1.28)	1.28(1.06,1.53)	1.34(1.08,1.67)	0.003
Model 3	1	1.06(0.87,1.29)	1.24(1.04,1.49)	1.25(1.00,1.56)	0.017
Reduced HDL					
Model 1	1	1.01(0.86,1.18)	1.04(0.86,1.26)	1.19(0.99,1.43)	0.083
Model 2	1	1.08(0.92,1.28)	1.20(0.99,1.46)	1.44(1.17,1.78)	<0.001
Model 3	1	1.05(0.88,1.26)	1.08(0.90,1.31)	1.13(0.90,1.42)	0.234
Elevated TG					
Model 1	1	1.23(1.00,1.51)	1.27(1.03,1.56)	1.38(1.18,1.62)	<0.001
Model 2	1	1.17(0.95,1.45)	1.18(0.94,1.48)	1.27(1.06,1.52)	0.019
Model 3	1	1.15(0.94,1.41)	1.10(0.89,1.36)	1.07(0.88,1.31)	0.477
Elevated WC					
Model 1	1	1.22(1.02,1.45)	1.45(1.18,1.78)	1.16(1.00,1.34)	0.005
Model 2	1	1.34(1.09,1.65)	1.66(1.32,2.11)	1.42(1.19,1.68)	<0.001
Model 3	1	1.37(1.11,1.68)	1.64(1.29,2.09)	1.36(1.11,1.67)	<0.001
Elevated BP					
Model 1	1	1.48(1.25,1.76)	1.95(1.62,2.35)	2.39(2.02,2.82)	<0.001
Model 2	1	1.32(1.13,1.54)	1.47(1.23,1.76)	1.77(1.50,2.08)	<0.001
Model 3	1	1.33(1.13,1.55)	1.46(1.21,1.75)	1.75(1.47,2.09)	<0.001

Notes: Model 1: Unadjusted model; Model 2: Adjusted for age, gender, race; Model 3: Adjusted for age, gender, race, smoking status, alcohol consumption, education, physical activity, and HEI-2015.
Abbreviations: OR, Odds Ratio; CI, Confidence Interval; MetS, metabolic syndrome; FPG, fasting blood glucose; HDL, high-density lipoprotein cholesterol; TG, triglycerides; WC, waist circumference; BP, blood pressure; AL, attachment loss.

were associated with the prevalence MetS, respectively ($P < 0.05$), although significant association were not observed with all components of MetS. Compared to the Q1, individuals in the Q4 quantile of AL had a 31% increased risk of MetS (OR=1.31, 95% CI: 1.06–1.61, Table 3). Similarly, individuals in the Q4 quantile of PD demonstrated a 32% increased risk of MetS (OR=1.32, 95% CI: 1.10–1.59, Table 4). However, the results of the RCS analysis shown in Figure 2A indicated

