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Research Article

Association of Periodontitis with Ambulatory Blood Pressure, Salt Intake, and Neutrophil-Lymphocyte Ratio in High-Risk Hypertensive Patients

Tiago Pinto-Ribeiro[1, *], Ricardo Faria-Almeida[1, 2], Ana Monteiro[3, 4, 5], Júlio César Matias Souza[6, 7, 8], António Felino[1], Jorge Polónia[9, 10, *]

[1]Department of Oral Surgery and Periodontology, Faculty of Dental Medicine (FMDUP), University of Porto, Porto, Portugal

[2]Associated Laboratory for Green Chemistry (LAQV) of the Network of Chemistry and Technology (REQUIMTE), Porto, Portugal

[3]Department of Clinical Neurosciences and Mental Health, Faculty of Medicine, University of Porto, Porto, Portugal

[4]Hospital Lusíadas Braga, Braga, Portugal

[5]Blueclinical, Matosinhos, Portugal

[6]Center for MicroElectroMechanical Systems (CMEMS-UMINHO), University of Minho, Campus Azurém, Guimarães, Portugal

[7]LABBELS Associate Laboratory, University of Minho, Guimarães, Braga, Portugal

[8]Center for Interdisciplinary Research in Health (CIIS), Faculty of Dental Medicine (FMD), Catholic University of Portugal (UCP), Viseu, Portugal

[9]Department of Medicine, CINTESIS, Faculty of Medicine, University of Porto, Porto, Portugal

[10]Blood Pressure Unit, Hospital Pedro Hispano, Matosinhos, Portugal

Abstract

Objective: Periodontitis and cardiovascular disease are prevalent entities that often coexist, with a common pro-inflammatory pathway. The objective of this study was to evaluate the association between periodontitis and cardiovascular pro-inflammatory parameters rarely considered within risk factors. *Methods*: Forty-three participants aged between 38-82 years were examined. An association between mean probing depth (MPD), mean attachment loss (MAL), bleeding on probing (BOP), and periodontal inflamed surface area (PISA) was correlated with the following cardiovascular disease factors and inflammatory promoters: neutrophil-to-lymphocyte ratio (NLR), 24h ambulatory blood pressure, global cardiovascular risk, daily salt intake, night-time systolic blood pressure (nSBP), and pulse wave velocity (PWV). A two-way ANOVA and multiple comparison tests were performed using SPSS statistics software. *Results*: A highly significant correlation ($p<0.05$) was found between BOP, MPD, and MAL with high salt intake, global cardiovascular risk estimation, nSBP, and PISA. Also, significantly statistical correlation ($p<0.05$) was found between BOP, NLR, and PWV while PISA was only associated with NLR. Logistic regression analysis identified absolute values of nSBP, salt intake and NLR as possible independent contributors to the increase in the *log* odds of developing BOP. *Conclusions*: Several periodontal disease parameters are linked to cardiovascular risk factors such as hypertension, neutrophil-to-lymphocyte ratio, daily salt intake and night-time systolic blood pressure.

[*]Corresponding author: tiagoribeiro@msn.com (Tiago Pinto-Ribeiro)

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Keywords

Periodontal Disease, Inflammation, Salt Intake, Hypertension, Cardiovascular Risk, Pulse Wave Velocity

1. Introduction

Periodontitis is a multifactorial chronic inflammatory disease, characterized by an inflammatory reaction at the teeth supportive tissues (periodontal ligament, cementum and alveolar bone) leading to bone loss [1, 2]. If untreated, periodontitis can cause irreversible damage of those structures with consequent tooth loss. It is a high prevalence disease (45-50%) and its most severe level affects 10-15% of the adult population [1, 2]. Periodontitis has been assumed as a possible factor implicated in the etiopathogenesis of atherosclerosis [3-6] with both disorders presenting some common risk factors such as smoking, age and diabetes mellitus [3]. Within the last decades, a potential association between periodontitis and cardiovascular disease (CVD) has received much attention [7, 3, 8]. Several studies have supported the existence of a relationship between periodontitis and an increased risk of CVD [7, 3, 8].

