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**Relationship between the severity of coronary artery
disease (CAD) and periodontal indices**

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Abstract

Background and objective: coronary artery disease (CAD) is the most common cause of death in developing countries. Periodontitis is a chronic gram-negative anaerobic infection with high prevalence, leading to inflammation, pocket formation, resorption of alveolar bone, and ultimately tooth loss. This study aimed to evaluate association between the CAD severity and periodontal indexes.

Materials and Methods: in this double-blind case-control study, 200 patients were divided into two groups: case (125 patients with positive angiographic findings) and control (75 patients without positive angiographic findings). Data were analyzed using SPSS version 22.

Results: the frequency of gingivitis and periodontitis was significantly higher in patients with abnormal angiography ($P < 0.001$). BOP in case group was significantly higher than controls ($P < 0.001$). The number of involved teeth in case group and the control group was 0.32 and 0.13, respectively ($P = 0.007$). The number of teeth with PM in the case group was significantly higher. The PM severity in this group was higher than the control group ($P = 0.016$ and $P = 0.016$, respectively). The frequency of patients with CAL > 3mm and < 3mm was significantly higher in patients with abnormal angiography ($P < 0.001$). No significant difference was seen between two groups in the number of missing teeth ($P = 0.16$) and PI ($P = 0.302$).

Conclusions: There is a positive relationship between periodontal disease and CAD.

Keywords: Coronary artery disease (CAD); Periodontal indices; Angiography; Periodontist

Introduction

Periodontitis is a chronic gram-negative anaerobic infection with high prevalence (as high as 75% in adults in the US, among whom approximately 20–30% have severe forms of the disease) (Brown L et al., 1988–91; Douglass CW et al., 1993; Papapanou PN et al., 1996) leading to inflammation, pocket formation, resorption of alveolar bone, and ultimately tooth loss (Joshipura K et al., 1995; Orbak R et al., 2002; Baker PJ et al., 2002). Oral bacteria make these changes by some known

mechanisms, including antigens, endotoxins, and inflammatory cytokines. Therefore, these pathogens and inflammatory factors spread in the whole body and may thereby increase the risk for some systemic diseases such as myocardial infarction, stroke (Beck JD et al., 1998). In the other hand, coronary artery disease (CAD) is the most common cause of death in developing countries. CAD has a multifactorial etiology such as response to injury and immuno-inflammatory, lipogenic

and infectious mechanisms (Hackam DG et al., 2003). In recent decades, an interest in the field of evaluating the association between oral health and ischemic heart disease has been increased (Persson GR et al., 2008). Previous studies have determined the role of inflammation and its biomarkers in cardiovascular disease (Danesh J et al., 2004). However, these studies were not conclusive due to a lack of homogeneity, eliminating the effects of confounding variables, such as smoking, small sample size, and antithesis results (Hujoel PP et al., 2000; Bahekar AA et al., 2007; Cueto A et al., 2005; Nonnenmacher C et al., 2007). Therefore, the association between chronic periodontitis and CAD remains inconclusive. As to the best of our knowledge, there is not enough study about this issue; therefore, this study was designed to evaluate a probable association between the severity of CAD and periodontal indexes.

Materials and Methods

Study design and the target group

This double-blind case-control study was conducted in the Cardiology Department of Ahvaz Golestan Hospital, southwest of Iran, from November 2015 to May 2016. The patients with initial diagnosis of CAD with abnormalities in angiography (the case group) were compared to healthy subjects without positive findings in angiography (the control group). Inclusion criteria consisted of patients referred to the Cardiology Department of Ahvaz Golestan Hospital with an initial diagnosis of CAD (based on clinical signs and symptoms and ECG findings), signed a consent form to participate in the study and having age >18 years, and having more than six teeth. Exclusion criteria consisted of consuming immunosuppressive drugs, the presence of autoimmune or neoplastic diseases, a history of infective endocarditis, pregnancy or lactation, age < 18 years, and dissatisfaction to continue participation in the study. We also excluded patients with uncompleted data. All patients enrolled in this study with an initial diagnosis of CAD, after receiving appropriate treatment and improving the symptoms, were referred to a cardiologist for angiography.

The study flowchart is shown in figure 1. Two hundred five patients with an initial diagnosis of CAD by a cardiologist and based on clinical and para-clinical findings and inclusion and exclusion criteria were included.

