

[DOI] 10.12016/j.issn.2096-1456.202440453

· 临床研究 ·

单核细胞/高密度脂蛋白胆固醇比值与牙周炎的关系:基于NHANES数据库的横断面研究

胡志强, 张琦, 李欣鹏, 崔宇琛, 袁佳敏, 朱宪春

吉林大学口腔医院正畸科, 吉林 长春(130021)

【摘要】 目的 探究单核细胞/高密度脂蛋白胆固醇比值(monocyte/high-density lipoprotein cholesterol ratio, MHR)与牙周炎的关联,为牙周炎的影响因素提供依据。**方法** 选取美国国家健康和营养调查(National Health and Nutrition Examination, NHANES)数据库中2009—2010年、2011—2012年、2013—2014年3个周期受试者的MHR、牙周炎情况及其他协变量数据,共纳入8 456名研究对象。根据牙周炎患病情况(有、无)对研究对象进行分组,采用加权logistic回归方法逐步调整混杂因素,构建3个回归模型(不调整协变量,部分调整协变量及完全调整协变量)分析MHR与牙周炎之间的关系。将MHR按照四分位法从小到大分为Q1~Q4四组进行加权趋势分析,使用限制性立方样条分析MHR(连续)与牙周炎之间的非线性关系,并进行了亚组分析及敏感性分析。**结果** 3个加权logistic回归模型均显示MHR与牙周炎间存在正相关关系[OR = 2.92, 95%CI: 2.14~3.99, $P < 0.001$ (不调整); OR = 1.97, 95%CI: 1.39~2.78, $P < 0.001$ (部分调整); OR = 1.62, 95%CI: 1.10~2.39, $P = 0.017$ (完全调整)]。趋势分析显示,与Q1组相比,Q4组的单因素分析(OR = 1.92, 95%CI: 1.58~2.33, $P < 0.001$)、多因素分析(OR = 1.30, 95%CI: 1.03~1.64, $P = 0.029$)均显示MHR升高会引起牙周炎患病风险显著升高。限制性立方样条结果显示,不支持MHR与牙周炎之间的非线性关系(P for nonlinear > 0.05),亚组分析显示各协变量与MHR无明显交互作用($P > 0.05$),敏感性分析也表明了MHR与牙周炎之间存在正相关关系(OR = 1.67, 95%CI: 1.31~2.14, $P < 0.001$)。**结论** MHR与牙周炎患病风险具有正相关关系。

【关键词】 牙周炎; 单核细胞; 高密度脂蛋白; 单核细胞/高密度脂蛋白胆固醇比值; 美国国家健康和营养调查; 横断面研究; 敏感性分析; 限制性立方样条

【中图分类号】 R78 **【文献标志码】** A **【文章编号】** 2096-1456(2025)03-0212-09

【引用著录格式】 胡志强, 张琦, 李欣鹏, 等. 单核细胞/高密度脂蛋白胆固醇比值与牙周炎的关系:基于NHANES数据库的横断面研究[J]. 口腔疾病防治, 2025, 33(3): 212-220. doi:10.12016/j.issn.2096-1456.202440453.

Association of monocyte/high-density lipoprotein cholesterol ratio with periodontitis: a cross-sectional study based on the NHANES database HU Zhiqiang, ZHANG Qi, LI Xinpeng, CUI Yuchen, YUAN Jiamin, ZHU Xianchun.

Department of Orthodontic, Hospital of Stomatology, Jilin University, Changchun 130021, China

Corresponding author: ZHU Xianchun, Email: zhuxc@jlu.edu.cn, Tel: 86-431-85579372

【Abstract】 Objective To investigate the association between monocyte to high-density lipoprotein cholesterol ratio (MHR) and periodontitis and to provide new epidemiologic evidence on the factors affecting periodontitis. **Methods** Data on MHR, periodontitis, and other covariates were selected from the NHANES(National Health and Nutrition Examination) database for 3 cycles of subjects in 2009–2010, 2011–2012, and 2013–2014, and a total of 8 456 study subjects were included. The study participants were grouped according to the prevalence of periodontitis (presence or absence), and three regression models (unadjusted covariates, partially adjusted covariates, and fully adjusted covariates) were constructed to analyze the relationship between MHR and periodontitis by using a weighted logistic regression method with stepwise adjustment for confounders. MHR was divided into four groups from Q1 to Q4 according to quartiles from



微信公众号

【收稿日期】 2024-11-14; **【修回日期】** 2025-01-10

【基金项目】 吉林省自然科学基金项目(YDZJ202201ZYTS057)

【作者简介】 胡志强, 住院医师, 硕士研究生, Email: huzq22@mails.jlu.edu.cn

【通信作者】 朱宪春, 主任医师, 博士, Email: zhuxc@jlu.edu.cn, Tel: 86-431-85579372

small to large for weighted trend analysis, and the nonlinear relationship between MHR (continuous) and periodontitis was analyzed using a restricted cubic spline with subgroup analysis and sensitivity analysis. **Results** All three logistic regression models showed a positive association between MHR and periodontitis ($OR = 2.92$, 95% CI : 2.14-3.99, $P < 0.001$ (not adjusted); $OR = 1.97$, 95% CI : 1.39-2.78, $P < 0.001$ (partially adjusted); $OR = 1.62$, 95% CI : 1.10-2.39, $P = 0.017$ (fully adjusted)). Trend analysis showed a significantly higher risk of developing periodontitis in the Q4 group compared with the Q1 group in both single ($OR = 1.92$, 95% CI : 1.58-2.33, $P < 0.001$) and multifactorial analyses ($OR = 1.30$, 95% CI : 1.03-1.64, $P = 0.029$). Restricted cubic spline results did not support a nonlinear relationship between MHR and periodontitis (P for nonlinear > 0.05), subgroup analysis showed no significant interaction between the covariates and MHR ($P > 0.05$), and sensitivity analysis also showed a positive correlation between MHR and periodontitis ($OR = 1.67$, 95% CI : 1.31-2.14, $P < 0.001$). **Conclusion** MHR is positively associated with the risk of developing periodontitis.

【Key words】 periodontitis; monocytes; high-density lipoprotein; monocyte/high-density lipoprotein cholesterol ratio; National Health and Nutrition Examination (NHANES); cross-sectional study; sensitivity analysis; restricted cubic spline

J Prev Treat Stomatol Dis, 2025, 33(3): 212-220.

【Competing interests】 The authors declare no competing interests.