Cardiovascular diseases affect the heart and the blood vessels and comprises ischemic heart disease, cerebrovascular diseases, peripheral vascular disease, and atherosclerotic vascular diseases which are the main cause of worldwide death, accounting for approximately 30% of the death of the world population [2]. Recently, periodontitis has been associated with CVD, as periodontal bacteria have been found in several components of the cardiovascular system such as human cardiac tissue, pericardial fluids, heart valves, and atherosclerotic lesions [9-11]. Thus, the consequent entry of periodontal bacterial products into the blood stream has been associated with the onset and progression of CVD on conditioning the induction and maintenance of a chronic inflammatory state [12-15]. Inflammatory reactions are also associated with CVD and the neutrophil – lymphocyte ratio (NLR) has been used as a marker of such disorder [16, 17]. Also, hypertension is an inflammatory disease [18] being the strongest indicator of CVD outcome while evaluated within 24 h monitoring mainly over night-time period [18, 19]. Additionally, high salt intake is a major factor that increases blood pressure being, therefore, responsible for strokes and heart attacks that involve proinflammatory mechanisms [20, 21]. Thus, cardiovascular risk estimators are used to raise population awareness of cardiovascular diseases that cause a significant burden of morbidity and mortality [22].

In healthy subjects, the depth of the gingival sulcus is approximately 3mm. The onset of an inflammatory condition in the connective tissue of the gingival sulcus causes the destruction of the gingival fibers. In the apical area to junctional epithelium, the collagen fibers degenerate and the area is filled with more inflammatory cells that migrate along the tooth root to the apical area, while the coronal area detaches from the root surface, causing loss of attachment [23]. In pathological conditions, the gingival sulcus is deeper, and a periodontal pocket is present. There are two types of periodontal pockets: supracrestal/suprabony (when the inferior part of the sulcus is coronal to the alveolar crest); and subcrestal/infrabony pockets (when the inferior part of the sulcus is apical to the alveolar crest) [24, 25]. Periodontal probing depth (PPD) is the measurement from the gingival margin to the apical portion of the gingival sulcus and has been used as the main indicator for the presence of periodontal inflammation. The clinical attachment loss (CAL) is a parameter which indicates the loss of periodontal support around a tooth being an indicator of periodontitis severity [26, 27] and concerns to the distance from the cemento-enamel junction to the bottom of the gingival sulcus. Bleeding on probing (BOP) refers to the number of bleeding sites relatively to the number of probed sites and is used as one of the key diagnostic parameters for periodontal disease. Thus, periodontal disease levels are classified by the association of clinical parameters of periodontal diagnosis such as BOP and periodontal pocket depth, CAL and gingival recession [28] and that has a relationship with parameters of vascular health and low-grade inflammatory systemic markers [29, 30].

The primary aim of this study was to investigate the association between periodontal disease indicators and cardiovascular pro-inflammatory parameters rarely considered within risk factors such as ambulatory blood pressure data, salt intake, neutrophil-lymphocyte ratio. It was hypothesized that cardiovascular disease risk factors are linked to periodontal disease markers.

2. Materials and Methods

A cross-sectional observational study was conducted in the Cardiovascular Disease Unit at Hospital Pedro Hispano, Matosinhos, Portugal, which is classified as an Excellence Center of the European Society of Hypertension. The research work plan was previously reviewed and approved by an institutional review board from the Hospital Pedro Hispano, Portugal, with the Ethics protocol reference namely 082/CE/JAS. The Hospital Ethics Committee approved the study protocol, which was carried out in accordance with the 1964 Helsinki declaration its later amendments on

comparable Ethics Standards. Routine clinical procedures were followed and written informed consent was gathered from the participants.

Between 2016 and 2022, a convenience sample of forty-three participants without previous history of cardiovascular or cerebrovascular events were included in this study, aged between 38 and 82 years. Demographic data were collected either by questionnaire at the first appointment or from existent clinical files: age, gender, height and weight, family history of cardiovascular risk and adverse outcomes, and calculated body mass index (BMI). Clinical aspects were recorded at baseline including the following data: glycated hemoglobin (HbA1C); fasting plasma glucose (FPG); serum creatinine (estimated glomerular function (eGFR) according to MDRD equation); cholesterol (Total, HDL and LDL); triglycerides, ionogram; uric acid; and 24h urinary sodium and potassium excretion controlled for creatinuria for evaluation of daily salt intake [31, 32]. Participants were also examined regarding chronic therapies and habitual dietary and daily physical habits. Diabetes mellitus was defined by two fasting plasma glucose (126mg/dl), 2h post-load plasma glucose (200mg/dl), HbA1C (6.5%), use of antidiabetic agents or personal history of diabetes. Participants exclusion criteria were the following: significant inflammatory disease; severe brain pathology (dementia by clinical criteria, brain tumor, traumatic brain injury, previous cerebral infection or neurodegenerative disease); previous cardiovascular events; changes in their ongoing therapy within the last 3 months; pregnancy; critical illness or a life expectancy lesser than 3 months; contraindication for magnetic resonance imaging (MRI); and inability to collaborate or to provide the informed consent.

