The Relationship Between the Severity of Atherosclerosis and Periodontal Disease Index in Diabetic Patients

Arda Güler[1](İD), Emre Yılmaz[2](İD), Ali Rıza Demir[1](İD), Neşe Bayıroğlu[3](İD), Ali Kemal Kalkan[1](İD), Fatih Uzun[1](İD), Mehmet Ertürk[1](İD)

[1] Clinic of Cardiology, İstanbul Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital, İstanbul, Türkiye
[2] Department of Cardiology, Giresun University Faculty of Medicine, Giresun, Türkiye
[3] Department of Dentistry, İstanbul Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital, İstanbul, Türkiye

ABSTRACT

Introduction: Although the link between coronary artery disease (CAD) and periodontal disease has previously been demonstrated, there is insufficient research on how the severity of both diseases impact each other. This study aimed to investigate the relationship between the severity of periodontal disease and the diffuseness of CAD in diabetic patients.

Patients and Methods: A total of 127 diabetic patients with CAD were included in this study. The SYNTAX score determined the diffuseness of CAD, and the patients were divided into two groups as the SYNTAX score ≤22 and >22. The plaque index and periodontal disease index were used in the dental evaluation. The relationship of these indexes to the diffuseness of coronary artery disease has been investigated.

Results: In this study, the plaque index and periodontal disease index correlate significantly with the high SYNTAX score in diabetic patients. In univariate logistic regression analysis, PDI was a predictive variable for the SYNTAX score above 22 in diabetic patients. According to the ROC curve analysis, it was shown that the periodontal disease index of 4.3 could predict a high SYNTAX score.

Conclusion: To sum up, we found a significant relationship between periodontal disease severity and coronary artery disease diffuseness. PDI was found to be a predictor of a high SYNTAX score.

Key Words: Coronary artery disease; SYNTAX score; periodontal disease; diabetes mellitus

Diyabetik Hastalarda Ateroskleroz Şiddeti ile Periodontal Hastalık İndeksi Arasındaki İlişki

ÖZET

Giriş: Koroner arter hastalığı (KAH) ile periodontal hastalık arasındaki ilişki daha önce gösterilmiş olsa da bu hastalıkların şiddetinin birbirini nasıl etkilediğine dair yeterli veri bulunmamaktadır. Bu çalışma, diyabetik hastalarda periodontal hastalık şiddeti ile KAH'ın yaygınlığı arasındaki ilişkiyi araştırmayı amaçlamıştır.

Hastalar ve Yöntem: Çalışmamızda diyabeti olan toplam 127 hasta değerlendirildi. KAH yaygınlığını belirlemede SYNTAX skoru kullanıldı ve hastalar SYNTAX skoru ≤22 ve >22 olarak iki gruba ayrıldı. Dental değerlendirmede plak indeksi ve periodontal hastalık indeksi kullanıldı. Bu indekslerin koroner arter hastalığının yaygınlığı ile ilişkisi araştırıldı.

Bulgular: Bu çalışmada, diyabetik hastalarda plak indeksi ve periodontal hastalık indeksi (PDI) yüksek SYNTAX skoru ile anlamlı bir şekilde ilişkili bulundu. Tek değişkenli lojistik regresyon analizinde PDI, diyabetik hastalarda 22'nin üzerindeki SYNTAX skoru için öngörücü bir değişkendi. ROC eğrisi analizine göre, 4.3 olan periodontal hastalık indeksinin yüksek bir SYNTAX skorunu öngörebileceği gösterildi.

Sonuç: Sonuç olarak, periodontal hastalık şiddeti ile koroner arter hastalığı yaygınlığı arasında anlamlı bir ilişki saptadık. PDI'nin yüksek bir SYNTAX skoru açısından da bağımsız bir öngördürücü olduğunu belirledik.