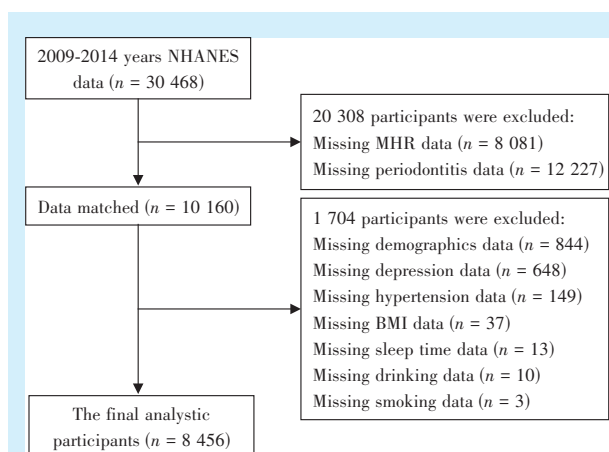
This study was supported by the grants from National Natural Science Foundation of Jilin Province (No. YDZJ202201ZYTS057).

牙周炎是全球第六大流行疾病,是牙周组织的慢性炎症性疾病^[1],同时也与心血管疾病、2型糖尿病、类风湿性关节炎、炎症性肠病和代谢综合征等多种慢性疾病有关^[2-4]。2011至2020年期间,全球成年人的牙周炎患病率为62%^[5]。牙周炎已经成为一个愈发重要的公共卫生问题^[6]。因此,有必要探索一种生物标志物用于牙周炎的预防、诊断及疗效评估。单核细胞/高密度脂蛋白胆固醇比值(monocyte/high-density lipoprotein cholesterol ratio, MHR)是一种新型炎症标志物,可以反映机体的炎症与氧化应激水平^[7-8]。多项研究表明,MHR可能是膝关节炎^[9]、代谢综合征的炎症标志物^[10],而关于MHR与牙周炎之间关联的研究鲜有报道。有研究显示MHR与牙周炎的患病风险具有相关性^[11],但两者之间的关系有待进一步研究且缺乏大样本量临床数据进行验证。本研究基于美国国家健康和营养调查(National Health and Nutrition Examination, NHANES)数据库探讨MHR与牙周炎之间的关联,以期为牙周炎的预防与诊断提供新的流行病学证据。

1 材料和方法

1.1 研究人群

分析采用2009—2010年、2011—2012年、2013—2014年3个周期收集的NHANES数据,共选取了30 468名参与者。纳入流程见图1,研究最终纳入



NHANES: National Health and Nutrition Examination; MHR: monocyte/high-density lipoprotein cholesterol ratio; BMI: body mass index

Figure 1 Flowchart showing process of screening research subjects

图1 研究对象筛选流程图

了8 456名参与者进行分析。

纳入标准:①年龄在30岁及以上;②有MHR测量数据;③口腔健康评估阶段接受过牙周检查。

排除标准:①未进行彻底牙周检查;②缺乏人口统计学数据、抑郁症数据、体重指数(body mass index, BMI)、饮酒量、吸烟、睡眠和高血压及糖尿病的协变量信息。

1.2 变量设置

1.2.1 单核细胞/高密度脂蛋白胆固醇比值

(MHR) 基于 NHANES 2009 至 2014 年数据,参与者至少禁食 9 h 后在上午接受检查;使用贝克曼库尔特 Max-M 仪器对参与者的血液样本进行全血细胞计数,并提供所有参与者的血细胞分布情况;高密度脂蛋白胆固醇的浓度通过直接沉淀法或免疫测定法进行测量。MHR 定义为单核细胞/高密度脂蛋白胆固醇(high density lipoprotein, HDL)比值,当 MHR 偏大时,说明研究对象的炎症稳态可能失衡。根据研究对象的 MHR 四分位数分为 MHRQ1 组: ≤ 0.283 ; MHR Q2 组: $> 0.283 \sim 0.392$; MHR Q3 组: $> 0.392 \sim 0.543$; MHR Q4 组: > 0.543 , 并进行趋势性分析。

1.2.2 牙周炎分类数据 牙周炎的分类数据是基于 NHANES 数据库中口腔健康组的牙周板块获取的。该板块自 2009 年重新开始调查,并于 2014 年之后暂停,即 2009 至 2014 年的牙周数据为现有最新数据。牙周病的分类基于 2012 年美国疾病控制与预防中心和美国牙周病学会的牙周炎病例定义^[12]。具体标准如下:轻度牙周炎是指两个邻间位点附着丧失达到 3 mm,两个邻间位点牙周袋深度达到 4 mm(不在同一牙齿上),或任意一个部位牙周袋深度达到 5 mm。中度牙周炎的定义是两个邻间位点的牙周袋深度为 4 mm(不在同一牙齿上)或两个邻间位点的牙周袋深度为 5 mm(不在同一牙齿上)。共有 2 个邻间位点的附着丧失值为 6 mm(不在同一牙齿上)和 1 个邻间位点的牙周袋深度值为 5 mm,则被归类为重度牙周炎。本研究将轻、中、重度牙周炎数据均定义为牙周炎组。

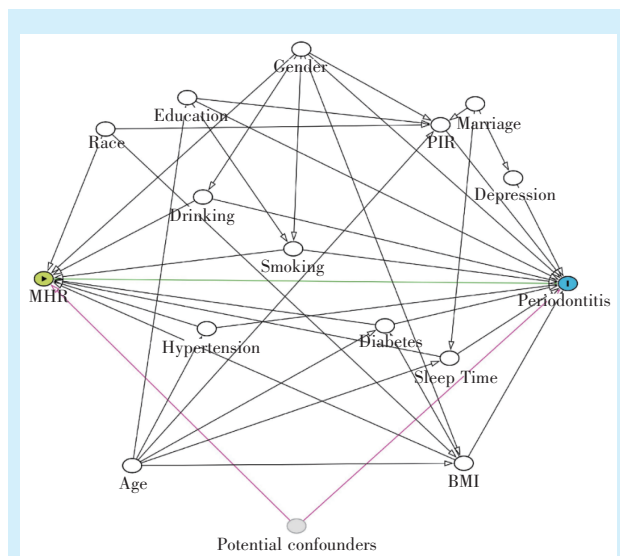
1.2.3 协变量 在本研究中,基于 NHANES 2009 至 2014 年数据,人口统计特征包括年龄、性别、种族、贫困收入比(poverty to income ratio, PIR)、教育水平和婚姻状况。①年龄分为 3 组:30 ~ 44 岁、45 ~ 59 岁、60 ~ 80 岁。②种族分为 5 类:墨西哥裔美国人、其他西班牙裔美国人、非西班牙裔白人、非西班牙裔黑人和其他种族。③PIR 分为 3 级:PIR < 1.3 为低家庭收入,PIR 为 1.3 ~ 3.5 为中等家庭收入,PIR > 3.5 为高家庭收入^[13]。④教育水平分为 5 类:小于 9 年级、9 ~ 11 年级、高中毕业/同等学历、大学经历或副学士学位、大学毕业或以上。⑤婚姻状况分为:已婚/与伴侣同居、丧偶/离婚/分居。