2.1. Periodontal Assessment

Information on periodontal condition was acquired by a single calibrated operator, blinded and well-trained on periodontal assessment at six locations per tooth: mesial, central and distal from vestibular and palatal/lingual regions. A reproductible and precise periodontal assessment was carried out using a hand-held pressure-controlled probe (Click-Probe^{TM}, Kerr, USA) with a unique click-system occurring at a pression of 20-25 g (0.2-0.25 N). A first assessment was obtained and two hours later a new one was registered. If differences between these two evaluations were found, a third measurement was performed and the mean between the three was considered. The following parameters were assessed for each participant: mean probing depth (MPD), mean attachment level (MAL), bleeding on probing (BOP), periodontal epithelial surface area (PESA), and periodontal inflamed surface area (PISA) [28]. Clinical measurements were then placed on a platform (www.perio-tools.com, Dept. of Periodontology, School of Dental Medicine, University of Bern, Switzerland).

MPD data was considered following the Community Periodontal Index for Treatment Needs (CPITN) criteria to classify the periodontal disease regarding its severity: no/mild periodontitis (PPD 0-3mm); moderate periodontitis (at least one pocket ≥4mm and <6mm) and severe periodontitis (at least one pocket ≥6mm) [33].

Also, BOP sites were assessed regarding the American Academy of Periodontology/European Federation of Periodontology (AAP/EFP) on the updated classification for periodontal diseases [34]. Two situations were considered for periodontal disease: no/mild periodontal disease (without bleeding sites or below 10% bleeding sites) and on periodontal disease (10% bleeding sites). In this study, BOP was categorized as a dichotomous variable [35].

PESA precisely quantifies the total surface area of pocket epithelium. On the other hand, PISA refers to the area of PESA that is affected by BOP, and its value, in square millimeters (mm^2), represents the degree of periodontal inflammation and as such quantifies the systemic inflammatory burden which can be used to distinguish subjects regarding its periodontal inflammatory condition. At last, both PESA and PISA were estimated using the average surface area of each tooth using a freely available Excel spreadsheet as previously described [28].

2.2. Cardiovascular Disease (CVD) Factors

The information on the participants was evaluated to estimate the overall atherosclerotic cardiovascular disease (ASCVD) risk over a period of ten years. Participants data included age, gender, race, total cholesterol, HDL cholesterol, systolic blood pressure, use of blood pressure lowering medication, diabetes status, and smoking status. The purpose of the 10-year ASCVD risk assessment was to establish a baseline set point. Estimates of 10-year risk for ASCVD are based on data from multiple community-based populations and are applicable to African, American, and non-Hispanic white men and women from 40 to 79 years of age.

Twenty-four-hour ambulatory blood pressure monitoring (ABPM) was carried out using Spacelabs 90207 and 90217 software (Spacelabs^{TM}, Redmond, USA) and automatic sphygmomanometer (OMRON 705-IT and M4-I^{TM}, Omron Healthcare, The Netherlands). Participants were categorized within four circadian patterns according to night systolic blood pressure (nSBP) fall, continuous night-to-day ratio (NDR). That was converted into percent reduction of daytime values: normal dippers (NDR [0.8; 0.9]); extreme dippers (NDR ≤ 0.8); reduced dippers (NDR [0.9; 1.0]); and reverse dippers (NDR>1.0). ABPM measurements were carried out following standard parameters as previously reported in literature [36, 37]. Pulse wave velocity (PWV) was considered as an indicator of target organ injury (atherosclerosis). A non-invasive device (Complior^{TM}, Colson, France) was used to evaluate the PWV which was based in two pulse flow waves recorded simultaneously at the level of the right common carotid and right femoral arteries, as previously reported [36].

2.3. Statistical Analysis

Normality tests were applied on the assumption that there was no relationship or difference between the elements and the variables. Most of the continuous variables assumed a non-normal distribution. After preliminary analyses and the Kolmogorov–Smirnov test, the following factors showed a normal distribution: age, 24h urinary sodium, day-time/night-time/24h pulse rate, in office SD diastolic blood pressure (DBP), night-time SD DBP, daytime DBP, and eGFR. Lilliefors was used to correct the Kolmogorov-Smirnov test when the distribution was normal, thus increasing the power of the test. A significance level (α) at 0.05 was considered and Pearson's chi-square and Mann–Whitney rank sum tests were applied to analyse the association between periodontal disease and clinical variables. A linear regression analysis was performed for significant clinical variables in univariate analysis and respective BP mean. Spearman's correlation coefficients (Rs) were calculated for the relationship between all variables after adjustment. Multivariate logistic regression was used to establish a predictive model for the periodontal disease markers by the cardiovascular risk markers. Backward stepwise elimination was used as an exploratory approach. The statistical treatment of the data was carried out with the Statistical Package for Social Sciences (SPSSTM) Version 25 program, from the manufacturer International Business Machines (IBM, Armonk, NY, USA).

