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Published in:
JOURNAL OF DENTISTRY

DOI:
10.1016/j.jdent.2021.103755

Journal of Dentistry 112 (2021) 103755

Contents lists available at ScienceDirect

Journal of Dentistry

journal homepage: www.elsevier.com/locate/jdent

Periodontal breakdown inter-tooth relationships in estimating periodontitis-related tooth loss

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ARTICLE INFO

Keywords:
Tooth loss
Periodontal disease
Epidemiology
Periodontal diagnosis

ABSTRACT

Objectives: The reasons for tooth extraction are rarely recorded in epidemiological datasets. It poses a diagnostic challenge to determine if tooth loss is related to periodontal disease (TLPD). The present study aimed to assess the inter-tooth relationships based on the periodontal characteristics of existing teeth.
Methods: A cross-sectional dataset of 8,978 participants with complete periodontal examination (including probing pocket depth [PPD] and clinical attachment loss [CAL]) in the NHANES 2009–2014 was used in this study. Spearman rank correlation was applied to assess the inter-tooth correlations of PPD/CAL among 28 teeth after adjustment for relevant confounders. We further verify our findings in the Java Project on Periodontal Disease with TLPD information available (the number of TLPD = 12).
Results: Strong PPD/CAL correlations were observed in adjacent teeth (r for PPD = 0.652, r for CAL = 0.597; false discovery rate [FDR] <0.05) rather than those on non-adjacent teeth (r for PPD = 0.515, r for CAL = 0.476; FDR <0.05). The correlations increased among severe periodontitis cases (CAL ≥5 mm or PPD ≥6 mm). In line with this, we further observed that the teeth adjacent to the TLPD tooth had the most alveolar bone loss in the Java dataset.
Conclusion: The periodontitis parameters (PPD/CAL) of adjacent teeth could be a potential indicator to estimate TLPD when actual reasons for tooth extraction are unknown.
Clinical Significance: Periodontally compromised teeth adjacent to a lost tooth may help estimate whether the loss could be related to periodontal disease when the actual extraction reasons are unknown.

1. Introduction

Periodontitis is an oral infection resulting in the loss of tooth-supporting tissue, loosening of teeth, and tooth loss ultimately [1, 2]. In turn, when a large number of teeth are lost/extracted in a population, this could mask the potentially high prevalence of severe periodontitis [3, 4]. Knowledge of the reasons of missing teeth could contribute to assessing the severity of periodontitis more accurately. Therefore, tooth loss related to periodontal disease (TLPD) was an essential component of the staging dimension in the classification proposed at the 2018 World Workshop [5]. Nevertheless, the reasons for tooth loss were rarely registered or otherwise neglected in relevant population datasets [6].

The periodontal status of existing teeth might be a reference indicator for estimating TLPD. The higher correlation of the periodontal

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https://doi.org/10.1016/j.jdent.2021.103755
Received 9 March 2021; Received in revised form 18 July 2021; Accepted 22 July 2021
Available online 3 August 2021
0300-5712/

parameters [i.e., probing pocket depth (PPD) and clinical attachment loss (CAL)] between two teeth, the more representative they are for each other. More specifically, when these periodontal parameters of different teeth are highly correlated, one specific tooth's values could represent the correlated tooth's value. A recent cross-sectional study showed significant correlations between the adjacent tooth's periodontal status and the peri-implant condition [7]. Furthermore, the colonization by the microorganisms at the implant sulcus was influenced by the periodontopathic bacteria of adjacent teeth [8]. Therefore, we hypothesized the adjacent teeth that have PPD/CAL similarities as an indicator to help estimate the reason for tooth loss. The current study aims:

1) to assess in dentitions of a general population, for each tooth the correlation of PPD/CAL with corresponding teeth: i.e., the same tooth in the other quadrants as well as with adjacent teeth.
2) to determine the tooth pairs with the highest PPD/CAL correlation in this population.