体重指数(body mass index, BMI)分为 3 组^[14]: BMI < 25 kg/m² 为体重不足和正常体重; BMI = 25 ~ 30 kg/m² 为超重; BMI > 30 kg/m² 为肥胖。吸烟状况:根据参与者一生中吸烟是否超过 100 支以及现

在是否吸烟,分为从不吸烟者、曾经吸烟者和现在吸烟者。饮酒量:根据文献分为不饮酒、1 ~ 5 次/个月、5 ~ 10 次/个月和 10 次以上/个月^[15]。睡眠时间:根据文献分为睡眠不足(0 ~ 6 h)、睡眠充足(7 ~ 9 h)和睡眠过度(> 9 h)^[16]。抑郁症、高血压、糖尿病按“是”和“否”进行分类。绘制有向无环图以解释研究变量之间的潜在联系(图 2)。

1.3 统计学分析

为确保研究结果的真实性和可靠性,研究采用 NHANES 抽样加权法,所有分析均使用 R Studio(4.2.3 版)进行。分类变量采用卡方检验进行统计分析。连续变量以平均值±标准差表示,使用多变量加权 logistic 回归模型探讨 MHR 与牙周炎之间的联系。模型 1 未调整任何协变量,模型 2 调整了年龄、种族、性别、PIR、教育水平和婚姻状况,模型 3 调整了模型 2 中的协变量以及其他混杂因素,如 BMI、睡眠时间、饮酒状况、吸烟状况、高血压、糖尿病和抑郁症。使用限制性立方样条来探索 MHR 与牙周炎患病风险之间是否具有非线性关系,使用亚组分析及敏感性分析探究 MHR 与牙周炎之间的关联在不同分组人群及非加权 logistic 回归模型中是否具有稳健性, $P < 0.05$ 为差异有统计学意义。



Green circles represent exposure variables, blue circles represent outcome variables, white circles represent confounding variables that require adjustment, and gray circles represent potential confounding variables. MHR: monocyte/high-density lipoprotein cholesterol ratio; PIR: poverty to income ratio; BMI: body mass index

Figure 2 Directed acyclic graphs between MHR and periodontitis and all confounders

图 2 单核细胞/高密度脂蛋白胆固醇比值与牙周炎和所有混杂因素之间的有向无环图

2 结 果

2.1 研究人群特征

分析最终纳入了 8 456 名参与者,其中 51% 为男性,49% 为女性;大多数受试者为非西班牙裔白人(71%);MHR 为 0.42 ± 0.23 ,牙周炎的患病率

为 41%。在非牙周炎组与不同程度牙周炎组患者中,性别、年龄、种族、PIR、BMI、教育程度、婚姻状况、睡眠时间、抑郁、吸烟状况、饮酒情况、糖尿病和高血压均有统计学差异($P < 0.05$) (表 1)。

表 1 单核细胞/高密度脂蛋白胆固醇比值与牙周炎关系研究人群特征

Table 1 Characteristics of the population in the study of the relationship between MHR and periodontitis

Characteristic	Non-periodontitis (<i>n</i> = 4 198)	Mild periodontitis (<i>n</i> = 388)	Moderate periodontitis (<i>n</i> = 2 956)	Severe periodontitis (<i>n</i> = 914)	Total (<i>n</i> = 8 456)	χ^2	<i>P</i>
Age/years						40.32	< 0.001
30-44	1 950 (46%)	203 (45%)	690 (24%)	161 (20%)	3 004 (37%)		
45-59	1 283 (33%)	114 (37%)	913 (36%)	374 (47%)	2 684 (36%)		
60-80	965 (21%)	71 (18%)	1 353 (40%)	379 (33%)	2 768 (27%)		
Gender						53.08	< 0.001
Female	2 450 (55%)	173 (43%)	1 298 (44%)	255 (27%)	4 176 (49%)		
Male	1 748 (45%)	215 (57%)	1 658 (56%)	659 (73%)	4 280 (51%)		
Race						16.58	< 0.001
Non-Hispanic White	2 232 (77%)	171 (67%)	1 213 (65%)	286 (55%)	3 902 (71%)		
Non-Hispanic Black	644 (8%)	79 (13%)	663 (13%)	282 (21%)	1 668 (10%)		
Mexican American	425 (5%)	75 (11%)	480 (10%)	188 (13%)	1 168 (8%)		
Other Hispanic	400 (4%)	37 (5%)	295 (5%)	71 (4%)	803 (5%)		
Other/Multiracial	497 (6%)	26 (4%)	305 (7%)	87 (7%)	915 (6%)		
Marriage						22.09	< 0.001
Married/living with partner	2 879 (74%)	251 (66%)	1 838 (65%)	542 (59%)	5 510 (70%)		
Widowed/divorced/separated	1 319 (26%)	137 (34%)	1 118 (35%)	372 (41%)	2 946 (30%)		
PIR						42.27	< 0.001
< 1.3	893 (12%)	112 (19%)	1 035 (25%)	397 (34%)	2 437 (18%)		
1.3-3.5	1 377 (33%)	160 (40%)	1 149 (40%)	331 (39%)	3 017 (35%)		
> 3.5	1 928 (55%)	116 (41%)	772 (35%)	186 (27%)	3 002 (47%)		
BMI						2.64	0.023
Underweight/normal	1 156 (26%)	75 (17%)	760 (27%)	227 (23%)	2 218 (26%)		
Overweight	1 443 (37%)	128 (37%)	1 012 (34%)	336 (35%)	2 919 (36%)		
Obese	1 599 (37%)	185 (46%)	1 184 (39%)	351 (42%)	3 319 (38%)		
Education						39.27	< 0.001
Less than 9th grade	189 (2%)	26 (4%)	365 (8%)	132 (10%)	712 (4%)		
9-11th grade	369 (6%)	50 (9%)	477 (14%)	205 (22%)	1 101 (10%)		
Highschool graduate/GED or equivalent	744 (17%)	98 (25%)	746 (25%)	255 (29%)	1 843 (20%)		
Some college or AA degree	1 298 (32%)	132 (34%)	808 (30%)	209 (28%)	2 447 (31%)		
College graduate or above	1 598 (43%)	82 (28%)	560 (23%)	113 (11%)	2 353 (35%)		
Depression						2.98	0.035
Yes	338 (6%)	39 (11%)	274 (8%)	77 (7%)	728 (7%)		
No	3 860 (94%)	349 (89%)	2 682 (92%)	837 (93%)	7 728 (93%)		
Sleep time/h						8.13	< 0.001
< 7	1 567 (32%)	162 (40%)	1 193 (37%)	417 (46%)	3 339 (35%)		
7-9	2 559 (67%)	215 (56%)	1 689 (61%)	475 (52%)	4 938 (64%)		
> 9	72 (1%)	11 (4%)	74 (2%)	22 (2%)	179 (1%)		
Smoking						49.43	< 0.001
Current smoker	526 (11%)	72 (15%)	666 (24%)	332 (39%)	1 596 (16%)		
Former smoker	982 (25%)	81 (20%)	879 (31%)	242 (28%)	2 184 (27%)		
Never smoker	2 690 (64%)	235 (65%)	1 411 (45%)	340 (33%)	4 676 (57%)		
Drinking/every month						2.24	0.038
0	1 054 (19%)	94 (18%)	846 (23%)	205 (17%)	2 199 (20%)		
1-5	2 119 (51%)	202 (56%)	1 435 (49%)	437 (51%)	4 193 (50%)		
5-10	356 (10%)	35 (9%)	174 (7%)	74 (7%)	639 (9%)		
> 10	669 (20%)	57 (17%)	501 (21%)	198 (25%)	1 425 (21%)		

