Is there a correlation between the periodontitis-related systemic inflammatory burden and future cardiovascular events' risk? A preliminary report

Periodontitisle ilişkili sistemik inflamatuvar yük ve ileride oluşabilecek kardiyovasküler olay riski arasında korelasyon var mı? Ön bulgular

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SUMMARY

Aim: To define a direct relationship or "cause-effect" relationship between the periodontitis and coronary artery disease (CAD) is hard due to the multifactorial nature of both inflammatory diseases. This study was aimed to test the hypothesis whether periodontitis related systemic inflammatory burden have a correlation with the future cardiovascular events.

Materials and Methods: Patients who undergo for coronary angiography with suspicion of coronary artery disease (CAD) between the ages 30-75 were included. The participants were divided into four groups: Group 1: CAD (+) P (+) (n=20), Group 2: CAD (+) P (-) (n=20), Group 3: CAD (-) P (+) (n=21), Group 4: CAD (-) P (-) (n=16). Clinical periodontal parameters and the periodontal inflamed surface area (PISA) were recorded. The parametric (analysis of variance, Tukey test) and non-parametric (Kruskall-Wallis and Bonferonni-Dunn) tests were used to determine the differences among the groups. The correlations between the parameters were tested with Pearson correlation analysis ($p<0.05$).

Results: FRS has shown significant positive correlations with all periodontal parameters, PISA, and significant negative number of teeth in CAD (-) groups ($p<0.05$). The number of teeth in the whole group has shown a negative correlation with FRS ($p<0.05$).

Conclusions: The correlations between PISA, number of teeth and FRS deserves further attention. The relationship between future CAD risk and periodontitis-related systemic inflammatory burden might be clarified in future studies with a careful adjustment of the shared risk factors in a larger study population.

Key words: Periodontitis, coronary artery disease, inflammation, Framingham Risk Score

ÖZET

Amaç: Periodontitis (P) ve koroner arter hastalığı (KAH) arasındaki ilişkinin doğrudan bir bir ilişki mi yoksa "neden-sonuç" ilişkisi mi olduğunu belirlemek, bu iki inflamatuvar hastalığın multifaktöriyel doğasından ötürü zordur. Bu çalışmanın amacı periodontitis ile ilişkili sistemik inflamatuvar yüklenme ile ileride oluşabilecek kardiyovasküler olay riski ile bir korelasyonu olduğu hipotezini test etmektir.

Gereç ve Yöntem: Yaşları 30-75 arasında değişen, KAH şüphesiyle koroner anjiyografi uygulanacak olan hastalar çalışmaya dahil edildi. Katılımcılar şu dört alt gruba ayrıldı: Grup 1: KAH (+) P (+) (n=20), Grup 2: KAH (+) P (-) (n=20), Grup 3: KAH (-)P (+) (n=21), Grup 4: KAH (-) P (-) (n=16). Klinik periodontal parametreler ve periodontal inflame yüzey alanı (PİYA) kayıtları alındı. Gruplar arası farkların belirlenmesinde parametrik olan (Varyans analizi ve Tukey) ve olmayan (Kruskall-Wallis ve Bonferonni-Dunn) testleri; korelasyonların incelenmesinde ise Pearson korelasyon analiz testi kullanıldı ($p<0,05$).

Bulgular: Framingham Risk Skoru (FRS) KAH (-) gruplarda

(Grup 3 ve 4) tüm periodontal parametrelerle ve PİYA ile anlamlı pozitif, diş sayısı ile anlamlı negatif korelasyonlar sergilerken (p<0,05); tüm grupta (Grup 1-4, N=77) sadece diş sayısı ile anlamlı negatif korelasyon gösterdi (p<0,05). **Sonuç**: Çalışmamızda belirlenen PİYA, diş sayısı ve FRS arasındaki korelasyonlar ileri çalışmalarda detayla araştırılmalıdır. Daha geniş bir popülasyonda ortak risk faktörlerinin de uyumlanmasıyla yapılacak olan çalışmalar periodontitis ile ilişkili sistemik inflamatuvar yük ve ileride oluşabilecek KAH riski arasındaki ilişkiyi daha net belirleyebilir.

