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Original Article

Association between vitamin D levels and risk of periodontitis in patients with metabolic syndrome

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KEYWORDS
Vitamin D;
Periodontitis;
Metabolic syndrome

Background/purpose: The relationship between Vitamin D (VD) and periodontitis in patients with metabolic syndrome (MetS) was unclear. This study was to investigate the relationship between VD and periodontitis in MetS patients.

Materials and methods: This cross-sectional study collected the data of 2165 MetS patients from the National Health and Nutrition Examination Survey (NHANES). The weighted univariate and multivariable Logistic regression models were applied to identify covariates and evaluate the association between 25-hydroxy vitamin D (25(OH)D) $[25(OH)D]_2 + 25(OH)D_3$ and periodontitis in patients. Odds ratio (OR) [95% confidence interval (CI)] was effect size. Subgroup analysis was performed in people with or without diabetes, dyslipidemia, hypertension, cardiovascular disease (CVD) and central obesity groups.

Results: In the unadjusted model, compared with patients with $25(OH)D_2 + 25(OH)D_3 < 50$ nmol/L, those with $25(OH)D_2 + 25(OH)D_3 \geq 50$ nmol/L might be associated with decreased risk of periodontitis in MetS patients (OR = 0.70, 95% CI: 0.57–0.85). After adjusting for confounders including age, gender, race, education, poverty income ratio (PIR), smoking, diabetes, VD intake and supplement and number of missing teeth, $25(OH)D_2 + 25(OH)D_3 \geq 50$ nmol/L was correlated with reduced risk of periodontitis in MetS patients (OR = 0.76, 95% CI: 0.60–0.97). Subgroup analysis revealed that in patients with CVD (OR = 0.60, 95% CI: 0.37–0.98), dyslipidemia (OR = 0.75, 95% CI: 0.57–0.97), and patients with central obesity (OR = 0.73, 95% CI: 0.57–0.95), decreased risk of periodontitis was identified in $25(OH)D_2 + 25(OH)D_3 \geq 50$ nmol/L.

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Conclusion: VD was associated with the risk of periodontitis in patients with MetS, which suggest the importance of VD supplement in patients with MetS and provide a reference for the management of periodontitis in patients with MetS.

Introduction

Periodontitis is the most prevalent disease of the oral cavity, and has emerged as a significant public health concern with an estimated global prevalence rate of 27%.[1] Patients with periodontitis are at an increased risk of tooth loss and masticatory dysfunction, which may negatively affect their quality of life.[2] Metabolic syndrome (MetS) is one of the non-communicable diseases known to be associated with periodontitis.[3] Han et al. reported a 48.8% prevalence of periodontitis in individuals with MetS.[4] The risk of periodontitis was significantly increased in patients with MetS compared with those without,[5,6] and the risk was elevated gradually with the number of MetS components.[7] To explore related factors that may affect the occurrence and development of periodontitis in patients with MetS is necessary.

Vitamin D (VD) level was recognized to be associated with the occurrence and development of a variety of inflammation-related chronic diseases.[8] There was evidence identified that serum 25-OH-vitamin D_3 ($25(OH)D_3$) levels were significantly reduced in patients with chronic periodontitis,[9] but the findings were not conducted in patients with MetS. Another study also found that insufficient VD supplement was associated with increased inflammation levels in patients with MetS.[10] In diabetic patients with periodontitis, serum $25(OH)D_3$ levels were negatively correlated with the levels of inflammatory cytokines and the severity of periodontitis.[11] The relationship between VD levels and the risk of periodontitis in patients with MetS was still unclear.

This study aimed to investigate the relationship between VD levels and the risk of periodontitis in patients with MetS based on the data from the National Health and Nutrition Examination Survey (NHANES) database. Subgroup analysis was performed according to the complications including diabetes, dyslipidemia, hypertension, and cardiovascular disease (CVD) and people with or without central obesity.