续表 1

Continued table 1

Characteristic	Non-periodontitis (<i>n</i> = 4 198)	Mild periodontitis (<i>n</i> = 388)	Moderate periodontitis (<i>n</i> = 2 956)	Severe periodontitis (<i>n</i> = 914)	Total (<i>n</i> = 8 456)	χ^2	<i>P</i>
Diabetes						33.39	< 0.001
Yes	510 (10%)	56 (16%)	682 (20%)	228 (22%)	1 476 (14%)		
No	3 688 (90%)	332 (84%)	2 274 (80%)	686 (78%)	6 980 (86%)		
Hypertension						24.10	< 0.001
Yes	1 337 (31%)	137 (36%)	1 319 (42%)	408 (44%)	3 201 (35%)		
No	2 861 (69%)	251 (64%)	1 637 (58%)	506 (56%)	5 255 (65%)		
MHR (continuous)	0.41 ± 0.20	0.45 ± 0.23	0.45 ± 0.24	0.51 ± 0.33	0.42 ± 0.23		< 0.001
MHR (categorical)						8.86	< 0.001
Q1	1 202 (29%)	82 (22%)	689 (24%)	166 (17%)	2 139 (26%)		
Q2	1 107 (26%)	96 (25%)	691 (24%)	209 (23%)	2 103 (25%)		
Q3	1 025 (25%)	102 (25%)	748 (25%)	233 (23%)	2 108 (25%)		
Q4	864 (20%)	108 (28%)	828 (27%)	306 (37%)	2 106 (24%)		

PIR: poverty-to-income ratio; BMI: body mass index; MHR: monocyte/high-density lipoprotein cholesterol ratio; Q1: $MHR \leq 0.283$; Q2: $0.283 < MHR \leq 0.392$; Q3: $0.392 < MHR \leq 0.543$; Q4: $MHR > 0.543$.

2.2 MHR 与牙周炎的关系

为了进一步探索 MHR 与牙周炎之间的潜在关联,本研究使用 3 个模型对 MHR 和牙周炎进行了 logistic 分析,均显示牙周炎与 MHR 具有相关性。在逐步调整混杂因素的过程中,MHR 与牙周炎的正相关作用逐渐减弱,但在完全调整混杂因素的模型中,MHR 每增加一个标准差,牙周炎的患病风险增加 62%,这表明 MHR 与牙周炎患病风险之间依然具有明显的正相关性。将连续变量 MHR 按照四分位数法从小到大分为 Q1 ~ Q4 四组并使用趋势分析发现,与 MHR 最低组(Q1)相比,MHR 最高组(Q4)患者牙周炎的患病风险最高且有统计学差异($P < 0.05$)。此外,趋势性检验结果提示 MHR 水平每增加一个等级,患者牙周炎风险呈现出逐渐增加的趋势($P\text{-trend} < 0.05$)。以上结果显示 MHR 与牙周炎之间具有相关性,且牙周炎的患病风险随 MHR 的分位数增加而增加,表明 MHR 与牙周炎

间可能存在剂量反应关系,见表 2。

采用四节点(节点设置在 MHR 总数据分布的 5%、35%、65%、95% 分位数上)的加权限制性立方样条图检验连续变量 MHR 与牙周炎之间是否具有非线性关系。完全调整协变量后的限制性立方样条结果显示,MHR 与牙周炎之间近似于“U”型关系,但 MHR 与牙周炎之间的非线性关系无统计学意义($P \text{ for Nonlinear} = 0.25$)(图 3)。

2.3 亚组分析与敏感性分析

为了探究 MHR 与牙周炎之间的正相关关系是否受到协变量的干扰,分别在年龄、性别、种族、婚姻情况、PIR 与受教育程度的亚组中进行协调其余协变量后的加权 logistic 回归分析,结果显示,各协变量与 MHR 无明显交互作用($P > 0.05$)。

亚组分析还表明,除大学毕业或以上及其他种族-包括多种族分组外,其余亚组中 MHR 与牙周炎间均保持正相关关系,虽然这种相关性不一定

表 2 单核细胞/高密度脂蛋白胆固醇比值与牙周炎的加权 logistic 回归分析

Table 2 Weighted logistic regression analysis of MHR and periodontitis

Group	Model 1 <i>OR</i> (95% <i>CI</i>)	<i>P</i>	Model 2 <i>OR</i> (95% <i>CI</i>)	<i>P</i>	Model 3 <i>OR</i> (95% <i>CI</i>)	<i>P</i>
MHR (continuous)	2.92 (2.14-3.99)	< 0.001	1.97 (1.39-2.78)	< 0.001	1.62 (1.10-2.39)	0.017
Q1	Ref		Ref		Ref	
Q2	1.22 (1.01-1.47)	0.036	1.06 (0.83-1.36)	0.638	1.04 (0.80-1.34)	0.762
Q3	1.22 (0.98-1.52)	0.068	1.01 (0.77-1.33)	0.953	0.97 (0.75-1.25)	0.784
Q4	1.92 (1.58-2.33)	< 0.001	1.48 (1.20-1.84)	< 0.001	1.30 (1.03-1.64)	0.029
<i>P-trend</i>	< 0.001		0.002		0.050	