3. Results

The present study included 18 (42%) female and 21 (50%) diabetic patients aged between 38 and 82 years (mean 63 ±9 years old). The descriptive analysis of the participants is shown in Table 1.

Table 1. *Descriptive analysis of the sample.*

	N=	Mean	SD
Age (years)	43	63.0	9.4
BMI (Kg/m2)	43	29.0	5.2
MMSE	41	27.9	2.0
MoCA	41	21.7	4.1
HbA1C (%)	42	6.4	1.2
Salt intake (g/day)	43	12.1	3.9
Creatinine (mg/dl)	42	1.0	0.4
GFR (ml/min/1.73)	42	78.0	22.9
Uric acid (mg/dl)	42	6.6	1.9
Total Cholesterol (mg/dl)	42	183.4	43.2
HDL- Cholesterol (mg/dl)	41	45.8	11.8
LDL- Cholesterol (mg/dl)	41	103.9	37.1
Triglycerides (mg/dl)	42	166.0	93.4
Albuminuria (mg/24h)	37	57.1	77.5
SBP 24 h (mm Hg)	39	132.8	12.2
DBP 24 h (mm Hg)	39	78.0	8.2
SBP daytime (mm Hg)	39	138.3	13.6
DBP daytime (mm Hg)	39	82.0	9.4
SBP night-time (mm Hg)	39	120.4	12.0
DBP night-time (mm Hg)	39	68.9	6.9
Night-time SBP fall (%)	39	12.7	7.2
Neutrophil / leucocytes ratio	39	0.5	0.2
Neutrophil / lymphocytes ratio	39	2.63	1.12
PESA (mm^2)	39	1163.7	551.4
PISA (mm^2)	39	82.7	106.9
MPD (mm)	39	2.5	0.6
MAL (mm)	39	2.8	0.8
BOP	39	6.4	8.4
Number of teeth	39	17.0	10.1
Global CV Risk calculator	42	31.5	15.9
Pulse Wave velocity (m/s)	42	11.3	2.6

In general, biochemical parameters were only slightly above the upper limits of normality. Concerning hypertension control, average data from 24 h ambulatory blood pressure were slightly above upper limits of normality either during daytime or night-time. Mean pulse wave velocity value (PWV) was above normal limits meaning an increase of aortic stiffness. All participants were under anti-hypertensive drugs of which 52% participants were taking statins. In average, the assessment of global cardiovascular risk was determined at 32% probability of a fatal or non-fatal CVD event within the next 10 years.

As shown in Table 2, obese participants with BMI equal or above 30 Kg/m^2 showed significantly detrimental periodontal disease parameters regarding MPD and MAL when compared with non-obese participants.

Table 2. *Comparison (with statistical significance) of PD values between subgroups of subjects according to BMI, gender and values above and below medians of neutrophil/ lymphocytes ratio (NLR), salt intake and night-time systolic BP.*

	PISA	MDP	MAL	BOP
Obese - BMI v=30 Kg/m^2 (n=23)		2.69 ±0.53	3.02 ±0.83	
Non-Obese - BMI v=30 Kg/m^2 (n=15)		2.16 ±0.62	2.30 ±0.68	
p =		0.046	0.015	
Female - (n=17)	128 ±111			
Male - (n=20)	45 ±71			
p=	0.025			
NLRatio - above median - 3.0 (n=18)	162 ±131			11.3 ±10.9
NLRatio - below median - 3.0 (n=18)	31 ±754			3.2 ±4.4
p=	0.006			0.035
Salt intake - above median - 11g/d (n=18)			3.76 ±0.913	
Salt intake - below median - 11g/d (n=18)			2.270 ±0.73	
p=			0.048	
SBP nighttime - above median – 118 mmHg (n=18)		2.70 ±0.65	3.10 ±0.68	
SBP nighttime - below median – 118 mmHg (n=18)		2.11 ±0.51	2.32 ±0.71	
p =		0.047	0.011	

The numeric values of significant linear correlations between periodontal disease parameters and CVD risk markers are shown in Table 3.