Materials and methods

Study design and population

This cross-sectional study collected the data of 2173 patients diagnosed of MetS from NHANES database between 2009 and 2014. The NHANES is a major program of the National Center for Health Statistics (NCHS), which evaluated the health and nutritional status of adults and children in the United States. The survey is unique in that it included interviews, physical examinations, and laboratory evaluations and obtained a large amount of quantitative and qualitative data.[12] In our study, patients without VD information, periodontal status information from oral health exam, and those with the number of missing teeth of 28 were excluded. Finally, 2165 samples were included.

Potential covariates and definitions

Age, gender (males or females), race (Mexican American, non-Hispanic Black, non-Hispanic White, other Hispanic and other races-including multi-racial), education level [9-11th grade (Includes 12th grade with no diploma), college graduate or above, high school graduate/general equivalent diploma (GED) or equivalent, less than 9th grade and some college or Associate of Arts degree (AA) degree], poverty income ratio (PIR), smoking (never smoking, former smoking, and continuous smoking), drinking consumption (high level, low level, median level, never drinking, or unknown), physical activity (high level, or low level), energy, VD intake and supplement, dental implants (no or yes), CVD (no or yes), diabetes (no or yes), hypertension (no or yes), dyslipidemia (no or yes), body mass index (BMI), waist circumference (cm), number of missing teeth (0, 1–5 or $\geq$6), and anti-periodontitis drug (no or yes) were potential covariates analyzed in this study.

Never smoking was defined based on the answer of "no" to SMQ020 (Smoked 100 cigarettes at further in life), former smoker was those answered "yes" to SMQ020 (Smoked 100 cigarettes at further in life) and "no" to SMQ040 (Do you now smoke Cigarettes choice). Current smoker was defined based on the answer of "yes" to SMQ040 (Do you now smoke Cigarettes choice). Those answered "no" to ALQ101 were defined as never drinking. People answered "yes" to ALQ101 were drinkers, and were divided into $<$1 glass (low level), 1–8 glasses (median level), and $\geq$8 glasses (high level) with ALQ120U was unified as weekly $\times$ times (days) and ALQ120Q $\times$ ALQ130 (alcoholic drink volume per day). High level of physical activity was defined based on the answer of "yes" to any one of the items of high intensity PAQ605 or PAQ650, or "yes" to any two of the items of moderate intensity PAQ620, PAQ635 or PAQ665. CVD was defined based on self-reported answer to MCQ160D (Ever told you had angina or heart failure), MCQ160E (Ever told you had heart attack, MCQ160C (Has a doctor or other health professional ever told you that you had coronary heart disease), MCQ160B (Ever told you had a stroke), MCQ160F (Ever told had congestive heart failure), or CVD drug codes: First Level Category ID-Name or 40-CARDIOVASCULAR AGENTS-41, 43, 44, 45, 46, 50, 51, 52, 53, 54, 56, 303, 340, 342, 430, 433 or 483. BMI = weight (kg)/height (cm^2). Central

obesity was defined as a waist circumference of ≥88 cm for women and ≥102 cm for men.[13]

Main and outcome variables

VD level was the main variable in this study, which was calculated based on serum $25(OH)D_2 + 25(OH)D_3$. $25(OH)D_2 + 25(OH)D_3 < 50$ nmol/L was defined as VD deficiency group and $25(OH)D_2 + 25(OH)D_3 \geq 50$ nmol/L was defined as the normal group.[14,15]

Periodontitis was defined based on the Centers for Disease Control and Prevention (CDC)/American Academy of Periodontology case definitions for surveillance of periodontitis.[16] Severe periodontitis was defined as having ≥2 interproximal sites with ≥6 mm of attachment loss (AL), and (not on the same tooth) and ≥1 interproximal site with ≥5 mm of probing depth (PD). Moderate periodontitis was defined as ≥2 interproximal sites with ≥4 mm of clinical AL (not on the same tooth) or ≥2 interproximal sites with PD ≥ 5 mm, also not on the same tooth. Mild periodontitis was defined as ≥2 interproximal sites with ≥3 mm of AL and ≥2 interproximal sites with ≥4 mm of PD or 1 site with ≥5 mm (not on the same tooth). Patients with no and mild periodontitis were combined into the non-periodontitis group, and patients with moderate and severe periodontitis were combined into the periodontitis group to reduce the risk of bias due to the possible excessive prevalence of mild periodontitis in the population.[17]