Anahtar kelimeler: Periodontitis, koroner arter hastalığı, inflamasyon, Framingham Risk Skoru

INTRODUCTION

Periodontitis is an infectious and inflammatory disease; the main etiologic factor is dental biofilm and eventuated with destruction of bone and connective tissues. The initiation and progression of periodontitis depend on the complex interactions between periodontopathogens and host immune system. The antigens, lipopolysaccharides and other virulence factors are known to be the potent stimulators of host inflammatory mediators.[1] For many years, it has been thought that periodontal infections are localized to the marginal periodontium and has not any systemic effects in healthy subjects; new evidences have reported the presence of systemic inflammation with the increased inflammatory markers in periodontitis subjects when compared to the control groups.[2,3]

Severe periodontal disease was reported to constitute 25-90% risk for cardiovascular disease (CVD) in case of adjustment of the shared confounding factors.[4] The mechanism(s) explaining this "relationship" was not determined clearly; but suggested as following: transient bacteremia in vascular cells and enhanced/accelerated atherogenesis related to the increased cytokine levels in circulation.[5]

Coronary artery diseases (CAD) have the highest mortality rates among the CVD.[5] The plaque formation, arterial wall thickening and atheroma formation are the known and accepted underlying predisposing factors of atherosclerosis resulting in CAD.[6] Besides, as potential reasons for atherosclerosis, inflammation and infection were reported and supported.[7] Periodontopathogens and their virulence factors might affect all of the steps of atherogenesis via the induction of systemic inflammation.[8,9] The isolation of *Porphyromonas gingivalis* from a human atheroma plaque has strengthened the role of periodontitis on the atherogenesis.[9] To define a direct relationship or "cause-effect" relationship between the periodontitis and CAD is hard due to the multifactorial nature of both inflammatory diseases. The statement of American Heart Association about the "cause-effect" relationship between the CAD and periodontitis regarding the surrogate end points, such as decreased CRP and LDL after periodontal therapy, give rise to think this issue should be evaluated with a great precaution: "...statements that imply a causative association between periodontal disease and specific atherosclerotic vascular disease events or claim that therapeutic interventions may be useful on the basis of that assumption are unwarranted."[10] Nevertheless, the proposed pathways connecting the diseases deserve to be investigated in a detailed manner.

The systemic inflammatory burden and its relationship with periodontitis have attracted more attention in time. The inflammatory periodontal surface area might be used to clarify this relationship.[11,12] A measurement and classification system developed by Hujoel[11] and modified by Nesse[12] was used for related periodontitis with systemic diseases in recent years.[12-14]

From this point of view, this study was aimed to test the hypothesis whether periodontitis related systemic inflammatory burden, measured by a scale using clinical periodontal parameters, have a correlation with the future cardiovascular events using Framingham Risk Score (FRS).

MATERIALS AND METHOD

This study was approved by Suleyman Demirel University Local Ethical Committee on Clinical Investigations (Date: 19.03.2014, Decision number: 38) and was performed in appropriate with the ethical rules of the Declaration of Helsinki. Seventy-seven consecutive patients, who undergo a coronary angiography with suspicion of CAD in Suleyman Demirel University, Faculty of Medicine, Department of Cardiology between June 2014 and August 2015, have participated in the study. The study was based on voluntariness; the informed consent forms were signed by all of the patients.

Patients who undergo for coronary angiography with suspicion of CAD between the ages 30 and 75 were included. The indication for coronary angiography was either the presence of typical angina or positive or equivocal results of noninvasive screening tests for myocardial ischemia. Patients, who were smoking before hospitalization, were accepted as smokers. To have the diagnosis and/or being under the therapy of CAD, having DM, using statins, using calcium channel blockers for hypertension therapy, pregnancy, lactation, being under age of 30, having rheumatologic diseases or malign diseases, used/using anti-inflammatory and/or antibiotics in the last three months/currently, having periodontal therapy in the last six months were the exclusion criteria. The detailed medical and dental anamneses of the patients were obtained.

Study groups

The volunteer participants fulfilling the study criteria were

divided into four groups considering the coronary angiography results and periodontal parameters recorded before coronary angiography as follows: Group 1: Subjects with CAD and periodontitis (n=20); Group 2: Subjects with CAD and without periodontitis (n=20); Group 3: Subjects without CAD and with periodontitis (n=21); Group 4: Subjects without CAD and without periodontitis (n=16)

Coronary angiography

Coronary angiography was routinely performed without the use of nitroglycerin. Selective coronary angiography was performed by means of the Judkins technique in multiple projections. Iohexol (Omnipaque, Opakim, İstanbul, Turkey) was used as contrast agent during coronary angiography in all patients and control subjects. Coronary angiograms were analyzed by two blinded interventional cardiologists without knowledge of the clinical status and laboratory measurements of the subjects. CAD was defined as >50% stenosis of one or more epicardial coronary artery. A normal segment was defined as a coronary artery segment without ectasia or stenosis on the basis of coronary angiography.