Anahtar Kelimeler: Koroner arter hastalığı; SYNTAX skoru; periodontal hastalık; diyabetes mellitus

Cite this article as: *Güler A, Yılmaz E, Demir AR, Bayıroğlu N, Kalkan AK, Uzun F, et al. The relationship between the severity of atherosclerosis and periodontal disease index in diabetic patients. Koşuyolu Heart J 2022;25(2):149-156.*

Correspondence

Arda Güler

E-mail: drardaguler@gmail.com
Submitted: 29.01.2022
Accepted: 03.04.2022
Available Online Date: 20.08.2022

INTRODUCTION

Coronary artery disease (CAD) is one of the leading causes of mortality and morbidity worldwide. Although the etiologic basis of atherosclerosis is rupture after inflammation in stable plaque and subsequent thrombosis, the contribution of many factors in this mechanism has been shown in clinical studies[1]. In addition to many traditional risk factors such as diabetes, obesity, hypertension, hyperlipidemia, and smoking, other pathogenic factors are influential in the development of CAD[2]. Especially in recent studies, infection and inflammation processes are shown to have an impact on the development and progression of thrombosis and atherosclerosis[3].

Periodontal disease (PD) is a chronic inflammation of the gum and supportive tissue with a silent course observed in approximately 60% of the population[4]. The disease has a broad spectrum ranging from gingival bleeding to gingivitis, tooth loss, and alveolar bone resorption[5]. There is increasing evidence that periodontal disease increases the severity of coronary artery disease[6,7].

Diabetes mellitus (DM) has been identified as a common risk factor for these two diseases. A two-way relationship between periodontal disease and diabetes has been shown in previous studies[8]. Although diabetes is a significant risk factor for coronary artery disease, diabetes has recently been described as an equivalent syndrome of coronary artery disease[9]. There is insufficient data on the relationship between PD and CAD[10-12]. PD is a common disease in the community, but the diagnosis is mostly missed. Considering the effect of its progression on the development of atherosclerosis, early recognition will be an essential step in the diagnosis and prevention of coronary artery disease[10]. In order to demonstrate this relationship, in this study, diabetic patients with more frequent periodontal disease were evaluated. This aim was to evaluate the relationship between the severity of periodontal disease and the diffuseness of coronary artery disease in diabetic patients.

PATIENTS and METHODS

Diabetic patients with suspected myocardial ischemia documented with non-invasive stress tests or clinical examination were prospectively evaluated in our study between January 2018 to June 2018. Among these individuals, patients with 50% or more stenosis in any coronary artery shown by coronary angiography were included in our study. The local ethics committee approved the study. All examinations were acknowledged and consented to by the patients, and consent forms were signed.

Patients were excluded if they met any of the following criteria: acute coronary syndrome patients, patients with a history of periodontal treatment in the last year, patients with malignancy, patients with autoimmune or rheumatologic disease, immunocompromised patients, patients with a history of coronary bypass graft surgery prior to study start date, patients with total or near-total dental prosthesis where periodontal disease cannot be evaluated, patients who did not consent to the informed consent form and did not want to participate in the study.

Clinical and Laboratory Assessment

Demographics and medical records of the patients were reviewed and noted. Physical exam measurements included height, weight, waist circumference, and systolic and diastolic blood pressure. Hypertension was defined as systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg, or treatment with anti-hypertensive medication[13]. Hyperlipidemia was considered positive for the use of antihyperlipidemic drugs or patients with total cholesterol ≥200 mg/dL or LDL-cholesterol ≥130 mg/dL or HDL-cholesterol <40 mg/dL[14].

Prior to coronary angiography, our hospital's laboratory performed routine blood counts (hemoglobin, WBC, platelet, neutrophil, lymphocyte, monocyte) and biochemical assays (fasting blood glucose, creatinine, total cholesterol, LDL, HDL, triglyceride, CRP) on all patients.

Diagnosis of Diabetes Mellitus

The diabetes mellitus inclusion criteria were as follows:

1. Fasting (≥8 hours fasting) plasma glucose ≥126 mg/dL

2. Oral glucose tolerance test (75 g glucose) second-hour plasma glucose ≥200 mg/dL

3. Random plasma glucose ≥200 mg/dL in the presence of diabetes symptoms

4. Based on the presence of any of the HbA1c 6-6.5% diagnostic criteria measured by the standardized method or whether the patient had been previously diagnosed with DM and was taking antidiabetic medication[15].

Evaluation of Atherosclerosis Severity

Standard selective coronary angiography (CAG) procedures were applied to all patients under elective conditions by transfemoral or transradial procedures in our hospital's catheter laboratory. Siemens coronary angiography device (Artis zee) was used for coronary angiography. Selective left coronary angiography was performed in standard six views, and right coronary angiography was performed in two views. Interpretation of coronary angiography was performed by two experienced cardiologists who did not know the inclusion and clinical status of the patients.