Model 1 was not adjusted for confounders; Model 2 was adjusted for gender, age, race, education, and marriage, PIR; and Model 3 was further adjusted for BMI, sleep time, smoking, drinking, diabetes, hypertension, and depression on the basis of Model 2. Ref: reference group; *P-trend*: *P*-value of trend analysis, Q1: $MHR \leq 0.283$, Q2: $0.283 < MHR \leq 0.392$, Q3: $0.392 < MHR \leq 0.543$, Q4: $MHR > 0.543$; MHR: monocyte/high-density lipoprotein cholesterol ratio

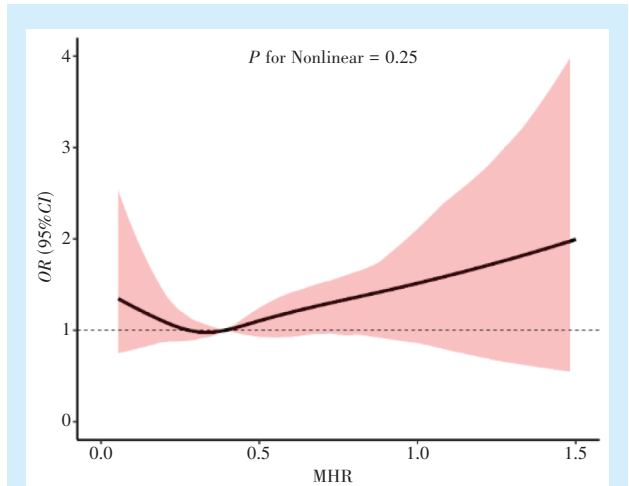
具有统计学意义。MHR 与牙周炎间的正相关关系在 45~59 岁、男性、PIR > 3.5、离婚/分居/未婚、受教育程度在高中毕业/同等学历和大学经历或副学士学位与非西班牙裔白人中显得更为明显且具有统计学意义(图 4)。

本研究还进行了敏感性分析,使用不加权的多变量 logistic 回归检验 MHR 与牙周炎之间的关联。结果显示,MHR 与牙周炎之间具有正相关性($P < 0.001$),趋势分析表明,MHR 与牙周炎可能呈线性正相关关系($P\text{-trend} < 0.001$),证明上述分析的结果稳健(表 3)。

3 讨论

本研究使用多种统计模型探究了 MHR 对美国成年人牙周炎患病率的影响。在加权多变量 logistic 回归中,MHR 与牙周炎患病率存在正相关关系,具体来说,MHR 每增加一个标准差,牙周炎的患病率增加 62%。限制立方样条图显示 MHR 与牙周炎之间不具有非线性关系,不加权的多变量 logistic 回归显示,MHR 与牙周炎患病率之间同样具有正相关关系,证明分析结果稳健。

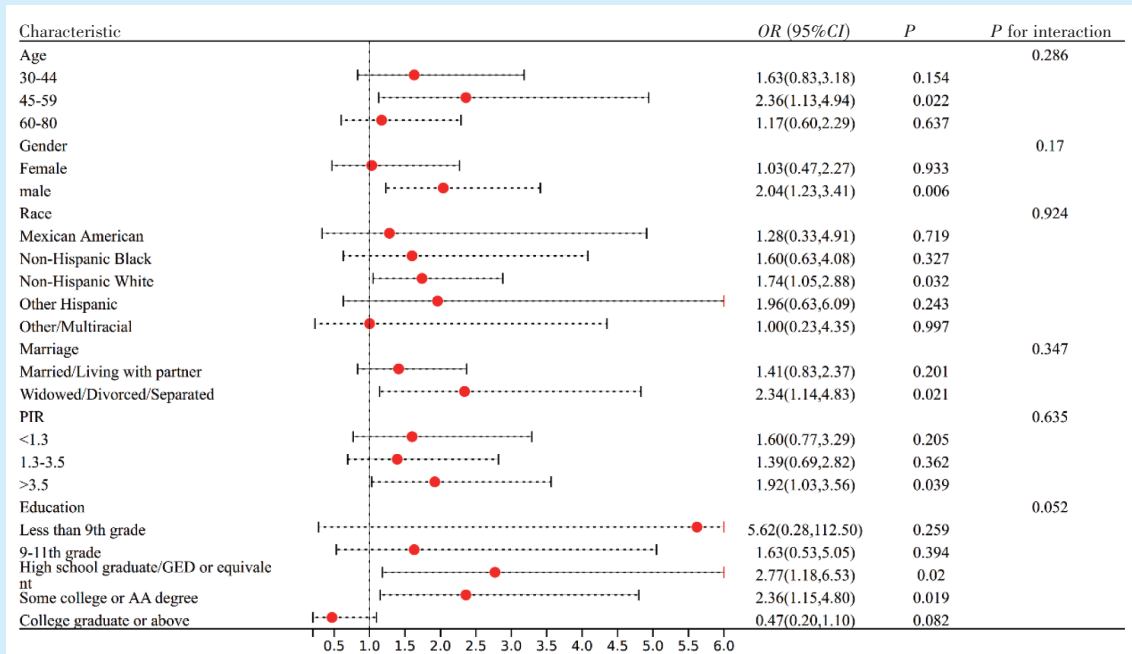
牙周炎的严重程度取决于微生物因子与宿主



Weighted restricted cubic splines after adjusting for gender, age, race, education, and marriage, PIR, BMI, sleep time, smoking, drinking, diabetes, hypertension, and depression. P for Nonlinear: P value of a Nonlinear relationship. PIR: poverty-to-income ratio; BMI: body mass index; MHR: monocyte/high-density lipoprotein cholesterol ratio

Figure 3 Restricted cubic spline plots of MHR and periodontitis

图 3 单核细胞/高密度脂蛋白胆固醇比值与牙周炎的限制立方样条图



Forest plot for subgroup analysis after adjusting for gender, age, race, education, and marriage, PIR, BMI, sleep time, smoking, drinking, diabetes mellitus, hypertension, and depression. P for interaction: P value for interaction. PIR: poverty-to-income ratio; BMI: body mass index; MHR: monocyte/high-density lipoprotein cholesterol ratio

