INSUFICIENCIA CARDIACA
Volume 21, Issue 03, Pages 01-06

ISSN Print: 1852-3862
ISSN Online: 1850-1044

Research Article

Periodontal Inflammatory Burden and NT-proBNP Levels in Patients with Chronic Heart Failure: A Cross-Sectional Study

Anurag Rawat[1], Sibani Sarangi[2], Ameya Tripathi[3], Bhupender Bhati[4], Jyoti Kasana[5*], Vikas Singh[6] and Ritik Kashwani[7]

[1]*Department of Cardiology, Himalayan Institute of Medical Science, Dehradun, Uttaranchal, India*
[2]*Department of Periodontics and Oral Implantology, Institute of Dental Sciences, SOA Deemed to be University, Bhubaneswar, India*
[3]*Department of Periodontology, Dental College Azamgarh, Azamgarh, Uttar Pradesh, India*
[4]*Department of Physiology, Ajay Sangaal Institute of Medical Sciences and Research and Ayushmaan Hospital, Jamalpur, Shamli, Uttar Pradesh, India*
[5]*Department of Dentistry, North DMC Medical College and Hindu Rao Hospital, Delhi, India*
[6]*Department of Public Health Dentistry, Teerthanker Mahaveer Dental College and Research Centre, Teerthanker Mahaveer University, Moradabad, Uttar Pradesh, India*
[7]*Department of Oral Medicine and Radiology, School of Dental Sciences, Sharda University, Greater Noida, India*

Abstract: Background: Neurohormonal activation, congestion and low-grade inflammation are hallmarks of Chronic Heart Failure (CHF). The association between periodontitis and N-terminal pro-B-type natriuretic peptide (NT-proBNP) in patients with stable CHF is not well established. **Objective:** To assess the relationship between Periodontal Inflammatory Burden (PIS) measured as Periodontal Inflamed Surface Area (PISA) and serum levels of NT-proBNP in adults with stable CHF. **Methods:** A cross sectional study was conducted with 120 dentate CHF patients aged 40-75 years who attended a cardiology outpatient clinic. Full mouth periodontal examination was performed to record probing pocket depth, clinical attachment level, recession, bleeding on probing and PISA. NT-proBNP and high-sensitivity C-reactive protein (hs-CRP) were measured on the same day. Patients were divided into low (<400 mm^2), moderate (400-899 mm^2) and high (≥900 mm2) PISA burden groups. **Results:** The mean age was 61.8±-9.7 years, 68 patients (56.7%) were male and 63 (52.5%) had heart failure with reduced ejection fraction. Mean PISA was 684±402 mm^2 and mean NT-proBNP was 1705±1056 pg/mL. NT-proBNP increased progressively across low, moderate and high PISA groups (1038 ±522, 1587±702 and 2476±1230 pg/mL, respectively; p<0.001). PISA correlated positively with NT-proBNP (r = 0.48, p<0.001) and hs-CRP (r = 0.44, p<0.001). PISA was independently associated with log10 NT-proBNP after adjustment for age, sex, BMI, smoking, diabetes, renal function, LVEF, heart failure phenotype and NYHA class (beta = 0.024 per 100 mm^2; 95% CI: 0.009-0.039; p = 0.002). **Conclusion:** NT-proBNP levels were independently related to greater periodontal inflammatory burden in stable CHF patients. In a multidisciplinary approach to CHF, periodontal assessment may offer more information about inflammation.

Key Words: Chronic Heart Failure, NT-proBNP, Periodontitis, Periodontal Inflamed Surface Area, PISA, Systemic Inflammation

Author Designation:
[1,6]Professor, [3-5]Assistant Professor

*Corresponding author:
Dr. Jyoti Kasana
Kasanajt@gmail.com

Received January 05, 2026
Accepted June 29, 2026
Published July 30, 2026

INTRODUCTION

Heart failure is a complex clinical syndrome that is a rapidly increasing public health problem worldwide. Current estimates suggest that heart failure affects around 64 million people globally, is a cause of recurrent hospitalization, reduces quality of life and contributes to significant health care cost [1]. Chronic heart failure is currently defined in Europe and America by symptoms, signs, structural or functional cardiac abnormalities and objective evidence (including elevated natriuretic peptides and imaging-based assessment of left ventricular ejection fraction) [2,3]. NT-proBNP is widely used among the available biomarkers, as it is a marker of myocardial wall stress, filling pressure, neurohormonal activation and offers prognostic information across heart failure phenotypes.