Serum samples

Before coronary angiography, fasting blood samples from antecubital vein were obtained. In scope of the present study, total cholesterol (TC), high density lipoprotein cholesterol (HDL-C) was used for the calculation of Framingham Risk Score (FRS).

Clinical periodontal parameters

Before coronary angiography, periodontal examination was conducted. In this examination, bleeding on probing (BOP), clinical attachment loss (CAL), and periodontal pocket depth (PD) were recorded from the six sites (mesiobuccal, mediobuccal, distobuccal, mesiolingual, midlingual, distolingual) of the present teeth. Williams's periodontal probe (Hu-Friedy, Chicago, IL, USA) was used for the PD measurement from free gingival margin to the bottom of the periodontal pocket, for the CAL measurement from cemento-enamel junction to the bottom of the periodontal pocket. The BOP was recorded for the measurement of systemic inflammatory burden from the six sites (mesiobuccal, mediobuccal, distobuccal, mesiolingual, midlingual, distolingual) of the present teeth as present (+) or absent (-). To calculate the percentage of BOP, even one site with bled on probing was recorded as (+) and used to calculate the percentage of bleeding teeth considering the number of teeth of the present dentition. The number of teeth (NT) was also recorded and patients having ≥8 teeth were included to the study.[14]

Determination of the systemic inflammatory burden

The classification reported by Hujoel[11] measures the total attachment loss surface area. This classification was modified to obtain a classification system regarding the periodontally inflamed surface area by Nesse[12] The modified version of the classification[12] was used to calculate the periodontally inflamed surface area (PISA) and periodontally epithelial surface area (PESA) using PD, CAL and BOP.

The Framingham Risk Score (FRS)

In this scoring system, the CAD (angina pectoris, myocardial infarction, coronary mortality) risk in 10 years is calculated considering the age, gender, TC, HDL-C, systolic blood pressure values (undergoing therapy for high blood pressure or not), smoking or not. The FRS was calculated as previously suggested.[15]

Statistical analysis

The sample size was calculated considering the Type I errors (0.05), targeted power (0.80), the estimated difference between the means (∂= 2), and the standard deviation (σ= 2). The sample size of each group was determined to be a minimum of.[16]

The investigated parameters were analyzed with the Anderson-Darling test to investigate the normality assumption, and with Levene's test to evaluate for homogeneity of variance assumption. The NT and FRS have not provided the assumptions for the parametric tests, while BOP and PD parameters had. The BOP and PD were analyzed using analysis of variance (one-way ANOVA). The Tukey test was used to determine the differences among the group means. The other parameters were analyzed with the Kruskall-Wallis test because they do not provide the assumptions of the parametric tests. Bonferonni-Dunn test was used to determine the differences among the groups' rank means.

The correlations between the parameters were tested in each group, in groups with CAD (Groups 1 and 2) and in groups without CAD (Groups 3+4) with Pearson correlation analysis. A commercial statistic program was used to analyze the parameters (https://www.minitab.com/en-us/products/minitab/).

RESULTS

Seventy-seven subjects (30 female, 47 male) between the ages 33 and 71 have participated in the study. The sociodemographic and anthropometric characteristics were presented in Table 1, the periodontal parameters, PISA and PESA values, FRS values and the comparison between the groups were shown in Table 2 (normal and homogenously distributed parameters) and Table 3 (values not presenting normal and homogenous distribution). The statistically significant differences were shown with roman characters on Tables.

The differences between the groups regarding BOP, CAL, PD, PISA, and PESA were found significantly higher in Groups 1 and 3 than Groups 2 and 4 ($p<0.01$, Table 2, Table 3). However, there were not found significant dif-

ferences between Groups 1 and 3, and Groups 2 and 4 (p>0.05, Table 2, Table 3). The NT was higher in Group 4 than Groups 1, 2, and 3 (p<0.01); but the difference among Groups 1, 2, and 3 was not significant (p>0.05).