Statistical analysis

Kolmogorov-Smirnov was used to test the normality of quantitative data. Normally distributed measurement data were described as Mean (standard error) [Mean (SE)]. Independent sample *t*-test was used for comparisons between the two groups. The non-normally distributed measurement data were described by median and quartiles [M (Q_1, Q_3)], and the Mann-Whitney U rank sum test was used for comparisons between groups. Enumeration data were described as number and percentages n (%), and Chi-square test and Wilcoxon rank sum test were used for comparisons between groups. The weighted univariate Logistic regression model was established and variable with $P < 0.05$ were identified. Potential confounding factors were screened out by backward stepwise regression method and identified as covariates. Model 1 was the univariate Logistic regression model without any adjustment. Model 2 adjusted for covariates including age, gender, race and education. In Model 3, covariates including age, gender, race, education, PIR, smoking, diabetes and number of missing teeth were adjusted. Odds ratio (OR) [95% confidence interval (CI)] was effect size for evaluating the association between $25(OH)D_2 + 25(OH)D_3$ and risk of periodontitis in patients. Missing value interpolation were performed using Python 3.9.12 (Python Software Foundation, Delaware, DE, USA). Difference comparison was performed by SAS 9.4 (SAS Institute Inc., Cary, NC, USA). Statistical modeling and subgroup analysis were performed by R version 4.2.2 (2022-10-31 ucrt) (R Foundation for Statistical Computing, Vienna, Austria).

Results

The baseline characteristics of patients in periodontitis group and non-periodontitis group

In total, the data of 2173 patients diagnosed of MetS were extracted from NHANES database. Patients without VD information (n = 8), those without periodontal status information from oral health exam (n = 0) and participants with the number of missing teeth of 28 (n = 0) were excluded. Finally, 2165 samples were included. All participants were divided into the periodontitis group (n = 1272) and the non-periodontitis group (n = 893). The screen process of the participants was shown in Fig. 1.

The mean age in the periodontitis group was higher than the non-periodontitis group (56.49 years vs 51.28 years). The percentage of participants in different numbers of missing teeth groups were statistically different between the periodontitis group and non-periodontitis group. The mean $25(OH)D_2 + 25(OH)D_3$ in the periodontitis group was lower than the non-periodontitis group (63.56 nmol/L vs 68.85 nmol/L). The percentages of participants with $25(OH)D_2 + 25(OH)D_3 \geq 50$ nmol/L in the periodontitis group was lower than the non-periodontitis group (68.02% vs 75.27%) (Table 1).

Potential covariates associated with the risk of periodontitis in MetS patients

To screen out potential confounding factors associated with the risk of periodontitis in MetS patients, a weighted univariate Logistic regression model was established. The results delineated that age, gender, race, education, PIR, smoking, physical activity, VD intake and supplement, CVD, diabetes, BMI, and number of missing teeth might be potential covariates associated with the risk of periodontitis in MetS patients. These variables were included in the weighted multivariable Logistic regression model, and covariates were screened out via the backward stepwise regression method. The data delineated that age (OR = 1.03, 95% CI: 1.02—1.05), gender (OR = 0.51, 95% CI: 0.40—0.65), race (OR = 0.46, 95% CI: 0.32—0.65),

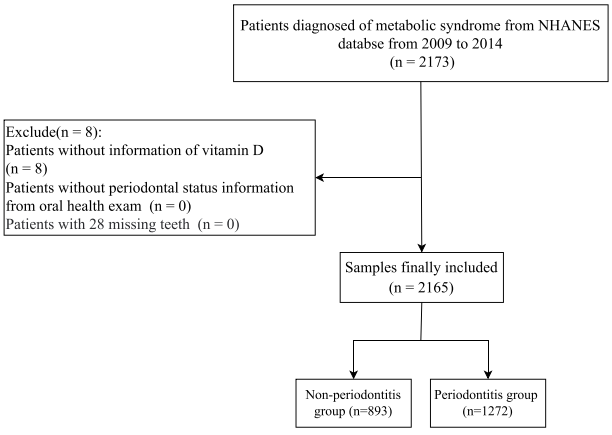

Figure 1 The screen process of the participants in our study.