Periodontitis is a chronic dysbiotic inflammatory disease of the tooth-supporting tissues. The 2018 classification focuses on disease staging, grading, severity, complexity and risk of progression, which enables periodontitis to be viewed as a systemic disease with chronic inflammatory nature [4,5]. The ulcerated pocket epithelium and subgingival biofilm can serve as a reservoir of microbial products, bacteremia and inflammatory mediators in susceptible individuals. Although probing pocket depth and bleeding on probing are clinically useful conventional indices, they fail to adequately reflect the entire surface area of the inflamed wound and are not easily interpreted by the physician.

To measure the surface area of bleeding periodontal pocket epithelium in square millimeters, the periodontal inflamed surface area (PISA) was introduced [6]. PISA combines periodontal pocket depth, clinical attachment loss, gingival recession and bleeding on probing and provides a continuous measure of active periodontal inflammatory burden. This is especially important for oral-systemic research as a continuous burden score may be more representative of the inflammatory exposure of periodontitis than a categorical diagnosis.

Epidemiological, mechanistic and interventional evidence has supported the periodontal-cardiovascular relationship. A consensus report from both groups found that severe periodontitis was independently linked to cardiovascular disease and that there were plausible mechanisms linking the two, such as transient bacteremia, systemic inflammation, oxidative stress and endothelial dysfunction [7]. While most of the evidence has been directed toward atherosclerotic cardiovascular disease, heart failure shares many of the same inflammatory, vascular dysfunction, renal interactions and repeated neurohormonal activation features. These overlapping pathways suggest that active periodontal inflammation could be linked to poor cardiac biomarker profiles in patients with chronic heart failure.

There is limited but growing evidence for the association of periodontal status and heart failure biomarkers. In the ARIC cohort, periodontal status was linked to incident HF and poor changes in C-reactive protein and NT-proBNP levels over follow-up [8]. In a recent cross-sectional study in early chronic heart failure, NT-proBNP and troponin T were found to be higher in patients with periodontitis than in those without periodontitis [9]. In isolation, PISA has been linked to high sensitivity C-reactive protein in community-dwelling older adults, which further validates the use of PISA as a bridge variable between periodontal and systemic inflammatory status [10]. To date, however, few studies have investigated the independent association of a quantitative periodontal inflammatory burden measure with NT-proBNP in stable chronic heart failure adjusted for major cardiac and systemic confounders [11].

The present study was thus designed to assess the relationship between PISA and serum NT-proBNP level in dentate adults with stable chronic heart failure. Secondary aims were to compare NT-proBNP and hs-CRP within the PISA burden groups and to assess if PISA remained associated with NT-proBNP after adjusting for demographic, metabolic, renal and heart failure-related variables.

METHODS

The Design and Setting of the Study

This was a cross-sectional study conducted in the outpatient department of cardiology and periodontology in a tertiary care teaching hospital from January 2025 to December 2025. The study design was a single visit assessment design, with cardiovascular, periodontal and biochemical variables measured on the same day. The protocol was approved by the Institutional Ethics Committee and written informed consent was obtained from all participants prior to enrolment.

Participants

Patients aged 40-75 years with clinically stable Chronic Heart Failure (CHF) for at least 6 months were screened. The definition of heart failure stability was no hospitalization, no use of intravenous diuretics, no acute coronary syndrome and no significant change in guideline-directed medical therapy within the past 8 weeks. Patients had to have 10 or more natural teeth to allow for adequate periodontal evaluation.

Inclusion and Exclusion Criteria

Inclusion criteria were confirmed chronic heart failure, NYHA class II or III symptoms, consent and willingness to perform full-mouth periodontal examination and venous blood sampling. Acute decompensated heart failure, recent myocardial infarction or stroke (within 3 months), active systemic infection, autoimmune disease, malignancy under active treatment, pregnancy, chronic immunosuppressive therapy, antibiotic use within 3 months, periodontal therapy within 6 months, edentulism and inability to complete periodontal probing were exclusion criteria.