In order to determine the severity of atherosclerosis, the SYNTAX scoring system was used, in which each coronary le-

sion was evaluated separately[16]. The calculation of the SYNTAX score was performed by two experienced cardiologists who were blinded to the patients, and inter-observer reproducibility of SYNTAX calculation was tested offline. As a result of the calculation, patients were divided into two groups: those with a high SYNTAX group with a score above 22 and a low SYNTAX group with patients with a SYNTAX score of 22 and below.

Dental Evaluation

The periodontal evaluation was performed by an experienced dentist in our clinic, who was blinded to the coronary angiography results of the patients. A dental evaluation of the patients was made before coronary angiography. The data obtained after the evaluation were recorded in the data form.

In the periodontal evaluation, plaque index (PI) and periodontal disease index (PDI) defined by Sigurd P. Ramfjord in 1959 were used[17,18]. The teeth numbered 16, 21, 24, 36, 41, and 44 described by the Ramfjord are called Ramfjord teeth. The buccal, lingual, and interproximal surfaces of these teeth were evaluated separately. Replacement teeth were not used in place of previously lost teeth. In this index system, attachment loss can be evaluated indirectly. Because of this feature is an effective index method to determine the periodontal status[17]. The evaluation was first made visually, and then the pocket depth was measured. Pocket depth measurement was made using a Medesy 548/4 CP15 brand periodontal probe.

The PI is defined as the amount of microbial dental plaque on the tooth surface; a scale of 0 to 3 was applied. A score of 0 indicates no plaque on the tooth; a score of 1, a hardly visible thin film of plaque; 2, the moderate plaque at the gingival margin; and 3, heavy plaque extending into the interdental area. For PDI, which represents the severity of gingivitis and periodontitis, a scale of 0 to 6 was applied. The PDI score of 0 indicates no inflammation; 1, mild gingivitis; 2, moderate gingivitis; 3, advanced gingivitis; 4, up to 3 mm attachment loss; 5, 3 to 6 mm attachment loss; and 6, more than 6 mm attachment loss. A PDI score of three or below indicates no periodontitis[19].

Statistical Analysis

Statistical analysis of the study was performed with SPSS Version 24.0 software (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as mean ± SD; categorical variables were presented as the number (percentage) of patients. Statistical analysis of numerical variables was performed by Student's t-test or Mann-Whitney U test, and categorical variables were analyzed by Chi-square or Fisher exact test. Pearson or Spearman analyses evaluated the correlation between periodontal disease index and other numerical variables. The logistic regression analysis was used to determine whether the periodontal disease index was an independent predictor for identifying diabetic patients with a SYNTAX score above 22. If the p-value was <0.1 in univariate analysis and <0.05 in multivariate analysis, it was considered significant. The receiver operating characteristic (ROC) curve was used to determine the predictive value of the periodontal disease index. The area under the ROC curve was above 0.5, and the p-value <0.05 was considered statistically significant.

RESULTS

The mean age of the study population was 58.3 ± 7.9 years. 76 (59.8%) of these patients were male, and 51 (40.2%) were female. According to the SYNTAX score calculated after coronary angiography, the patients were divided into two groups. A high SYNTAX score was found in 38 (29.9%) patients. Table 1 presents data on the baseline characteristics, demographics, and clinical features of the two groups. In the group with high SYNTAX score, the number of male (p= 0.013), smoking (p= 0.015), hypertensive (p= 0.018) and hyperlipidemic (p= 0.023) patients were found to be significantly higher than the group with low SYNTAX score. Neutrophil (p= 0.021) and C reactive protein (p< 0.001) levels were also significantly higher in the high SYNTAX score group. The group with high SYNTAX had a significantly higher periodontal disease index (p< 0.001), and plaque index values (p< 0.001).

The correlation of plaque index and periodontal disease index with other variables is shown in Table 2. It was found that PDI had a significant correlation with SYNTAX score (p< 0.001), periodontal disease index was high (r= 0.737) (Figure 1), and plaque index was found to have a poor correlation (r= 0.473).