Table 4 The Association Between PD and the Prevalence of MetS and Its Components

Variable	Q1	Q2	Q3	Q4	*P* for trend
	OR (95% CI)				
MetS					
Model 1	1	1.04(0.85,1.29)	1.33(1.10,1.60)	1.48(1.27,1.74)	<0.001
Model 2	1	1.05(0.85,1.30)	1.31(1.08,1.59)	1.53(1.30,1.81)	<0.001
Model 3	1	1.03(0.83,1.28)	1.23(1.01,1.50)	1.32(1.10,1.59)	0.003
Elevated FPG					
Model 1	1	0.98(0.82,1.16)	1.28(1.09,1.50)	1.38(1.13,1.69)	<0.001
Model 2	1	0.91(0.76,1.09)	1.11(0.93,1.32)	1.16(0.93,1.45)	0.076
Model 3	1	0.90(0.75,1.08)	1.07(0.90,1.27)	1.07(0.86,1.34)	0.293
Reduced HDL					
Model 1	1	1.05(0.89,1.24)	1.16(0.98,1.37)	1.44(1.21,1.70)	<0.001
Model 2	1	1.10(0.93,1.31)	1.26(1.05,1.51)	1.64(1.36,1.98)	<0.001
Model 3	1	1.07(0.91,1.26)	1.16(0.96,1.41)	1.34(1.10,1.64)	0.008
Elevated TG					
Model 1	1	1.06(0.86,1.30)	1.19(0.98,1.45)	1.36(1.13,1.64)	0.001
Model 2	1	1.00(0.81,1.24)	1.11(0.90,1.38)	1.24(0.99,1.54)	0.048
Model 3	1	0.98(0.80,1.21)	1.05(0.85,1.30)	1.06(0.84,1.34)	0.512
Elevated WC					
Model 1	1	1.16(0.99,1.34)	1.35(1.15,1.58)	1.16(0.98,1.37)	0.016
Model 2	1	1.31(1.11,1.55)	1.61(1.35,1.93)	1.59(1.32,1.90)	<0.001
Model 3	1	1.32(1.11,1.56)	1.57(1.32,1.88)	1.52(1.25,1.84)	<0.001
Elevated BP					
Model 1	1	1.20(1.01,1.42)	1.44(1.20,1.71)	1.43(1.24,1.66)	<0.001
Model 2	1	1.19(1.00,1.40)	1.36(1.15,1.60)	1.43(1.23,1.67)	<0.001
Model 3	1	1.18(1.00,1.40)	1.33(1.13,1.57)	1.39(1.17,1.64)	<0.001

Notes: Model 1: Unadjusted model; Model 2: Adjusted for age, gender, race; Model 3: Adjusted for age, gender, race, smoking status, alcohol consumption, education, physical activity, and HEI-2015.
Abbreviations: OR, Odds Ratio; CI, Confidence Interval; MetS, metabolic syndrome; FPG, fasting blood glucose; HDL, high-density lipoprotein cholesterol; TG, triglycerides; WC, waist circumference; BP, blood pressure; PD, probing depth.

a nonlinear association between AL and the prevalence of MetS (P for non-linearity < 0.001). However, PD was significantly positively associated with the prevalence of MetS (Figure 2B, P for overall = 0.004).

Association Between Periodontitis and the Prognosis of MetS

KM survival curves analysis and Cox proportional hazards regression models were used to compare the impact of periodontitis on the prognosis for survival in individuals in the MetS. As displayed in Figure 3A and B, the KM analysis revealed that individuals with periodontitis had significantly higher all-cause and cardiovascular mortality compared to those without periodontitis among individuals with MetS ($P < 0.001$). As seen in Table 5, three models all demonstrated that periodontitis was associated with an increased risk of all-cause mortality (Model 1: HR = 2.67, 95% CI: 1.92–3.70; Model 2: HR = 2.29, 95% CI: 1.58–3.32; Model 3: HR = 2.03, 95% CI: 1.40–2.92) and cardiovascular mortality (Model 1: HR = 3.29, 95% CI: 1.59–6.82; Model 2: HR = 2.46, 95% CI: 1.12–5.41; Model 3: HR = 2.32, 95% CI:1.05–5.10). Table 6 indicated that individuals in the Q4 quartile of AL demonstrated a significantly higher risk of both all-cause mortality (HR = 3.77, 95% CI: 2.43–5.84) and cardiovascular mortality (HR = 4.28, 95% CI: 1.73–10.61) compared to Q1. Meanwhile, a similar trend was observed for PD, where individuals in the Q4 quartile suggested an increased risk of all-cause mortality (HR = 1.90, 95% CI: 1.21–3.00) and cardiovascular mortality (HR = 3.13, 95% CI: 1.21–8.05) compared to those in Q1. In addition, we further investigated the impact of changes in AL and PD on the prognosis of MetS individuals by RCS analysis. Figure 4A and B demonstrated nonlinear associations between AL and the risks of