Sample Size

The sample size was determined for the detection of a minimum correlation coefficient of 0.30 between PISA and NT-proBNP at 90% power and 2-sided α of 0.05. A sample size of 109 was the minimum required. The number of patients recruited was 124, with biochemical assay failure and incomplete data, 120 patients had complete periodontal and NT-proBNP data and were included in the final analysis.

Cardiovascular Assessment

Demographic data, smoking, BMI, comorbidities, duration of heart failure, current medication and NYHA class were obtained on a structured case record form. Two-dimensional transthoracic echocardiograms were used to obtain the left ventricular ejection fraction within 4 weeks prior to or at the time of the study visit if a recent echocardiogram was not available. Heart failure phenotype was classified as reduced ejection fraction, mildly reduced ejection fraction or preserved ejection fraction. Serum creatinine was used to estimate GFR.

Periodontal Examination

Full-mouth periodontal examination was performed at six sites per tooth (excluding third molars) by a calibrated periodontist. The pocket depth, gingival recession, clinical attachment level and bleeding on probing were measured with a manual UNC-15 periodontal probe. Oral hygiene and gingival inflammation were described by plaque index and gingival index respectively. Pocket depth, clinical attachment level, gingival recession and bleeding on probing were used to calculate PISA. The participants

were divided into three groups: low PISA burden (<400 mm^2), moderate PISA burden (400-899 mm^2) and high PISA burden (≥900 mm^2). Periodontitis stage was determined based on clinical attachment loss, radiographic bone loss, tooth loss due to periodontitis and complexity factors.

Biochemical Assessment

Venous blood samples were taken after the periodontal examination and prior to any dental treatment between 9:00 am and 12:00 pm. An electrochemiluminescence immunoassay was used to measure serum NT-proBNP. The high sensitivity C-reactive protein was determined using an immunoturbidimetric assay. Periodontal burden group was blinded to the laboratory personnel.

Statistical Analysis

SPSS version 26.0 was used for data analysis. Data for continuous variables were presented as Mean±standard deviation or median (interquartile range) as appropriate and categorical variables were presented as numbers and percentages. Due to the right-skewed distribution of NT-proBNP, it was log10 transformed for correlation and regression analyses. One-way ANOVA with Tukey post hoc test, Kruskal-Wallis test or chi-square test was used for between-group comparisons, depending on the data type. Pearson or Spearman correlation was used based on the distribution of data. The independent association of PISA with log10 NT-proBNP was examined using multivariable linear regression. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 124 patients were recruited. Four were excluded from final analysis because of incomplete blood sampling or incomplete periodontal recordings, leaving 120 participants. The mean age was 61.8±9.7 years and 68 participants (56.7%) were male. The most common comorbidities were hypertension (65.0%), diabetes mellitus (35.0%) and chronic kidney disease stage 3 or higher (24.2%). The mean left ventricular ejection fraction was 42.7±11.6% and 63 patients (52.5%) were classified as having heart failure with reduced ejection fraction.

Thirty-nine participants were categorized as low PISA burden, 42 as moderate burden and 39 as high burden. The three groups were comparable for age, sex distribution, hypertension, diabetes, heart failure phenotype and use of beta-blockers or renin-angiotensin system inhibitors. Current smoking, NYHA class III symptoms and loop diuretic use were more frequent in the high PISA group. Baseline demographic and heart failure characteristics are presented in Table 1.

Periodontal severity increased stepwise across PISA groups. Compared with the low PISA group, the high PISA group had fewer remaining teeth, deeper periodontal pockets, greater clinical attachment loss and a higher percentage of bleeding sites. Mean hs-CRP and NT-proBNP levels also increased significantly across PISA burden groups. Mean NT-proBNP was 1038±522 pg/mL in the low PISA group, 1587±702 pg/mL in the moderate PISA group and 2476±1230 pg/mL in the high PISA group (p<0.001). The periodontal and biomarker profile is summarized in Table 2.

