The effect of non-surgical therapy on plasma C-reactive protein levels in periodontitis patients. A single arm prospective clinical trial.

Bansari Shah[*†], Monali Shah[†], Maria Geisinger[‡], Muhammad H. A. Saleh [§], Mohamed Meghil[**], Hom-Lay Wang[§]

Corresponding author:

Hom-Lay Wang, DDS, MSD, PhD

Department of Periodontics and Oral Medicine,

University of Michigan School of Dentistry

1011 North University Avenue

Ann Arbor, Michigan 48109-1078, USA.

TEL: (734) 763-3325; FAX: (734) 936-0374 E-mail address: homlay@umich.edu

Abstract word count: 190

Total word count: 2602

---

[*] Department of Periodontics, University of Louisville School of Dentistry, Louisville, KY

[†] Department of Periodontology K. M. Shah Dental College and Hospital, Sumandeep Vidyapeeth, Vadodara, Gujarat, India

[‡] Department of Periodontology, University of Alabama at Birmingham School of Dentistry, Birmingham, AL, USA

[§] Department of Periodontics and Oral Medicine, University of Michigan School of Dentistry, Ann Arbor, MI, USA

[**] Department of Periodontics, the Dental College of Georgia at Augusta University, Augusta, GA

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1002/jper.11020.

Total number of tables and figures: 3 Tables; 2 Figures

Supplementary tables: 4 Tables

Number of references: 29

Running title: Effect of SRP on CRP levels.

Key words (MeSH): clinical trial, periodontitis, C-reactive protein, systemic inflammation

Authors' contributions: BS, MS contributed to the conception and design of the work. BS and MS collected and analyzed the data; BS, MM, MHS contributed to manuscript preparation, HLW and MG made critical changes and gave final approval to the manuscript. All authors gave their final approval and agreed to be accountable for all aspects of the work.

Conflict of Interest and Source of Funding: The authors do not have any financial interests, either directly or indirectly, in the products or information listed in the paper.

One sentence summary: Non-surgical Periodontal therapy can significantly reduce CRP levels.

Data availability: The data that support the findings of this study are available from the corresponding author upon request.

ABSTRACT

Background: This study aimed to evaluate the effect of scaling and root planing (SRP) on levels of plasma C-reactive protein (CRP).

Methods: A total of 30 patients with advanced periodontitis as determined by Clinical Periodontal Sum Score (CPSS) were recruited. Venous whole blood samples were drawn from to obtain serum samples were obtained from all participants at baseline and 1 month after SRP (post-SRP). High-

sensitivity CRP (hs-CRP) was measured by highly sensitive immunoturbidimetric assay. Wilcoxon signed-rank test was used for data analysis. Spearman's rank correlation analysis was conducted to test the correlations between CPSS and hs-CRP at baseline and post-SRP.

Results: There was a statistically significant reduction in the post-SRP CPSS values from the baseline values ($z = 4.783$, $p < 0.0001$). Similarly, there was a statistically significant reduction in the post-SRP hs-CRP levels from the baseline levels ($z = 4.782$, $p < 0.0001$). Moreover, there was positive association between the baseline levels of CPSS and hs-CRP ($\rho = 0.5703$) and the post-SRP values of CPSS and hs-CRP ($\rho = 0.7507$).

Conclusion: The present study suggests that SRP can significantly reduce the levels of CRP.

INTRODUCTION

Periodontitis is a chronic inflammatory disease characterized by the destruction of periodontal tissues that is attributed to a host immune-inflammatory response[1]. The local inflammatory response to bacteria or bacterial by-products is characterized by infiltration of the periodontal tissues of inflammatory cells including: polymorphonuclear neutrophils (PMNs), macrophages, lymphocytes, and plasma cells[2]. Activated macrophages release cytokines, and the heterogeneity in response may be due to variable responses to a microbial challenge of inflammatory mediators, such as prostaglandin E_2 (PGE_2), IL-1 and tumor necrosis factor-α (TNF-α). These cytokines not only induce destruction of periodontal soft and hard tissues[3] but also initiate a systemic acute phase response. These proinflammatory cytokines enter the blood stream and often triggers a systemic inflammatory response, characterized by increased levels of acute phase proteins such as C-reactive protein (CRP) and related vascular dysfunction[4, 5]. CRP production is part of the non-specific acute-phase response to most forms of inflammation, infection, and tissue damage[4, 5]. CRP levels reflect the burden of inflammation within atherosclerotic lesions and is a biomarker used to measure the atherosclerotic