Table 1 Comparisons of the characteristics in the periodontitis group and non-periodontitis group.

Variables	Total (n = 2165)	Non-periodontitis group (n = 893)	Periodontitis group (n = 1272)	Statistics	*P*
Age, years, Mean (S.E)	53.84 (0.35)	51.28 (0.48)	56.49 (0.49)	t = −7.11	<0.001
Gender, n (%)				χ^2 = 6.524	0.011
Female	1106 (48.84)	510 (51.97)	596 (45.59)		
Male	1059 (51.16)	383 (48.03)	676 (54.41)		
Race, n (%)				χ^2 = 70.499	<0.001
Mexican American	371 (9.51)	111 (6.49)	260 (12.66)		
Non-Hispanic Black	417 (9.98)	140 (7.84)	277 (12.20)		
Non-Hispanic White	962 (69.39)	489 (77.34)	473 (61.14)		
Other Hispanic	246 (5.68)	88 (4.44)	158 (6.98)		
Other races-including multi-racial	169 (5.43)	65 (3.89)	104 (7.03)		
Education level, n (%)				χ^2 = 95.000	<0.001
9–11th grade (Includes 12th grade with no diploma)	372 (13.00)	124 (9.42)	248 (16.71)		
College graduate or above	359 (21.34)	207 (28.17)	152 (14.25)		
High school graduate/ GED or equivalent	517 (24.40)	189 (21.44)	328 (27.49)		
Less than 9th grade	266 (6.82)	56 (3.14)	210 (10.63)		
Some college or AA degree	651 (34.44)	317 (37.83)	334 (30.92)		
PIR, ratio, Mean (S.E)	2.84 (0.06)	3.13 (0.06)	2.54 (0.07)	t = 9.25	<0.001
Smoking, n (%)				χ^2 = 39.873	<0.001
Continuous smoking	438 (17.98)	132 (12.37)	306 (23.81)		
Former smoking	602 (29.65)	233 (27.70)	369 (31.67)		
Never smoking	1125 (52.37)	528 (59.94)	597 (44.52)		
Drinking consumption, n (%)				χ^2 = 14.431	0.006
High drinking	238 (13.03)	91 (12.23)	147 (13.86)		
Low drinking	515 (25.81)	244 (27.90)	271 (23.65)		
Median drinking	402 (21.10)	195 (24.02)	207 (18.06)		
Never drinking	615 (24.07)	234 (23.14)	381 (25.03)		
Unknown	395 (16.00)	129 (12.72)	266 (19.40)		
Physical activity, n (%)				χ^2 = 10.771	0.001
High level	864 (42.48)	393 (46.99)	471 (37.80)		
Low level	1301 (57.52)	500 (53.01)	801 (62.20)		
Energy, kcal, Mean (S.E)	2126.42 (25.55)	2158.94 (34.65)	2092.65 (31.57)	t = 1.55	0.128
VD intake and supplement, mcg, Mean (S.E)	15.77 (1.04)	17.84 (1.78)	13.62 (0.82)	t = 2.28	0.027
Dental implants, n (%)				χ^2 = 3.686	0.055
No	2124 (98.06)	865 (97.27)	1259 (98.88)		
Yes	41 (1.94)	28 (2.73)	13 (1.12)		
CVD, n (%)				χ^2 = 7.559	0.006
No	1561 (72.65)	684 (76.81)	877 (68.34)		
Yes	604 (27.35)	209 (23.19)	395 (31.66)		
Diabetes, n (%)				χ^2 = 33.252	<0.001
No	1360 (68.04)	636 (75.36)	724 (60.45)		
Yes	805 (31.96)	257 (24.64)	548 (39.55)		
Hypertension, n (%)				χ^2 = 3.586	0.058
No	356 (16.96)	173 (19.03)	183 (14.81)		
Yes	1809 (83.04)	720 (80.97)	1089 (85.19)		
Dyslipidemia, n (%)				χ^2 = 1.025	0.311
No	179 (7.55)	76 (6.70)	103 (8.42)		
Yes	1986 (92.45)	817 (93.30)	1169 (91.58)		
Height, cm, Mean (S.E)	169.15 (0.39)	169.98 (0.46)	168.29 (0.51)	t = 2.78	0.008