PISA showed a moderate positive correlation with NT-proBNP (r = 0.48, p<0.001) and hs-CRP (r = 0.44, p<0.001). Bleeding on probing, mean probing pocket depth and mean clinical attachment level also correlated positively with NT-proBNP but the correlation coefficients were lower than that observed for PISA. Left ventricular ejection fraction and estimated glomerular filtration rate showed inverse correlations with NT-proBNP.

In multivariable linear regression, PISA remained independently associated with log10 NT-proBNP. In the fully adjusted model including demographic, metabolic, renal and heart failure variables, each 100 mm^2 increase in PISA was associated with a 0.024 increase in log10 NT-proBNP (95% CI: 0.009-0.039; p = 0.002). High PISA burden was also associated with significantly higher log10 NT-proBNP compared with low PISA burden after adjustment. Correlation and regression findings are shown in Table 3.

DISCUSSION

The present cross-sectional study showed that there was a significant relationship between periodontal inflammatory burden and NT-proBNP level in patients with stable chronic heart failure. Patients with high PISA burden presented with more advanced periodontal destruction, higher hs-CRP and significantly higher NT-proBNP compared to patients with low PISA burden. Importantly, the association between PISA and log transformed NT-proBNP remained after adjustment for age, sex, BMI, smoking, diabetes, renal function, EF, NYHA class, heart failure phenotype and diuretic use. The results indicate that there is a relationship between active periodontal inflammation and an unfavorable cardiac biomarker profile in CHF beyond common demographic and metabolic risk factors.

There is a plausible biological association between the two. Periodontitis results in a large ulcerated epithelial surface that is exposed to dysbiotic subgingival biofilm. This can help to allow the re-entry of bacterial products and inflammatory mediators into the systemic circulation. PISA is a more direct measure of this active inflamed wound surface than pocket depth or attachment loss [6]. In this study, PISA was more strongly correlated with mean probing pocket depth or mean clinical attachment level, suggesting that the inflammatory burden of active bleeding may be more important than historical periodontal destruction in systemic biomarker disturbance.

Our results are in line with the general cardiovascular-periodontal literature. The consensus report on periodontitis and cardiovascular diseases highlighted the potential of systemic inflammation, oxidative stress, bacteremia and endothelial dysfunction as possible mechanisms [7]. The ARIC study was the first to report associations between periodontal status, incident heart failure, CRP and NT-proBNP in heart

Table 1: Baseline Demographic and Heart Failure Characteristics According to Periodontal Inflammatory Burden

Characteristic	Total (n = 120)	Low PISA <400 mm² (n = 39)	Moderate PISA 400-899 mm² (n = 42)	High PISA ≥900 mm² (n = 39)	p-value
Age (years)	61.8±9.7	60.6±9.1	62.0±10.4	62.9±9.8	0.563
Male sex (n (%))	68 (56.7)	21 (53.8)	25 (59.5)	22 (56.4)	0.872
Body mass index (kg/m²)	26.1±3.8	25.1±3.5	26.2±3.6	27.1±4.0	0.041
Current smoker (n (%))	23 (19.2)	4 (10.3)	7 (16.7)	12 (30.8)	0.049
Diabetes mellitus (n (%))	42 (35.0)	10 (25.6)	15 (35.7)	17 (43.6)	0.236
Hypertension (n (%))	78 (65.0)	24 (61.5)	27 (64.3)	27 (69.2)	0.769
eGFR (mL/min/1.73 m²)	68.4±18.9	73.2±17.1	68.0±17.9	64.1±20.4	0.082
HFrEF (n (%))	63 (52.5)	19 (48.7)	23 (54.8)	21 (53.8)	0.836
LVEF (%)	42.7±11.6	44.1±10.8	42.8±11.7	41.2±12.2	0.548
NYHA class III (n (%))	43 (35.8)	8 (20.5)	16 (38.1)	19 (48.7)	0.029
Heart failure duration (years)	4.1±2.6	3.8±2.4	4.0±2.7	4.5±2.8	0.490
Beta-blocker use (n (%))	88 (73.3)	28 (71.8)	31 (73.8)	29 (74.4)	0.966
ACEI/ARB/ARNI use (n (%))	86 (71.7)	29 (74.4)	29 (69.0)	28 (71.8)	0.859
Loop diuretic use (n (%))	72 (60.0)	18 (46.2)	25 (59.5)	29 (74.4)	0.036

