ACTA SCIENTIFIC DENTAL SCIENCES

Volume 8 Issue 8 August 2024

Research Article

Unveiling the 2017 Periodontitis Classification: A Deep Dive into Risk and Prognostic Factors

Young Joon Cho[1], Hyun Woo Cho[2], Sung Min Lee[3], Hyun Nyun Woo[4] and Philip Kang[4]

[1]*Mac Dental Clinic, Dalgubul-daero, Susung-gu, Daegu, S. Korea*

[2]*Department of Periodontics, School of dentistry, Kyungpook National University, Daegu, S. Korea*

[3]*New York University College of Dentistry, New York, NY*

[4]*Division of Periodontics, Section of Oral, Diagnostic and Rehabilitation Sciences, Columbia University College of Dental medicine, New York*

***Corresponding Author:** Young Joon Cho, Mac Dental Clinic, Dalgubul-daero, Susung-gu, Daegu, S. Korea.

Received: June 24, 2024

Published: July 04, 2024

Abstract

Background: The 2017 classification of periodontitis is a system consisting of 2 vectors, stage and grade, determined by risk and prognostic factors. This study aimed to examine the possibilities and limits of the 2017 classification from the perspective of risk and prognostic factors. This study also explains a third implicit vector—prognosis—which is spontaneously generated by combining the 2 vectors.

Methods: We selected articles through a search of digital databases. We used key words such as "risk factor/prognostic factor and periodontitis." We utilized a color scale to understand the degree of risk of each factor for tooth loss and periodontitis.

Results: 147 articles were selected. The 2017 classification includes 3 essential patient-related factors and 6 principal tooth-related factors. By analyzing the odds ratio of each parameter using color scale and systematic review, the categories of smoking, diabetes, pocket depth, clinical attachment loss, and furcation involvement were classified adequately to predict the risk/prognosis of periodontitis. However, evidence was insufficient for other factors.

Conclusion: In this analysis of risk and prognostic factors of the 2017 classification, we confirmed that it not only contains most of the essential factors for diagnosis but can also estimate the rate of progression and tooth loss.

Keywords: Periodontitis; Prognosis; Periodontal Risk Factors; Risk Factor; Systematic Review

Introduction

In the 2017 World Workshop, a novel classification of periodontitis (the 2017 classification) was developed [1]. The 2017 classification changed the paradigm of diagnosis of periodontitis and presented the direction of progress for periodontics. The 2017 classification is a unique system, adopting an unprecedented 2-vector system. The first is stage which reflects the severity and complexity of periodontitis, and the other is grade which describes the progression and risk factors of disease [2].

A risk factor is defined as one that causes disease, such as environmental exposure, behavioral aspect, and genotype [3]. There are two types of risk factors. The first are modifiable risk factors, such as diabetes and smoking. The second type are immutable risk factors, such as the IL-1 genotype and they are also known as determinants, or background factors [3]. Risk factors are usually confirmed through longitudinal research [4]. As the term suggests, risk factors can increase the probability of periodontitis, and the probability could be decreased if they are removed [5]. However, although dentists intervene to remove the risk factors of periodontitis, the results are not always altered in a favorable way, because there are multiple factors for both onset and cure for disease. Unlike risk factors, risk indicators and risk predictors (risk markers) are not based on clear evidence and longitudinal studies. Rather, risk indicators are probable factors which are determined by cross-sectional research, and risk predictors are results that come from

disease, such as mobility and tooth loss (TL) [6]. Nonetheless, risk indicators and risk predictors are frequently used for epidemiology.

Prognostic factors are similar to risk factors, but there is a higher chance of intervention leading to improved outcomes. Initial severity of periodontitis, compliance from the patient, and therapy performed by periodontists are good examples of prognostic risk factors. In addition, some risk factors such as smoking, could sometimes be regarded as prognostic factors, as intervention may affect the outcomes of periodontal disease [4].

Numerous studies on risk and prognostic factors have been conducted [4,7,8]. However, in recent years, not many studies on risk and prognostic factors have been reported, even though the classification of periodontitis has changed. Moreover, to our best knowledge, no studies have yet analyzed the 2017 classification in terms of risk factors and prognostic factors.

The 2017 classification also has a third implicit vector-prognosis-which is which is spontaneously generated by combining the two vectors (Figure 1). By using the 2-vector system, clinicians not only can accurately diagnose the current state of periodontitis, but also can determine the periodontal prognosis to some extent.

The purpose of this study is to examine the possibilities and limits of the 2017 classification from the perspective of risk factors and prognostic factors through the systematic review of associated articles reported thus far.

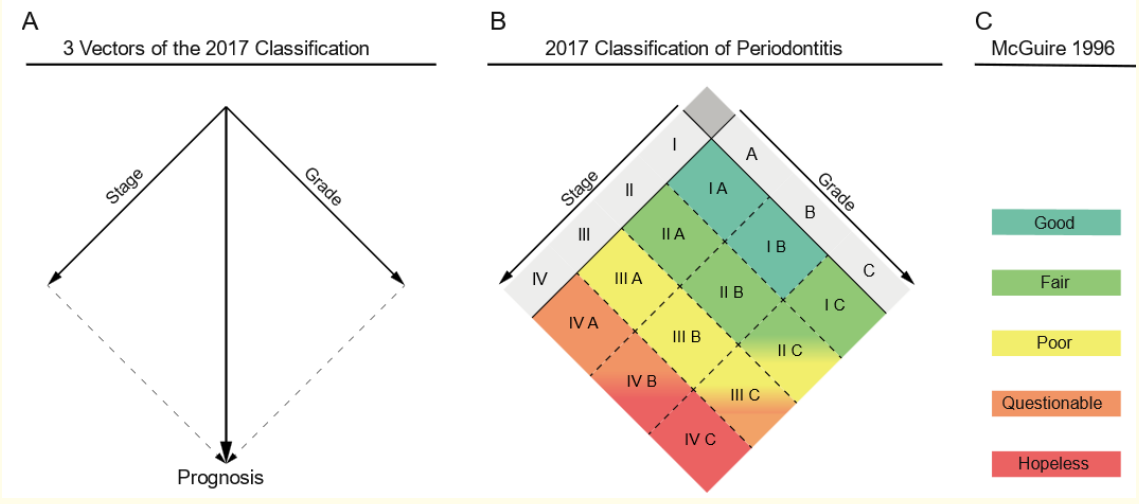

Figure 1: The new 2017 classification is a 3-vector system. 1A) Combining the 2 vectors of stage and grade generates the third vector of prognosis. 1B, 1C) It is possible to compare the prognostic capabilities of the 2017 classification to other prognostic systems. The rationale for comparing 1B and 1C is in table S1.