2. Methods

2.1. Study design and population

Three waves of survey data, acquired from the National Health and Nutrition Examination Survey (NHANES), were used to explore inter-tooth correlation. The NHANES is a national cross-sectional study administered by the National Center for Health Statistics (NCHS) to assess the health and nutritional status of the U.S. population through a variety of questionnaires and examinations. The NCHS collected data from a stratified, multistage, clustered probability sample of the non-institutionalized civilians. Details regarding the NHANES protocol,

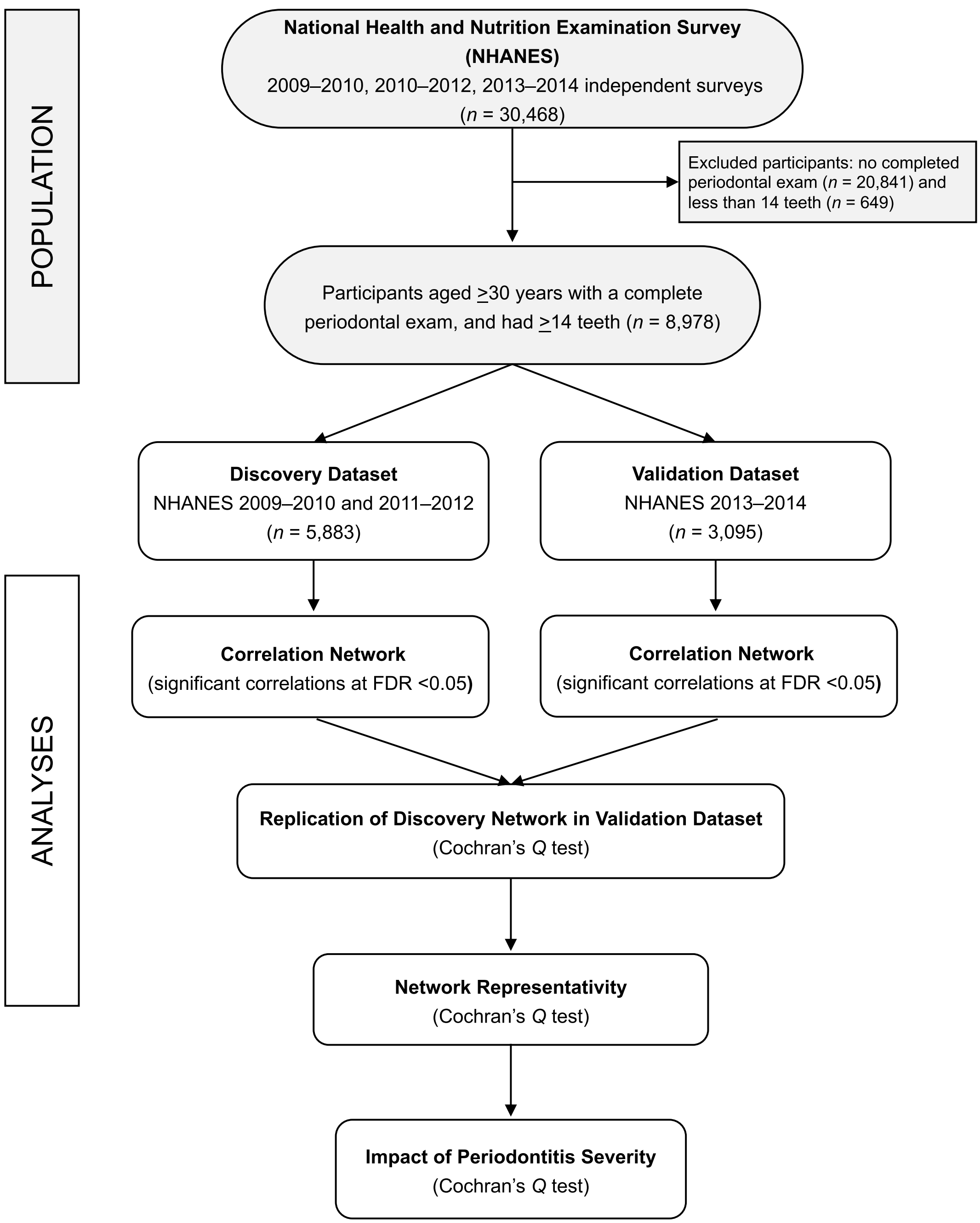

Fig. 1. Population and analysis workflow of the present study using the National Health and Nutrition Examination Survey 2009–2014 dataset.

testing procedures, and consent documents have been specified elsewhere [9]. The NCHS Ethics Review Board approved all NHANES protocols. Since this study analyzed public-use data, an additional research ethics review was not necessary for our analysis. Individuals who had fewer than 14 teeth and for whom no periodontal measurement data were available were excluded from our dataset [10]. In brief, the three waves from NHANES 2009–2014 enrolled 8,978 participants (Fig. 1). Two waves were used for a discovery dataset (NHANES 2009–2012, $n =$ 5,883) and one wave for a validation dataset (NHANES 2013–2014, $n =$ 3,095) to test the robustness and reproducibility of the results in the correlation analyses.