Table 1. Characteristics of the study groups

	Group (n=20)	Group 2 (n=20)	Group 3 (n=21)	Group 4(n=16)
Age	59.5 (46-68) a	57.5 (44-65) a	50 (42-71) b	49 (33-65) b
Income (TL, x1000)	13.8 (2.4-60)	13.2(8.4-48)	12 (2.4-36)	14.4 (6-48)
Height (m)	1.671 (1.5-1.8)	1.7 (1.5-1.84)	1.65 (1.5-1.8)	1.62(1.5-1.8)
Weight (kg)	75 (56-103)	77.5 (45-103)	75 (67-88)	72(60-97)
BMI (kg/m²)	27.021 (18.29-40.23)	26.99 (19.2-36.06)	28.04 (21.6-34.37)	29.341 (22.08-39.11)
Waist (cm)	93.5 (65-122)	96 (61-120)	93 (78-120)	88.5 (68-115)
Hip (cm)	110 (85-120)	109 (89-114)	109 (87-125)	109.5 (94-125)
Total cholesterol (mg/dl)	186 (106-291)	164 (109-389)	171 (109-232)	182 (129-261)
HDL (mg/dl)	46.5 (31-56)	42 (25-65)	46 (33-54)	46 (34-75)
W/H	0.86 (0.08-1.1)	0.89 (0.68-1.09)	0.86 (0.72-1.09)	0.81 (0.7-1.17)

BMI: body mass index; cm: centimeter; dl: desiliter; HDL: high density lipoprotein; kg: kilogram; m: meter; mg: milligram; W/H: waist and hip ratio; TL: Turkish Lira

Table 2. Descriptive statistics and comparisons among the groups of CAL, NT, PISA, PESA, and FRS

Variable	Groups	N	N*	Mean	SEMean	Average of Rank	StDev	Minimum	Median	Maximum
CAL	1	20	0	3.6905	0.0991	55.6 [a]	0.4434	3.0300	3.5900	4.4600
	2	20	0	2.2285	0.0857	20.8 [b]	0.3835	1.6500	2.1250	2.8400
	3	21	0	3.860	0.155	58.2 [a]	0.708	2.750	3.730	6.350
	4	16	0	2.0544	0.0623	15.9 [b]	0.2493	1.7300	1.9900	2.5700
FRS	1	20	0	8.20	1.32	47.4 [ab]	5.88	1.00	7.00	20.00
	2	20	0	8.55	1.19	49.5 [a]	5.34	1.00	9.00	20.00
	3	21	0	5.190	0.938	36.5 [b]	4.297	1.000	3.000	16.000
	4	16	0	1.813	0.368	18.6 [c]	1.471	1.000	1.000	5.000
NT	1	20	0	21.30	1.35	35.0 [b]	6.04	10.00	22.50	30.00
	2	20	0	21.25	1.31	34.1 [b]	5.87	9.00	23.50	31.00
	3	21	0	21.67	1.21	35.3 [b]	5.53	9.00	24.00	28.00
	4	16	0	26.00	1.00	55.1 [a]	4.02	16.00	28.00	30.00
PISA	1	20	0	718.9	64.3	57.0 [a]	287.5	174.0	691.8	1212.1
	2	20	0	167.8	26.0	17.9 [b]	116.3	28.1	124.7	427.3
	3	21	0	689.0	67.8	55.3 [a]	310.6	305.4	625.0	1787.1
	4	16	0	195.8	27.3	21.4 [b]	109.1	28.1	200.2	427.1
PESA	1	20	0	1464	117	50.7 [a]	522	564	1526	2555
	2	20	0	838.6	62.4	24.2 [b]	279.3	326.3	944.4	1225.1
	3	21	0	1462.1	97.2	52.1 [a]	445.3	598.9	1434.5	2398.9
	4	16	0	905.8	43.3	25.7 [b]	173.2	674.8	875.2	1224.7

BOP: Bleeding on Probing; CAL: Clinical Attachment Loss; FRS: Framingham Risk Score; NT: number of teeth; PD: Probing Depth; PESA: Periodontal epithelial Surface Area; PISA: Periodontal inflamed Surface Area; Kruskall-Wallis and Bonferonni-Dunn tests (p<0.05). Superscripts with the same letter indicate that there is no statistically significant difference (p>0.05).

