

Research on the Correlation Between Periodontitis and Cerebral Small Vessel Disease

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Abstract. In recent years, the proposed "Oral-Brain- Axis" hypothesis has provided a new theoretical perspective on the relationship between oral health and cerebrovascular diseases. This study employs a combination of literature review and empirical research to explore the association between periodontitis and cerebral small vessel disease (CSVD). The research compared the periodontal status of patients with CSVD and non-CSVD patients, as well as tooth loss and periodontal indicators in patients with varying degrees of CSVD. Statistical validation was conducted using Spearman correlation analysis and Binary logistic regression analysis. The results indicate that the CSVD group had significantly higher levels of tooth loss and more severe periodontitis compared to the non-CSVD group. Patients with moderate to severe CSVD exhibited poorer oral health. Correlation analysis revealed a positive relationship between periodontal indicators, tooth loss, and the severity of CSVD. Further regression analysis confirmed that severe periodontitis is an independent risk factor for moderate to severe CSVD. Patients with moderate to severe periodontitis had a 1.501 times higher risk of developing moderate to severe CSVD compared to those with no or mild periodontitis.

Keywords: Periodontitis, Cerebral small vessel disease, Correlation analysis, Binary logistic regression analysis.

1. Introduction

CSVD refers to a group of pathological processes affecting small arteries, arterioles, capillaries, and venules in the brain. Its clinical manifestations include lacunar infarcts, white matter hyperintensities, cerebral microbleeds, and others [1]. The incidence of CSVD exceeds 70% among middle-aged and elderly populations in China, and with the accelerating aging of the population, its prevalence continues to rise [2]. Thus, CSVD has become a public health issue that cannot be ignored. Moreover, CSVD is one of the major causes of cognitive impairment, gait abnormalities, and disability in later life, severely affecting patients' quality of life. Meanwhile, periodontitis is also a common chronic inflammatory disease, particularly prevalent among the elderly. It not only leads to tooth loss and reduced masticatory function, impacting nutritional intake and quality of life [3], but recent studies have also suggested that its systemic inflammatory effects may be associated with various systemic diseases [4].

In recent years, various scholars have systematically summarized potential pathways through which periodontitis may affect brain health, explicitly proposing the concepts of the "Oral-Brain Axis" or "Periodontitis-Brain Connection" [5]. Thus, this paper is the first to employ the CSVD total burden scoring system to quantitatively assess the overall severity of CSVD. It aims to analyze the correlation between CSVD severity and both tooth loss status and periodontal health indicators in older adults, while further exploring the underlying pathophysiological mechanisms. This paper seeks to provide a scientific basis for early intervention and comprehensive prevention strategies.

2. Research design and methods

2.1 Study Participants

The paper participants comprised 100 patients with periodontal disease who were treated at the Department of Stomatology of XX Hospital between January 2022 and December 2024. The inclusion criteria were as follows: (1) availability of cranial Magnetic Resonance Imaging (MRI) data

within the preceding two months; (2) age over 40 years; (3) no history of cerebrovascular events attributable to large vessel stenosis $\geq 50\%$; (4) absence of acute stroke, autoimmune malignancies, severe infectious diseases, or severe hepatic/renal insufficiency. The exclusion criteria included: (1) presence of large cortical or subcortical infarct lesions; (2) intracranial hemorrhagic lesions, significant craniocerebral trauma, or history of brain tumors; (3) severe sensory impairments (e.g., visual or hearing impairments) affecting evaluation outcomes; (4) recent acute infections; (5) pregnancy or lactation; (6) recent periodontal treatment, refusal to undergo oral examination, or incomplete data.

This study categorized patients into those with arteriosclerotic CSVD and non-CSVD lesions based on cranial MRI findings. The diagnosis of arteriosclerotic CSVD adhered to the standards for small artery arteriosclerotic CSVD outlined in the *Chinese Expert Consensus on Diagnosis and Treatment of Cerebral Small Vessel Disease 2021*. The paper protocol was approved by the Ethics Committee, and written informed consent was obtained from all participants.