To verify the findings of the NHANES study, a dataset of a longitudinal study is necessary, which has a verified reason for extractions. Therefore, we used the data from the Java Project on Periodontal Diseases [11]. The study population consisted of 98 subjects from a tea estate on West Java, Indonesia, that had been part of a prospective longitudinal study and provided full datasets of clinical assessments from 1987, 1994 and 2002. In 2011, complete sets of dental radiographs were made which was combined with the survey forms and clinical slides from the previous assessments in order to estimate reasons for tooth loss. As previously described [11], a tooth was considered to be lost due to periodontitis if in the preceding examinations the presence of caries and/or root remnant of the tooth were never noted and if the tooth showed an increased pocket depth as well as attachment loss during the follow-up years, resulting in the last examination before the tooth was lost in pockets ≥6 mm with attachment loss ≥5 mm.

2.2. Demographics and health-related variables

Demographic variables included age (year), gender, ethnicity/race (non-Hispanic white, Hispanic, African American, and other races), education (≤ high school, college, and > college), annual household income (<20,000$, 20,000–75,000$, and >75,000$). Health-related characteristics included health behaviors such as smoking status (never smoked, former smoker, and current smoker), and medical history mainly comprised doctor-diagnosed diseases, such as arthritis, hypertension, hyperlipidemia, diabetes mellitus, and stroke. Physician-diagnosed myocardial infarction and coronary heart disease were defined as heart disease.

2.3. Periodontal examination

Trained and calibrated dentists from the NCHS examined each patient's dentition and periodontal status. In the dentition assessment, the tooth-positions presenting edentulous or with dental implants were recorded as tooth loss [12]. The full mouth (four quadrants) was evaluated in each participant. The periodontal examination included probing assessments for PPD and CAL at six sites per tooth (mesio-, mid-, disto-buccal and mesio-, mid-, disto-lingual). As the third molars were excluded, a maximum of 28 teeth and 168 sites per individual could be examined to assess periodontal status. The maximum PPD and CAL per tooth were applied in the analyses to simplify the hierarchical structure of the periodontal data [13]. According to the 2018 World Workshop Classification System [5, 14], the patients with the maximum CAL of 1–2 mm were defined as stage I periodontitis, 3–4 mm as stage II, and ≥5 mm as stage III/IV. The complexity of management was also evaluated. The patients of stage II periodontitis were reclassified as stage III if the maximum PPD was ≥6 mm [15]. In the present study, we defined stage III/IV as severe periodontitis (CAL ≥5 mm or PPD ≥6 mm); the others were set as non-severe periodontitis.

2.4. Data analysis

For the present study correlation analyses were performed in the NHANES datasets regarding PPD and CAL. Since PPD and CAL may relate to the previously mentioned demographic and health-related variables [16, 17], we first inverse-rank transformed PPD and CAL values and further applied a linear regression model to adjust confounding factors [18], including age, sex, BMI, tooth number, ethnicity, education, income, smoking, alcohol intake, as well as presence of diseases (arthritis, hypertension, diabetes, dyslipidemia, and heart disease). Subsequently, we took residues of PPD and CAL generated from the linear regression model and determined the correlation of 28 teeth using Spearman rank correlation (378 random tooth pairs in total, $C_2(28) = 378$). The Benjamini-Hochberg procedure was further applied to calculate the false discovery rate (FDR) [19]. Next a correlation matrix was built to present the results of all tooth pairs.

In the current dataset, 2,805 out of 8,978 participants (31%) had lost no teeth at all (Fig. *S*1). However, the missing teeth with unrecorded reasons in this population may bias the strength and direction of correlation. To further validate the representative of established correlations, we split the cohort into two parts (with and without tooth loss) to check whether there are significant differences in correlation strength and direction between two parts. Cochran-Q test was applied to assess the heterogeneity of effect sizes and direction between two parts for each correlation coefficient [20]. The Cochran-Q test calculated the squared difference between individual study effect and the pooled effect using inverse variance weighting (Fig. 1).

Periodontitis severity could be a potential factor influencing the correlation of periodontal parameters. Since the findings from correlation analyses would be applied to periodontitis patients, subgroup analyses were performed to assess the variability of the PPD/CAL correlation coefficients across the tooth-relationships based on the degree of periodontitis severity. We divided the population into two groups: severe periodontitis (SP) and non-SP. The Cochran-Q test was further applied to assess the difference between the two groups (Fig. 1).