The Kruskall-Wallis test has revealed that the FRS scores were significantly different among the median ranks of the groups (p<0.01). Bonferonni-Dunn test results were shown with Latin letters on Tables 2 and 3. The FRS values were significantly higher in Groups 1, 2 and 3 than Group 4 (p<0.01), and higher in Group 2 than Group 3 (p<0.01); however, not statistically significantly different in Group 1 than the Groups 2 and 3 (p<0.01).

Table 3. Descriptive statistics for BOP and PD

Variable	Group	N	N*	Mean	SEMean	StDev	Minimum	Median	Maximum
BOP	1	20	0	47.15 [a]	3.18	14.22	27.01	45.86	79.48
	2	20	0	19.05 [b]	2.28	10.21	6.14	16.66	45.37
	3	21	0	46.81 [a]	4.15	19.00	15.97	45.83	87.03
	4	16	0	22.01 [b]	2.85	11.39	7.50	19.77	40.47
PD	1	20	0	3.248 [a]	0.110	0.493	2.230	3.185	4.160
	2	20	0	2.143 [b]	0.0866	0.3873	1.4000	2.1200	2.7500
	3	21	0	3.409 [a]	0.0923	0.4232	2.7500	3.4100	4.2600
	4	16	0	1.974 [b]	0.0765	0.3058	1.3300	1.9550	2.4500

BOP: Bleeding on Probing; PD: Probing Depth; One-way ANOVA and Tukey test (p<0.05). Superscripts with the same letter indicate that there is no statistically significant difference (p>0.05).

Table 4. The correlations between FRS and NT, systemic inflammatory burden and periodontal parameters

Groups	Parameters	r	p
CAD (+) P(+/-) (Group 1+2, n= 40)	PESA-NT	0.585	<0.0001
	FRS-NT	-0.468	0.004
	FRS-PISA	0.503	0.002
CAD (-) P(+/-) (Group 3+4, n= 37)	FRS-PD	0.393	0.016
	FRS-CAL	0.604	<0.0001
	FRS-BOP	0.508	<0.0001
Whole group (N=77)	FRS-NT	-0.253	0.027

BOP: Bleeding on Probing; CAD: Coronary Artery Disease; CAL: Clinical Attachment Loss; FRS: Framingham Risk Score; NT: number of teeth; P: periodontitis; PD: Probing Depth; PESA: Periodontal epithelial Surface Area ; PISA: Periodontal inflamed Surface Area; r: Pearson Correlation coefficient. Pearson correlation analysis, p<0.05

The statistically significant correlations were shown in Table 4. FRS has shown significant strong correlations with all periodontal and systemic inflammatory burden parameters and NT in CAD (-) groups (p<0.05, Table 4). The number of teeth in the whole group has shown a negative correlation with FRS (p<0.05).

DISCUSSION

In the present study, periodontitis and related systemic inflammatory burden were investigated regarding their correlation with the future cardiovascular events' risk. Systemic inflammatory burden has presented significant strong correlations with NT and FRS. Besides, the parameters investigated (PISA, PESA, and FRS) have shown successful functions in discriminating the groups.

The immuno-inflammatory response and homeostasis were thought to associate with the atherosclerosis and

periodontitis when the cellular mechanisms taken into consideration. This association suggested by experimental studies become complicated when the multifactorial nature of both diseases in humans taken into account. Low-level chronic inflammation plays a role and included in the risk factors for atherosclerosis.[16] The platelet aggregation induced by oral bacteria, the increased serum levels of the pro-inflammatory mediators and related strong inflammatory response development, and the effect of the increased circular levels of bacterial and inflammatory products related to bacteremia on the endothelial cells are suggested to be the atherogenic mechanisms.[17] Currently, periodontitis has gained a great interest because it might have the potential to get a substructure for the atherosclerosis and cardiovascular diseases regarding its infectious and inflammatory features.[18]