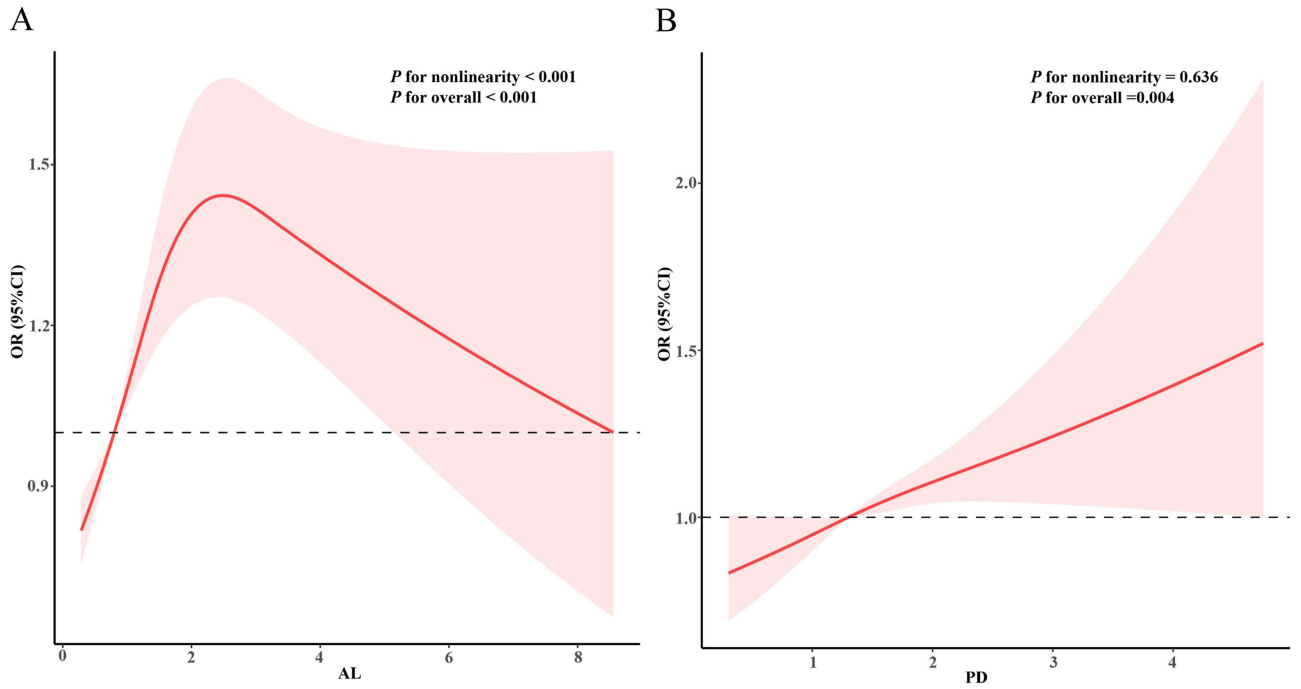

Figure 2 Restricted cubic spline curves for the associations of AL and PD with the risk of MetS. OR were adjusted for age, gender, race, education, smoking status, alcohol consumption, physical activity, and HEI-2015. (**A**) AL and the risk of MetS; (**B**) PD and the risk of MetS.
Abbreviations: AL, attachment loss; PD, probing depth; OR, Odds Ratio; CI, Confidence Interval.