2.2 Research Methods and Indicators

2.2.1 Periodontal Indicators

A trained periodontist assessed the periodontal health status of all enrolled patients. The periodontal indicators included: Probing Depth (PD): The distance from the gingival margin to the base of the periodontal pocket. Clinical Attachment Loss (CAL): The distance from the base of the periodontal pocket to the cemento-enamel junction. It is the gold standard for assessing the extent of periodontal tissue destruction. Bleeding Index (BI): Bleeding upon probing, reflecting current inflammatory activity. Plaque Index (PLI): Indicating oral hygiene status. Tooth Loss: An indicator of the number of permanent teeth lost. It was categorized as follows: Simple Tooth Loss: Loss of ≤ 4 teeth. Complex Tooth Loss: Loss of ≥ 5 teeth. Complete Dentition: No teeth missing. Periodontitis and its severity were defined according to the CDC/AAP classification criteria.

2.2.2 Assessment of Cerebral Small Vessel Disease

All enrolled patients underwent cranial MRI examinations. The imaging evaluation of cerebral small vessel disease strictly adhered to the internationally recognized STRIVE standards and was performed by an experienced neuroradiologist who was blinded to the patients' periodontal status. Designated multimodal MRI sequences were utilized, encompassing various imaging techniques: T1-Weighted Imaging (T1WI), T2-Weighted Imaging (T2WI), Diffusion-Weighted Imaging (DWI), Fluid-Attenuated Inversion Recovery (FLAIR), and Susceptibility-Weighted Imaging (SWI). These sequences were applied to detect cerebral atrophy, intracranial hemorrhage (ICH), and exclude acute cerebral infarction. The following core biomarkers were identified and assessed: Enlarged Perivascular Spaces (PVS), Cerebral Microbleeds (CMB), Lacunes of presumed vascular origin.

The total CSVD burden score was then calculated according to the following criteria, with one point assigned for each of the following four features: lacune ≥ 1 , Deep white matter hyperintensities (WMH) with Fazekas score 2-3 or periventricular WMH with Fazekas score 3, cerebral microbleed ≥ 1 , enlarged perivascular spaces in a single region ≥ 11 . The scores for each patient were summed to obtain a total burden score (range 0-4). Patients were categorized into a mild group (0-1 points) and a moderate-to-severe group (2-4 points) based on this score. This approach enables a comprehensive and scientific evaluation of the presence and severity of cerebral small vessel disease in patients.

2.2.3 Covariate Data Collection

This paper collected baseline demographic information of enrolled patients, including age and sex. Laboratory tests were performed, comprising fasting blood glucose, glycated hemoglobin (HbA1c), and a full lipid panel. Conventional vascular risk factors were documented, including: Hypertension, Diabetes mellitus, Hyperlipidemia (diagnostic criteria based on the Chinese Guidelines for Lipid Management [2023]), Smoking history (defined as cumulative smoking ≥ 100 cigarettes). Alcohol

consumption history (defined as alcohol use for >3 months with a frequency of at least once per week). Physical examination data were also collected, including height, weight, and blood pressure.

3. Empirical Analysis

This paper divides the subjects into two groups: patients with CSVD and non-CSVD, and analyzes the data using SPSS. First, Univariate analysis is conducted to examine the relationship between each independent variable and the dependent variable. Chi-square tests, Independent samples t-tests, and One-way ANOVA are employed to investigate whether the proportion of hypertensive patients is higher in the CSVD group compared to the non-CSVD group, and whether there are differences in the proportions of smokers, alcohol consumers, individuals with hyperlipidemia, and diabetes mellitus between the CSVD and non-CSVD groups. A comparative analysis is also performed on the status of dentition defects and periodontal indicators between the CSVD and non-CSVD groups. Next, a comparative study is conducted on dentition defects and periodontal indicators among patients with varying degrees of CSVD. Additionally, a correlation analysis is carried out between periodontal indicators (PD, CAL, BI), dentition loss, and the total burden of CSVD to preliminarily explore the relationship between them. Finally, binary logistic regression analysis is used to determine whether the severity of periodontitis is independently correlated with the occurrence and severity of CSVD.

3.1 Univariate Analysis

3.1.1 Comparative Analysis of Baseline Characteristics Between Patients with CSVD and Non-CSVD

As shown in Table 1, a comparative analysis of baseline characteristics was conducted between patients with CSVD and non-CSVD. The variables age, hypertension, hyperlipidemia, and alcohol consumption yielded p-values of less than 0.05, indicating statistically significant differences in these four indicators. Compared to the non-CSVD group, the CSVD group was older and had higher proportions of hypertension, hyperlipidemia, and alcohol consumption. In contrast, the variables sex, diabetes mellitus, and smoking showed p-values greater than 0.05, suggesting no statistically significant differences.