Univariate logistic regression analysis was performed to determine the variables predicting high SYNTAX score in diabetic patients. The analysis resulted with male gender [p= 0.043, OR (95% CI)= 5.263 (1.051-26.370)], hypertension [p= 0.034, OR (95% CI)= 6.489 (1.154-36.481)] and periodontal disease index [p< 0.001, OR (95% CI)= 8.169 (3.107-21.479)] as independent predictors for the high SYNTAX score (Table 3).

Figure 2 shows the ROC curve for PDI estimation for the high SYNTAX score. According to this analysis, PDI can detect a SYNTAX score above 22 with 92% sensitivity and 90% specificity at a value of 4.3 [p< 0.001, AUC (95% CI)= 0.934 (0.888-0.980)].

DISCUSSION

Our study discovered that periodontal disease index and plaque index, both significant dental evaluation criteria, were

Table 1. Demographic, laboratory, drug use, and dental evaluation characteristics of patients according to SYNTAX scores

	Total (n= 127)	SYNTAX score≤ 22 (n= 89)	SYNTAX score> 22 (n= 38)	p
Age, (years)	58.33 ± 7.87	58.30 ± 8.08	58.39 ± 7.44	0.952
Gender (male), n (%)	76 (59.8)	47 (53.3)	29 (76.3)	**0.013**
BMI, kg/m^2	30.07 ± 3.15	29.92 ± 3.17	30.40 ± 3.12	0.432
Smoking, n (%)	56 (41.1)	33 (37.1)	23 (60.5)	**0.015**
Hypertension, n (%)	77 (60.6)	48 (53.9)	29 (76.3)	**0.018**
Hyperlipidemia, n (%)	64 (50.4)	39 (43.8)	25 (65.8)	**0.023**
Beta-blocker use n (%)	32 (25.2)	20 (22.5)	12 (31.6)	0.279
ACEi-ARB use, n (%)	64 (50.4)	47 (52.8)	17 (44.7)	0.405
Statin use, n (%)	48 (37.8)	30 (33.7)	18 (47.4)	0.146
CCB use, n (%)	28 (22.0)	18 (20.2)	10 (26.3)	0.448
OAD, n (%)	118 (92.9)	84 (94.4)	34 (89.5)	0.450
Insulin, n (%)	24 (18.9)	14 (15.7)	10 (26.3)	0.163
Glucose, mg/dL	154 (134-191)	151 (132-184.5)	170.5 (140-207)	0.085
Creatinine, mg/dL	0.81 ± 0.27	0.81 ± 0.30	0.82 ± 0.19	0.907
T. Cholesterol, mg/dL	185.6 ± 40.1	184.8 ± 40.7	187.4 ± 39.3	0.740
LDL, mg/dL	109 ± 37.7	106.9 ± 38.3	113.8 ± 36.5	0.352
HDL, mg/dL	43.5 ± 11.9	44.2 ± 12.3	41.8 ± 10.8	0.296
Triglyceride, mg/dL	150 (116-195)	150 (117-207)	147 (115-184)	0.796
Hemoglobin, g/dL	13.64 ± 1.55	13.54 ± 1.51	13.87 ± 1.61	0.271
WBC cells, 10^3/uL	8.57 ± 2.02	8.6 ± 2.14	8.49 ± 1.75	0.780
Neutrophils, 10^3/uL	4.89 ± 1.21	4.72 ± 1.21	5.26 ± 1.14	**0.021**
Lymphocytes, 10^3/uL	2.54 ± 0.81	2.52 ± 0.81	2.60 ± 0.83	0.626
CRP, mg/L	5.0 (3.0-11.0)	4.0 (2.0-8.0)	11.5 (4.0-16.0)	**<0.001**
PDI	3.31 ± 1.70	2.57 ± 1.42	5.05 ± 0.78	**<0.001**
PI	2.01 ± 0.87	1.77 ± 0.85	2.58 ± 0.65	**<0.001**

ACEi: Angiotensin-converting-enzyme inhibitors, ARB: Angiotensin II receptor blockers, BMI: Body-mass index, CCB: Calcium channel blocker, CRP: C reactive protein, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, OAD: Oral antidiabetic drugs, PDI: Periodontal disease index, PI: Plaque index, T: Total, WBC: White blood cell.

associated with a high SYNTAX score and that the periodontal disease index was an independent predictor of a SYNTAX score of > 22.