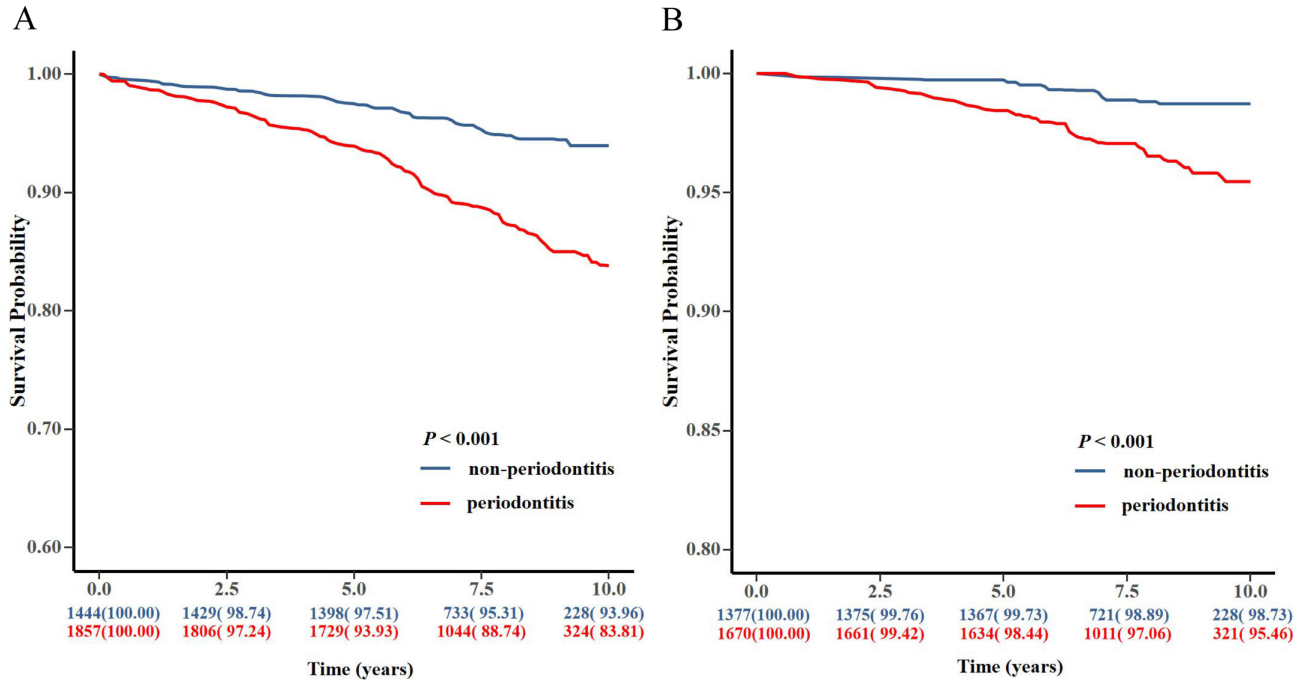

Figure 3 Kaplan–Meier survival curves of MetS patients with/without periodontitis. (**A**) All-cause mortality; (**B**) Cardiovascular mortality.
Abbreviations: AL, attachment loss; PD, probing depth.

Table 5 The Association Between Periodontitis and the Prognosis of MetS

Variable	Non-periodontitis	Periodontitis	*P-value*
	HR (95% CI)		
All-cause mortality			
Model 1	1	2.67(1.92,3.70)	<0.001
Model 2	1	2.29(1.58,3.32)	<0.001
Model 3	1	2.03(1.40,2.92)	<0.001
Cardiovascular mortality			
Model 1	1	3.29(1.59,6.82)	0.001
Model 2	1	2.46(1.12, 5.41)	0.024
Model 3	1	2.32(1.05,5.10)	0.037

Note: Model 1: Unadjusted model; Model 2: Adjusted for age, gender, race; Model 3: Adjusted for age, gender, race, smoking status, alcohol consumption, education, physical activity, and HEI-2015.
Abbreviations: HR, Hazard ratio; CI, Confidence Interval.