2017 classification of periodontitis	Conditions	Compared with McGuire 1996
Stage I Grade A, B	1~2mm CAL +<2mm/5years additional CAL + no complexity	Good
Stage I Grade C, Stage II Grade A, B	1-2mm CAL + ≥2mm/5years CAL (or 3-4mm CAL + <2mm/5 years CAL) + no complexity	Fair
Stage II Grade C	3-4mm CAL + ≥2mm/5years + no complexity	Fair or Poor
Stage III Grade A, B	≥5mm CAL + < 2mm/5years + simple (complexity)	Poor
Stage III Grade C	≥5mm CAL + ≥ 2mm/5years + simple (complexity)	Poor or Questionable
Stage IV Grade A	≥5mm CAL + 0mm/5years + complex (complexity)	Questionable
Stage IV Grade B	≥5mm CAL + <2mm/5years + complex (complexity)	Hopeless (retaintion) or hopeless (extraction)
Stage IV Grade C	≥5mm CAL + ≥2mm/5years + complex (complexity)	Hopeless (retaintion) or hopeless (extraction)

Table S1: Comparing the 2017 classification of periodontitis with McGuire's prognostic system (1996).

Methods

For this study, we selected articles through direct search and a search of databases, such as Medline, Sciencedirect, Web of science and Google scholar. We used key words such as "risk factor and periodontitis/periodontal disease," "prognostic factor and periodontitis/periodontal disease," "tooth-related factor and periodontitis/periodontal disease," "patient-related factor and periodontitis/periodontal disease," "smoking and periodontitis/periodontal disease," "diabetes and periodontitis/periodontal disease," "genetic factor and periodontitis/periodontal disease," "phenotype and periodontitis/periodontal disease." We found 4760 articles, and 597 articles were selected for evaluation after reading their abstracts. We evaluated the quality of journals, considering the 6 categories and 27 checklists of PRISMA [9]. In order to see the overall trend, we especially focused on searching journals including "odds ratio (OR)." The final number of articles used for this study was 147.

A descriptive review was accomplished by summarizing the studies. Although we did not perform a meta-analysis because the data and analyzing methods in the studies were heterogeneous, we attempted to find a trend regarding the degree of risk of each factor by using color scales.

		Assessement items	Category of factors	Periodontitis stage			
				I	II	III	IV
Stage	Severity	Interdental clinical attachment loss	Risk predictor (marker). Could be risk factor or prognostic factor	1-2 mm	3-4 mm	≥5 mm	≥5 mm
		Radiographic bone loss	Risk predictor. Could be risk factor or prognostic factor	<15%	15-33%	Extending to mid-third of root and beyoud	Extending to mid-third of root and beyoud
		Number of tooth loss due to periodontitis	Risk predictor. Could be risk factor or prognostic factor	0	0	≤4 teeth	≥5 teeth
	Complexity	Probing depth	Risk predictor. Could be risk factor or prognostic factor	≤4 mm	≤5 mm	≥6 mm	≥6 mm
		Horizontal bone loss	Risk predictor. Could be risk factor or prognostic factor	Mostly	Mostly	Combined	Combined
		Vertical bone loss	Risk predictor. Could be risk factor or prognostic factor			≥3 mm	≥3 mm
		Furcation involvement	Risk predictor. Could be risk factor or prognostic factor			Class II or III	Class II or III
		Ridge defect	Probably risk predictor			Moderate	Severe
		Need for complex rehabilitation; masticatory dysfunction, secondary occlusal trauma (mobility degree ≥2)	Risk predictor				Combined
		Bite collapse, drifting, flaring	Risk predictor				Combined
		Less than 20 remaining teeth (10 opposing pairs)	Risk predictor. Could be risk factor or prognostic factor				Combined
	Extent and distribution	Localized(<30% of teeth involved) or generalized	Risk indicator				
		Molar/incisor pattern (tooth type)	Risk predictor				

		Assessement items	Category of factors	Periodontitis grade		
				A	B	C
Grade	Primary criteria	Longitudinal data (radiographic bone loss or clinical attachment loss)	Could be risk factor or Prognostic factor	No loss over 5 years	<2 mm loss over 5 years	≥2 mm loss over 5 years
		% bone loss/age	Risk predictor	<0.25	0.25 to 1	>1.0
		Case phenotype (level of destruction following biofilm deposits)	Risk factor (determinant)	Low level of destruction	Commensurate level of destruction	Exceeded destruction
	Grade modifiers	Smoking	Risk factor and prognostic factor	Non-smoker	<10 cigarettes/day	≥10 cigarettes/day
		Diabetes	Risk factor and prognostic factor	Normoglycemic	HbA1c <7%	HbA1c ≥7%

Table 1: All assessment items in the 2017 classification of periodontitis were organized according to the definition of terms from the perspective of risk factors and prognostic factors. The categories were distinguished and categorized based on Locker., *et al*. 1998, Beck 1998, Heitz-Mayfield., *et al*. 2005, Eickholz., *et al*. 2008 and Genco., *et al*. 2013.

Review

The 2017 classification includes 12 contributing factors related to risk and prognosis, which are clinical attachment loss (CAL), bone loss (BL), %bone loss/age, TL, probing depth (PD), furcation involvement (FI), secondary occlusal trauma along with mobility of degree≥2, molar/incisor pattern, bite collapse, smoking, diabetes and case phenotype (Table 1). While smoking, diabetes and case phenotype are patient-related factors, the remaining factors are tooth-related factors.

Patient-Related Factors

Smoking

Although Labriola., *et al*. concluded that there is no evidence for difference in gain in clinical attachment and a reduction of bleeding on probing (BOP) between smokers and nonsmokers after nonsurgical therapy [10], most papers about smoking have revealed that smoking does have negative impacts on periodontitis and therapy [11]. It is already well known why smoking has many adverse effects on the periodontium. Chemotactic migration and phagocytic ability of polymorphonuclear leukocytes can be negatively affected by smoking [12]. Eggert., *et al*. argued that smoking creates molecular byproducts which interfere with mechanisms that suppress growth of harmful bacteria in gingival crevices. They concluded that smoking can promote periodontal lesions and increases the risk of development and progression of periodontitis [13]. Their claim has been confirmed by other research [7].

For this reason, smokers have higher risk ratio (RR) than nonsmokers regarding TL and disease progression [14]. Analyzing related papers using a color scale showed that the risk of periodontitis and TL increased dose-dependently and time-dependently. In addition, we found that ≥20 and ≥30cigaerettes/day also increased the risk but were not included in the 2017 classification (Table 2).

Diabetes

There has been much evidence supporting that diabetes is a strong risk factor for periodontitis [15]. While periodontitis is initiated by biofilm, most of the destruction comes from host immune response against bacteria. There are several mechanisms through which diabetes is related to periodontitis. One of them is the activation of chronic host immune system, which increases pro-inflammatory cytokines and causes damage to the microvascular endothelium. It then could destruct periodontal tissue after promoting alterations of normal periodontium. Even though Matuliene., *et al*. reported that the OR of periodontal disease progression for patients with diabetes was 0.7, [16] the ORs of diabetes in most research for relationship between diabetes and periodontitis is apparently high [17]. We used a color scale to evaluate the relationship between diabetes and periodontitis, and as HbA1c increased, the risk of periodontitis and TL clearly increased (Table 3).