plaques instability[6]. Current evidence supports the link between vascular events and periodontal disease. This is because oral bacteria can cause platelet aggregation and thromboembolic events via expression of proteins associated with platelet aggregation[7, 8]. Furthermore, local periodontal inflammation has been associated with major adverse cardiovascular events through a mechanism of increased arterial inflammation[9]. Therefore, CRP levels has been suggested as one of the tolls to assess the risk of cardiovascular disease due to periodontitis [10], since CRP serum levels are elevated in patients with periodontal disease. [11,12]. A meta-analysis investigating the relation of CRP with periodontitis have shown that CRP in periodontitis patients of different severity is elevated compared with controls[13]. The benefit of periodontal therapy for patients with severe periodontitis was demonstrated compared with untreated subjects[14]

Conversely, periodontal therapy itself is associated with short-term increases in systemic inflammation, likely due to subsequent bacteremias.[15, 16] In patients with periodontitis, intensive nonsurgical therapy "non-surgical therapy full-mouth subgingival instrumentation delivered within a 6-h period" an acute systemic inflammatory response that lasted for approximately 1 week[17].

Therefore, the aim of the present study was to assess the effect of scaling and root planing (SRP) on serum CRP levels.

MATERIALS AND METHODS

Ethical Approval and Registration

Approval for the experimental protocol of the present study was obtained from the K. M. Shah Dental College and Hospital, Sumandeep Vidyapeeth, Vadodara, Gujarat, India Institutional Review Board (SVUEC/ON/DENT/BN09/D1007). This study was conducted in accordance with the Helsinki Declaration for the ethical principles for medical research involving human subjects, as revised in 2013.

Experimental design, Eligibility Criteria, and Recruitment

This study was designed as a single arm prospective clinical trial to assess the effect of SRP on plasma CRP levels. Adult subjects who agreed to participate in this study were informed about the study design, risks, benefits, and timeline and provided informed consent prior to inclusion in the study. A comprehensive periodontal examination was performed including medical history as assessed via a questionnaire and a full-mouth periodontal probing chart on six sites/tooth performed. Subjects were recruited from consecutive individuals presenting at the Department of Periodontics, K.M. Shah Dental College and Hospital seeking periodontal care. The case definition of periodontitis was done in accordance with the 2017 World Workshop[1]. The severity of the inflammation was assessed and categorized by Clinical Periodontal Sum Score (CPSS). The CPSS utilizes the following clinical parameters: probing pocket depths (PPD), bleeding on probing (BOP), suppuration, and furcation involvement (FI)[18].

The CPSS gives the ability to have a clinical periodontal sum score that includes parameters pointing to inflammation (BOP, SUP, and PD), which is currently not possible using the Stage and Grade classification. A total score was assigned to each patient through the weighted score for those clinical parameters. PPD measurements were assessed by means of a manual, calibrated UNC 15-mm probe¶. Six sites per tooth (disto-buccal, mid-buccal, mesio-buccal, mesio-lingual, mid-lingual, disto-lingual) were examined in all teeth in the dentition. FI was assessed by Nabers probe¶ using the Hamp classification[19]. CPSS was calculated through the sum of the number of sites per patient with PPD ≥ 4mm, the number of sites with BOP, the number of sites with visible suppuration on probing, and the number of FI exceeding grade 1. No CPSS cutoff limit was put to the inclusion of patients. In addition to the CPSS, patients were initially recruited if (i) they had at least 20 teeth present; and (ii) good general health as assessed by the examining clinician.

Subjects were excluded if they were (i) older than 70 years; (ii) pregnant or lactating females; (iii) females using contraceptive methods; (iv) suffering from systemic illnesses that may affect CRP levels; (v) underwent any antimicrobial treatment within the 3 months prior to the study; (vi) treated for periodontal disease in the previous 6 months; and (vii) heavy smokers (i.e., ≥10 cigarettes/day). These exclusion criteria were established to avoid the confounding effects of other diseases/conditions or the medications.

Sample size

A previous study conducted to evaluate the systemic inflammatory response to nonsurgical therapy was used to determine the sample size. Study power 80% with confidence interval 95% and alfa error 5% making 24 patients is minimum accepted number. Based on that, a total of 30 patients were recruited for the study to reach a significance level[20]. A total of 30 patients were included in this study, 19 of which were females, and 11 were males.

Non-surgical therapy & serum collection.