(*continued on next page*)

Table 1 (*continued*)

Variables	Total (n = 2165)	Non-periodontitis group (n = 893)	Periodontitis group (n = 1272)	Statistics	*P*
Weight, kg, Mean (S.E)	95.95 (0.59)	97.81 (0.85)	94.01 (0.90)	t = 2.99	0.004
BMI, kg/m^2, Mean (S.E)	33.42 (0.22)	33.79 (0.34)	33.04 (0.22)	t = 1.98	0.053
Waist circumference, cm, Mean (S.E)	111.43 (0.46)	111.62 (0.70)	111.24 (0.61)	t = 0.39	0.695
Central obesity n(%)				χ^2 = 4.288	0.038
No	218 (8.92)	62 (7.50)	156 (10.39)		
Yes	1947 (91.08)	831 (92.50)	1116 (89.61)		
Number of missing teeth, n (%)				χ^2 = 143.377	<0.001
0	504 (29.49)	330 (42.15)	174 (16.33)		
1–5	862 (41.73)	365 (40.36)	497 (43.15)		
≥6	799 (28.78)	198 (17.48)	601 (40.51)		
Anti-periodontitis drug, n (%)				χ^2 = 1.353	0.245
No	2111 (96.90)	864 (96.20)	1247 (97.63)		
Yes	54 (3.10)	29 (3.80)	25 (2.37)		
25(OH)D_2 + 25(OH)D_3, nmol/L, Mean (S.E)	66.26 (1.07)	68.85 (1.39)	63.56 (1.08)	t = 3.63	<0.001
25(OH)D_2, nmol/L, Mean (S.E)	4.81 (0.61)	4.92 (0.84)	4.69 (0.56)	t = 0.31	0.760
25(OH)D_3, nmol/L, Mean (S.E)	61.45 (1.18)	63.93 (1.63)	58.87 (1.09)	t = 3.10	0.003
25(OH)D_2 + 25(OH)D_3, n (%)				χ^2 = 14.939	<0.001
<50	738 (28.29)	266 (24.73)	472 (31.98)		
≥50	1427 (71.71)	627 (75.27)	800 (68.02)		

S.E: standard error; GED: general equivalent diploma; PIR: poverty income ratio; VD: vitamin D; CVD: cardiovascular disease; BMI: body mass index; 25(OH)D: 25-OH-vitamin D.

education, PIR (OR = 0.90, 95% CI: 0.83–0.97), smoking (OR = 2.55, 95% CI: 1.82–3.56), diabetes (OR = 1.50, 95% CI: 1.12–1.99), VD intake and supplement (OR = 0.76, 95% CI: 0.60–0.97) and the number of missing teeth were associated with the risk of periodontitis in MetS patients (Table 2).

The association between 25(OH)D_2 + 25(OH)D_3 and the risk of periodontitis in MetS patients

As exhibited in Table 3, in the unadjusted model, compared with patients with 25(OH)D_2 + 25(OH)D_3 < 50 nmol/L, those with 25(OH)D_2 + 25(OH)D_3 ≥ 50 nmol/L might be associated with decreased risk of periodontitis in MetS patients (OR = 0.70, 95% CI: 0.57–0.85). After adjusting for confounding factors including age, gender, race, education, PIR, smoking, diabetes, VD intake and supplement and number of missing teeth, 25(OH)D_2 + 25(OH)D_3 ≥ 50 nmol/L was correlated with reduced risk of periodontitis in MetS patients (OR = 0.76, 95% CI: 0.60–0.97).