Case phenotype

The characteristics of a disease varies from patient to patient due to different phenotypes [18]. The phenotype is the observable expression of a person's genotype, and each expression is affected by both their genotype and the surrounding environment [19]. Periodontitis, which is a multifactorial disease, also has a diverse phenotype across patients. Toxin producing bacteria and environmental factors are mainly related to periodontitis, but genetic factors are also involved in the etiology and characteristics of periodontitis as well [20].

In terms of adult periodontitis, it is estimated to have about 50% heritability following adjustments for behavioral variables [21]. Laine., *et al*. reported that polymorphisms in the IL-1, IL-6 and IL-10 genes may be associated with chronic periodontitis susceptibility [22]. We performed a review of research related to well-known genetic factors like the IL-1 genotype and neutrophil abnormalities (Table 4). Phenotype/genotype were clearly associated with periodontitis, and the risk became significantly greater when environmental factors such as smoking were involved [23,24]. However, we failed to find articles assessing the RR regarding the relationship between biofilm and phenotype.

Tooth-related factors

Probing depth/clinical attachment loss

Although there have been some research that PD has little predictive capacity and diagnostic accuracy [25], there are many longitudinal studies concluding that increased PD is associated with future CAL [26]. The categories of stage regarding PD that consider the complexity in the 2017 classification is divided into three situations: ≤4mm, ≤5mm, and ≥6mm. According to most research, PD of ≤3mm was considered as normal or mild periodontitis, PD of 4~6mm was regarded as moderate periodontitis, and PD of ≥7mm was assumed as severe periodontitis [16]. A color scale showed that the risk tends to increase as the PD deepens. PD≤3mm and PD≥7mm affected the risk of TL and BL, but this was not included in the 2017 classification (Table 5).

Authors	Category (cigarettes/day)						Study design/analysis	No. of Pt	Sex	Age	Duration	Method of evaluation: TL, CAL/PD, or BL	OR, RR, or HR, respectively	CAL (mm), respectively	Remarks
2017 new classification of periodontitis	NS	1~9	≥10				N/A					N/A	N/A	N/A	N/A
Horning 1992	NS	Smoker					Logistic regression	1984. (1788 with complete data set)		13~84	3 years	PD, BL, FI	OR: 1.809		Moderate or advanced, periodontitis vs. early periodontitis or gingivitis
Locker 1993	NS	Ever smoked	Current smoker				Longitudinal, logistic regression analysis	624		over 50		CAL	OR: 1, 2.3, 2.7		
Holm 1994	NS	1~15	>15				Longitudinal, logistic regression analysis	273	149 (M), 124 (F)	20~40, 50~70	10 years	TL	RR: 2.66, 4.55 (Age 20~40), 1.6, 2.16 (Age 50~70)		
Grossi 1994	NS	Very light smoker or occasional smoker (>0~<5.2 pack/years)	Light smoker (5.3~15pack/years)	Moderate smoker (15.1~30pack/years)	Heavy smoker (30.1~150pack/years)		Cross-sectional, logistic regression	Total: 1426, Smoking: 1312		25~74		CAL and BL	OR: 1.48 (very light;BL), 7.18 (heavy;BL), 2.05 (very CAL), 4.75 (heavy;CAL)		
Martinez-Canut 1995	NS	1~10	11~20	>21				889	340 (M), 549 (F)	21~76		CAL		3.85, 3.72, 4.36, 4.5	
Gelskey 1998	NS	1~300 cigarette index	301~500 cigarette index	>500 cigarette index			Logistic regression	637		35~87	3 years	PD ≥7mm	OR: 1, 1.24, 1.78, 3.80 (Ever smoked; 1.82, ≥16/day; 2.10)		Cigarette index= No. of Cig./day X No. of years
Tomar 2000	NS	1~9	10~19	20	21~30	≥31	Multiple logistic Regression	12329	6460 (M), 7190 (F)	≥18	6 years	AL ≥4mm	OR: 1, 2.79, 2.96, 4.72, 5.10, 5.88		NHANES III
Saito 2001	NS	1~199	200~399	≥400			Multiple logistic regression analysis	643	131 (M), 512 (F)	19~79					No. of Cig./day X No. of years, study for obesity
Yoshida 2001	NS	Quit smoking	Smoking				Logistic regression analysis	2015	Male	20~59	10 days	TL	OR: 1, 1.27, 1.54		
	NS	1~10	11~20	>21									OR: 1, 1.04, 1.48, 1.72		
	NS	≤10 years	11~20 years	≥21 years									OR: 1, 1.22, 1.94, 1.39		
Calsina 2002	NS	1~10	11~20	21~30	>30		Logistic regression analysis	240	119 (M), 121 (F)	20~71		CAL and PD	OR: 1, 1.8, 1.6, 1.9, 11		
Hyman 2003	NS	quit ≥6 years ago	quit 0~5 years ago	Current smoker			Cross-sectional, multinomial logistic regression (NHANES III)	12325		20~49, ≥50	6 years	CAL	OR: 1, 2.67, 4.61, 18.55		NHANES III
	NS	quit ≥13 years ago	quit 0~12 years ago	Current smoker									OR: 1, 2.11, 10.27, 25.64		
Lang 2003	NS	FS (≥5 years since cessation)	<10	11~20	≥20										Periodontal risk assessment model
Susin 2004	NS	1~2734 packs	2735~7300 packs	≥7300 packs			Cross sectional, mutivariable model	853	388 (M), 465 (F)	30~103		CAL	RR: 2.1(mod. smoker for mod. periodontitis), 3.4(mod. smoker for severe periodontitis), 3.0(heavy smoker for mod. periodontitis), 8.2(heavy smoker for severe periodontitis)		No. of Cig./day X No. of years/20 cig. In a lifetime
Krall 2006	NS	Smoking cessation (for 15 years or more)	Smoking cessation (for 13 years)	Smoking cessation (for 9 years)	Smoking cessation (for 1 year)	Current smoker	Longitudinal, multivariate proportional hazards regression model	789	Male	(Initially) 21 to 84	Up to 35 years	TL	HR: 2.1 (smoker), 1.3 (former), 2.0 (after 1year), 1.0 (after15 years)		Not sig. after 9 years, constantly near 1.0 (HR) after 13 years
Chandra 2007	NS	FS	<10	10~19	20	>20		26							Modified periodontal risk assessment
Jansson 2008	NS	<10	≥10					20		33~69	5 years	TL, PD, and BL			Periodontal risk assessment
Trombelli 2009	NS	FS	1~9	10~19	≥20		Linear and multiple regression analysis	107	34 (M), 73 (F)	mean age 45.5					Compared UniFe & PAT
Matuliene 2010	NS, FS	<10	10~20	>20			Retrospective cohort study, logistic regression analysis	160	72 (M), 88 (F)	15~71	9.5 years	TL	OR: 1.28 (any TL), 1.52 (loss of more than one tooth), 3.03 (recurrence of periodontitis)		
Bergstrom 2003	NS	1~9	10~19	>20			Logistic regression analysis	375 (S: 133, NS: 242)		20~69	10 years	1% of PD≥5mm	OR: 3		It rises dose dependently on the graph
	NS	1~170 cig./year	171~350 cig./year	>350 cig./year								15% of PD≥5mm	OR: 12.1		

Color Scale						
OR, RR, or HR	1	1.04~1.94	2~3.8	4.55~7.18	8.2~12.1	18.55~25.64
LOG Scale Range	0	0.001~0.300	0.301~0.600	0.601~0.900	0.901~1.200	1.201~1.500

Table 2: Summary and comparison of articles that are related to the effects of smoking on periodontal disease. The ORs between studies were not normalized, and the color scale only shows a general trend. The ORs were compared and categorized using a log scale. PD, probing depth; CAL, clinical attachment loss; BL, bone loss; FI, furcation involvement; OR, odds ratio; HR, hazard ration; N/A, non-available.