Periodontal status for study subjects was recorded by CPSS at baseline and 1-month after SRP using a calibrated periodontal probe¶. Examination was done by a single examiner (MS). All non-surgical therapy was provided by a single periodontal resident (BS). The study procedures were followed for each patient. Baseline examinations included CPSS and collection of whole blood sample. Blood samples were collected, centrifuged, serum was separated and transferred to transport media to be sent out to the lab. Coolants were used to transport the serum samples at 15-25°C. Once it reached the lab high-sensitivity CRP (hs-CRP) was assessed using immunoturbidimetric assay.

After the baseline examination, subjects received phase I periodontal therapy, which included patient education and motivation, plaque control, supra- and sub-gingival scaling and root planing, elimination of all plaque-retentive sites on teeth and restorations, and supragingival polishing. All phase I procedures were performed by the same operator (BS). No antibiotics or anti-inflammatory medications were given during or after the treatment. Patient were seen two weeks after SRP was completed to assess plaque control. One month after completion of SRP, CPSS was recorded after comprehensive periodontal examination and blood was drawn for a follow-up assessment of hs-CRP levels.

Blood collection and analysis of hs-CRP levels

Serum samples were collected from a single, clean venipuncture with minimal stasis through the skin and in the antecubital fossa at baseline and 2 and 6 months after completion of treatment. 3 ml of blood was drawn using a 5cc disposable syringe and 23-gauge needles. The blood was allowed to clot and then centrifuged at 3,000 RPM for 10 minutes. The serum was then separated and tested for CRP levels using the commercially available kits. hs-CRP levels were assessed from the serum separated from the acquired blood samples from baseline and 1-month post-SRP by commercially available immunoturbidimetric assay. The reagent CRP-turbidilatex agglutination assay is a quantitative turbidimetric assay for measurement of CRP in human serum. Latex particles coated with specific human anti-CRP are agglutinated when mixed with sample containing CRP. The agglutination causes an absorbance change that allows quantification of CRP levels within the samples through utilization a calibrator of known CRP concentration.

Statistical analysis

Data analyses were performed using a statistical software[#]. Kolmogorov-Smirnova and the Shapiro-Wilk tests were applied to determine the data distribution of CPSS and hs-CRP. Nonparametric tests were used since the variables did not follow a normal distribution. Wilcoxon signed-rank test was used for data analysis. The correlations between CPSS and hs-CRP at baseline and post-SRP were performed using the Spearman's rank correlation analysis.

RESULTS

All 30 patients, age ranged from 16-56 years, successfully completed the study. Table 1 lists CPSS and hs-CRP data for each patient at baseline and post-SRP time points. The data was tested for normality using the Kolmogorov-Smirnova and the Shapiro-Wilk test (see Tables S1 & S2 in online Journal of Periodontology). Wilcoxon signed-rank test was used for data analysis due to non-parametric data obtained. The baseline CPSS ranged from 38 to 162 whereas the post-SRP CPSS ranged from 9 to 121 (Figure 1). In addition, the baseline hs-CRP values ranged from 0.37 to 5.69 mg/l whereas the post-SRP hs-CRP values ranged from 0.14 to 3.49mg/l (Figure 2). There was a statistically significant reduction in post-SRP CPSS values from the baseline values ($z = 4.783$, $p < 0.0001$). Similarly, there was a statistically significant reduction in the post-SRP hs-CRP levels from the baseline levels ($z = 4.782$, $p < 0.0001$) (see Tables S3 & S4 in online Journal of Periodontology).

A positive association was found between the baseline levels of CPSS and hs-CRP ($\rho = 0.57$) and the post-SRP values of CPSS and hs-CRP ($\rho = 0.75$) by using Spearman's correlation. There was moderate agreement between the baseline levels of CPSS and hs-CRP ($\rho = 0.57$) and substantial agreement ($\rho = 0.75$) in the correlation between the post-SRP values of CPSS and hs-CRP by using Spearman's

correlation (Table 2). Furthermore, in the present study, 8 out of 30 patients (26.6%) had clinically elevated CRP (≥ 3 mg/l) before intervention. One-month post-SRP, only one patient showed elevated CRP (≥3mg/l) which accounts to 3.3% of the subjects. Consequently, 87.5% of the individuals who demonstrated elevated CRP at baseline showed normal (< 3mg/L) CRP levels after SRP. These changes in elevated CRP were statistically significant ($p < 0.01$) (Table 3).

DISSCUSSION

The present study showed that SRP can effectively reduce the levels of CRP and that the severity of periodontal inflammation as indicated by the CPSS score was correlated with a proportional elevation in serum CRP levels.