Table 3. *Linear correlations statistically significant between periodontal and CVD risk markers.*

N=39		BMI	Salt intake (g/d)	Night-time SBP	Neutrophil/ lymphocytes ratio	Overall CVD RisK	PWV
PISA	r2	,385*			,511**		,443*
	p=	0,022			0,003		0,021
MDP	r2	,468**	,403*	,441*		,409*	,502**
	p=	0,005	0,016	0,013		0,023	0,008
MAL	r2	,349*	,375*	,461**		,495**	
	p=	0,040	0,027	0,009		0,005	
BOP	r2	,441**	,344*	,435*	,571**	,389*	,470*
	p=	0,008	0,031	0,014	0,002	0,021	0,013

Female participants showed lower values of PISA compared with male participants ($p < 0.05$). NLRatio values above median and values below median were associated with significant compromised values of PISA and BOP. Night-time systolic BP values above median and values below median were associated with unfavourable values of MPD and MAL ($p < 0.05$). Daily salt intake values above median and values below median were associated with lower values of MAL ($p < 0.05$). No significant differences of periodontal disease parameters were found between diabetics when compared with

non-diabetics, neither between age values or educational levels. The influence of smoking habits was not analysed since only 4 participants were actual smokers (n=1) or previous smokers (n=3). Scatter plots on the correlation between some of the variables described in Table 2 are shown in Figures 1 and 2.

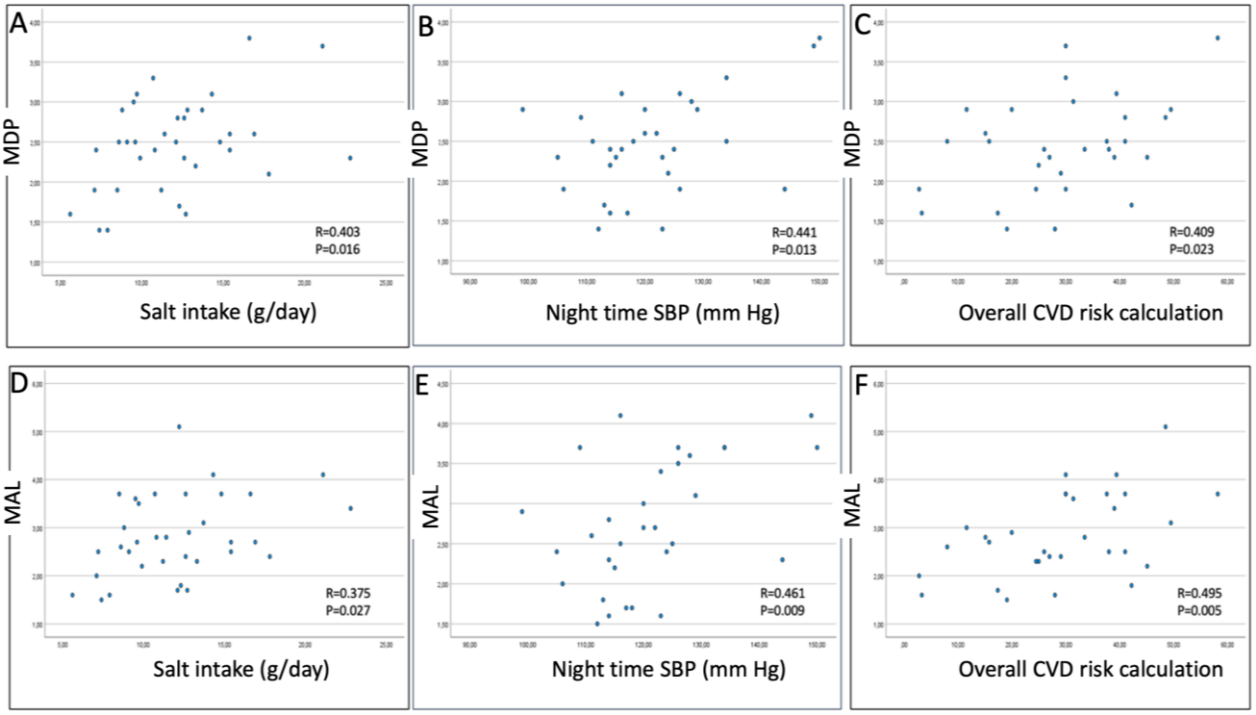

Figure 1. *Scatter plots on the correlation between MDP or MAL and salt intake, nighttime systolic blood pressure (SBP), and overall CVD risk.*