Authors	Category (HbA1c%)					Study design/analysis	No. of Pt	Sex	Age	Duration	Evaluation: TL, CAL/PD, or BL	OR, respectively	CAL(mm), respectively	Remarks
2017 new classification of periodontitis	Normogrycemic	HbA1c<7%	HbA1c≥7%			N/A					N/A	N/A	N/A	N/A
Nelson 1990	Nondiabetic	Diabetic				Longitudinal	2273	949 (M), 1324 (F)	≥15	6 years	Periodontal disease	2.6 (incidence rate)		Catetory added arbitrariliy, as original paper lacks one
Emrich 1991	N/A	<140mg/dl	140~200mg/dl			linear logistic regression analysis	1342		≥15		CAL and BL	2.81 (CAL), 3.43 (BL)		2-hour plasma glucose concentration
Tervonen 1993	N/A	<8% (Good controlled)	8~10% (Moderate controlled)	>10% (Poor controlled)		Forward stepwise multiple regression analysis	75		20~70	2~5 years	PD≥4mm, AL≥3mm & 5mm			4.151 (Regression coefficient of poor control), calculus is important
Grossi 1994	Nondiabetic	Diabetic				Cross-sectional, logistic regression	1426	685 (M), 741 (F)	25~74		CAL	2.32		
Oliver 1994	N/A	<8%	8~10%	>10%							site of PD≥ 4mm			
Christgau 1998	N/A	<6%	6~7.9%	8~9.9%	≥10%	Prospective parallel study	40	24 (M), 16 (F)	mean 52.5	4 months	CAL & PD after nonsurgical			Well controlled; normally healing after nonsurgical
Gelskey 1998	Nondiabetic	Diabetic				Case control, logistic regression analysis	637		35~87	3 years	PD ≥7mm	1.65		
Taylor 1998 (Ann Periododontol)	Nondiabetic	<9% (Better controlled)	≥9% (Poorly controlled)			Longitudinal, ordinal logistic regression model	359	145 (M), 214 (F)	15~57	1.2~6.9 years	BL	1, 2.2, 5.3		
Taylor 1998 (J Periodontol)	Nondiabetic	Diabetic				Ordinal logistic regression model	362	146 (M), 216 (F)	15~57	2 years	BL	4.23		
Katz 2001	Nondiabetic	≥120mg/dl					10590				Severe periodontitis	2.46		
Tsai 2002	Nondiabetic	<9% (Better controlled)	≥9% (Poorly controlled)			Multivariable logistic regression (NHANESIII)	4343	2188 (M), 2155 (F)	45~90	6 years	PD≥5mm (at least 1 site) & AL≥6mm (at least 2 sites)	1, 1.56, 2.6		
Guzman 2003	N/A	7.72% (Healthy)	8.19% (Moderate periodontitis)	9.21% (Severe periodontitis)			100	45 (M), 56 (F)	Mean 54.62		CAL ≥5mm			High prevalence, overrepresented IL-1B
Hyman 2003	Nondiabetic	Diabetic				Cross-sectional, multinomial logistic regression (NHANES III)	12325		20~45	6 years	CAL	1.05 (CAL: 1.0~1.99mm), 2.03 (CAL: 2.0~2.99mm), 2.5 (CAL: ≥3mm)		
									≥50		CAL	1.03 (CAL: 1.0~1.99mm), 1.40 (CAL: 2.0~2.99mm), 2.06 (CAL: ≥3mm)		
Torrungruan 2005	Nondiabetic	Diabetic				Cross-sectional, multinomial logistic regression analysis	2005	1492 (M), 513 (F)	50~73		CAL	1.3 (CAL: 2.5~3.9mm), 1.6 (CAL: ≥4mm)		
Lalla 2006	N/A	<7.5%	7.5~9.5%	>9.5%		Case control	182		6~18		AL>2mm (at least 2 teeth)	5.23 (All), 4.8 (Age: 12~18)		Periodontal destruction can start very early
Faggion 2007	Nondiabetic	Diabetic				Linear logistic regression analysis	198		Mean 47.58	11.8 years	TL	4.17		
Matuliene 2008	Nondiabetic	Diabetic				Multivariable logistic regression	172	77 (M), 95 (F)	14~69	3~27 years	Periodontal disease progression	0.7		
Trombelli 2009	Nondiabetic	<7% (Controlled diabetic)	≥7% (Poor controled diabetic)			Linear and multiple regression analysis	107	34 (M), 73 (F)	Mean 45.5					Compared UniFe & PAT
Matuliene 2010	Nondiabetic	Diabetic				Longitudinal, logistic regression analysis	160	72 (M), 88 (F)	15~71	9.5 years	TL and reccurence of periodontitis	6.56 (Any TL), 3.43 (One TL), 1.07 (Recurrence)		
Morita 2012	Nondiabetic	≥6.5%				Longitudinal	5856		30~69	5 years	PD	1.17 (≥6.5%), 2.47 (PD≥4~5mm), 3.45 (PD≥6mm)		

Color Scale					
OR	0.7~1	1.03~1.56	1.6~2.5	2.6~3.45	4.17~6.56
LOG Scale Range	≤0	0.001~0.200	0.201~0.400	0.401~0.600	≥0.6

Table 3: Summary and comparison of articles that are related to the effects of diabetes on periodontal disease. The ORs between studies were not normalized, and the color scale only shows a general trend. The ORs were compared and categorized using a log scale. PD, probing depth; CAL, clinical attachment loss; BL, bone loss; FI, furcation involvement; OR, odds ratio; N/A, non-available; HbA1c = glycated hemoglobin A1c.