Table 6 The Association of AL and PD With the Prognosis of MetS

Variable	Q1	Q2	Q3	Q4	*P* for trend
	HR (95% CI)				
AL					
All-cause mortality					
Model 1	1	2.82(1.75, 4.55)	3.72(2.39, 5.78)	5.31(3.57, 7.90)	<0.001
Model 2	1	2.60(1.60, 4.25)	3.11(1.94, 4.97)	4.51(2.94, 6.91)	<0.001
Model 3	1	2.68(1.64, 4.37)	2.84(1.78, 4.55)	3.77(2.43, 5.84)	<0.001
Cardiovascular mortality					
Model 1	1	1.51(0.49, 4.64)	5.52 (2.35,12.97)	6.69(3.05,14.69)	<0.001
Model 2	1	1.27(0.40, 4.09)	3.90 (1.54, 9.87)	4.60(1.95,10.83)	<0.001
Model 3	1	1.42(0.45, 4.47)	3.69 (1.52, 8.94)	4.28(1.73,10.61)	<0.001
PD					
All-cause mortality					
Model 1	1	1.40(0.87,2.24)	1.84(1.24,2.74)	1.99(1.32,3.00)	0.002
Model 2	1	1.49(0.93,2.39)	1.89(1.23,2.91)	2.22(1.40,3.54)	0.001
Model 3	1	1.42(0.88,2.27)	1.80(1.19,2.74)	1.90(1.21,3.00)	0.005
Cardiovascular mortality					
Model 1	1	1.04(0.35,3.10)	2.61(1.02,6.69)	3.21(1.33,7.75)	0.001
Model 2	1	1.15(0.39, 3.39)	2.61(1.04, 6.55)	3.32(1.29, 8.53)	0.004
Model 3	1	1.04(0.33, 3.31)	2.52(1.00, 6.36)	3.13(1.21, 8.05)	0.003

Notes: Model 1: Unadjusted model; Model 2: Adjusted for age, gender, race; Model 3: Adjusted for age, gender, race, smoking status, alcohol consumption, education, physical activity, and HEI-2015.
Abbreviations: HR, Hazard ratio; CI, Confidence Interval; AL, attachment loss; PD, probing depth.

all-cause (P for non-linearity < 0.001) and cardiovascular (P for non-linearity = 0.007) mortality. Specifically, when AL exceeded a value of 2, the effect of further increases of AL on all-cause and cardiovascular mortality gradually stabilized in MetS. In contrast, PD displayed linear associations with both all-cause (P for overall = 0.004) and cardiovascular (P for overall < 0.001) mortality, with risk continuously escalating as PD levels increased (Figure 4C and D).