Figure 4 Subgroup analysis of the relationship between MHR and periodontitis

图 4 亚组分析单核细胞/高密度脂蛋白胆固醇比值与牙周炎之间的关系

表 3 单核细胞/高密度脂蛋白胆固醇比值与牙周炎的 logistic 回归分析

Table 3 Logistic regression analysis of MHR and periodontitis

Group	Model 1 OR(95%CI)	P	Model 2 OR(95%CI)	P	Model 3 OR(95%CI)	P
MHR(continuous)	2.89(2.37-3.54)	< 0.001	1.93(1.54-2.44)	< 0.001	1.67(1.31-2.14)	< 0.001
Q1	Ref		Ref		Ref	
Q2	1.16(1.02-1.30)	0.019	1.04(0.91-1.20)	0.539	1.03(0.90-1.19)	0.667
Q3	1.36(1.20-1.53)	< 0.001	1.18(1.03-1.36)	0.018	1.15(1.00-1.33)	0.051
Q4	1.85(1.63-2.09)	< 0.001	1.48(1.20-1.84)	< 0.001	1.34(1.15-1.56)	< 0.001
P-trend	< 0.001		< 0.001		< 0.001	

Model 1 was not adjusted for confounders, and Model 2 was adjusted for gender, age, race, education, marriage, PIR; Model 3 was further adjusted for BMI, sleep time, smoking, drinking, diabetes, hypertension, and depression on the basis of Model 2; Ref: reference group; P-trend: P-value of trend analysis, Q1: $MHR \leq 0.283$, Q2: $0.283 < MHR \leq 0.392$, Q3: $0.392 < MHR \leq 0.543$, Q4: $MHR > 0.543$; MHR: monocyte/high-density lipoprotein cholesterol ratio

免疫系统之间的相互作用^[17]。单核细胞和巨噬细胞在这一过程中起着重要作用^[18]。Steinmetz 等^[19]发现在小鼠牙周组织炎症过程中, CX3CR1hi 型单核/巨噬细胞亚群通过调节早期中性粒细胞反应来支持牙龈卟啉单胞菌的存活。人单核细胞可分为 3 种类型亚群, 即经典、中间和非经典亚群^[20-21]。Jagannathan 等^[22]比较了患和不患慢性牙周炎个体的外周血单核细胞亚群百分比, 发现非经典单核细胞在牙周炎组中的数量更多, 非手术牙周治疗可显著降低血液中的非经典单核细胞计数和 C 反应蛋白(C-reactive protein, CRP)水平^[23]。

单核细胞进入组织可以转化为巨噬细胞^[24]。牙周巨噬细胞主要位于牙龈沟或牙周袋中, 是抵御微生物疾病的一线防御者^[25], 受不同刺激时主要表现为 M1 促炎型与 M2 抗炎型两种极化方式^[26]。牙周炎症与 M1 和 M2 巨噬细胞表型的增强有关^[27], 其中 M1 和 M2 巨噬细胞相关细胞因子表达失衡可能是介导牙周组织损伤的关键机制^[28]。

HDL 长期被认为是心血管疾病的预测因子^[29], 具有多效性, 包括胆固醇外排能力、抗氧化活性、抗炎活性、抗血栓形成活性和抗凋亡活性, 这些有助于 HDL 对动脉粥样硬化的保护作用^[30]。它的抗炎、抗氧化和抗感染特性也为其作为新的生物标志物和治疗靶点开辟了新的途径^[31]。

近年来, 人们对 HDL 和牙周炎之间的联系越来越感兴趣, 尽管有相关孟德尔随机化研究指出包括 HDL 在内的血清脂质水平与牙周炎间并未发现因果关系^[32], 但依然有许多横断面研究表明二者之间具有相关性^[33-34], 即低 HDL 水平与牙周炎的高患病风险有关。原因可能有以下两种: 一种是牙龈卟啉单胞菌可以通过改变脂质结构来加速动

脉粥样硬化的形成, 从而降低血清 HDL 水平, 另一种是牙周炎可上调全身炎症, 通过抑制血清 HDL 水平和甘油三酯水平升高来影响脂质代谢^[35]。

单核细胞在炎症过程中产生大量炎症因子, 加剧炎症反应。血清 HDL 具有抗炎和抗氧化作用^[36], 将两个值同时纳入的 MHR 同时兼顾免疫与保护机制, 可能具有更大的临床价值。MHR 作为一种新兴的炎症标志物, 被认为是动脉粥样硬化发生、发展的预测因子^[37], 也是与炎症状态相关的心血管疾病临床预后的预测因子^[38], 更是全身炎症的标志物^[39], 与 CRP 呈正相关。最近的一项 meta 分析表明, 牙周炎与全身炎症有关, 表现为血清 CRP 水平的升高^[40], 根据以上研究, 推测 MHR 与牙周炎之间可能存在直接或间接的联系, 但具体机制仍需要进一步探究。

在本研究中, 牙周炎患者的 MHR 值显著大于非牙周炎患者, 这与 Lalitha 等^[11]的研究结果一致。MHR 与牙周炎的较高相关性在本研究的多种统计方法中均得到验证。限制性立方样条图中, MHR 与牙周炎近似于“U”型关系, 且最低点 OR 值低于 1。这表明 MHR 在一定的正常范围内, 不会对牙周炎产生显著影响, 只有 MHR 因单核细胞计数或 HDL 升高或降低变得异常时, 才与牙周炎患病率之间呈现正相关关系。亚组分析中, 对于大部分亚组人群, MHR 与牙周炎患病率呈正相关, 表明分析结果的稳健。对于 NHANES 数据, 使用加权多变量 logistic 分析得到结果以代表美国人群的一般水平, 但纳入了性别、年龄、种族等协变量的多变量 logistic 回归更能反应独立个体中 MHR 与牙周炎的相关性^[41]。在敏感性分析中, MHR 无论作为连续变量还是分类变量, 都显示了其与牙周炎之间具

有一定的正相关作用($P < 0.001$)。作为连续变量时,相较于加权 logistic 回归模型,不加权的 logistic 模型显示,随着 MHR 的升高,牙周炎患病风险增加的可能性更大。基于 MHR 与牙周炎的相关性且白细胞计数与血脂指标的易获取性,MHR 有可能作为临床诊疗中牙周炎的预测因子。

本研究使用的牙周炎数据,已在多项高水平研究中被广泛报告^[42-43]。NHANES 是一项国家级数据库,虽然最新的牙周炎数据仅覆盖至 2014 年,但由于其严格的质量控制措施,确保了数据的高准确性和可靠性。而牙周炎的慢性进展性特点决定了其在人群中的流行病学特征在短期内不会发生显著变化,因此 2009 至 2014 年的 NHANES 数据可以为本研究的结论提供可靠依据。

总之,本研究表明 MHR 与美国成年人群牙周炎患病风险具有正相关作用,即随着 MHR 的升高,牙周炎的患病风险也随之升高。希望未来有进一步的大规模前瞻性队列研究来验证这一发现,并探究 MHR 与牙周炎之间的潜在联系,揭示单核细胞亚群与 HDL 成分与牙周炎间的具体机制。

[Author contributions] Hu ZQ performed the research, analyzed the data and wrote the article. Zhang Q, Li XP, Cui YT, Yuan JM designed the research study and revised the article. Zhu XC conceptualized and reviewed the article. All authors read and approved the final manuscript as submitted.