The serum levels of CRP can increase by other conditions other than periodontitis. The exclusion criteria for this study specifically included systemic diseases and inflammatory conditions that may affect CRP levels to rule out any potential influence. Furthermore, patients with a past history of recent periodontal therapy were also excluded because previous therapy may have resulted in a reduction of systemic inflammatory burden and thus diminishing of the impact of SRP on CRP levels [21]. In addition, periodontal therapy may cause tissue injury that would again lead to an inflammatory response and lead to increase of CRP levels immediately post-treatment [22]. Hence, in this study, the outcomes were assessed one month post-SRP.

The mean baseline value of hs-CRP found for subjects in this study was slightly less than the previously reported[13], which may be attributed to more severe form of periodontal destruction was studied in the previous study. Moreover, statistically significant reduction in the post-SRP hs-CRP levels relative to the baseline levels is found to be comparable to the results of the systematic review and meta-analysis of CRP in relation to periodontitis and several other studies[13, 23-25]. This study also revealed a statistically significant reduction in the post-SRP CPSS values relative to the

baseline values, indicating an improvement in the clinical parameters after SRP. CPSS includes clinical parameters of BOP, PPD, suppuration and FI. These findings are consistent with the review of several studies reporting improvement in the clinical parameters after SRP[26]. Additionally, our results showed a positive association and moderate agreement between the baseline levels of CPSS and hs-CRP and the post-SRP values of CPSS and hs-CRP. Similar findings were also reported in a systematic review and meta-analysis that studied the relationship between CRP and periodontitis [13].

In the present study, 8 out of 30 patients (26.6%) had elevated CRP (≥3mg/l) at baseline whereas post-SRP, only one patient (3.3%) showed elevated CRP (≥3mg/l). So, the reduction in occurrence of higher CRP after intervention is 87.5%, which is statistically significant and clinically applicable. It should be noted that the sole patient who had higher CRP value post-SRP had hs-CRP value of 4.63 at baseline, which was reduced to 3.49, accounting to 24.6% reduction in that individual's hs-CRP value.

The results of the present study highlight three points. First, elevated CRP levels were associated with an increasing severity of periodontal inflammation as measured by the CPSS. Second, SRP resulted in improvement of the periodontal parameters irrespective of the state of the disease. Third, SRP led to a reduction of systemic inflammation as evidenced by the reduction in CRP. Some studies have failed to confirm the decrease in CRP with periodontal treatment[23, 27], however it is important to highlight that these studies did not account for the CRP influencing conditions such as obesity, hypertension and cholesterol. Additionally, previous studies demonstrated residual diseased periodontal sites remained after the periodontal treatment, which may have had some bearing on the results. However, one of the limitations of the present study is that the presented results can only suggest that the severity of periodontal inflammation (CPSS) was correlated elevation in serum CRP levels, but this does not necessarily apply to the severity of periodontitis.

One of the factors that could have influenced the results of this study was the age of the participants (ranged from 16 to 56 years). Given the vagaries of the pathogenesis of periodontal disease in terms of age, rate of progression and the episodic nature of the disease, it would be very difficult to gather all the samples of same age having similar periodontal status. Also, the patients enrolled in this study have periodontal status ranging from gingivitis to severe periodontitis, which may have allowed for significant heterogeneity and may have obscured more significant reactions seen with treatment of various forms of periodontal diseases. Moreover, strong correlation between the severity of periodontitis and the reduction of hs-CRP accordingly couldn't be established. Another limitation of this study might be that it adopted the Clinical Periodontal Sum Score (CPSS) instead of the 2017 world workshop classification (2017 WWC)[1]. Currently, the 2017 WWC does not include parameters that indicate inflammation (either bleeding or suppuration). For instance, a treated Stage III, with advanced bone loss and CAL ≥5mm would remain a Stage III after treatment, resolution of PD and BOP, which would be considered a treated stable periodontitis patient[28, 29]. Grade is based, mainly, on co-morbidities like diabetes mellitus and smoking that were excluded in this study for obvious reasons. Instead of giving a reference for proportions of diseased periodontal areas in the sites examined, the CPSS sums up the number of various recordings that are indicating periodontal inflammation[18]. This may have concealed findings and/or limited the ability to determine correlation. For example, given that it would not be anticipated that FI would change after SRP, this composite periodontal disease assessment may have underestimated the clinical response to therapy.

An additional limitation to the widespread generalizability of the present study was related to its exclusion of subjects with systemic factors known to have an up-regulatory effect on CRP level. In the general population, for subjects with pre-existing known risk factors for cardiovascular disease,

presence of periodontitis may add to the cumulative effect of such factors thus further increasing the risk. This aspect should be examined further in future studies.