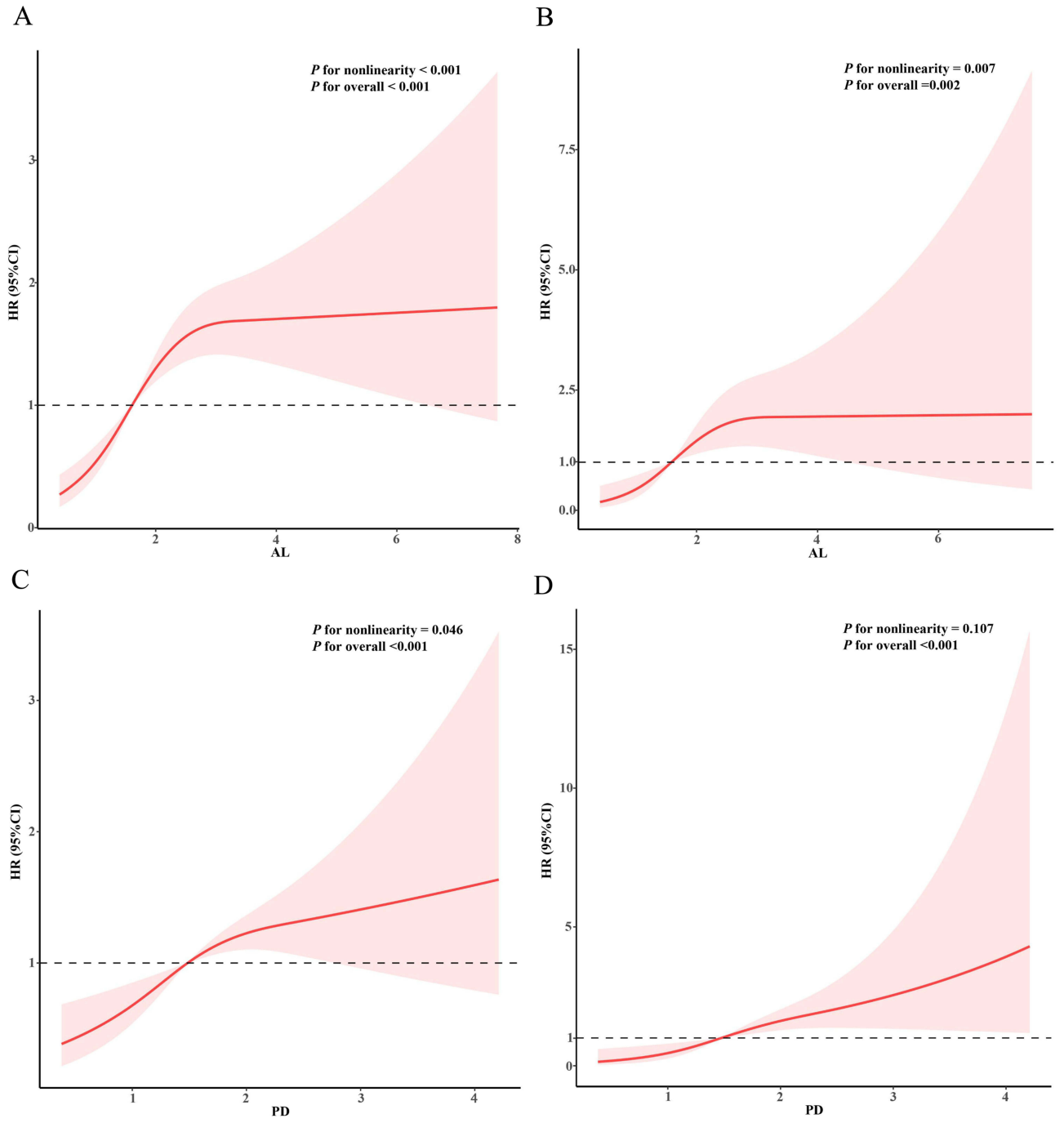

Figure 4 Restricted cubic spline curves for the associations of AL and PD with the prognosis of MetS. (**A**) AL and the risk of all-cause mortality. (**B**) AL and the risk of cardiovascular mortality. (**C**) PD and the risk of all-cause mortality. (**D**) PD and the risk of cardiovascular mortality. HR were adjusted for age, gender, race, education, smoking status, alcohol consumption, physical activity, and HEI-2015.
Abbreviations: AL, attachment loss; PD, probing depth.

Discussion

MetS has become a global health concern as Western lifestyles become more prevalent and economic growth accelerates.[20] It is a complex disorder that brings together several distinct health issues. Without proper management, it could gradually develop into metabolic imbalances, eventually increasing mortality.[21] In this study, we investigated the effect of periodontitis on MetS using the NHANES database.

Considering that variables such as age, gender, race, smoking, alcohol consumption, education, physical activity, and diet are shared influence factors for various chronic diseases,[22] we constructed three models to minimize potential interference in this study. Consistent with the findings of most research,[12,23] all models in our analysis indicated periodontitis could increase the risk of MetS compared to non-periodontitis. MetS comprises five components: WC, BP, FBG, TG, and HDL. Therefore, we also investigated the association between periodontitis and each component of MetS. The results showed that periodontitis was significantly associated with abdominal obesity, elevated blood pressure, and high blood glucose levels. There is strong evidence supporting these findings. For instance, a recent 8-year longitudinal study conducted in Japan by Saito M et al revealed an association between periodontitis and abdominal obesity, suggesting that the underlying mechanisms may involve inflammatory cytokines and reactive oxygen species (ROS),[5] Furthermore, periodontitis may worsen diabetes progression by increasing the levels of tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and resistin. These mediators interfere with insulin receptors and their downstream signaling pathways, resulting in insulin resistance and subsequent increases in blood glucose levels.[24] Some studies reported that periodontitis could increase the prevalence of hypertension and identified that c-reactive proteins and leukocyte levels, markers of systemic inflammation, could serve as biological mediators in this relationship.[25,26] Similarly, a recent cohort study demonstrated that BP was higher in participants with periodontitis compared to those without, which may be related to oral-gut microbial transmission.[27] In summary, the increased risk of MetS associated with periodontitis may be attributed to the involvement of inflammatory cytokines, oxidative stress, microbial dysbiosis and so on. Moreover, periodontitis has been considered to potentially affect lipid metabolism in previous studies, including the ability to elevate TG levels and reduce HDL levels.[28,29] Notably, this association was not observed in our study. A possible and sensible interpretation of these results might be that differences in study populations and confounding factors in the analysis may have influenced the results.