Table 2: Periodontal Findings and Biomarker Levels According to Periodontal Inflammatory Burden

Variable	Total (n = 120)	Low PISA <400 mm² (n = 39)	Moderate PISA 400-899 mm² (n = 42)	High PISA ≥900 mm² (n = 39)	p-value
Remaining teeth (n)	21.3±5.7	23.5±4.9	21.6±5.4	18.8±5.8	<0.001
Mean probing pocket depth (mm)	3.8±0.9	2.9±0.5	3.7±0.6	4.9±0.8	<0.001
Mean clinical attachment level (mm)	4.1±1.1	3.2±0.7	4.0±0.8	5.2±1.0	<0.001
Bleeding on probing (% sites)	43.6±20.1	22.3±8.9	43.1±10.7	65.4±12.6	<0.001
PISA (mm²)	684±402	245±88	612±137	1196±255	<0.001
Stage III-IV periodontitis (n (%))	71 (59.2)	8 (20.5)	27 (64.3)	36 (92.3)	<0.001
hs-CRP (mg/L)	5.4±3.1	3.6±1.8	5.1±2.4	7.6±3.8	<0.001
NT-proBNP (pg/mL)	1705±1056	1038±522	1587±702	2476±1230	<0.001
Log10 NT-proBNP	3.18±0.31	3.00±0.23	3.17±0.25	3.35±0.30	<0.001

Table 3: Correlation and Regression Analysis for Determinants of log10 NT-proBNP.

Analysis/predictor	Coefficient or r	95% CI	p-value	Model note
PISA vs NT-proBNP	r = 0.48	-	<0.001	Spearman correlation
BOP % vs NT-proBNP	r = 0.42	-	<0.001	Spearman correlation
Mean PPD vs NT-proBNP	r = 0.37	-	<0.001	Spearman correlation
Mean CAL vs NT-proBNP	r = 0.32	-	0.001	Spearman correlation
hs-CRP vs NT-proBNP	r = 0.45	-	<0.001	Spearman correlation
LVEF vs NT-proBNP	r = -0.39	-	<0.001	Spearman correlation
eGFR vs NT-proBNP	r = -0.28	-	0.002	Spearman correlation
PISA per 100 mm2	beta = 0.038	0.024 to 0.052	<0.001	Model 1: unadjusted
PISA per 100 mm2	beta = 0.032	0.017 to 0.047	<0.001	Model 2: adjusted for age, sex, BMI, smoking, diabetes, eGFR
PISA per 100 mm2	beta = 0.024	0.009 to 0.039	0.002	Model 3: Model 2+LVEF, NYHA class, HF phenotype, loop diuretic use
High PISA vs low PISA	beta = 0.224	0.091 to 0.357	0.001	Fully adjusted model
Stage III-IV periodontitis	beta = 0.096	0.010 to 0.182	0.029	Fully adjusted model

failure [8]. In another cross-sectional study, the early chronic heart failure patients with periodontitis had higher levels of NT-proBNP than those without periodontitis [9]. The current study contributes to this evidence by measuring periodontal inflammatory burden as a continuous quantitative measure using PISA in patients with a known diagnosis of stable CHF.

The current data further support this inflammatory interpretation as the relationship between PISA and hs-CRP is observed. Previous population-based studies in adults >70 years of age demonstrated the relationship between PISA and hs-CRP and proposed that PISA could be used as a medical-dental communication tool [10]. Systematic reviews have also demonstrated that periodontitis is linked to increased systemic CRP, suggesting that periodontal disease can lead to a measurable low-grade inflammation [12]. In our study, the high PISA group had higher levels of hs-CRP and a positive correlation was observed between hs-CRP and NT-proBNP. While this does not establish a causal relationship between periodontal burden and cardiac stress biomarkers, it does indicate that systemic inflammation may be one pathway by which these are associated.