	Study design/ analysis	Type of gene	No. of Pt	Sex	Age	Duration	Methods of evaluation: TL, CAL/PD, BL	Outcomes/results	Remarks
Ehmke 1999	Longitudinal	IL-1 haplotype	48 total, (33 studied)		Mean: 50~53	2 years	AL ≥2mm	No significant difference	
McGuire 1999	Longitudinal	IL-1 genotype	100		30~69		TL	OR: 2.7 (IL-1), 2.9 (heavy smoking), 7.7 (combined IL-1 & heavy smoking)	Effect amplified when factors are combined
Laine 2001	Systematic review	IL gene polymorphism	105 (experimental), 53 (control)	Experimental: 54 (M), 51 (F), Control 16 (M), 37 (F)	Experimental: 28-66, Control: 25~77			polymorphisms in the IL1, IL6, IL10, VDR, and CD14 genes may be associated with CP susceptibility.	24 articles
Preiss 1994		IL-1B	33		15~39			22.8~150ng/ml (healthy patients), 85.8~882.2ng/ml (periodontitis patients)	Concentration of gingival crevicular fluid
Lang 2000	Prospective longitudinal	IL-1	323	115 (M), 208 (F)	24~81	4 consecutive SPT visits every 3~4 months apart	BOP	BOP is related to IL-1, BOP % deteriorated; 31% (IL-1 poisitive) vs.15% (IL-1 negative)	
Pretzl 2008 (JCP)	Logistic multilevel regression	IL-1	100	41 (M), 59 (F)	Mean: 46.5	10 years	TL	OR: 1.71	
Nickles 2017	Retrospective, multiple regression analysis		41	24 (M), 17 (F)	49~68	5 years	CAL	IL-1 is associated with less stability (IL-1 positives: AL 2mm/5years, IL-1 negatives: AL 0.5mm/5years)	Long-term stability after regeneration
Mcdevitt 2000	Multivariate logistic regression	IL-1A, IL-1B	90		≥35, 35~55 (test group)		BL ≥3mm	OR: 3.75 (moderate periodntitis), 5.27 (severe periodontitis), 7.43 (moderate to severe periodontitis for former moderate smoker), 1.68 (moderate to severe periodontitis for former moderate smoker compared to IL-1 positives who are nonsmoker or light smoker)	Phenotype effect (IL-1 & former moderate smoker (5~10pack/yr))
Huynh-Ba 2007	Systematic review	IL-1						Insufficient evidence (5 articles: association, 5 articles: no assocition, 1 article: unclear)	11 longitudinal studies
Cattabriga 2001	Retrospective	IL-1	60	29 (M), 31 (F)	40~58	10 years	TL, BL	No significant difference (TL)	Healing effect after therapy
Persson 2003 (OHPD)	Prospective longitudinal	IL-1	323 total, (224 studied)	Among studied: 84 (M), 140 (F)	30~87	4 years	BL/age	No significant difference	Periodontal risk assessment
Cullinan 2008	Longitudinal	IL-1	295			5 years	AL	Non essential factor for periodontal disease progression, but showed interaction with age, smoking, Pg	Phenotype effect
De Sanctis 2000	Multivariate logistic regression model	IL-1	40	19 (M), 21 (F)	Mean: 45	4 years	CAL	In a 3-year period, patients with positive IL1 genotype lost about 50% of the first year gained CAL and were about 10 times more likely of experiencing ≥2 mm CAL loss	Long-term stability after GTR
Eickholz 2001	Longitudinal	IL-1	9	3 (M), 9 (F)	34~58	5 years		Two of the IL-1-positive patients (four) showed remarkable CAL-H losses in 1 of 2 furcation defects. But, stable attachment levels despite the IL-1 genotype.	Long-term stability after GTR
Eickholz 2007	Mutilevel analysis	IL-1	37		23~64	5 years	CAL, Bone density	No significantly influenced	Long-term stability after GTR
Eickholz 2008	Poisson and logistic regressions	IL-1 polymorphism	100	41 (M), 59 (F)	15~67	10 years	TL	OR: 1.237	
Karimbux 2012	Meta-analysis	IL-1A, IL-1B					Chronic periodontitis	OR: 1.48 (IL-1A), 1.54 (IL-1B) Significant contribuor to chronic periodontitis in whites	27 studies
Galbraith 1999		IL-1B, TNF-A	85		35~65			Significant increase in advanced periodontitis (both IL-1b & TNF-a), no significant association between genotype and cytokine production	
Taiete 2019	Stepwise logistic regression analysis	IL-1B, IL-10	24	7 (M), 17 (F)	Mean: 27.5	6 months	CAL/PD	Dropped level of IL-1b after therapy. The higher the IL-10 concentration at baseline, the higher the reduction in PPD at 6 months	Generalized aggressive periodontitis
Michalowicz 2000	Regression analysis	Familial aggregation	234 (128 (MZ), 106 (DZ))	104 (F for MZ), 68 (F for DZ)	35~59		AL, PD	Adult periodontitis has about 50% heredity.	Compared monozygotic & dizygotic twins
Beaty 1987		Familial aggregation	372 (28 Families)		Mean 20 (JP), 25 (not JP)		Test a series of medelian model	JP is an autosomal recessive disorder	62 patients (JP)
Genco 2013	Review	Familial aggregation & genome-wide association						Clearly associate with genetic factors, but mechanisms are unclear.	
Deas 2003	Review	Neutrophil dysfunction						Associated between neutrophil dysfuction & periodontitis	
Cogen 1986		Neutrophil dysfunction	18 (JP), 18 (control)	JP: 7 (M), 11 (F)	13~22		HLA phenotypes	Phagocyte and chemotactic abilities of polymorphonuclear leukocytes in both LJP and GJP were significantly decreased	Host factors in JP
Boughman 1992		Neutrophil dysfunction	116		13~48		Phenotypic assessment (*Aa* seropositive proband)	83% of affected siblings and 65% of healthy siblings were seropositive.	Family background is one of risk factors of early onset periodontitis
Shibutani 2000	Case report	Neutrophil dysfunction	1	Female	9~21			Professional tooth cleaning could not prevent periodontal destruction.	Chediak-Higashi syndrome

Table 4: Summary and comparison of articles that are related to the effects of genetics and phenotype on periodontal disease. PD, probing depth; CAL, clinical attachment loss; AL, attachment loss; BL, bone loss; BOP, bleeding on probing; JP, juvenile periodontitis; MZ, monozygotic twins; DZ, dizygotic twins; OR, odds ratio; GTR, guided tissue regeneration; IL-1, interleukine-1; TNF-A, tumor necrotic factor-alpha.

In terms of CAL, the categories of stage regarding CAL in the 2017 classification is divided into three situations: 1~2mm, 3~4mm, and ≥5mm. Using a color scale, we found that the risk tends to increase as CAL increases. CAL≥6mm affected the risk of TL and further attachment loss, but this was also not included in the 2017 classification (Table 5).

Bone Loss and %bone loss/age

The 2017 classification includes baseline radiographic BL for stage and longitudinal BL data for grade. The category of baseline BL is divided into three situations: <15%, 15~33%, and extending mid-third of root length and beyond. When categorizing BL, different authors have used slightly different ways to divide the categories for periodontitis. Martinez-Canut divided BL into 3 categories to evaluate the rate of TL: BL <30%, 30~50%, and >50%, [27] and Graetz., *et al*. also used 4 categories: ≤25%, ≤50%, ≤75%, and >75%.[28] There were few studies that investigated the RR according to the degree of BL, so this study could not evaluate the risk of different levels of BL on periodontitis.