参考文献

- [1] Heitz-Mayfield LJA. Conventional diagnostic criteria for periodontal diseases (plaque-induced gingivitis and periodontitis)[J]. *Periodontol* 2000, 2024, 95(1): 10-19. doi: 10.1111/prd.12579.
- [2] Jepsen S, Suvan J, Deschner J. The association of periodontal diseases with metabolic syndrome and obesity[J]. *Periodontol* 2000, 2020, 83(1): 125-153. doi: 10.1111/prd.12326.
- [3] Hajishengallis G, Chavakis T. Local and systemic mechanisms linking periodontal disease and inflammatory comorbidities[J]. *Nat Rev Immunol*, 2021, 21(7): 426-440. doi: 10.1038/s41577-020-00488-6.
- [4] Tanwar H, Gnanasekaran JM, Allison D, et al. Unravelling the oral-gut axis: interconnection between periodontitis and inflammatory bowel disease, current challenges, and future perspective[J]. *J Crohns Colitis*, 2024, 18(8): 1319-1341. doi: 10.1093/ecco-jcc/jjae028.
- [5] Trindade D, Carvalho R, Machado V, et al. Prevalence of periodontitis in dentate people between 2011 and 2020: a systematic review and meta-analysis of epidemiological studies[J]. *J Clin Periodontol*, 2023, 50(5): 604-626. doi: 10.1111/jcpe.13769.
- [6] Genco RJ, Sanz M. Clinical and public health implications of periodontal and systemic diseases: an overview[J]. *Periodontol* 2000, 2020, 83(1): 7-13. doi: 10.1111/prd.12344.
- [7] Meng X, Sun H, Tu X, et al. The predictive role of hematological parameters in hypertension[J]. *Angiology*, 2024, 75(8): 705-716. doi: 10.1177/00033197231190423.
- [8] Guo X, Ma L. Inflammation in coronary artery disease-clinical implications of novel HDL-cholesterol-related inflammatory parameters as predictors[J]. *Coron Artery Dis*, 2023, 34(1): 66-77. doi: 10.1097/MCA.0000000000001198.
- [9] Cao J, Hua L, Dong L, et al. The value of the monocyte to high-density lipoprotein cholesterol ratio in assessing the severity of knee osteoarthritis: a retrospective single center cohort study[J]. *J Inflamm Res*, 2023, 16: 595-604. doi: 10.2147/JIR.S395229.
- [10] Wang W, Chen ZY, Guo XL, et al. Monocyte to high-density lipoprotein and apolipoprotein A1 ratios: novel indicators for metabolic syndrome in Chinese newly diagnosed type 2 diabetes[J]. *Front Endocrinol(Lausanne)*, 2022, 13: 935776. doi: 10.3389/fendo.2022.935776.
- [11] Lalitha TA, Balakrishnan A, Parthiban S, et al. Monocyte-to-high-density lipoprotein cholesterol ratio as a novel inflammatory marker in periodontal disease: a pilot study[J]. *J Contemp Dent Pract*, 2022, 23(7): 709-712.
- [12] Eke PI, Page RC, Wei L, et al. Update of the case definitions for population-based surveillance of periodontitis[J]. *J Periodontol*, 2012, 83(12): 1449-1454. doi: 10.1902/jop.2012.110664.
- [13] Liu B, Wang J, Li YY, et al. The association between systemic immune-inflammation index and rheumatoid arthritis: evidence from NHANES 1999-2018[J]. *Arthritis Res Ther*, 2023, 25(1): 34. doi: 10.1186/s13075-023-03018-6.
- [14] Zhu S, Ji L, He Z, et al. Association of smoking and osteoarthritis in US (NHANES 1999 - 2018)[J]. *Sci Rep*, 2023, 13: 3911. doi: 10.1038/s41598-023-30644-6.
- [15] Christensen K, Gleason CE, Mares JA. Dietary carotenoids and cognitive function among US adults, NHANES 2011-2014[J]. *Nutr Neurosci*, 2020, 23(7): 554-562. doi: 10.1080/1028415X.2018.1533199.
- [16] Xu JN, Huang YQ, Wang J, et al. Association between healthy lifestyle combinations and periodontitis in NHANES[J]. *BMC Oral Health*, 2024, 24(1): 182. doi: 10.1186/s12903-024-03937-z.
- [17] Di Stefano M, Polizzi A, Santonocito S, et al. Impact of oral microbiome in periodontal health and periodontitis: a critical review on prevention and treatment[J]. *Int J Mol Sci*, 2022, 23(9): 5142. doi: 10.3390/ijms23095142.
- [18] Cekici A, Kantarci A, Hasturk H, et al. Inflammatory and immune pathways in the pathogenesis of periodontal disease[J]. *Periodontol* 2000, 2014, 64(1): 57-80. doi: 10.1111/prd.12002.
- [19] Steinmetz O, Hoch S, Avniel-Polak S, et al. CX3CR1hi monocyte/macrophages support bacterial survival and experimental infection-driven bone resorption[J]. *J Infect Dis*, 2016, 213(9): 1505-1515. doi: 10.1093/infdis/jiv763.
- [20] Almubarak A, Tanagala KKK, Papapanou PN, et al. Disruption of monocyte and macrophage homeostasis in periodontitis[J]. *Front Immunol*, 2020, 11: 330. doi: 10.3389/fimmu.2020.00330.