Table 1. Comparison of Baseline Characteristics Between CSVD and Non-CSVD Groups

Variable	Non-CSVD (n=37)	CSVD (n=63)	Statistic	P-values
Age ($\bar{x}\pm s$)	60.06 $\pm$ 9.36	66.25 $\pm$ 10.23	t=2.341	0.025
Male [n(%)]	16 (43.2%)	35 (55.5%)	$\chi^2=0.029$	0.147
Hypertension [n(%)]	9 (24.3%)	43 (68.2%)	$\chi^2=9.486$	0.001
Diabetes mellitus [n(%)]	12 (32.4%)	20 (31.7%)	$\chi^2=0.061$	0.762
Hyperlipidemia [n(%)]	10 (27%)	20 (31.7%)	$\chi^2=4.362$	0.006
Smoking [n(%)]	14 (37.8%)	29 (46.0%)	$\chi^2=2.485$	0.097
Alcohol consumption [n(%)]	8 (21.6%)	18 (28.6%)	$\chi^2=3.982$	0.036

3.1.2 Comparison of Tooth Loss and Periodontal Indicators Between Patients With CSVD and Non-CSVD

As shown in Table 2, the p-values for the selected periodontal indicators (tooth loss and moderate-to-severe periodontitis) were all less than 0.05, indicating statistically significant differences in these parameters. Specifically, compared to the non-CSVD group, the CSVD group exhibited higher values in PD, CAL, BI, and PLI, suggesting more severe periodontal pathology and a higher proportion of patients with moderate to severe periodontitis. Furthermore, the proportions of patients with simple tooth loss and complex tooth loss were higher in the CSVD group, while the proportion of patients

with complete dentition was lower compared to the non-CSVD group. These results indicate that tooth loss and periodontitis are more severe and prevalent among CSVD patients.

Table 2. Comparison of Tooth Loss and Periodontal Indicators Between CSVD and Non-CSVD Groups

Variable	Non-CSVD (n=37)	CSVD (n=63)	Statistic	P-values
PD ($\bar{x}\pm s$)	3.31 $\pm$ 0.14	5.49 $\pm$ 0.72	t=8.362	<0.001
CAL ($\bar{x}\pm s$)	3.11 $\pm$ 0.56	4.81 $\pm$ 1.16	t=9.124	0.027
BI ($\bar{x}\pm s$)	2.08 $\pm$ 0.11	2.32 $\pm$ 0.13	t=7.015	<0.001
PLI($\bar{x}\pm s$)	1.53 $\pm$ 0.19	2.25 $\pm$ 0.23	t=9.428	0.004
Tooth loss [n(%)]			$\chi^2=8.037$	0.015
Simple tooth loss	13 (35.1%)	13 (20.6%)		
Complex Tooth loss	10 (27.0%)	30 (47.6%)		
Complete dentition	14 (37.8%)	20 (31.7%)		
Moderate to Severe Periodontitis [n(%)]	15 (40.5%)	46 (73.0%)	$\chi^2=10.104$	<0.001

3.1.3 Comparative of Tooth Loss and Periodontal Indicators in Patients with Different Degrees of CSVD

As shown in Table 3, a comparative analysis of tooth loss and periodontal indicators was conducted between patients with mild CSVD and those with moderate-to-severe CSVD. The p-values for all selected parameters related to dentition defects and periodontal indicators were less than 0.05, indicating statistically significant differences. Specifically, patients with moderate-to-severe CSVD exhibited higher values in PD, CAL, BI, and PLI compared to those with mild CSVD. The proportion of patients with complete dentition was higher in the mild CSVD group, while the proportions of those with simple tooth loss and complex dentition defects were lower than in the moderate-to-severe CSVD group. Additionally, the moderate-to-severe CSVD group had a higher prevalence of moderate-to-severe periodontitis compared to the mild CSVD group. These results suggest that periodontal inflammation and dentition defects are more severe in patients with moderate-to-severe CSVD than in those with mild CSVD.