Two hundred patients were included in the study, and five patients were excluded from the study due to having exclusion parameters; then, angiography was performed for all patients, and finally patients were divided into two groups; 125 individuals with positive findings in angiography (as the case group) and 75 individuals without positive findings in angiography (as the control group). The study received ethics approval from the Ethics Committee of Ahvaz University of Medical Sciences, and all participants gave written informed consent.

After obtaining informed consent, eligible patients were enrolled. Then oral health was evaluated for all patients. The oral health was determined by clinical examination that included visual and tactile inspection performed by a periodontist. The periodontist evaluated the number of missing teeth, clinical attachment loss, plaque index, bleeding on probing (BOP) (the presence or absence of bleeding on probing examination), pocket depth, pathologic mobility, the type of periodontal disease (normal, gingivitis, periodontitis), and furcation grading-Gilckman classification.

For evaluating clinical attachment loss (CAL), which is the extent of periodontal support destroyed around a tooth), the distance from the cemento-enamel junction (CEJ) to the gingival sulcus depth for each tooth was measured. Therefore, CAL was divided into three groups: without CAL (normal group), a clinical attachment of < 3 mm (mild group), and a clinical attachment >3 mm (the moderate to severe group).

For evaluating plaque index (PI) (an index for estimating the status of oral hygiene by measuring dental plaque that occurs in the areas adjacent to the gingival margin), scores from 0-3 are assigned to each of the four surfaces of the teeth (buccal, lingual, mesial and distal). The scores from the four areas of the tooth are added and divided by four in order to give the plaque index for the tooth with the following scores and criteria:

Scores	Criteria
0	No plaque
1	A film of plaque adhering to the free gingival margin and adjacent area of the tooth. The plaque may be seen in situ only after application of disclosing solution or by using the probe on the tooth surface.
2	Moderate accumulation of soft deposits within the gingival pocket, or the tooth and gingival margin which can be seen with the naked eye.
3	The abundance of soft matter within the gingival pocket and/or on the tooth and gingival margin.

For evaluating pocket depth (PD), the distance between the edges of the gingival margin to the epithelial attachment for four surfaces of each tooth was measured by the probe.

For evaluating pathologic mobility (PM), the handle of a metal mirror was put on one side and the finger on the other side of the teeth and movement in any direction were measured and graded based on the following criteria:

Grade	Criteria
0	No apparent mobility
1	Perceptible mobility <1mm
2	Vertical displacement (severe backlash in buccolingual direction and mesiodistal with vertical displacement)

Furcation grading- Gilckman classification was graded with the following criteria:

Grade	Criteria
1	<ul style="list-style-type: none"> • Incipient. • Just barely detectable with examination hand instruments
2	<ul style="list-style-type: none"> • Early bone loss • Examination hand instrument goes partially into the furcation, but not all the way through. • Furcation may be grade II on both sides of the tooth, but are not connected.
3	<ul style="list-style-type: none"> • Advanced bone loss • Examination hand instrument goes all the way through furcation, to the other side of the tooth. • Furcation is through-and-through.
4	<ul style="list-style-type: none"> • Through-and-through, plus furcation is clinically visible due to gingival recession

Data analysis

Data were analyzed and reported only for patients who completed the trial. Statistical analysis of data was performed using SPSS version 22. To compare qualitative variables between groups, the Chi-square test was performed. The normal distribution of all

studied parameters was checked with the Kolmogorov-Smirnov test. The student t-test and the paired t-test were used for variables distributed in a normal way; in addition, the Mann-Whitney and the Wilcoxon test were performed for non-normally distributed variables. The two- tailed p-value < 0.05 were considered significant.