CONCLUSION

Within the limitations of this study, periodontitis is associated with elevation in serum CRP levels and that scaling and root planing is able to bring down the levels of CRP. The long-term impact of such a CRP reduction in reducing cardiovascular risk, its morbidity, and mortality can only be assessed by well-controlled longitudinal trials.

Legends:

Table 1: Patient demographics with pre and post CPSS and hs-CRP levels.

Table 2: Correlation between the post-SRP values of CPSS and hs-CRP using Spearman's correlation.

Table 3: The occurrence of hs-CRP at baseline versus post treatment.

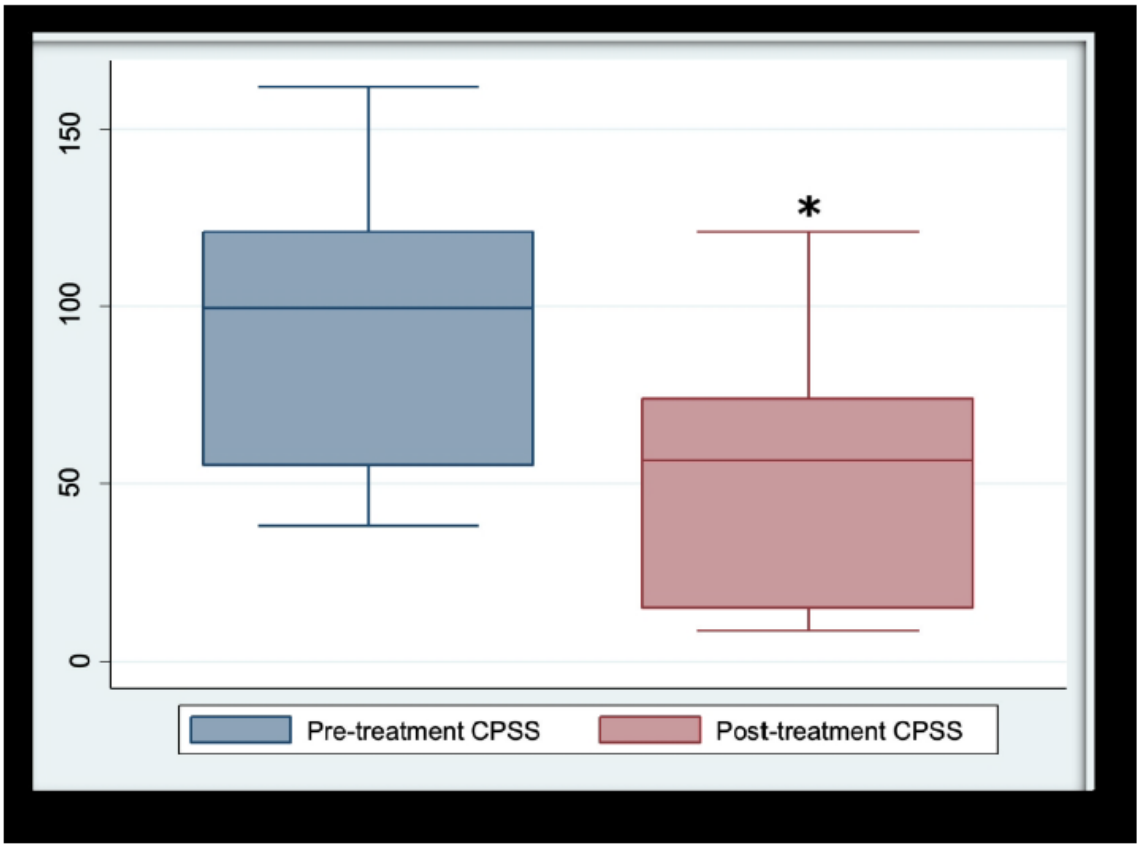

Figure 1: Mean & confidence interval of pre-treatment & post-treatment CPSS.