Table 3. Comparison of Tooth Loss and Periodontal Indicators Between Patients with Mild CSVD and Moderate-to-Severe CSVD

Variable	Mild CSVD (n=31)	Moderate-to-Severe CSVD (n=32)	Statistic	P-values
PD ($\bar{x}\pm s$)	4.98 $\pm$ 1.04	5.74 $\pm$ 1.93	t=3.014	0.003
CAL ($\bar{x}\pm s$)	4.42 $\pm$ 0.58	4.88 $\pm$ 0.44	t=4.952	0.005
BI ($\bar{x}\pm s$)	2.39 $\pm$ 0.09	2.61 $\pm$ 0.11	t=2.637	0.027
PLI ($\bar{x}\pm s$)	2.02 $\pm$ 0.24	2.31 $\pm$ 0.33	t=2.057	<0.001
Tooth loss [n(%)]			$\chi^2=13.173$	0.001
Simple tooth loss	5	8		
Complex tooth loss	14	16		
Complete dentition	12	8		
Moderate to severe periodontitis [n(%)]	18	28	$\chi^2=10.279$	0.001

3.2 Correlation Analysis

To comprehensively investigate the relationship between periodontal indicators, tooth loss, and cerebral small vessel disease (CSVD), this paper employed Spearman correlation analysis for preliminary exploration and description of variable associations. The analysis aimed to identify linear trends between periodontal indicators, tooth loss, and CSVD, and to evaluate the strength and direction of these associations. Correlation strength was interpreted based on the absolute value of the correlation coefficient (r_s): 0.00 – 0.19 as very weak, 0.20 – 0.39 as weak, 0.40 – 0.59 as moderate, 0.60 – 0.79 as strong, and 0.80 – 1.00 as very strong. A p -value < 0.01 was considered statistically significant.

The results are presented in Table 4. All examined periodontal indicators showed significant positive correlations with the total CSVD burden score (all $p < 0.01$). That is, higher values of periodontal indicators were associated with higher CSVD burden scores, indicating more severe conditions. Similarly, more severe tooth loss was associated with higher CSVD burden scores. Among these, CAL demonstrated the strongest correlation with total CSVD burden ($r_s = 0.63$, $p = 0.002$), indicating a strong positive association. PD ($r_s = 0.47$, $p < 0.001$), BI ($r_s = 0.51$, $p = 0.001$), and PLI ($r_s = 0.40$, $p < 0.001$) showed moderate positive correlations with total CSVD burden. Tooth loss ($r_s = 0.32$, $p = 0.001$) exhibited a weak positive correlation with total CSVD burden.

Table 4. Correlation Analysis of Periodontal Indicators and Tooth Loss with CSVD

Variable	r_s	P-values
PD ($\bar{x} \pm s$)	0.47	< 0.001
CAL ($\bar{x} \pm s$)	0.63	0.002
BI ($\bar{x} \pm s$)	0.51	0.001
PLI ($\bar{x} \pm s$)	0.40	< 0.001
Tooth loss [n(%)]	0.32	0.001

3.3 Binary Logistic Regression Analysis of Tooth Loss, Periodontal Indicators, and CSVD

To investigate whether tooth loss and periodontal indicators are independent risk factors for CSVD, this paper employed a multivariate binary logistic regression model. The presence or absence of CSVD was set as the dependent variable (0 = no, 1 = yes). Independent variables included factors with $p < 0.1$ in the univariate analysis of general characteristics and the severity of periodontitis. After adjusting for smoking and alcohol consumption, the logistic regression analysis revealed that age, hypertension, hyperlipidemia, and moderate-to-severe periodontitis were independent risk factors for CSVD.

Furthermore, with the presence of moderate-to-severe CSVD as the dependent variable (moderate-to-severe CSVD = 1, mild CSVD = 0) and age, hypertension, hyperlipidemia, and moderate-to-severe periodontitis as independent variables, a binary logistic regression analysis was performed. The results are shown in Table 5.

Age (OR = 1.07, 95% CI: 1.02 – 1.12, $p = 0.006$), hypertension (OR = 4.82, 95% CI: 2.15 – 10.82, $p < 0.001$), hyperlipidemia (OR = 2.95, 95% CI: 1.30 – 6.68, $p = 0.010$), and moderate-to-severe periodontitis (OR = 1.54, 95% CI: 1.55 – 7.89, $p = 0.002$) were all identified as independent risk factors for moderate-to-severe CSVD. Specifically, patients with moderate-to-severe periodontitis had a 1.501 times higher risk of developing moderate-to-severe CSVD compared to those with no or mild periodontitis.