In the NHANES datasets, the normality of the continuous variables' distributions was assessed using a Kolmogorov-Smirnov test. Continuous variables with normal distribution were reported as mean (standard deviation [SD]), whereas non-normal variables were presented as median (interquartile range [IQR]). Categorical variables were described as number and frequency. Multiple imputation was used to handle the missing data of the covariables. Tooth-relationships are described as follows [21]: adjacent teeth (AD), contralateral teeth in the same jaw (CS) or the opposite jaw (CO), and ipsilateral opposing teeth (IO) (Fig. 2A, B). Evaluation of alveolar bone loss (ABL) was performed as described previously [22]. ABL of teeth in four relationships (AD, CS, CO, and IO) linked to each TLPD tooth was assessed radiographically. A one-way analysis of variance was used to compare the correlation coefficients and ABL of the four tooth-relationship categories. Significance was defined as P <0.05 (two-tailed). All statistics were computed in R Project for Statistical Computing (version 3.6.0).

3. Results

3.1. Characteristics of study populations

Of the 5,883 participants in the discovery dataset (NHANES 2009–2012), 2,962 (50.3%) were female, and 2,604 (44.3%) were non-Hispanic white. Subjects ranged in age from 30 to 85 years, with a mean (SD) age of 50.62 (13.85) (Table 1). The characteristics of the population in the validation dataset (NHANES 2013–2014) are also shown in Table 1. Results of the Java data set showed that most teeth were lost due to caries or the co-occurrence of caries and periodontitis. Solely 12 missing teeth of only five subjects were assigned to be lost due to periodontal disease.

3.2. Inter-tooth PPD/CAL correlations

Following the workflow presented in Fig. 1, the Spearman rank correlation was applied to assess inter-tooth correlations of PPD and CAL. We observed significant PPD/CAL correlations (FDR <0.001) for