Cardiovascular diseases (CVD) are the most important cause of morbidity and mortality worldwide. Coronary artery disease (CAD) is the leading cause of mortality in this group of patients[20]. The primary mechanism of CAD formation is atherosclerosis. Inflammation takes an important place in the development of atherosclerosis[21]. This process suggests that there may be a relationship between CAD and other inflammatory diseases. Periodontal diseases (PD) are similar to atherosclerosis after an inflammatory process[22]. Moreover, it has been shown in some studies that PD triggers systemic inflammation and contributes to the development of other inflammatory diseases[23,24]. However, the inconsistent results obtained in previous studies between CAD and PD indicate that more comprehensive studies are needed to explain the relationship between these two diseases.

Firstly, the point should be emphasized is that diabetic patients with high-risk conditions for both periodontal diseases and coronary artery disease were included to our study in terms of compliance with real-life data. Epidemiological studies have

Table 2. Correlation of periodontal disease index and plaque index with other variables

	Periodontal Disease Index		Plaque Index	
	r	p	r	p
Age (years)	0.128	0.151	0.029	0.746
BMI	0.182	**0.041**	0.099	0.268
Glucose	0.151	0.090	0.166	0.062
Creatinine	0.021	0.812	0.076	0.398
T. Cholesterol	-0.155	0.083	-0.118	0.186
LDL	-0.108	0.226	-0.116	0.196
HDL	-0.093	0.299	-0.085	0.341
Triglyceride	-0.093	0.296	-0.015	0.868
Hemoglobin	0.100	0.261	0.105	0.239
WBC	-0.005	0.957	-0.010	0.907
Neutrophil	0.295	**0.001**	0.139	0.120
Lymphocyte	-0.001	0.991	0.014	0.875
CRP	0.462	**<0.001**	0.205	**0.021**
SYNTAX Score	0.737	**<0.001**	0.473	**<0.001**

BMI: Body-mass index, CRP: C-reactive protein, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, T: Total, WBC: White blood cell.

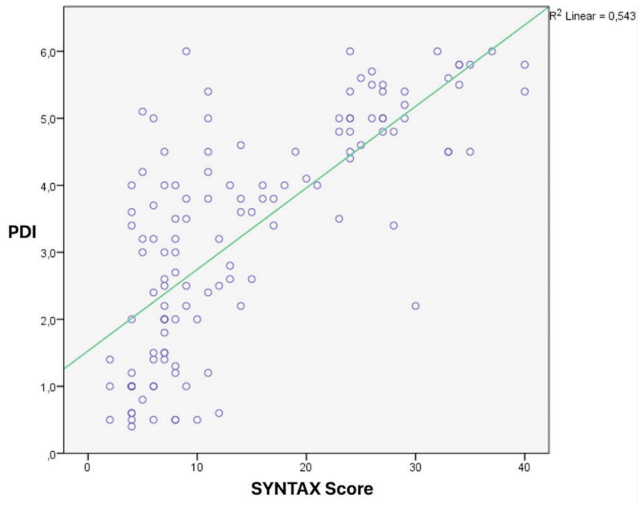

Figure 1. Correlation chart between periodontal disease index (PDI) and SYNTAX score.

shown that DM is a risk factor for PD[25]. It has been shown that periodontal disease is more frequent, and alveolar bone loss is high, especially in patients with poor glycemic control. Many factors increase the frequency and severity of periodontal disease in diabetic patients. These include increased oxidative stress, altered polymorphonuclear leukocyte functions, changes in immune response, formation of atheroma due to increased LDL levels, collagen of the periodontal ligament, and AGE accumulation in gingival capillaries.