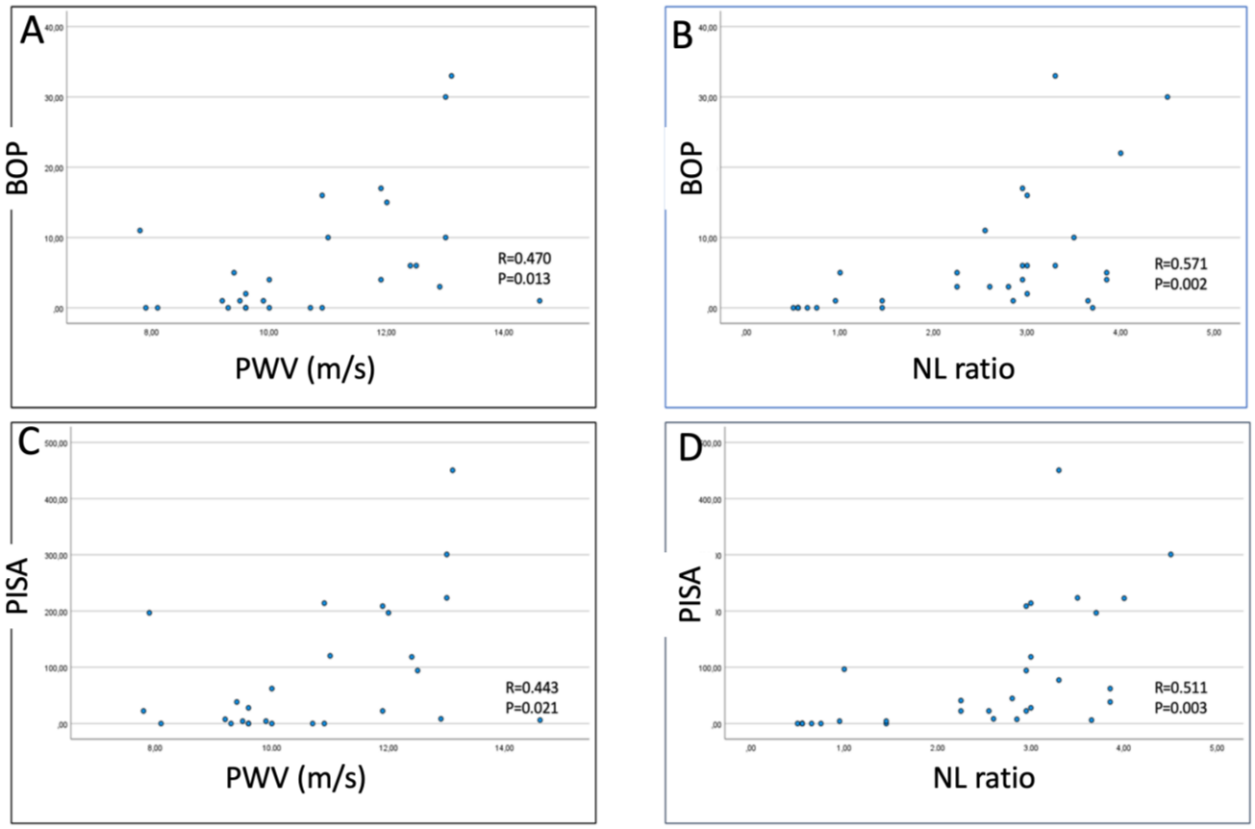

Figure 2. *Scatter plots on the correlation between BOP or PISA and PWV or NL ratio.*

As shown in Table 3, body mass index significantly correlated linearly with all four periodontal disease markers. Night-time systolic BP, daily salt intake, and overall CVD risk correlated significantly with MPD, MAL and BOP. Neutrophil-lymphocyte ratio (NLR) correlated with PISA and BOP while PWV correlated with PISA, MAL, and BOP. As seen in Table 4, multivariate logistic regression analysis revealed that BMI, salt intake, NLR, and night-time systolic BP were independently and significantly (at level of 5%) correlated with BOP. All other variables were eliminated from the final model according to Wald ś criteria. The logistic coefficients for the values of BMI, salt intake, NLR and nighttime systolic blood pressure (SBP) are positive indicating an increase in the log odds of developing BOP values.