In terms of %BL/age, the 2017 classification divides %bone loss/age into <0.25, 0.25 to 1.0, and >1.0. Unfortunately, not many studies have assessed the relationship between %bone loss/age and RR. Lang., *et al*. divided %bone loss/age into 6 categories: 0.25, 0.5, 0.75, 1, 1.25, and >1.5 for his periodontal risk assessment (PRA) model and considered <0.5 as low risk, 0.5~1.0 as moderate risk, and >1.0 as high risk [8]. Jansson., *et al*. also used %bone loss/age and divided the categories into 0, 0.5, and 1 [29]. Hirata., *et al.* reported that the hazard ratio (HR) was 3.19 when %bone loss/age is ≥1.0 compared to <1.0 [30].

Number of tooth loss due to periodontitis

The 2017 classification divided the number of TL into 3 situations: no TL for stage I and II, TL of ≤4 teeth for stage III, and TL of ≥5 teeth for stage IV [1]. Although Lang., *et al*. adopted the number of TL in PRA based on the concept of shortened dental arch (SDA) related to occlusal unit [8,31], we could not find studies assessing the relationship between SDA and periodontal risk. However, using modified PRA, Hirata., *et al*. reported that the HR was 4.06 when number of TL was ≥8, compared to <8. Using therapy-resistant periodontitis assessment, they reported that the HR for TL of ≥8 for favorable prognosis was 3.70, while the HR for TL of ≥8 for poor prognosis was 20.17 [30]. Thus, although the number of TL does seem to be a risk factor for periodontitis in a positively correlated manner, the relationship of periodontitis with the concept of occlusal unit has not been sufficiently assessed and further research is needed.

Furcation involvement

FI is one of tooth-related factors that affect both TL and BL, since furcation involved teeth respond less favorably to periodontal treatment than molars without FI or single-rooted teeth and are at greater risk for further attachment loss compared with other teeth [32]. Therefore, the 2017 classification states that for FI, shifting to a higher/lower stage is possible [1]. In risk analysis using a color scale, associated articles clearly showed the tendency of increased risk as the degree of FI increased (Table 6).

Secondary occlusal trauma and mobility

There have been no studies assessing the risk of TL and periodontitis following secondary occlusal trauma. In addition, although Matuliene., *et al*. reported that the ORs increased to 1.5, 3.8, and 5.3 as the degree of mobility increased to degree 1, 2, and 3, [16], there have not been many studies on the risk of TL and periodontitis according to the degree of mobility. Therefore, this study could not evaluate the relationship between secondary occlusal trauma along with mobility and the risk of periodontitis.

Molar/Incisor pattern (Tooth type)

Molar/incisor pattern is included to evaluate the extent and distribution of stage and the case phenotype of grade in the 2017 classification. Molar/incisor patten is a typical indicator of juvenile periodontitis (JP) which was included in the 1986 classification of periodontal disease.[33] Studies on the effect of the molar/incisor pattern caused by JP on TL or periodontitis were insufficient, so it was not evaluated in this study. However, we evaluated several studies on risks of periodontitis according to tooth type (Table 6). The risk of molars is higher than incisors because the periodontal structure of posterior teeth is more complicated, and the root length is shorter than anterior teeth [34].

Miscellaneous Factors and Other Risk/Prognostic Factors Which Are Not Included in the 2017 classification

It was difficult to review the remaining factors, such as masticatory dysfunction, bite collapse, drifting, and flaring, because there has not been any research assessing the risk of these factors to periodontitis. However, posterior bite collapse, drifting, and flaring of anterior teeth are important factors to periodontitis. Therefore, while it is appropriate to include these factors to assess the com-

plexity of periodontitis, further studies will be needed to provide objective and sufficient data on these factors.

We also found several risk/prognostic factors that are not included in the 2017 classification but are still important. They are age, gender, BOP, alcohol, compliance, osteoporosis, and obesity. They are summarized in table S2.

Discussion

According to our analysis, the 2017 classification contains essential 3 patient-related factors consisting of smoking, diabetes and phenotype, and principal 6 tooth-related factors including PD/CAL, BL, the number of TL, FI, secondary occlusal trauma with mobility, and molar/incisor pattern.

We utilized color scales to evaluate the risk of each factor. Since different studies adopted different research methods, it was virtually impossible to perform a meta-analysis through data normalization. Therefore, we chose to use color scales to see the general trend towards the difference in the amount of risk posed by different levels of each risk factor. Data visualization through the use of color scales allows an intuitive understanding on a data set, and color scales have recently been adopted in medical fields for their potential for providing insight on complicated sets of data [35]. The color scales used in this study not only provides insight on the degree of risk that different categories of each factor poses on periodontitis, but also shows whether the categories of a risk factor are divided in a reasonable way.

A color scale can be used for mainly 4 types of data: normal data, ordinal data, interval data and ratio data [35]. For this study, we used them to visualize ORs reported in various papers, which made it possible to recognize categories of risk factors that were not included in the 2017 classification but were reported to have a statistically significant difference in their risks on periodontitis. For example, while the 2017 classification only classifies smoking up to ≥10 cigarettes/day, analysis using a color scale showed that the risk rapidly increases in categories of ≥20 and ≥30 cigarettes/day (Table 2).

Smoking is a patient-related factor and affects the onset of periodontitis, the progression of periodontitis, periodontal therapy, and even maintenance [5]. As a result of analyzing related articles using a color scale, the risk of periodontitis and TL increased in a dose-dependent and time-dependent manner (Table 2). The 2017 classification divides smoking into 3 categories: nonsmoker, 1~9, ≥10 cigarettes/day [1]. However, many articles on smoking have divided smokers in their own way, and the common categories for smoking were nonsmoker, former smoker (FS), less than 10 cigarettes/day, 10 to 19 cigarettes/day, and 20 cigarettes or more/day [8]. In addition, the duration of smoking cessation also affected the risk for TL and periodontitis. Krall., *et al*. reported that the HR was significantly higher up to 9 years after quitting smoking, and the HR became similar to that of non-smokers after at least 13 years [36]. Thus, it seems appropriate to include the category of FS into the 2017 classification. Also, as mentioned earlier, the risk of periodontitis increased further in ≥20 cigarettes/day, which makes it necessary to also add the category of ≥20 cigarettes/day.

For diabetes, the color scale showed that as HbA1c increased, the risk of TL and the progression of periodontitis increased (Table 3). The 2017 classification categorizes diabetes into 3 situations: normoglycemic, HbA1c < 7.0%, and HbA1c ≥ 7.0%. According to the 2020 American Diabetes Association guideline, HbA1c of 5.7~6.4% are diagnosed as prediabetic, and HbA1c ≥ 6.5% is diagnosed as diabetic [37]. As shown in table 3, the 2017 classification does not include HbA1c 6.5~7%. Moreover, there is no additional categories above 7%, although the risk increases up to ≥9% [17]. Therefore, it seems appropriate to add these categories to the 2017 classification.