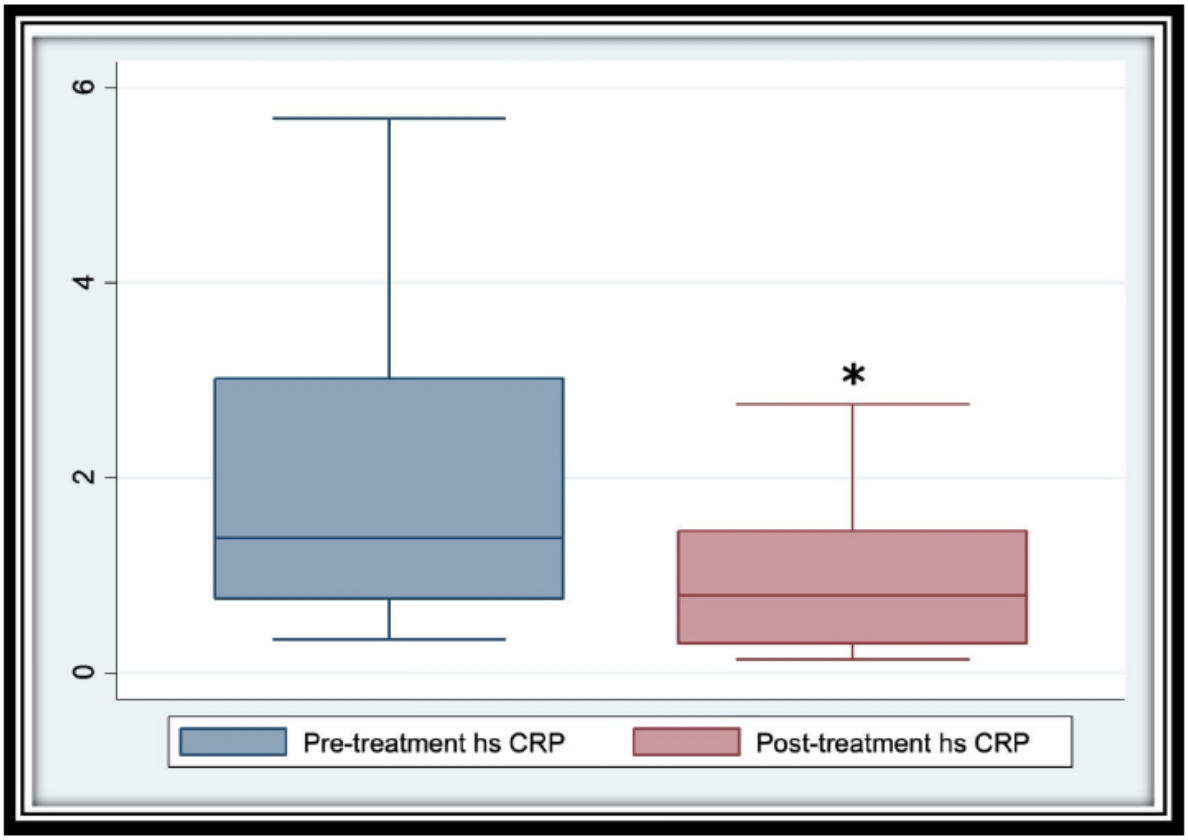

Figure 2: Mean & confidence interval of pre-treatment & post-treatment hs-CRP

Supplementary Table 1: Kolmogorov-Smirnova Shapiro-Wilk tests for assessing the normality of data of CPSS.

Supplementary Table 2: Kolmogorov-Smirnova Shapiro-Wilk tests for assessing the normality of data of hs-CRP.

Supplementary Table 3: Wilcoxon signed rank test for assessing CPSS.

Supplementary Table 4: Wilcoxon signed rank test for assessing hs-CRP.

Conflict of Interest and Source of Funding: The authors do not have any financial interests, either directly or indirectly, in the products or information listed in the paper.

REFERENCES

1. Tonetti MS, Greenwell H, Kornman KS. Staging and grading of periodontitis: Framework and proposal of a new classification and case definition. *J Periodontol* 2018;89 Suppl 1:S159-S172.
2. Gemmell E, Yamazaki K, Seymour GJ. The role of T cells in periodontal disease: homeostasis and autoimmunity. *Periodontol 2000* 2007;43:14-40.
3. Reynolds JJ, Meikle MC. Mechanisms of connective tissue matrix destruction in periodontitis. *Periodontol 2000* 1997;14:144-157.
4. Slade GD, Offenbacher S, Beck JD, Heiss G, Pankow JS. Acute-phase inflammatory response to periodontal disease in the US population. *Journal of dental research* 2000;79:49-57.
5. Graziani F, Cei S, La Ferla F, Vano M, Gabriele M, Tonetti M. Effects of non-surgical periodontal therapy on the glomerular filtration rate of the kidney: an exploratory trial. *Journal of clinical periodontology* 2010;37:638-643.
6. Soehnlein O, Libby P. Targeting inflammation in atherosclerosis - from experimental insights to the clinic. *Nat Rev Drug Discov* 2021;20:589-610.

7. Lourbakos A, Potempa J, Travis J, et al. Arginine-specific protease from Porphyromonas gingivalis activates protease-activated receptors on human oral epithelial cells and induces interleukin-6 secretion. *Infection and immunity* 2001;69:5121-5130.