Table 4. *Variables (cardiovascular risk markers) considered as significant predictors of BOP (multiple logistic regression analysis.*

BOP	Coefficient	t	Sig.	CI 95% for B	
	Beta			Low	High
(Constant)		-4.480	0.000	-129.08	-46.661
BMI	0.324	2.154	0.045	0.013	1.033
SBP nighttime	0.329	2.270	0.036	0.021	0.555
Neutr/Lymph	0.326	2.317	0.032	1.202	24.533
Salt intake	0.339	2.483	0.023	19.468	233.624

4. Discussion

The present study enrolled a population of hypertensive participants without previous CVD events. Periodontal disease level was significantly associated with the severity of overall CVD risk within 10-years regarding fatal and non-fatal events. Also, periodontal disease was associated with CVD risk factors such as ambulatory blood pressure particularly on night-time values and target organ damage markers such as aortic stiffness (pulse wave velocity). Periodontal disease was also correlated with inflammatory promoters such as high salt intake and abnormal immune system homeostasis determined by neutrophil-to-lymphocyte ratio (NLR). Moreover, multivariate regression analysis emphasized an independent direct relationship between CVD risk variables and periodontal bleed on probing severity. Thus, the findings validate the hypothesis of the present study considering the association of periodontal disease and CVD risk pro-inflammatory parameters rarely studied in this context, such as salt intake, NLRatio, and ABPM.

Periodontal disease has been classified as an inflammatory disease [14, 15]. Recently, inflammatory reactions have been considered an important contributing factor for both periodontal disease and CVD events. Considering correlation appraisals, the present study intended to evaluate the relationship between periodontal disease and CVD risk markers in which the input of the inflammatory factors is well established, regarding both pathophysiology and its consequences. This study revealed a significant and independent association between severity of periodontal disease and the neutrophil-lymphocyte ratio (NLR). NLR is a simple index for assessing inflammatory reactions and it can be measured by dividing absolute neutrophil count to absolute lymphocyte count. In this study, NLR values above median were linked to critical values of PISA and BOP. Indeed, the data confirmed a noticeable association between periodontal disease and NLR-indicated inflammatory reactions. Emerging evidence suggests that increased NLR is a potential marker for poor prognosis in multiple tumors, being associated with a high risk of CVD events and mortality rate [17, 38, 39].

In the present research, a significant and strong independent association of high blood pressure values was linked to periodontal disease. That was particularly relevant for night-time systolic blood pressure values which are those with a better performance for diagnosis of hypertension among the different ways of measuring blood pressure, among the different ways of measurement. For instance, night-time systolic blood pressure values show the highest predictive value for CVD outcome and events when compared with blood pressure which was recorded in office, at home, or over daytime periods [18, 19, 36]. Night-time blood pressure values were significantly correlated with periodontal disease parameters (i.e., MPD, MAL and BOP) and independently associated with BOP in multivariate analysis. Also, night-time blood pressure values above median were associated with critical levels of MAL.

In the present study, it should also be emphasized a striking finding on the association of periodontal disease with 24h ambulatory blood pressure, as well as among the ABPM data

and night-time blood pressure i.e., the blood pressure values that have the optimum indicators for CVD events [18, 19, 36]. Those results were reinforced by the relationship found between the various markers of periodontal disease and the aortic stiffness evaluated by the PWV. Since PWV is a marker of target organ damage and an integrated indicator of CVD and atherosclerosis, the relationship found between PWV and periodontal disease is in accordance with the results of other authors.

Moreover, high salt intake was significantly associated with periodontal disease (MPD, MAL and BOP) and independently associated with BOP within the present study. Salt intake values above median were associated with unwarranted levels of MAL. High salt intake is particularly common in our country being around 10.8 g/day [32], almost twice the optimal recommended intake level [37]. As in previous studies [31, 32, 40], daily salt intake was measured in this study by the most accurate method namely, by determining the sodium excretion in at least two valid 24-h urinary samples. In the present study, average salt intake was even higher than the mean daily salt intake of the Portuguese population [32]. High salt intake has been implicated not only on the blood pressure rise but also by promoting CVD and cerebral damage through some well stablished pro-inflammatory pathways [21, 31, 41]. Interestingly, a relationship between high salt intake and periodontitis was found in the present study. Pro-inflammatory markers appear to link periodontal disease and high salt intake, thereby being possible, although still speculative. A high salt intake may importantly contribute to the inflammatory reaction within the spectrum of periodontal disease.

This study revealed a clear association between periodontal disease markers and overall CVD risks. The present data confirm a pronounced evidence that patients with severe periodontal disease revealed susceptibility to CVD events [3-6, 8, 14, 42]. Beyond the oral careless habits, factors contributing to periodontal disease include socioeconomic status, gender, education, diet, and smoking [43]. In the present study, female participants showed low-grade indices of some periodontal disease markers (PISA and BOP) when compared to those recorded or male participants. However, no statistical differences were found on periodontal disease status between diabetics and non-diabetics or even between high and low educational level. That may be due to the small numerical size of the test population.