We also performed a systematic review to find out the characteristics of phenotypes resulting from the relationship between environmental factors and genotypes. Unfortunately, to our best knowledge, no studies have assessed the risks of various case phenotypes on periodontitis. However, it was possible to conduct a systematic review regarding the relationship between genotype and periodontitis (Table 4). There are many genetic markers which affect periodontal disease such as the IL-1 genotype, tumor necrotic factor-a, and neutrophil abnormalities. Among them, IL-1 is the genetic factor that is most likely associated with periodontitis [23]. Despite the controversy, most articles have reported that IL-1 genotype increased the risk for TL and periodontitis [23,24]. Furthermore, the risk of periodontitis becomes much greater when genetic factors such as IL-1 are combined with environmental factors. McGuire reported that a positive IL-1 genotype alone increased the risk of TL by a factor of 2.66, while heavy smoking on its own increased the risk by a factor of 2.88. However, the combined effect of IL-1 genotype positive and heavy smoking increased the risk of TL by a factor of 7.7 [23]. McDevitt., *et al*. reported that former moderate smokers who were IL-1 genotype positive had an increased odds of having moderate to severe periodontitis of 1.68

compared to non-smokers or former light smokers who were IL-1 genotype negative, and they concluded that there was a statistically significant interaction between past smoking history status and IL-1 genotype status [24]. Therefore, it seems that adopting the concept of phenotype in the 2017 classification is essential for accurate diagnosis and prognosis of periodontitis.

We also analyzed tooth-related factors included in the 2017 classification. The color scale shows that, as PD increases, the risk for periodontitis and TL tends to increase (Table 5). Therefore, it is reasonable that the 2017 classification includes PD, which is easy to measure and evaluate in clinics. However, future adjustments seem necessary as studies have reported that the risk of PD ≤ 3mm was lower than the risk of PD > 3mm and the risk of PD ≥ 7mm was higher than the risk of PD < 7mm [16].

Regarding CAL (for stage), it is indisputable that CAL is a much more reliable parameter of severity of periodontitis than PD [38]. Comparing various articles with a color scale, it was confirmed that the risk increases as CAL increases. Since the OR also increases further in CAL of more than 6~10mm and ≥10mm, the categories of the 2017 classification needs to be adjusted (Table 5) [16].

In terms of longitudinal CAL data (for grade), there has not been many studies about the threshold of disease progression rate. Löe., *et al*. judged the difference between no progression and mild periodontitis based on attachment loss of 2mm [39]. Joss., *et al*. regarded attachment loss of ≥2mm as the indicator of disease progression.[40] The 2017 classification says CAL of 2mm over 5 years is the criterion for the progression of periodontitis. If CAL of 2mm occurs additionally in stage I where CAL is ≤2mm, CAL progresses to 3~4mm and becomes stage II. If CAL of 2mm occurs additionally in stage II where CAL is 3~4mm, CAL progresses to 5~6mm and becomes stage III. Therefore, setting 2mm of CAL as the threshold is not only consistent with other studies, but also within the 2017 classification, as the grade system is coherent with the stage system.

The 2017 classification categorized BL into 15%, 15~33%, and extending to mid-third of root and beyond. Pretzl., *et al.* used 4 categories to assess the rate of TL: BL = 20%, 40%, 60%, and 80% and they reported that the OR of BL for TL was 2.4 [32]. Faggion., *et al*. also reported that the OR of reduced alveolar bone levels for each 1% increment was 1.04 [15]. However, since there have been few studies investigating the RR according to the degree of BL, additional studies are needed. In addition, the 2017 classification includes %BL/age instead of age. Although there is controversy, most studies have assumed that increase in BL with age is not due to the risk of aging, but because of the accumulation of periodontal tissue destruction as one ages [3]. Thus, it is a brilliant attempt to adopt %BL/age as the primary criterion for judging the progression of disease, but due to lack of data, it is necessary to verify the risk of %BL/age through additional research.

Regarding the number of TL, Lang and Tonetti adopted the number of TL as a risk factor based on SDA [8]. The concept of SDA explains that at least 20 teeth including anterior teeth are necessary to safely maintain dentition for a prolonged time [31]. Kayser defined one occlusal unit as a pair of two occluding premolars and two occlusal units as a pair of two occluding molars. He concluded that four occlusal units including anterior teeth are absolutely necessary for esthetics, stable TMJ, and occlusion [31]. Following Kayser' research, Lang., *et al*. considered ≤4 teeth loss as low risk, >4 to 8 teeth loss as moderate risk, and loss > 8 teeth as high risk [14]. However, to our best knowledge, there has not been any research on whether the number of TL is an appropriate indicator of the severity of a disease or not. Therefore, although the 2017 classification adopts number of TL as a parameter to evaluate severity of periodontitis, further research is needed.

Regarding FI, Matuliene., *et al*. reported that the ORs of FI I, II, and III for TL were 2.3, 4.8 and 12.3, respectively [16]. Salvi., *et al*. reported that the ORs of FI II and III are 2.92 and 6.85. In the case of non-compliers who did not visit their dental office, the ORs of FI II and III increased to 10.11 and 17.18, respectively [41]. Therefore, although most PRA models do not utilize FI as one of risk factors [29], it is reasonable that FI is included in the 2017 classification, as the risk tends to increase as the degree of FI increases (Table 6).

The 2017 classification has another peculiar characteristic. Although it is a diagnostic system, it is possible to estimate a certain degree of disease progression and TL. The 2017 classification is created as a 2-vector system using stage and grade [1,42]. However, we found that as the 2 vectors are combined, a third vector is spontaneously generated, which represents the prognostic capability of the 2017 classification (Figure 1A). To better illustrate this finding, we aligned the 2017 classification with McGuire's prognostic system and compared the sets of stage and grade with each prognostic category using a color gradient scale (Figure 1B, 1C). As periodontitis is a multifactorial disease, a clear and simple periodontal prognostic system which can be easily used by clinicians has not yet been developed. Since the 2017 classification has a limited prog-

nostic capacity, it seems reasonable to review previous prognostic systems and compare them with the 2017 classification to verify the effectiveness of its prognostic function in clinical settings.

Conclusion

Unlike previous diagnostic systems, the 2017 classification utilizes both risk and prognostic factors, which allows an accurate diagnosis of periodontitis. In this study, we have conducted a systematic review of risk and prognostic factors to verify the effectiveness of the 2017 classification. We concluded that essential 3 patient-related factors and principal 6 tooth-related factors for diagnosis are included in the 2017 classification and that the categories of each factor are mostly consistent with other literature. Although the 2017 classification is somewhat complicated and does not perfectly account for every situation, it is highly valuable from the perspective of clinical application, because not only does it provide an accurate diagnostic capacity, it also contains a prognostic capability to a certain degree. Overall, we find that the 2017 classification includes much information and therefore is a highly efficient system for clinicians.

Acknowledgements

The authors did not receive funding and have no conflict of interest to declare in relation to this systematic review.

Bibliography

1. Papapanou PN., *et al*. "Periodontitis: Consensus report of workgroup 2 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions". *Journal of Periodontology* 89.1 (2018): S173-s182.

2. Kornman KS and Papapanou PN. "Clinical application of the new classification of periodontal diseases: Ground rules, clarifications and "gray zones". *Journal of Periodontology* 91 (2020): 352-360.