8. Lourbakos A, Yuan YP, Jenkins AL, et al. Activation of protease-activated receptors by gingipains from Porphyromonas gingivalis leads to platelet aggregation: a new trait in microbial pathogenicity. *Blood* 2001;97:3790-3797.

9. Van Dyke TE, Kholy KE, Ishai A, et al. Inflammation of the periodontium associates with risk of future cardiovascular events. *J Periodontol* 2021;92:348-358.

10. Da Venezia C, Hussein N, Hernández M, et al. Assessment of Cardiovascular Risk in Women with Periodontal Diseases According to C-reactive Protein Levels. *Biomolecules* 2021;11.

11. Noack B, Genco RJ, Trevisan M, Grossi S, Zambon JJ, De Nardin E. Periodontal infections contribute to elevated systemic C-reactive protein level. *Journal of periodontology* 2001;72:1221-1227.

12. Ebersole JL, Machen RL, Steffen MJ, Willmann DE. Systemic acute-phase reactants, C-reactive protein and haptoglobin, in adult periodontitis. *Clin Exp Immunol* 1997;107:347-352.

13. Paraskevas S, Huizinga JD, Loos BG. A systematic review and meta-analyses on C-reactive protein in relation to periodontitis. *J Clin Periodontol* 2008;35:277-290.

14. Vidal F, Figueredo CM, Cordovil I, Fischer RG. Periodontal therapy reduces plasma levels of interleukin-6, C-reactive protein, and fibrinogen in patients with severe periodontitis and refractory arterial hypertension. *J Periodontol* 2009;80:786-791.

15. Shamaei-Tousi A, D'Aiuto F, Nibali L, et al. Differential regulation of circulating levels of molecular chaperones in patients undergoing treatment for periodontal disease. *PLoS One* 2007;2:e1198.

16. Yamazaki K, Honda T, Oda T, et al. Effect of periodontal treatment on the C-reactive protein and proinflammatory cytokine levels in Japanese periodontitis patients. *J Periodontal Res* 2005;40:53-58.

17. D'Aiuto F, Nibali L, Mohamed-Ali V, Vallance P, Tonetti MS. Periodontal therapy: a novel non-drug-induced experimental model to study human inflammation. *J Periodontal Res* 2004;39:294-299.

18. Mattila KJ, Asikainen S, Wolf J, Jousimies-Somer H, Valtonen V, Nieminen M. Age, dental infections, and coronary heart disease. *J Dent Res* 2000;79:756-760.

19. Hamp SE, Nyman S, Lindhe J. Periodontal treatment of multirooted teeth. Results after 5 years. *J Clin Periodontol* 1975;2:126-135.

20. Yashima A, Morozumi T, Yoshie H, et al. Biological responses following one-stage full-mouth scaling and root planing with and without azithromycin: Multicenter randomized trial. *J Periodontal Res* 2019;54:709-719.

21. Hussain Bokhari SA, Khan AA, Tatakis DN, Azhar M, Hanif M, Izhar M. Non-surgical periodontal therapy lowers serum inflammatory markers: a pilot study. *Journal of periodontology* 2009;80:1574-1580.

22. Graziani F, Cei S, Tonetti M, et al. Systemic inflammation following non-surgical and surgical periodontal therapy. *Journal of clinical periodontology* 2010;37:848-854.

23. Ide M, McPartlin D, Coward PY, Crook M, Lumb P, Wilson RF. Effect of treatment of chronic periodontitis on levels of serum markers of acute-phase inflammatory and vascular responses. *Journal of clinical periodontology* 2003;30:334-340.

24. D'Aiuto F, Ready D, Tonetti MS. Periodontal disease and C-reactive protein-associated cardiovascular risk. *Journal of periodontal research* 2004;39:236-241.

25. D'Aiuto F, Parkar M, Andreou G, Brett PM, Ready D, Tonetti MS. Periodontitis and atherogenesis: causal association or simple coincidence? *Journal of clinical periodontology* 2004;31:402-411.

26. Cobb CM. Non-surgical pocket therapy: mechanical. *Annals of periodontology* 1996;1:443-490.

27. Christgau M, Palitzsch KD, Schmalz G, Kreiner U, Frenzel S. Healing response to non-surgical periodontal therapy in patients with diabetes mellitus: clinical, microbiological, and immunologic results. *Journal of clinical periodontology* 1998;25:112-124.

28. Chapple ILC, Mealey BL, Van Dyke TE, et al. Periodontal health and gingival diseases and conditions on an intact and a reduced periodontium: Consensus report of workgroup 1 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. *J Periodontol* 2018;89 Suppl 1:S74-S84.