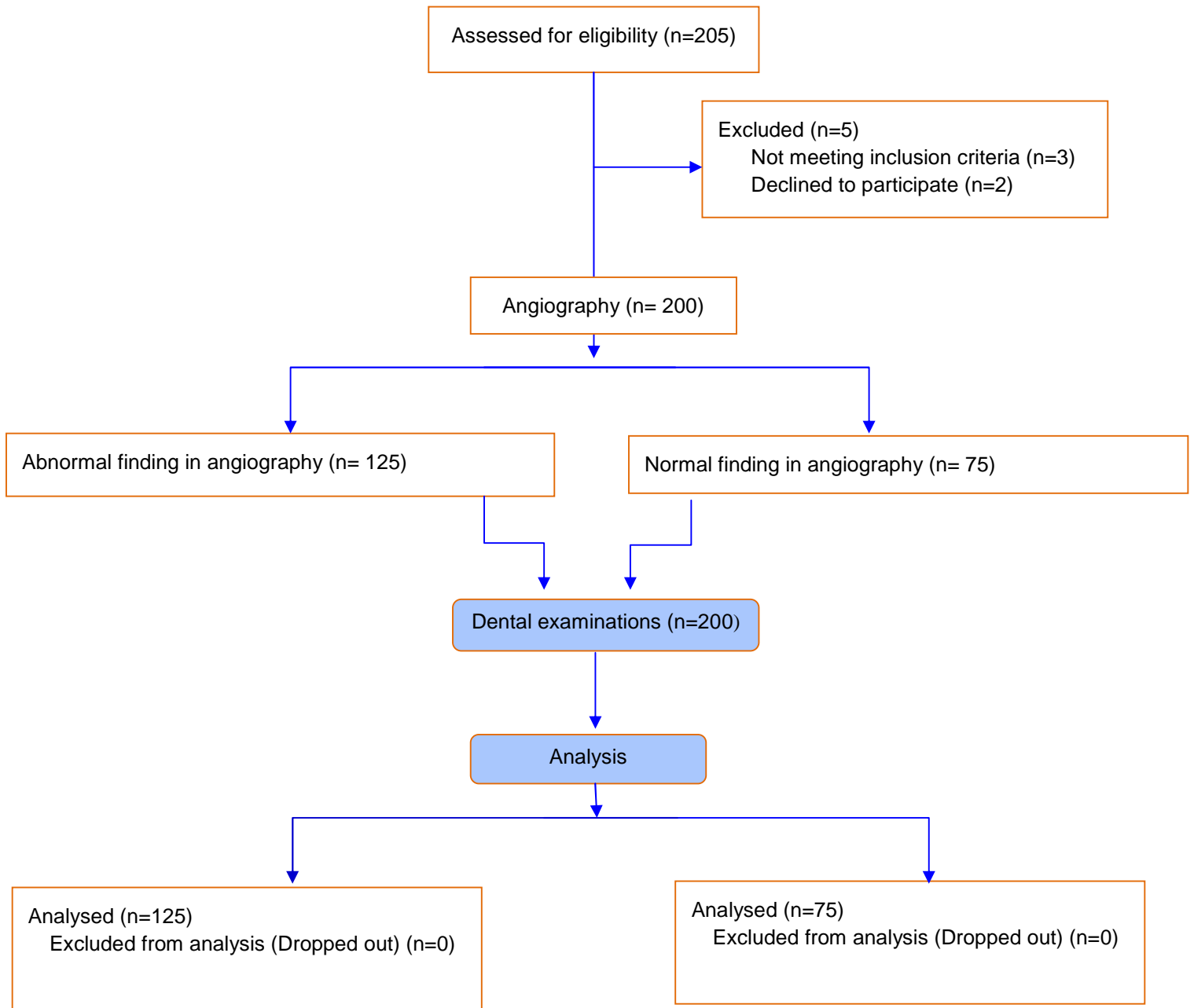


Figure 1. The study flowchart

Results

Demographic features in terms of sex ($P=0.826$) were similar in both groups, while the patients' age in case group was significantly higher (57.86 versus 47.63; $P<0.001$) (Table 1). Five patients were excluded and finally, 200 patients were included in the study.

Results showed that the frequency of gingivitis and periodontitis was significantly higher in patients with abnormal angiography (36% versus 25.3% and 52.2% versus 16%, respectively; $P<0.001$). Moreover, BOP was significantly higher in the case group compared to control (78.29 versus 31.26; $P<0.001$).

The number of involved teeth in case group was 0.32 and in the control group it was 0.13 ($P=0.007$). Furthermore, the number of teeth with PM in the case group was significantly higher; in addition, the severity of PM in this group was higher than the control group (0.24 versus 0.05; $P=0.016$ and 0.29 versus 0.05; $P=0.016$, respectively). By evaluating CAL, we found that the frequency of patients with $CAL>3\text{mm}$ and $<3\text{mm}$ was significantly higher in patients with abnormal angiography (28.8% versus 0% and 26.4% versus 17.3%, respectively; $P<0.001$). On the other hand, we did not find significant differences between two groups in the term of the number of missing teeth ($P=0.16$) and PI ($P=0.302$).