Subgroup analysis on the association between 25(OH)D_2 + 25(OH)D_3 and the risk of periodontitis in MetS patients

Subgroup analysis revealed that in patients complicated with CVD (OR = 0.60, 95% CI: 0.37–0.98), dyslipidemia (OR = 0.75, 95% CI: 0.57–0.97), and central obesity (OR = 0.73, 95% CI: 0.57–0.95), decreased risk of periodontitis was identified in those with 25(OH)D_2 + 25(OH)D_3 ≥ 50 nmol/L. In patients with diabetes, or hypertension, or those without CVD, diabetes, hypertension or central obesity, no significant association was observed between 25(OH)D_2 + 25(OH)D_3 ≥ 50 nmol/L and the risk of periodontitis in MetS patients (all $P > 0.05$) (Fig. 2).

Discussion

The present study assessed the association between 25(OH)D_2 + 25(OH)D_3 and the risk of periodontitis in patients with MetS based on the data of 2165 participants from NHANES database. The results delineated that 25(OH)D_2 + 25(OH)D_3 ≥ 50 nmol/L was associated with decreased risk of periodontitis in MetS patients. Subgroup analysis revealed that in MetS patients complicated with CVD, dyslipidemia, and central obesity, decreased risk of periodontitis was observed in 25(OH)D_2 + 25(OH)D_3 ≥ 50 nmol/L group. The findings might provide a reference for the prevention and treatment of periodontitis in patients with MetS.

VD is a generic name comprising Vitamin D_2 and D_3, and Vitamin D_2 is manufactured through ultraviolet irradiation of ergosterol from yeast while Vitamin D_3 results from ultraviolet irradiation of 7-dehydrocholesterol from lanolin.[18] A widely accepted biomarker analysis for VD status is to

Table 2 Potential covariates associated with the risk of periodontitis in patients with MetS.

Variables	OR (95% CI)	*P*
Age	1.03 (1.02–1.04)	<0.001
Gender		
Male	Ref	
Female	0.77 (0.64–0.94)	0.012
Race		
Mexican American	Ref	
Non-Hispanic Black	0.80 (0.58–1.09)	0.164
Non-Hispanic White	0.41 (0.30–0.54)	<0.001
Other Hispanic	0.81 (0.60–1.08)	0.151
Other races-including multi-racial	0.93 (0.53–1.61)	0.788
Education level		
9–11th grade (Includes 12th grade with no diploma)	Ref	
College graduate or above	0.29 (0.19–0.43)	<0.001
High school graduate/GED or equivalent	0.72 (0.50–1.05)	0.097
Less than 9th grade	1.91 (1.19–3.07)	0.011
Some college or AA degree	0.46 (0.33–0.64)	<0.001
PIR	0.78 (0.74–0.82)	<0.001
Smoking		
Never smoking	Ref	
Former smoking	1.54 (1.19–1.98)	0.002
Continuous smoking	2.59 (1.95–3.45)	<0.001
Drinking consumption		
High drinking	Ref	
Low drinking	0.75 (0.51–1.10)	0.149
Median drinking	0.66 (0.42–1.05)	0.090
Never drinking	0.95 (0.56–1.62)	0.863
Unknown	1.34 (0.85–2.12)	0.211
Physical activity		
High level	Ref	
Low level	1.46 (1.15–1.85)	0.003
Energy	1.00 (1.00–1.00)	0.128
VD intake and supplement	1.00 (0.99–1.00)	0.040
Dental implants		
No	Ref	
Yes	0.40 (0.15–1.07)	0.074
CVD		
No	Ref	
Yes	1.53 (1.13–2.09)	0.009
Diabetes		
No	Ref	
Yes	2.00 (1.54–2.60)	<0.001
Hypertension		
No	Ref	
Yes	1.35 (0.99–1.84)	0.064
Dyslipidemia		
No	Ref	
Yes	0.78 (0.48–1.26)	0.319
BMI	0.98 (0.97–1.00)	0.042
Circumference	1.00 (0.99–1.01)	0.694
Number of missing teeth		
≥6	Ref	
0	0.17 (0.12–0.24)	<0.001
1–5	0.46 (0.37–0.58)	<0.001
Anti-periodontitis drug		
No	Ref	
Yes	0.62 (0.27–1.41)	0.258

(*continued on next page*)

Table 2 (*continued*)

MetS: metabolic syndrome; OR: odd ratio; CI: confidence interval; Ref: reference; GED: general equivalent diploma; PIR: poverty income ratio; VD: vitamin D; CVD: cardiovascular disease; BMI: body mass index.