Table 5. Multivariable Binary Logistic Regression Analysis of Factors Associated With Moderate-to-Severe CSVD

Variable	β	S.E.	Wald χ^2	P-values	OR-values	95% CI
Age	0.068	0.025	7.524	0.006	1.070	1.020 - 1.123
hypertension	1.573	0.402	15.320	<0.001	4.821	2.194 - 10.815
hyperlipidemia	1.082	0.421	6.613	0.010	2.951	1.294 - 6.732
moderate-to-severe periodontitis	1.253	0.404	9.623	0.002	1.501	1.587 - 7.723
Constant	-10.521	2.105	25.007	<0.001	0.000	

3.4 Conclusion

Firstly, this paper employed a literature review method to summarize research status on the correlation between periodontitis and cerebral CSVD. Secondly, an empirical approach was adopted to compare and analyze the periodontal status of patients with CSVD and non- CSVD, as well as the tooth loss and periodontal indicators among patients with varying degrees of CSVD. Then, Spearman correlation analysis was used to preliminarily assess the relationship between periodontal indicators, tooth loss, and CSVD. Finally, binary logistic regression analysis was applied to investigate whether tooth loss and periodontal indicators are independent risk factors for arteriosclerotic CSVD. The main findings are as follows: (1) The proportion of patients with complete dentition was higher in the non-CSVD group. Compared to the non-CSVD group, the CSVD group exhibited more severe periodontal pathology and a higher proportion of patients with severe periodontitis. This conclusion is consistent with the study on the potential impact of periodontitis on cerebral small vessel disease by the Molecular Oral Microbiology team [6] and the preliminary findings on the correlation between periodontitis and cerebral small vessel disease by Zhang Jiyu [7]. That is, the degree of tooth loss and periodontitis was more severe in the CSVD group than in non-CSVD patients.(2)Compared to patients with mild CSVD, those with moderate-to-severe CSVD had more severe periodontitis and tooth loss. Correlation studies also indicate that higher periodontal index values are associated with higher CSVD scores and more severe conditions. Similarly, more severe tooth loss is correlated with higher CSVD scores and worsened outcomes. A positive correlation was observed, suggesting that as periodontitis progresses, the severity of CSVD may also increase.(3)moderate-to-severe periodontitis is an independent risk factor for moderate-to-severe CSVD. Patients with moderate-to-severe periodontitis had a 1.501-fold higher risk of developing moderate-to-severe CSVD compared to those with no or mild periodontitis. Similarly, Yago, Leira et al. conducted a study using clinical data from patients with periodontitis and stroke between 1946 and 2015, showing that individuals with periodontitis had a 2.88-fold higher risk of ischemic stroke [8]. Leira et al. examined 147 elderly individuals aged 58 – 71 and found a strong association between chronic periodontitis and lacunar infarction [9]. Ya-Ling Lee’s research results indicated that patients with untreated periodontitis had a significantly higher probability of developing ischemic stroke [10]. Thus, controlling periodontal inflammation may reduce the risk of stroke.

Therefore, from a clinical perspective, it is essential to raise public awareness of oral health protection, strengthen oral hygiene maintenance in CSVD patients, and implement early oral interventions to prevent the onset of CSVD and delay its progression from mild to moderate-to-severe stages.

4. Conclusion

Substantial research and clinical evidence indicate that periodontal diseases and dental hard tissue diseases are infectious conditions that severely compromise oral health. These diseases not only affect local oral tissues but are also associated with various systemic and chronic conditions. Oral pathogens contribute to intracranial inflammatory responses, which can lead to the development of CSVD. Periodontopathic bacteria, such as *Porphyromonas gingivalis* (Pg) and *Treponema denticola* (T. denticola), can enter the bloodstream, cross the Blood-Brain Barrier (BBB), and infiltrate brain tissue, where they activate endothelial cells and trigger cerebrovascular inflammatory responses [11]. Periodontitis promotes the production of abundant inflammatory mediators, including Tumor Necrosis Factor (TNF)- α , Interleukin (IL)-1 β , and IL-6, which disrupt the BBB, increase its permeability, and induce a state of systemic chronic inflammation [12]. Furthermore, periodontopathic bacteria activate the immune system, damage vascular endothelial cells, and cause structural and functional alterations in the cerebrovascular endothelium [13]. Thus, periodontitis may directly or indirectly facilitate the onset and progression of CSVD.

Therefore, oral health represents an important modifiable factor in CSVD. Early prevention and treatment of oral diseases—such as standardized management of periodontal inflammation and effective rehabilitation of tooth loss—may help mitigate the progression of CSVD and improve overall quality of life.

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