Table 1. Demographic and studied variables in both case and control groups

Group		Case	Control	P-value
Variables				
Age (year)		57.86 ± 9.58	47.63 ± 8.19	<0.001
Sex (male)		67 (53.6%)	39 (52%)	0.826
Periodontal disease	Normal	11 (8.8%)	44 (58.7%)	<0.001
	Gingivitis	45 (36%)	19 (25.3%)	
	Periodontitis	69 (52.2%)	12 (16%)	
Number of missing tooth		8.27 ± 5.09	7.15 ± 4.17	0.16
BOP		78.29 ± 20.8	31.26 ± 28	<0.001
PI		72.18 ± 7.26	71.76 ± 8.1	0.302
Number of involved tooth		0.32 ± 0.7	0.13 ± 0.577	0.007
Number of PM		0.24 ± 0.67	0.05 ± 0.32	0.016
Severity of PM		0.29 ± 0.78	0.05 ± 0.32	0.016
PD		3.8 ± 1.38	2.13 ± 0.82	<0.001
CAL	Normal	56 (44.8%)	62 (82.7%)	<0.001
	< 3 mm	33 (26.4%)	13 (17.3%)	
	>3 mm	36 (28.8%)	0	

Bleeding on probing (BOP); plaque index (PI); pathologic mobility (PM); pocket depth (PD); and clinical attachment loss (CAL).

Discussion

According to our results, the frequency of gingivitis, periodontitis, $CAL>3\text{mm}$ and $<3\text{mm}$, the mean of BOP, the number of involved teeth, tooth with PM, and the severity of PM was higher in patients with abnormal angiography compared to the control group.

In a study, Bokhari et al. showed that there is an intensive association between BOP in coronary heart disease (CHD) patients with periodontitis with systemic CRP levels; this association possibly reflects the potential significance of the local periodontal inflammatory burden for systemic inflammation (Bokhari SAH et al., 2014). In another study, Jung YS et al. demonstrated that the number of missing teeth was associated with common carotid artery intima-media thickness (CCA IMT), and BOP% was associated with CCA IMT in females only. These

associations have been robust in never-smokers. Finally, they concluded that tooth loss due to oral disease may play a role in subclinical carotid atherosclerosis (Jung YS et al., 2014). Costa TH et al. showed that the prevalence of chronic apical periodontitis was 41.7%, and about with coronary artery disease, it was 65%. The patients with chronic apical periodontitis had 2.79 times higher risk of developing coronary artery disease (Costa THR et al., 2014). Moreover, in another study in Iran, Ketabi et al. showed an association between periodontal disease and dental parameters with the severity of coronary artery obstruction measured by angiography. They found a significant positive correlation between the variables such as gingival recession, PD, CAL, decayed, missing, decayed-missing-filled, BOP, and degree of coronary artery obstruction (Ketabi M et al., 2016).

On the other hand, Ramesh A et al. demonstrated that no significant association was found between periodontal disease and acute coronary syndrome. Finally, they proposed that properly powered longitudinal case-control and intervention trials are needed to identify how periodontitis and periodontal interventions may have an impact on cardiovascular diseases (Ramesh A et al., 2013). These differences in the results of Ramesh A et al. and our study may be due to the different sample size, and different race with different demographic features. Moreover, lacked accurate diagnostic criteria for periodontal disease and CAD (not validated criteria) and lack of controlling for risk factors common in both conditions may cause different results.

In total, the association between periodontal disease and CAD is controversial. While some studies have not shown an association (Joshi KJ et al., 1996; Hujuel PP et al., 2002; Beck JD et al., 2005), other researchers have identified the opposite. Moreover, some meta-analyses which have done recently, have indicated a positive association between periodontal disease and CAD (Bahekar AA et al., 2007; Humphrey LL et al., 2008; Khader YS et al., 2004).

The interaction between bacterial products and various homeostatic mechanisms is currently believed to be the link between periodontal disease and CAD (Kweider M et al., 1993; Herzberg MC et al., 1996; Loos BG et al., 2000). The products of bacteria found in the subgingival plaque, particularly endotoxin associated with Gram-negative bacteria, have access to the vasculature in the gingival connective tissue. The factors, released from Gram-negative bacteria, stimulate monocytes to secrete pro-inflammatory cytokines such as tumor necrosis factor (TNF) and interleukin 1, and prostaglandin E₂ and thromboxanes, which initiate platelet adhesion and aggregation and increase the risk of CAD (Seymour R et al., 1998).

Conclusions

The results of this study showed the positive association between periodontal disease and CAD. Therefore, paying attention seriously to periodontal disease in earlier ages and treating it fast, may decrease the risk of CAD and stroke in the elderly.

Conflicts of interest

The authors declare that they have no conflicts of interests regarding the content of this article.

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