- [21] Belge KU, Dayyani F, Horelt A, et al. The proinflammatory CD14⁺ CD16⁺ DR⁺⁺ monocytes are a major source of TNF[J]. *J Immunol*, 2002, 168(7): 3536-3542. doi: 10.4049/jimmunol.168.7.3536.
- [22] Jagannathan R, Lavu V, Rao SR. Comparison of the proportion of non-classic (CD14⁺ CD16⁺) monocytes/macrophages in peripheral blood and gingiva of healthy individuals and patients with chronic periodontitis[J]. *J Periodontol*, 2014, 85(6): 852-858. doi: 10.1902/jop.2013.120658.
- [23] Jagannathan R, Balaji TM, Rao SR, et al. Effect of non-surgical periodontal therapy on CD14⁺ CD16⁺ monocyte counts in peripheral blood samples: a clinical interventional study[J]. *BMC Oral Health*, 2024, 24(1): 94. doi: 10.1186/s12903-023-03793-3.
- [24] Peet C, Ivetic A, Bromage DI, et al. Cardiac monocytes and macrophages after myocardial infarction[J]. *Cardiovasc Res*, 2020, 116(6): 1101-1112. doi: 10.1093/cvr/cvz336.
- [25] Luo W, Du C, Huang H, et al. The role of macrophage death in periodontitis: a review[J]. *Inflammation*, 2024, 47(6): 1889-1901. doi: 10.1007/s10753-024-02015-4.
- [26] Sun X, Gao J, Meng X, et al. Polarized macrophages in periodontitis: characteristics, function, and molecular signaling[J]. *Front Immunol*, 2021, 12: 763334. doi: 10.3389/fimmu.2021.763334.
- [27] 贺欣然, 李元, 张武阳, 等. 牙周炎中巨噬细胞极化、焦亡、胞葬的研究进展[J]. *口腔疾病防治*, 2024; 32(11): 886-893. doi: 10.12016/j.issn.2096-1456.202330511.
- He XR, Li Y, Zhang WY, et al. Research progress on macrophage polarization, pyroptosis, and efferocytosis in periodontitis[J]. *J Prev Treat Stomatol Dis*, 2024; 32(11): 886-893. doi: 10.12016/j.issn.2096-1456.202330511.
- [28] Zhang W, Guan N, Zhang X, et al. Study on the imbalance of M1/M2 macrophage polarization in severe chronic periodontitis[J]. *Technol Health Care*, 2023, 31(1): 117-124. doi: 10.3233/THC-220092.
- [29] Pownall HJ, Rosales C, Gillard BK, et al. High-density lipoproteins, reverse cholesterol transport and atherogenesis[J]. *Nat Rev Cardiol*, 2021, 18(10): 712-723. doi: 10.1038/s41569-021-00538-z.
- [30] Thakkar H, Vincent V, Sen A, et al. Changing perspectives on HDL: from simple quantity measurements to functional quality assessment[J]. *J Lipids*, 2021, 2021: 5585521. doi: 10.1155/2021/5585521.
- [31] Endo Y, Sasaki K, Ikewaki K. Bridging the gap between the bench and bedside: clinical applications of high-density lipoprotein function[J]. *J Atheroscler Thromb*, 2024, 31(9): 1239 - 1248. doi: 10.5551/jat.RV22020.
- [32] Chen Z, Song J, Tang L. Investigation on the association between serum lipid levels and periodontitis: a bidirectional mendelian randomization analysis[J]. *BMC Oral Health*, 2023, 23(1): 827. doi: 10.1186/s12903-023-03575-x.
- [33] Zhu H, Ye G, Xie Y, et al. Association of high-density lipoprotein cholesterol and periodontitis severity in Chinese elderly: a cross-sectional study[J]. *Clin Oral Investig*, 2022, 26(7): 4753-4759. doi: 10.1007/s00784-022-04439-4.
- [34] Guan X, Wang X, Li Y, et al. Glucose and lipid metabolism indexes and blood inflammatory biomarkers of patients with severe periodontitis: a cross-sectional study[J]. *J Periodontol*, 2023, 94(4): 554-563. doi: 10.1002/JPER.22-0282.
- [35] Mikami R, Mizutani K, Matsuyama Y, et al. Association between periodontal inflammation and serum lipid profile in a healthy population: a cross-sectional study[J]. *J Periodontol Res*, 2021, 56(6): 1037-1045. doi: 10.1111/jre.12917.
- [36] Yurtdaş M, Yaylali YT, Özdemir M. The role of monocyte to HDL ratio in predicting clinically significant carotid stenosis in patients with asymptomatic carotid artery disease[J]. *Rev Assoc Med Bras* (1992), 2020, 66(8): 1043 - 1048. doi: 10.1590/1806 - 9282.66.8.1043.
- [37] Zhao S, Tang J, Yu S, et al. Monocyte to high-density lipoprotein ratio presents a linear association with atherosclerosis and nonlinear association with arteriosclerosis in elderly Chinese population: the Northern Shanghai study[J]. *Nutr Metab Cardiovasc Dis*, 2023, 33(3): 577-583. doi: 10.1016/j.numecd.2022.12.002.
- [38] Jiang M, Yang J, Zou H, et al. Monocyte-to-high-density lipoprotein-cholesterol ratio (MHR) and the risk of all-cause and cardiovascular mortality: a nationwide cohort study in the United States [J]. *Lipids Health Dis*, 2022, 21(1): 30. doi: 10.1186/s12944-022-01638-6.
- [39] Wei Y, Gao H, Luo Y, et al. Systemic inflammation and oxidative stress markers in patients with unipolar and bipolar depression: a large-scale study[J]. *J Affect Disord*, 2024, 346: 154 - 166. doi: 10.1016/j.jad.2023.10.156.
- [40] Machado V, Botelho J, Escalda C, et al. Serum C-reactive protein and periodontitis: a systematic review and meta-analysis[J]. *Front Immunol*, 2021, 12: 706432. doi: 10.3389/fimmu.2021.706432.
- [41] Gelman A. Struggles with survey weighting and regression modeling[J]. *Statist Sci*, 2007, 22(2): 153 - 164. doi: 10.1214/088342306000000691
- [42] Huang Z, Peng S, Cen T, et al. Association between biological ageing and periodontitis: evidence from a cross-sectional survey and multi-omics mendelian randomization analysis[J]. *J Clin Periodontol*, 2024, 51(10): 1369-1383. doi: 10.1111/jcpe.14040.
- [43] Wu Y, Yang H, Jin W, et al. Association between polycyclic aromatic hydrocarbons and periodontitis: results from a large population-based study[J]. *J Clin Periodontol*, 2024, 51(4): 441-451. doi: 10.1111/jcpe.13919.

(编辑 罗燕鸿, 刘洁)



Open Access

This article is licensed under a Creative Commons
Attribution 4.0 International License.

Copyright © 2025 by Editorial Department of Journal of
Prevention and Treatment for Stomatological Diseases



官网