3. Burt B. "Research, Science and Therapy Committee of the American Academy of Periodontology". *Position Paper: Epidemiology of Periodontal Diseases Journal of Periodontology* 76 (2005): 1406-1419.

4. Beck JD. "Risk revisited". *Community Dental Oral Epidemiology* 26 (1998): 220-225.

5. Nunn ME. "Understanding the etiology of periodontitis: an overview of periodontal risk factors". *Periodontology 2000* 32 (2003): 11-23.

6. Page RC and Beck JD. "Risk assessment for periodontal diseases". *International Dental Journal* 47 (1997): 61-87.

7. Genco RJ and Borgnakke WS. "Risk factors for periodontal disease". *Periodontology 2000* 62 (2013): 59-94.

8. Lang NP and Tonetti MS. "Periodontal risk assessment (PRA) for patients in supportive periodontal therapy (SPT)". *Oral Health and Preventive Dentistry* 1 (2003): 7-16.

9. Moher D., *et al*. "Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement". *PLoS Medicine* 6 (2009): e1000097.

10. Labriola A., *et al*. "Systematic review of the effect of smoking on nonsurgical periodontal therapy". *Periodontology 2000* 37 (2005): 124-137.

11. Van Der Weijden GA., *et al*. "Periodontitis in smokers and nonsmokers: intra-oral distribution of pockets. A retrospective study". *Journal of Clinical Periodontology* 28 (2001): 955-960.

12. Kenney EB., *et al*. "The effect of cigarette smoke on human oral 23polymorphonuclear leukocytes". *Journal of Periodontal Research* 12 (1977): 227-234.

13. Eggert FM., *et al*. "Effects of smoking and treatment status on periodontal bacteria: evidence that smoking influences control of periodontal bacteria at the mucosal surface of the gingival crevice". *Journal of Periodontology* 72 (2001): 1210-1220.

14. Tomar SL and Asma S. "Smoking-Attributable Periodontitis in the United States: Findings From NHANES III". *Journal of Periodontology* 71 (2000): 743-751.

15. Faggion CM., *et al*. "Prognostic model for tooth survival in patients treated for periodontitis". *Journal of Clinical Periodontology* 34 (2007): 226-231.

16. Matuliene G., *et al*. "Influence of residual pockets on progression of periodontitis and tooth loss: Results after 11 years of maintenance". *Journal of Clinical Periodontology* 35 (2008): 685-695.

17. Taylor GW., *et al*. "Glycemic control and alveolar bone loss progression in type 2 diabetes". *Annals of Periodontology* 3 (1998): 30-39.

18. Torkamani A. "Drilling for Insight: Forecasting Phenotype from Genotype". *Trends Genetics* 34 (2018): 821-822.

19. Wojczynski MK and Tiwari HK. "Definition of Phenotype". In: Elsevier (2018): 75-105.

20. Laine ML., *et al*. "Gene polymorphisms in chronic periodontitis". *International Journal of Dentistry* 2010 (2010): 324719.

21. Michalowicz BS., *et al*. "Evidence of a substantial genetic basis for risk of adult periodontitis". *Journal of Periodontology 2000* 71 (2000): 1699-1707.

22. Laine ML., *et al*. "Gene Polymorphisms in Chronic Periodontitis". *International Journal of Applied Dental Sciences* 2010 (2010): 1-22.

23. McGuire MK and Nunn ME. "Prognosis versus actual outcome. IV. The effectiveness of clinical parameters and IL-1 genotype in accurately predicting prognoses and tooth survival". *Journal of Periodontology* 70 (1999): 49-56.

24. McDevitt MJ., *et al*. "Interleukin-1 genetic association with periodontitis in clinical practice". *Journal of Periodontology* 71 (2000): 156-163.

25. Vanooteghem R., *et al*. "Bleeding on probing and probing depth as indicators of the response to plaque control and root debridement?". *Journal of Clinical Periodontology* 14 (1987): 226-230.

26. Claffey N., *et al*. "Diagnostic predictability of scores of plaque, bleeding, suppuration and probing depth for probing attachment loss. 31/2-years of observation following initial periodontal therapy". *Journal of Clinical Periodontology* 17 (1990): 108-114.

27. Martinez-Canut P. "Predictors of tooth loss due to periodontal disease in patients following long-term periodontal maintenance". *Journal of Clinical Periodontology* 42 (2015): 1115-1125.

28. Bergstrom J and Floderus-Myrhed B. "Co-twin control study of the relationship between smoking and some periodontal disease factors". *Community Dentistry and Oral Epidemiology* 11 (1983): 113-116.

29. Jansson H and Norderyd O. "Evaluation of a periodontal risk assessment model in subjects with severe periodontitis". *Swedish Dental Journal* 32 (2008): 1.

30. Hirata T., *et al*. "Predictive factors for tooth loss during supportive periodontal therapy in patients with severe periodontitis: a Japanese multicenter study". *BMC Oral Health* (2019): 19.

31. Kayser A. "The shortened dental arch: a therapeutic concept in reduced dentitions and certain high-risk groups". *International Journal of Prosthodontics and Restorative Dentistry* 9 (1989): 427-449.

32. Pretzl B., *et al*. "Tooth loss after active periodontal therapy. 2: tooth-related factors". *Journal of Clinical Periodontology* 35 (2008): 175-182.

33. Consensus Report, Discussion Section I. In: Nevins R, Becker W, Kornman K, eds. *World Workshop in Clinical Periodontics*. Princeton, NJ, USA: American Academy of Periodontology (1989): 1-325.

34. Wood WR., *et al*. "Tooth loss in patients with moderate periodontitis after treatment and long-term maintenance care". *Journal of Periodontology* 60 (1989): 516-520.

35. Silva S., *et al*. "Using color in visualization: A survey". *Computers and Graphics* 35 (2018): 320-333.

36. Krall EA., *et al*. "Risk of tooth loss after cigarette smoking cessation". *Preventing Chronic Disease* 3 (2006): A115.

37. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2020". *Diabetes Care* 43 (2020): S14-S31.

38. Matthews DC., *et al*. "Tooth loss in periodontal patients". *Journal-Canadian Dental Association* 67 (2001): 207-210.

39. Loe H., *et al*. "Natural history of periodontal disease in man. Rapid, moderate and no loss of attachment in Sri Lankan laborers 14 to 46 years of age". *Journal of Clinical Periodontology* 13 (1986): 431-440.

40. Joss A., *et al*. "Bleeding on probing. A parameter for monitoring periodontal conditions in clinical practice". *Journal of Clinical Periodontology* 21 (1994): 402-408.

41. Salvi GE., *et al*. "Risk factors associated with the longevity of multi-rooted teeth. Long-term outcomes after active and supportive periodontal therapy". *Journal of Clinical Periodontology* 41 (2014): 701-707.

42. Cho YJ., *et al*. "A Novel System for Predicting Periodontal Outcomes: Analysis of the 2017 Periodontitis Classification based on a Systematic Review". *Journal of Clinical Dentistry and Oral Care* 2.3 (2024): 01.