Groves et al. investigated patients with type 1 DM to find the association of periodontal disease with coronary artery calcium score and the progression of calcium score[26]. In that study, 473 of the 1021 patients had type 1 DM, and periodontal disease was associated with coronary artery calcium score ($p< 0.001$). Similarly, our study found that periodontal disease is associated with the prevalence of coronary artery disease in diabetic patients. Furthermore, the periodontal disease index which demonstrates the severity of the periodontal disease was found to be a parameter that can predict the prevalence of coronary artery disease. Moreover, in the study conducted by Groves et al., the periodontal disease level was evaluated with the patient declaration, and in our study, periodontal evaluation was made using the clinical criteria. In addition, the evaluation of patients with coronary angiography, which is the definitive diagnostic method of coronary artery disease, rather than coronary artery calcium score, increases the power of our study. In conclusion, both studies showed that periodontal disease significantly correlates with coronary artery disease in diabetic patients.

J. Yang et al. conducted a study to investigate the relationship between CAD and the severity of PH in the Chinese population, where 115 patients were retrospectively evaluated[27]. In that study, the Gensini score was used to determine the severity of CAD, while the severity of periodontal disease was determined by Armitage classification[28]. Clinical attachment loss,

Table 3. Univariate and multivariate regression analysis to determine the prediction of high SYNTAX score

	Univariate analyses		Multivariate analyses	
	OR (CI 95%)	**p**	**OR (CI 95%)**	**p**
Age (years)	1.001 (0.954-1.051)	0.952		
Gender (male)	2.879 (1.224-6.776)	**0.015**	5.263 (1.051-26.370)	**0.043**
BMI	1.050 (0.930-1.186)	0.429		
Smoking	2.602 (1.193-5.675)	**0.016**	1.483 (0.338-6.509)	0.601
Hypertension	2.752 (1.169-6.479)	**0.020**	6.489 (1.154-36.481)	**0.034**
Hyperlipidemia	2.465 (1.119-5.434)	**0.025**	2.091 (0.396-11.033)	0.385
Glucose	1.005 (0.999-1.011)	0.133		
Creatinine	1.088 (0.270-4.392)	0.906		
T. Cholesterol	1.002 (0.992-1.011)	0.737		
LDL	1.005 (0.995-1.015)	0.351		
HDL	0.981 (0.948-1.017)	0.297		
Triglyceride	1.000 (0.996-1.004)	0.940		
Hemoglobin	1.155 (0.894-1.493)	0.270		
WBC	0.973 (0.805-1.177)	0.778		
Neutrophil	1.469 (1.051-2.053)	**0.024**	1.308 (0.560-3.056)	0.535
Lymphocyte	1.124 (0.705-1.792)	0.623		
CRP	1.170 (1.087-1.259)	**<0.001**	1.013 (0.899-1.142)	0.830
PDI	7.207 (3.417-15.201)	**<0.001**	8.169 (3.107-21.479)	**<0.001**
PI	3.705 (2.066-6.643)	**<0.001**		

BMI: Body-mass index, CRP: C-reactive protein, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, PDI: Periodontal disease index, PI: plaque index, T: Total, WBC: White blood cell.

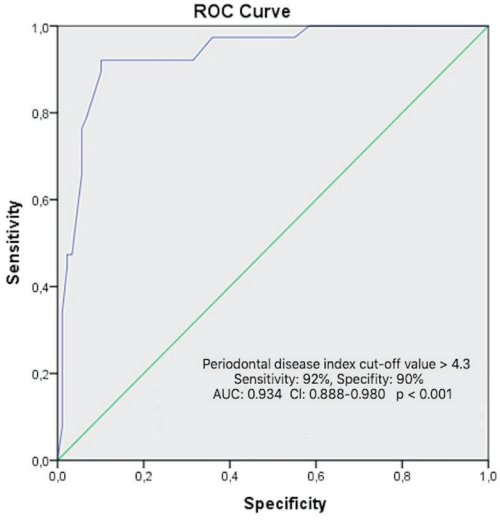

Figure 2. Periodontal disease index (PDI) ROC curve analyses for high SYNTAX score (Blue line periodontal index, green line reference line).

pocket depth, bleeding index, calculus index, and plaque index were the parameters used in the dental evaluation. As a result of this study, a significant correlation was found between generalized coronary artery disease and severe periodontal disease determined by the Gensini score (p< 0.001). In the multivariable regression analysis, pocket depth and plaque index were found to be predictive parameters of the Gensini score.