measure the serum 25[OH]D.[19] Recently, VD levels have been gaining growing attention in oral health especially periodontitis. There was evidence identified the association of VD deficiency with a myriad of acute and chronic illnesses including periodontitis.[20] A comprehensive review depicted that VD deficiency was associated with higher prevalence of periodontitis.[21] Another randomized double-blind placebo-controlled study revealed that 6-month VD supplement improved the treatment of periodontitis in patients with initial 25(OH) vitamin $D_3 < 30$ ng/mL.[22] In the current study, $25(OH)D_2 + 25(OH)D_3$ was evaluated to identity the association between VD levels and risk of

Table 3 The association between $25(OH)D_2 + 25(OH)D_3$ and the risk of periodontitis in patients with MetS.

Periodontitis	$25(OH)D_2 + 25(OH)D_3$			
	<50 (n = 738)		≥50 (n = 1427)	
	OR (95% CI)	*P*	OR (95% CI)	*P*
Model 1	Ref		0.70 (0.57–0.85)	0.001
Model 2	Ref		0.68 (0.53–0.87)	0.004
Model 3	Ref		0.76 (0.60–0.97)	0.038

25(OH)D: 25-OH-vitamin D; MetS: metabolic syndrome; OR: odd ratio; CI: confidence interval; Ref: reference.
Model 1: Unadjusted.
Model 2: Adjusted for age, gender, race, and education level.
Model 3: Adjusted for age, gender, race, education level, PIR, smoking, diabetes, number of missing teeth.