Periodontitis results in loss of teeth if not treated.[19] Thus, it was thought that number/loss of teeth might have an association with CVD.[20,21] Studies have revealed a relationship between loss of teeth and CVD mortality.[22] Moreover, Holmlund[19] have investigated this relationship with stratification of the NT (<10, 10-14 teeth,[15-19] teeth etc.), and reported that the mortality risk increased while the NT decreased (approximately 7 fold higher risk when the number of teeth <10 than >25). Janket[23] have reported that the CVD survival was ameliorated 27% in every increase of 10 teeth. Zanella[24] have recently reported that tooth loss was significantly associated with a higher chance of having at least one obstructed vessel and with vessel obstruction ≥ 50%. Substantially, the evaluation of number/loss of teeth should be evaluated carefully in the relationship between periodontitis and CAD, since the reason of teeth loss might be related to orthodontic reasons, caries or periodontal treatment. Although extracted teeth for periodontal reasons might eliminate the cumulative systemic effect, the systemic effect of periodontal disease still might be partially exist.[21] If the study sample for the present study was obtained only from the Periodontology Clinic, we might suggest that the teeth loss might be related to periodontal reasons. However, our study group was selected from the Cardiology Clinic, so the teeth loss might depend on other reasons. The recruitment of the population from medical offices rather than dental offices provides more reliable results. The stratification and related evaluation was not aimed, and the number of our study group was not enough for such an analysis. NT was correlated with FRS in the whole group (N=77); and the patients without CAD and without periodontitis (Group 4) has the highest NT. Larger populations should be evaluated to clarify the relationship between the future CVD risk and NT.

The widely used measurements/indexes PD, CAL and BOP provide inside for the past and current activity of periodontitis.[25] The whole mouth examination has prevented the underestimation of the present periodontal status in the present study.[26] The PISA value obtained using BOP, CAL and PD is a measurement suggested to classify periodontitis and note the systemic effect of periodontitis, since the inflammatory surface area could be measured. The bacteria and bacterial products use the route constituted by inflamed and ulcerated periodontal pocket surface to the circulation and result in systemic inflammatory response.[11] In the present study, the periodontal disease classification regarding PISA was not made; the effect of PISA on future CAD risk was evaluated. However, the full-mouth recording and not having evaluated the "self-reported periodontal health" are the strengths of the present study.

The correlation between the PISA and FRS values was an interesting finding in CAD (-) groups (Group 3 and Group 4). The absence of CAD was verified by coronary angiography in these groups. All of the other risk factors (gender, increased LDL, HDL, smoking, presence of hypertension and usage of anti-hypertensives) have not presented significant differences between the groups. Besides, the adjustment of groups regarding age was also made. Thus, the positive correlations between the future CAD risks with PISA might be evaluated to be related with the presence of the periodontitis. The PD, CAL and BOP were used to calculate the PISA values and have presented strong correlations with FRS. Besides, the insignificance between the Group 1 and Group 2 regarding FRS was an expected finding, because the patients in these groups were verified with angiography having CAD. The similarity between the Group 1 and 3 regarding FRS was an interesting finding, because Group 3 was verified angiographically not having CAD, however, both of the groups have periodontitis. The age was found significantly higher in the Groups 1 and 2 than the Groups 3 and 4 ($p<0.05$). however, after the adjustment regarding age, the investigated modifiable and un-modifiable risk factors, such as gender, smoking, usage of anti-hypertensive drugs, BMI, waist/hip ratio, serum lipid parameters, and serum hs-CRP levels (data not shown) have not presented any significant difference among the groups ($p>0.05$). Besides, the adjustment regarding age and gender has not changed the results (data not shown).

The epidemiologic studies have reported that periodontitis might have associations with CVD.[27,28] However, the American Heart Association has also stated in 2012, that there is no class A or B evidence that periodontal disease causes atherosclerotic vascular disease, and cautioned that statements that imply a causative association, or that specific therapeutic interventions may be useful, are unwarranted.[10] Currently, Ryden[29] have reported the possibility of an independent relationship between peri-

odontitis and CVD manifestations. In a current meta-analysis,[28] it has been also suggested that PD was significantly and independently associated with an increased risk of CAD, and further studies are warranted which would have significant implications on current clinical practice as to whether patients with periodontal disease should have frequent dental check-up with an emphasis on CAD assessment. Nguyen[30] have also suggested further interventional and longitudinal studies to clarify the exact biological mechanisms and confirm a direct or causal relationship.

The observational character of the present study and the limited sample size might be considered as limitations. This relationship/contribution might be clarified when the associations of the PISA values with FRS (or with other scoring systems) would be evaluated before and after periodontal therapy in case of the careful adjustment of the shared risk factors in a larger study population.

CONCLUSIONS

Despite the above mentioned limitations, our results and similar studies are important, although they have suggested indirect contribution of periodontitis on CAD development or an independent relationship between the periodontitis and CAD. The correlation between the PISA and FRS values was an interesting finding in CAD (-) groups deserve further attention. The consideration about periodontitis and referral to the Periodontology Clinics from the Cardiology Clinics should have taken a place in routine practice.

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