Similarly, in our study, statistically significant data obtained demonstrated a link between the prevalence of coronary artery disease and the severity of periodontal disease. We used the periodontal disease index defined by Ramfjord for evaluating the PD severity, rather than the Armitage method. There is no clear consensus on which method is more successful in periodontal evaluation. SYNTAX score was used to evaluate the prevalence of CAD, rather than the Gensini score. The Gensini score is a widely recognized scoring system for assessing atherosclerotic plaque burden in coronary arteries. However, the SYNTAX score has become a popular and fre-

quently used method in recent years. In the SYNTAX score, each coronary artery lesion is evaluated in detail with its characteristic features, and the severity of CAD is examined in several aspects[29]. In addition, the SYNTAX score is predictive of cardiac prognosis. As a result, it has regularly appeared in guidelines in recent years and remains an important reference in the treatment of coronary artery patients[29-31].

Study Limitations

The current study has potential limitations. In our study, the conditions that may be related to periodontal diseases, such as the education level of the individuals with periodontal disease, dental care, and regular dentist control, were not included in the demographic evaluations. The degree of tooth loss associated with CAD due to previous studies has not been evaluated in our study. In our study, a single physician performed the dental evaluations, and the level of inter-observer compliance and variability was not included in the dental evaluations.

CONCLUSION

Periodontal disease severity, periodontal disease index, and plaque index, which are the parameters we use to evaluate in our study, may be a factor in determining the severity of coronary artery disease determined by SYNTAX score in diabetic patients. The periodontal disease index was an independent predictor of the prevalence and severity of coronary artery disease among these dental parameters.

Ethics Committee Approval: The approval for this study was obtained from, İstanbul Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital Ethics Committee (Decision no: 2018-17, Date: 13.11.2018).

Informed Consent: This is retrospective study, we could not obtain written informed consent from the participants.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept/Design - FU; Analysis/Interpretation - EY; Data Collection - AG, NB; Writing - AG; Critical Revision - AKK; Final Approval - ME; Statistical Analysis - ARD; Overall Responsibility - AG.