Natriuretic peptides are secreted when there is a stress in the ventricular wall, higher filling pressures and activation of neurohormones. They play an important role in the diagnosis, risk stratification and follow-up of heart failure but are influenced by renal function, age, body mass, rhythm disorders and disease phenotype [2,3,15]. This is the reason renal function, BMI, EF, NYHA class and heart failure phenotype were included in the fully adjusted analysis. The association between PISA-NT and the PISA score remained after these adjustments, indicating that this relationship is independent of the conventional markers of severity of heart failure. However, there is the possibility of reverse causation: patients with more symptomatic CHF may have poor self-care, xerostomia due to medication effects, increased mouth breathing, nutritional issues and decreased access to dental care, all of which could negatively impact periodontal status.

The clinical significance of these results is not causal but rather in terms of risk recognition. Periodontal examination should not be used to replace cardiac evaluation and PISA should not be considered as a biomarker for heart failure. But, high periodontal inflammatory burden may be a marker for a subset of CHF patients who have other systemic inflammatory exposures. There is systematic review evidence that periodontal treatment modestly decreases CRP following anti-infective therapy [13]. Intensive periodontal therapy has also been linked to a later improvement in endothelial function but an inflammatory increase has been seen in the short term after therapy [14]. The results of this study are consistent with the concept of coordinated care, especially in medically complex patients with CHF who require periodontal intervention.

One of the practical implications is that the cardiology and dental teams should communicate when CHF patients present with severe periodontitis, high bleeding burden or poor oral hygiene. Oral health assessment may be particularly useful in the pre-procedure setting for advanced cardiac procedures, repeated hospitalizations and prior to the start of complex therapies. A recent review of the oral health and cardiovascular disease highlighted the potential benefits of periodontal therapy and oral hygiene reinforcement to lower systemic inflammatory and cardiovascular risk burden and the need for more robust outcome trials [16]. Future interventional studies in CHF should investigate whether PISA reduction following periodontal therapy is associated with improved NT-proBNP trajectory, hs-CRP, functional status and hospitalization risk.

There are some limitations to this study. It is cross sectional in design, so cannot draw conclusions about temporal sequence or causality. NT-proBNP was measured at one time and serial values could be more sensitive to chronic cardiac stress. There was potential for residual confounding due to diet, socioeconomic status, oral hygiene behavior, burden of atrial fibrillation, medication adherence and unmeasured inflammatory diseases. The sample was taken from a tertiary hospital and may not be representative of all CHF patients. Edentulous patients were excluded, which could underestimate the lifetime periodontal burden in older CHF patients. Last but not least, the accuracy of the probing and bleeding assessment is crucial for PISA calculation and requires examiner calibration.

The study has strengths, however, despite these limitations. It employed full-mouth periodontal examination, same-day biomarker sampling, clinically relevant heart failure phenotyping and multivariable adjustment for renal and cardiac factors that may affect NT-proBNP. The findings suggest that PISA could be a useful quantitative exposure variable in future oral-systemic studies in patients with chronic heart failure.

CONCLUSIONS

In a cross-sectional study of patients with stable chronic heart failure, the higher the periodontal inflammatory burden (PISA), the higher the levels of NT-proBNP and hs-CRP. This relationship between PISA and log-transformed NT-proBNP was also significant after adjusting for demographic, metabolic, renal and heart failure-related factors. The results of this study support the need for periodontal assessment as part of the multidisciplinary management of dentate CHF patients and warrant longitudinal and interventional studies to determine if periodontal inflammation reduction can positively affect cardiac biomarker trends and clinical outcomes.

REFERENCES

[1] Shahim, B. *et al.* "Global Public Health Burden of Heart Failure: An Updated Review." *Cardiac Failure Review*, vol. 9, 2023. https://doi.org/10.15420/cfr.2023.05.

[2] McDonagh, T.A. *et al.* "2021 ESC Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure." *European Heart Journal*, vol. 42, no. 36, 2021, pp. 3599-3726. https://doi.org/10.1093/eurheartj/ehab368.