29. Ravida A, Travan S, Saleh MHA, et al. Agreement among international periodontal experts using the 2017 World Workshop classification of periodontitis. *J Periodontol* 2021;92:1675-1686.

Table 1: Patient demographics with pre and post CPSS and hs-CRP levels.

Sr. No.	Age	Sex	Pre-treatment CPSS	Post-treatment CPSS	Pre-treatment hs-CRP (mg/l)	Post-treatment hs-CRP (mg/l)
1	42	M	88	42	1.47	0.84
2	20	F	38	10	1.06	0.54
3	47	M	102	60	0.76	0.49
4	16	F	51	14	0.49	0.19
5	25	M	38	21	1.25	0.84
6	29	F	117	59	0.98	0.42
7	54	M	128	107	4.04	2.34
8	40	F	111	70	1.46	0.5
9	41	F	46	17	1.32	0.64
10	38	F	141	94	4.78	2.69
11	38	F	98	62	1.21	1
12	32	M	135	101	3.46	2.1
13	24	M	49	9	1.05	0.15
14	42	M	105	89	3.02	2.19
15	48	M	131	74	4.17	1.54
16	45	F	57	25	1.85	0.86
17	35	M	147	113	4.8	1.46
18	23	F	67	12	0.58	0.16
19	28	F	119	80	4.63	3.49
20	51	F	51	25	1.14	0.95
21	26	F	55	15	0.72	0.18
22	25	M	74	10	0.34	0.14
23	56	F	162	121	5.69	2.76
24	28	F	112	54	0.7	0.17
25	24	F	121	68	1.9	0.3
26	17	F	54	12	0.37	0.3
27	26	M	101	74	1.44	1.15
28	31	F	132	63	0.62	0.41
29	31	F	72	18	1.53	0.76
30	35	F	65	12	1.52	0.86

Table 2: Correlation between the post-SRP values of CPSS and hs-CRP using Spearman's correlation.

	Baseline CPSS	Post-SRP CPSS	Baseline hs-CRP	Post-SRP hs-CRP
Baseline CPSS	**1.0000**			
Post-SRP CPSS	**0.8616**	**1.0000**		
Baseline hsCRP	**0.5703**	**0.7432**	**1.0000**	
Post-SRP hsCRP	**0.4814**	**0.7507**	**0.8561**	**1.0000**
0.41-0.60		**Moderate agreement**		
0.61-0.90		**Substantial agreement**		
0.91-1.00		**Almost perfect agreement**		

Table 3: The occurrence of hs-CRP at baseline versus post treatment.

Hs-CRP at Baseline and Post-SRP

	Hs-CRP ≥3	Hs-CRP <3	Total	Occurrence of increased hs-CRP
Baseline	**8**	**22**	**30**	**26.6%**
Post-SRP	**1**	**29**	**30**	**3.3%**

Reduction in occurrence of elevated hs-CRP is 87.5%

Supplementary Table 1:

	Kolmogorov-Smirnova			Shapiro-Wilk		
	Statistic	Df	Sig.	Statistic	Df	Sig.
Baseline CPSS	.131	30	.200	.937	30	.078
Post-NSPT CPSS	.199	30	.004	.898	30	.008

Test for assessing the normality of data of CPSS

Supplementary Table 2:

	Kolmogorov-Smirnova			Shapiro-Wilk		
	Statistic	Df	Sig.	Statistic	Df	Sig.
Baseline hsCRP	.271	30	.000	.819	30	.000
Post-NSPT hsCRP	.206	30	.002	.843	30	.000

Test for assessing the normality of data of hs-CRP

Supplementary Table 3:

Sign	Obs	Sum ranks	Expected
Positive	30	465	232.5
Negative	0	0	232.5
Zero	0	0	0
All	30	465	465

Unadjusted variance: 2363.75

Adjustment for ties: -0.75

Adjustment for zeroes: 0.00

Adjusted variance: 2363.00

Ho: Baseline CPSS = Post-NSPT CPSS
z = 4.783, p < 0.0001

Wilcoxon signed rank test for CPSS

Supplementary Table 4:

Sign	Obs	Sum ranks	Expected
Positive	30	465	232.5
Negative	0	0	232.5
Zero	0	0	0
All	30	465	465

Unadjusted variance:	2363.75
Adjustment for ties:	0.00
Adjustment for zeroes:	0.00
Adjusted variance:	2363.75

Ho: Baseline hs-CRP = Post-NSPT hs-CRP z = 4.782, p < 0.0001

Wilcoxon signed rank test for hs-CRP