Conflict of Interest: The authors declared that there was no conflict of interest during the preparation and publication of this article.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. Taqueti VR, Di Carli MF. Coronary microvascular disease pathogenic mechanisms and therapeutic options: JACC state-of-the-art review. J Am Coll Cardiol 2018;72:2625-41. [Crossref]
2. Smith SC Jr, Greenland P, Grundy SM. AHA Conference Proceedings. Prevention conference V: Beyond secondary prevention: Identifying the high-risk patient for primary prevention: executive summary. American Heart Association. Circulation 2000;101(1):111-6. [Crossref]
3. O'Connor S, Taylor C, Campbell LA, Epstein S, Libby P. Potential infectious etiologies of atherosclerosis: A multifactorial perspective. Emerg Infect Dis 2001;7:780-8. [Crossref]
4. Kinane DF, Stathopoulou PG, Papapanou PN. Periodontal diseases. Nat Rev Dis Primer 2017;3:17038. [Crossref]
5. Van Dyke TE. Control of inflammation and periodontitis. Periodontol 2000 2007;45:158-66. [Crossref]
6. Kodovazenitis G, Pitsavos C, Papadimitriou L, Vrotsos IA, Stefanadis C, Madianos PN. Association between periodontitis and acute myocardial infarction: A case-control study of a nondiabetic population. J Periodontal Res 2014;49:246-52. [Crossref]
7. Shrihari TG. Potential correlation between periodontitis and coronary heart disease-an overview. Gen Dent 2012;60:20-4.
8. Preshaw PM, Alba AL, Herrera D, Jepsen S, Konstantinidis A, Makrilakis K, et al. Periodontitis and diabetes: A two-way relationship. Diabetologia 2012;55:21-31. [Crossref]
9. Howard BV, Best LG, Galloway JM, Howard WJ, Jones K, Lee KT, et al. Coronary heart disease risk equivalence in diabetes depends on concomitant risk factors. Diabetes Care 2006;29:391-7. [Crossref]
10. Saffi MAL, Rabelo-Silva ER, Polanczyk CA, Furtado MV, Montenegro MM, Ribeiro IWJ, et al. Periodontal therapy and endothelial function in coronary artery disease: A randomized controlled trial. Oral Dis 2018;24:1349-57. [Crossref]
11. Pietiäinen M, Kopra KAE, Vuorenkoski J, Salminen A, Paju S, Mäntylä P, et al. Aggregatibacter actinomycetemcomitans serotypes associate with periodontal and coronary artery disease status. J Clin Periodontol 2018;45:413-21. [Crossref]
12. Li C, Lv Z, Shi Z, Zhu Y, Wu Y, Li L, et al. Periodontal therapy for the management of cardiovascular disease in patients with chronic periodontitis. Cochrane Database Syst Rev 2017;11:CD009197. [Crossref]
13. Oparil S, Acelajado MC, Bakris GL, Berlowitz DR, Cífková R, Dominiczak AF, et al. Hypertension. Nat Rev Dis Primer 2018;4:18014. [Crossref]
14. Nelson RH. Hyperlipidemia as a risk factor for cardiovascular disease. Prim Care 2013;40:195-211. [Crossref]
15. American Diabetes Association. Standards of medical care in diabetes-2012. Diabetes Care 2012;35:S11-63. [Crossref]
16. Sianos G, Morel M-A, Kappetein AP, Morice M-C, Colombo A, Dawkins K, et al. The SYNTAX Score: An angiographic tool grading the complexity of coronary artery disease. Euro Intervention J Eur Collab Work Group Interv Cardiol Eur Soc Cardiol 2005;1:219-27.
17. Ramfjord SP. Indices for prevalence and incidence of periodontal disease. J Periodontol 1959;30:51-59. [Crossref]
18. Löe H. The Gingival index, the plaque index and the retention index systems. J Periodontol 1967;38:610-6. [Crossref]
19. laffey N, Polyzois I, Ziaka P. An overview of nonsurgical and surgical therapy. Periodontol 2000 2004;36:35-44. [Crossref]
20. Malakar AK, Choudhury D, Halder B, Paul P, Uddin A, Chakraborty S. A review on coronary artery disease, its risk factors, and therapeutics. J Cell Physiol 2019;234:16812-23. [Crossref]
21. Hansson GK. Inflammation, atherosclerosis, and coronary artery disease. N Engl J Med 2005;352:1685-95. [Crossref]
22. Dentino A, Lee S, Mailhot J, Hefti AF. Principles of periodontology - Periodontol 2000 2013;61:16-53. [Crossref]
23. Periodontics Text and Evolve eBooks Package - 6th Edition. Available from: https://www.elsevier.com/books/periodontics-text-and-evolve-ebooks-package/eley/978-0-7020-4472-4 (Accessed date: 02 Kasım 2020).
24. Kim J, Amar S. Periodontal disease and systemic conditions: A bidirectional relationship. Odontology 2006;94:10-21. [Crossref]
25. Löe H. Periodontal disease. The sixth complication of diabetes mellitus. Diabetes Care 1993;16:329-34. [Crossref]

26. Groves DW, Krantz MJ, Hokanson JE, Johnson LR, Eckel RH, Kinney GL, et al. Comparison of frequency and duration of periodontal disease with progression of coronary artery calcium in patients with type 1 diabetes mellitus versus non-diabetics. Am J Cardiol 2015;116:833-7. [Crossref]

27. Yang H, Xiao L, Zhang L, Deepal S, Ye G, Zhang X. Epidemic trend of periodontal disease in elderly Chinese population, 1987-2015: a systematic review and meta-analysis. Sci Rep 2017;7:45000. [Crossref]

28. Rampidis GP, Benetos G, Benz DC, Giannopoulos AA, Buechel RR. A guide for Gensini Score calculation. Atherosclerosis 2019;287:181-3. [Crossref]

29. Chakrabarti AK, Gibson CM. The SYNTAX score: Usefulness, limitations, and future directions. J Invasive Cardiol 2011;23:511-2.

30. Authors/Task Force members, Windecker S, Kolh P, Alfonso F, Collet J-P, Cremer J, et al. 2014 ESC/EACTS Guidelines on myocardial revascularization: The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS) Developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI). Eur Heart J 2014;35:2541-619. [Crossref]

31. Escaned J, Collet C, Ryan N, De Maria GL, Walsh S, Sabate M, et al. Clinical outcomes of state-of-the-art percutaneous coronary revascularization in patients with de novo three vessel disease: 1-year results of the SYNTAX II study. Eur Heart J 2017;38:3124-34. [Crossref]