In addition, periodontitis, as a chronic inflammatory disease, has been widely recognized as associated with increased all-cause mortality and cardiovascular mortality in the general population.[30] Therefore, we further explored the impact of periodontitis on the prognosis of MetS. Our study indicates that periodontitis increases the risk of all-cause and cardiovascular mortality in MetS participants. The mechanisms by which periodontitis contributes to mortality in individuals with MetS remain unclear. However, it is well-established that periodontitis is associated with poor prognoses in various chronic diseases, including diabetes and hypertension.[31,32] Further comprehensive and in-depth research is undoubtedly needed in the future.

After evaluating the effects of periodontal parameters on MetS, PD and AL were found to be significantly associated with the prevalence and prognosis of MetS, further supporting our conclusions. Additionally, RCS analysis revealed PD was positively associated with the prevalence, all-cause mortality, and cardiovascular mortality in MetS. However, beyond a certain threshold of AL, the risk for MetS gradually decreases, which was similar to the findings of Fukui N.[33] A plausible explanation is that deep PD signifies the current state of inflammation in periodontal tissues, whereas the presence of AL indicates cumulative periodontal tissue damage caused by periodontitis, which may not necessarily reflect the current inflammatory status.[33,34]

This study utilized a weighted design based on the NHANES sample to ensure nationwide representativeness.[35–37] Furthermore, we not only investigated the association between periodontitis and the risk of MetS but also evaluated the potential impact of periodontitis on the poor prognosis of MetS, providing valuable insights and references for further research in this field. However, there are several limitations should be acknowledged. First, although our results indicated a positive association between periodontitis and MetS parameters, as a cross-sectional study, we cannot infer causality from this association. Second, rigorous adjustments were performed to account for confounding factors, but the potential impact of unmeasured or residual confounders cannot be entirely eliminated. Additionally, the absence of oral imaging data in the NHANES 2009–2014 dataset restricted the utilization of the most recent classification criteria for periodontitis.[38] Therefore, large-scale prospective studies are required to establish the causal relationship between periodontitis and MetS and to elucidate the underlying mechanisms.

Conclusion

In conclusion, periodontitis may be linked to a higher risk of MetS and increased all-cause and cardiovascular mortality. It is advised that healthcare professionals consider periodontitis as a potential factor when preventing and managing MetS. Early intervention and treatment of periodontitis may, to some extent, improve the prognosis of MetS, thereby contributing to the overall health improvement of patients.

Data Sharing Statement

Publicly available datasets were analyzed in this study. This data can be found here: www.cdc.gov/nchs/nhanes/.

Ethics Approval and Consent to Participate

The NHANES 2009-2014 was approved by the NCHS Research Ethics Review Board (NHANES 2009-2010: Continuation of Protocol #2005-06; NHANES 2001-2014: Protocol #2011-17) and acquired all the eligible individuals' informed consent. And The Ethics Committee of The First Affiliated Hospital, Jiangxi Medical College, Nanchang University deemed that this research is based on open-source data, so the need for ethics approval was waived.

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Author Contributions

All authors reviewed the manuscript. All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

All authors declare no conflict of interest in this study.

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