[3] Heidenreich, P.A. *et al.* "2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure." *Circulation*, vol. 145, no. 18, 2022, pp. e895-e1032. https://doi.org/10.1161/CIR.0000000000001063.

[4] Caton, J.G. *et al.* "A New Classification Scheme for Periodontal and Peri-Implant Diseases and Conditions-Introduction and Key Changes from the 1999 Classification." *Journal of Clinical Periodontology*, vol. 45, suppl. 20, 2018, pp. S1-S8. https://doi.org/10.1111/jcpe.12935.

[5] Papapanou, P.N. *et al.* "Periodontitis: Consensus Report of Workgroup 2 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions." *Journal of Periodontology*, vol. 89, suppl. 1, 2018, pp. S173-S182. https://doi.org/10.1002/JPER.17-0721.

[6] Nesse, W. *et al.* "Periodontal Inflamed Surface Area: Quantifying Inflammatory Burden." *Journal of Clinical Periodontology*, vol. 35, no. 8, 2008, pp. 668-673. https://doi.org/10.1111/j.1600-051X.2008.01249.x.

[7] Sanz, M. *et al.* "Periodontitis and Cardiovascular Diseases: Consensus Report." *Journal of Clinical Periodontology*, vol. 47, no. 3, 2020, pp. 268-288. https://doi.org/10.1111/jcpe.13189.

[8] Molinsky, R.L. *et al.* "Periodontal Status, C-Reactive Protein, NT-proBNP and Incident Heart Failure: The ARIC Study." *JACC: Heart Failure*, vol. 10, no. 10, 2022, pp. 731-741. https://doi.org/10.1016/j.jchf.2022.05.008.

[9] Schulze, A. *et al.* "Assessment of the Relationship between Periodontitis and Cardiac Parameters in Patients with Early Chronic Heart Failure: A Cross-Sectional Study." *Journal of Functional Morphology and Kinesiology*, vol. 9, no. 1, 2024. https://doi.org/10.3390/jfmk9010052.

[10] Miki, K. *et al.* "Periodontal Inflamed Surface Area Is Associated with hs-CRP in Septuagenarian Japanese Adults in Cross-Sectional Findings from the SONIC Study." *Scientific Reports*, vol. 11, 2021. https://doi.org/10.1038/s41598-021-93872-8.

[11] A. Kadhim and Shatha R. Zaidan. "A Review of Cholesterol Biosynthesis Pathway." *International Journal of Clinical and Medical Research*, vol. 1, no. 1, June 2024, pp. 39-45. https://doi.org/10.66590/ijcmr2024010103

[12] Paraskevas, S. *et al.* "A Systematic Review and Meta-Analyses on C-Reactive Protein in Relation to Periodontitis." *Journal of Clinical Periodontology*, vol. 35, no. 4, 2008, pp. 277-290. https://doi.org/10.1111/j.1600-051X.2007.01173.x.

[13] Demmer, R.T. *et al.* "The Influence of Anti-Infective Periodontal Treatment on C-Reactive Protein: A Systematic Review and Meta-Analysis of Randomized Controlled Trials." *PLoS ONE*, vol. 8, no. 10, 2013. https://doi.org/10.1371/journal.pone.0077441.

[14] Tonetti, M.S. *et al.* "Treatment of Periodontitis and Endothelial Function." *New England Journal of Medicine*, vol. 356, no. 9, 2007, pp. 911-920. https://doi.org/10.1056/NEJMoa063186.

[15] Tsutsui, H. *et al.* "Natriuretic Peptides: Role in the Diagnosis and Management of Heart Failure: A Scientific Statement from the Heart Failure Association of the European Society of Cardiology, Heart Failure Society of America and Japanese Heart Failure Society." *European Journal of Heart Failure*, vol. 25, no. 5, 2023, pp. 616-631. https://doi.org/10.1002/ejhf.2848.

[16] Hopkins, S. *et al.* "Oral Health and Cardiovascular Disease." *American Journal of Medicine*, vol. 137, no. 4, 2024, pp. 304-307. https://doi.org/10.1016/j.amjmed.2023.11.022.