Thus, several previous studies have reviewed the available data on the correlation between periodontal disease and hypertension [7, 13, 44]. Both periodontal disease and hypertension share a common inflammatory pattern [14, 15, 45]. Hypertension is a major risk factor for CVD [37] being associated with increased systemic or local vascular inflammation and oxidative stress [45]. Severe periodontitis is strongly associated with hypertension [44] and some studies have claimed to notice a decline of blood pressure after periodontal disease therapy [46]. Multiple studies have proven the existence of a close association between periodontal disease and CVD [3-7, 9]. On the other hand, the question of causality is still unclear particularly because most of studies have used only stand-in markers/biomarkers as endpoints. The possible practical solution to this issue has ethical constraints that limit the accomplishment of studies involving untreated groups. Hence, it remains unclear in this study whether the relationship found between the inflammatory parameters and periodontal disease is purely circumstantial because of the simple coexistence of high prevalent phenomena. This study has some limitations such as enrolling a small population within a narrow age limit. All the patients studied were hypertensive with high cardiovascular risk and submitted to several medications, so the overview of the results to other populations is obviously limited. Since it is a cross-sectional observational study, the causality between periodontal disease, the studied CVD risk, and pro-inflammatory markers is not entirely determined. Thus, the question of a possible causal relationship between periodontal disease and cardiovascular disease remains clearly unsolved.

5. Conclusions

Within the limitations of the present cross-sectional observational study, the results indicate an association between periodontal disease and cardiovascular risk factors considering the evaluation of pro-inflammatory parameters rarely studied in this context, such as salt intake, neutrophil-to-lymphocyte ratio, and abnormal immune system homeostasis. Also, periodontal disease was associated with cardiovascular risk factors such as ambulatory blood pressure particularly on night-time values and target organ damage markers. Nevertheless, future studies are therefore needed to enhance the current state of evidence regarding periodontal disease and CVD risk markers.

Abbreviations

CVD: Cardiovascular Disease
NLR: Neutrophil-Lymphocyte Ratio
PPD: Periodontal Probing Depth
CAL: Clinical Attachment Loss
BOP: Bleeding on Probing
BMI: Body Mass Index
HbA1C: Glycated Hemoglobina
FPG: Fasting Plasma Glucose
eGFR: Estimated Glomerular Function
MDRD: Modification of Diet in Renal Disease
HDL: High Density Lipoprotein
LDL: Low Density Lipoprotein
MRI: Magnetic Resonance Imaging
MPD: Mean Probing Depth
MAL: Mean Attachment Level

PESA: Periodontal Epithelial Surface Area
PISA: Periodontal Inflamed Surface Area
CPITN: Community Periodontal Index for Treatment Needs
AAP/EFP: American Academy of Periodontology/European Federation of Periodontology
ASCVD: Atherosclerotic Cardiovascular Disease
ABPM: Ambulatory Blood Pressure Monitoring
nSBP: Night Systolic Blood Pressure
NDR: Night-to-Day Ratio
PWV: Pulse Wave Velocity
DBP: Diastolic Blood Pressure
SPSS: Statistical Package for Social Sciences
SBP: Systolic Blood Pressure

Declarations

Ethics Approval and Consent to Participate

All procedures performed involving human participants followed the ethics standards of the research committee of the Cardiovascular Disease Unit at Hospital Pedro Hispano, Matosinhos, Portugal, Portugal, and therefore with the 1964 Helsinki declaration and its later amendments or comparable ethics standards. The project for the present study was previously reviewed and approved by the IUCS Ethics committee with the following Ethics Protocols Reference number: 082/CE/JAS. The Hospital Ethics Committee approved the study protocol, which was carried in accordance with the 1964 Helsinki declaration its later amendments on comparable Ethics Standards.

Consent for Publication

Written informed consent was gathered from the participants.

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Author Contributions

Conceptualization, T. P.-R, R. F.-A.; A. F., J. P, Methodology, T. P.-R, A. M., J. C. M. S., J. P.; Writing - original draft preparation, T. P.-R, A. M., R. F.-A.; Writing - review and editing, J. C. M. S., R. F.-A., J. P.; Supervision, A. F., R. F.-A., J. P. All authors have read and agreed to the published version of the manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this published article. The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.

Conflicts of Interests

The authors declare no conflicts of interests.

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