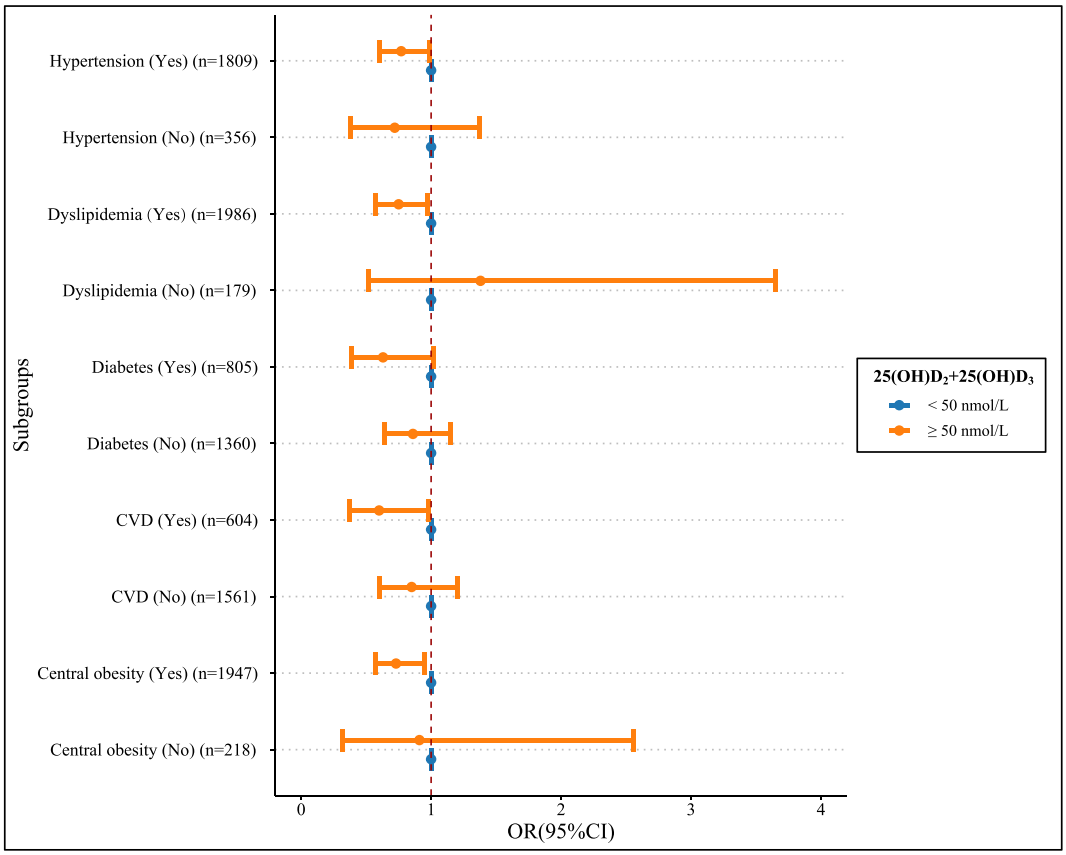

Figure 2 Forest plot showing the subgroup analysis of the association between $25(OH)D_2 + 25(OH)D_3$ and the risk of periodontitis in MetS patients.

periodontitis in patients with MetS. We found that $25(OH)D_2 + 25(OH)D_3 \geq 50$ nmol/L was associated with reduced risk of periodontitis in patients with MetS. We suspected that the potential mechanism might be that VD could participate in the inflammation processes, decrease the inflammatory levels including RANKL, TNF-α, IL-1, MMP-9, and IL-6 and stimulate the healing of periodontal tissues, which played a vital part in maintaining healthy periodontal tissues.[23] VD was reported to exhibite apparent fine-tuning, anti-inflammatory and mineralization effects on the periodontium, and may decrease the number of live porphyromonas gingivalis through active autophagy.[24] Other studies also revealed that VD participated in the oxidative stress,[25,26] and systemic inflammation in patients with MetS,[27] and these might also help decrease the risk of periodontitis. Bone metabolism might be another mechanism that VD has impact on oral health.[28] Subgroup analysis showed that in MetS patients complicated with CVD, dyslipidemia, and central obesity, $25(OH)D_2 + 25(OH)D_3 \geq 50$ nmol/L was correlated with decreased risk of periodontitis. Inflammation exerted significant roles in CVD, dyslipidemia, and central obesity.[29–31] VD was identified to be a potential anti-inflammatory mediator of CVD.[32] A previous study demonstrated the beneficial effects of VD supplementation in anti-inflammation in overweight and obese paediatric populations.[33]

Our study showed the association between $25(OH)D_2 + 25(OH)D_3$ and the risk of periodontitis in patients with MetS based on data from a large sample size using multi-stage complex sampling, and the representativeness was good. The evaluation of periodontitis covered 28 teeth with 6 locations per tooth, and the results might be more comprehensive. Additionally, VD level was evaluated based on the detection of 25-(OH)-D, which could more objectively reflect the VD level of the body. We found that $25(OH)D_2 + 25(OH)D_3 \geq 50$ nmol/L was associated with decreased risk of periodontitis in MetS patients. The findings suggested the potential importance of VD in MetS patients. VD is a steroid hormone obtained mainly from exposure to sunlight, but also from diet and dietary supplements.[34] Foods naturally containing VD is rare, and it can be found in oily fish including salmon, mackerel, and herring and oils from fish.[35] Both metabolic syndrome and periodontitis are urgent issues for the global burden of disease, and to identify more reliable biomarkers that might help better manage patients with these diseases are important. Considering the association of VD with periodontal health, nutritional advice might be given for the management of periodontal diseases. Regular and timely VD during dental practice might help improve the quality of life, hence benefitting the MetS patients. In the case of a deficiency of any micronutrients, dietary sources, exposure to sunlight, or $25(OH)D_3$ supplement must be considered.

There were limitations in this study. Firstly, this was a cross-sectional study, and only the association between $25(OH)D_2 + 25(OH)D_3$ and the risk of periodontitis in

patients with MetS could be identified, while the causal relationship between them could not be inferred. Secondly, the information on certain dental diseases of participants was not reported in the database, such confounding factors could not be included in the analysis. Thirdly, the underlying mechanisms between VD and the risk of periodontitis in patients with MetS could not be verified in our study, and in the future, more well-designed studies were required to verify the results in the present study.

The current study identified that VD level was associated with the risk of periodontitis in patients with MetS, which might suggest the importance of VD supplement in patients with MetS and provide a reference for the prevention and treatments of periodontitis in patients with MetS.

Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

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