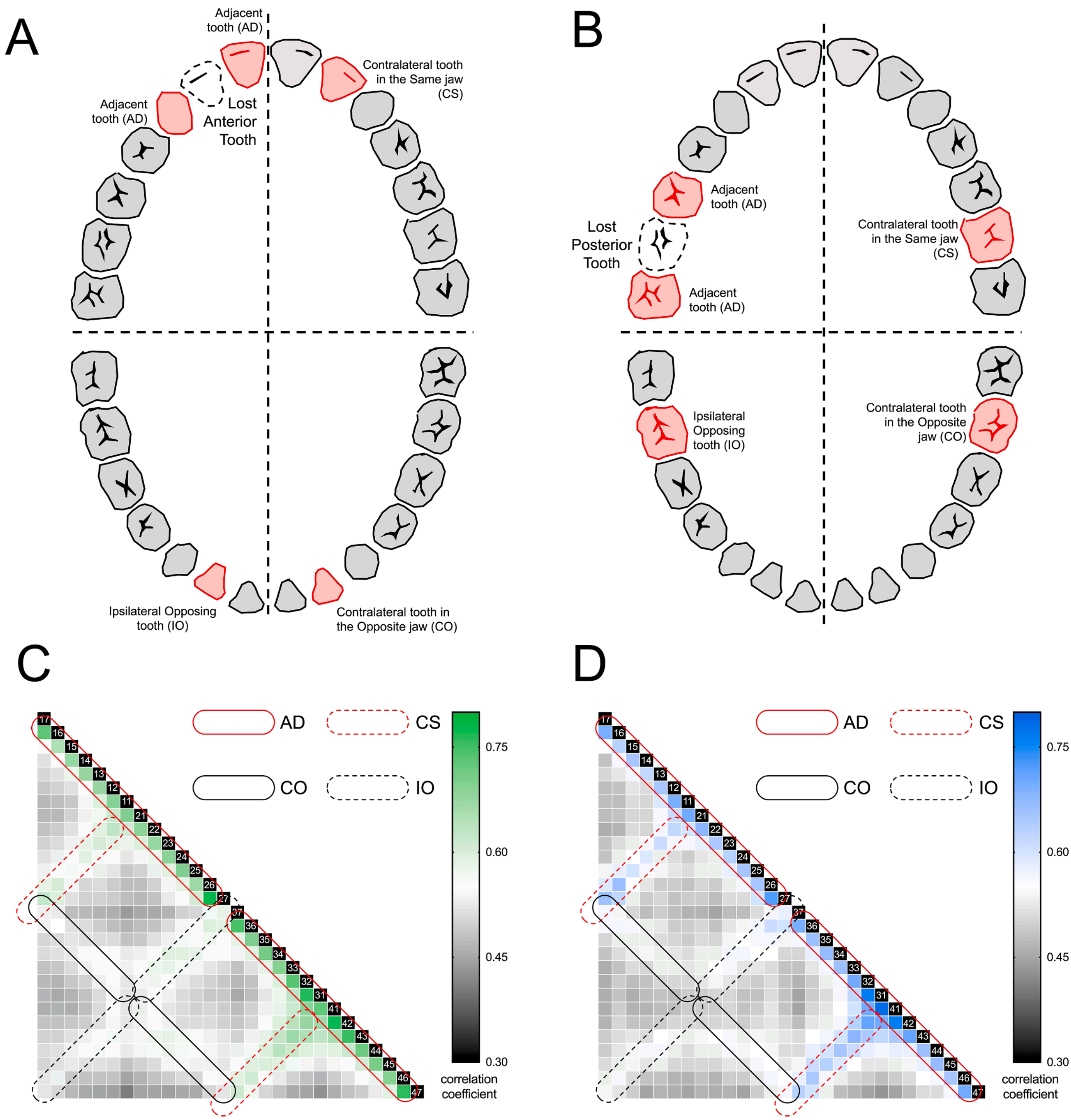

Fig. 2. Diagram of the tooth-positions examples the lost lateral incisor (A) and the first molar (B) in the right maxillary quadrant. The positions of remaining teeth are classified into four categories: adjacent teeth (AD), the contralateral teeth in the same jaw (CS) and the opposite jaw (CO), and ipsilateral opposing teeth (IO). Spearman rank correlation matrices were used to present the correlation coefficients of PPD (C) and CAL (D) among all 28 teeth (n = 378) in the discovery dataset (NHANES 2009–2012). Abbreviations: NHANES, National Health and Nutrition Examination Survey; PPD, probing pocket depth; CAL, clinical attachment loss.

all 378 tooth pairs in the discovery dataset (2009–2012, n = 5,883, Fig. 2C, D and Supplementary Data 1) with different confounding factors adjusted (age, gender, ethnicity, education, income, BMI, tooth number, smoking, alcohol intake, and chronic diseases). Strong PPD/CAL correlations were observed in adjacent teeth (r for PPD = 0.652, r for CAL = 0.597) instead of non-adjacent teeth (r for PPD = 0.515, r for CAL = 0.476, Table S1).

PPD/CAL correlations of tooth pairs in four tooth-relationships were further visualized in the tooth charts using a correlation network where the weight of each dash depended on the coefficient (AD-teeth, the number of tooth pairs [n] = 26; CS-teeth, n = 12; CO-teeth, n =14; and IO-teeth, n = 14. Fig. 3A, B). The dashes of AD-teeth and CS-teeth are more evident in the tooth charts than those of CO-teeth and IO-teeth, particularly in the lower jaw. A stronger PPD/CAL correlation was seen for the AD-teeth when compared to the CS-teeth, IO-teeth, and CO-teeth (P <0.001 for PPD and P <0.01 for CAL, Fig. 3C, D). Consider tooth

Table 1
Characteristic of the NHANES 2009–2014 subjects (n = 8,978).

VARIABLES	Discovery Dataset NHANES 2009–2012 (n = 5,883)	Validation Dataset NHANES 2013–2014 (n = 3,095)
Continuous variables, mean (SD)		
Age (year)	50.62 (13.85)	50.76 (13.90)
Body mass index (kg/m^2)	29.27 (6.48)	29.46 (7.06)
Tooth number*	26 (5)	26 (5)
Categorical variables, n (%)		
Gender		
Male	2,921 (49.7)	1,480 (47.8)
Female	2,962 (50.3)	1,615 (52.2)
Ethnicity		
Non-Hispanic White	2,604 (44.3)	1,350 (43.6)
Hispanic	1,504 (25.6)	699 (22.6)
African American	1,126 (19.1)	566 (18.3)
Others	649 (11.0)	480 (15.5)
Education		
≤ high school	2,525 (43.0)	1,198 (38.7)
college	1,660 (28.3)	948 (30.6)
> college	1,690 (28.8)	948 (30.6)
Annual household income		
≤20,000$	1,006 (17.8)	448 (15.2)
20,000-75,000$	2,929 (52.0)	1,476 (49.9)
≥75,000$	1,702 (30.2)	1,033 (34.9)
Smoking habit		
Non smoker	3,404 (57.9)	1,834 (59.3)
Former smoker	1,420 (24.1)	733 (23.7)
Current smoker	1,058 (18.0)	526 (17.0)
Arthritis	1,423 (24.2)	793 (25.7)
Hypertension	2,065 (35.1)	1,176 (38.0)
Hyperlipidemia	2,471 (42.0)	1,368 (44.2)
Diabetes mellitus	588 (10.0)	314 (10.1)
Stroke	124 (2.1)	64 (2.1)
Heart disease	318 (5.4)	170 (5.5)

* Non-normal distribution continuous variable, median (interquartile range).
Abbreviations: SD, standard deviation; NHANES, National Health and Nutrition Examination Survey

16 as an example: the PPD correlation coefficients of AD-teeth include 16–17 = 0.678 and 16–15 = 0.594, CS-teeth is 16–26 = 0.549, CO-teeth is 16–36 = 0.520, and IO-teeth is 16–46 = 0.504.

To further validate the robustness of all 378 significant periodontal correlations, another dataset (NHANES 2013–2014, n = 3,095) was included as replication, and all significant correlations in the discovery could be replicated at P <0.05 (Table *S*2 and Supplementary Data 1). Importantly, correlation strength was highest in the adjacent teeth when compared with other pairs (Fig. *S*3). Furthermore, 84.39% and 99.21% of correlations were comparable (Cochran-Q test FDR >0.05) between participants with (n = 6,173) and without (n = 2,805) tooth loss for PPD and CAL, respectively (Supplementary Data 2). This consistent effect was observed between participants with and without tooth loss (Fig. *S*3), indicating that the adjacent teeth were identified as the best correlated teeth in term of periodontal parameters.

3.3. Inter-tooth PPD/CAL correlations increased in severe periodontitis

Since this general population contains both SP and non-SP participants, we further hypothesized that inter-tooth PPD and CAL correlations may show difference between SP and non-SP potentially due to disease severity. To assess this, we first divided the participants into severe and non-severe cases based on the 2018 classification. As expected, similar results were obtained in the SP subgroup analyses (Supplementary Data 3) that adjacent teeth have higher PPD/CAL correlation coefficients than the other teeth among the participants with both non-SP and SP (P <0.001 for PPD and P <0.05 for CAL, Fig. 4A, B). Notably, the heterogeneity across two subgroups for each correlation coefficient shows stronger PPD/CAL correlations in patients with SP than individuals without SP ($P_{heterogeneity}$ <0.001 for PPD and $P_{heterogeneity}$ <0.05 for CAL, Fig. 4C, D). Again, consider tooth 16 as an example: the correlation coefficient of 16–17 (AD) increased from 0.659 in non-SP to 0.711 in SP, and 16–15 (AD) increased from 0.586 to 0.629. In brief, the adjacent tooth pairs had the highest PPD/CAL correlations; the correlation increased with increasing periodontitis severity. Table *S*3 presents more detailed analyses.

3.4. Periodontally compromised teeth adjacent to TLPD tooth in the Java cohort

As found in the correlation analysis of the NHANES study, the adjacent teeth of TLPD tooth were found as to be the most correlated concerning PPD and CAL. We further investigated whether the teeth adjacent to the lost tooth have the greatest amount of bone loss compared to other teeth in the Java cohort. Given the highly correlated teeth clustered in the AD, CS, CO, and IO tooth-relationships (Fig. 2C, D), the teeth correlations analyzed in the Java study were only limited to these four categories. The other teeth (not AD, CS, CO, and IO) have lower correlation with each other from the statistical perspective, so they were not the focus of this study, even in case they had a more periodontal breakdown. In the Java study with twelve TLPD teeth from five subjects, the teeth adjacent to the TLPD tooth presented evident ABL, with a mean (SD) ABL of 45.6% (27.5%). In contrast, the mean (SD) ABL of CS is 36.6% (34.4%), CO is 43.82% (22.5%), and IO is 36.6% (17.8%). The teeth adjacent to TLPD tooth tended to have the most alveolar bone loss among the predefined four-relationship categories, although the difference did not reach statistical significance (P >0.05). *Supplementary Data 4* displays more details.

4. Discussion

The present study found that higher correlation coefficients of PPD and CAL were observed in adjacent teeth than those in the other tooth-relationships using NHANES data of a large-scale population. There was a consistent difference in the correlation network, both overall and in the subgroup with no tooth loss. More importantly, the periodontal correlation coefficients increased with increasing periodontitis severity. In addition, it was found that the teeth adjacent to TLPD tooth presented evident alveolar bone loss in the Java study. From this, we propose a potential indicator: the periodontally compromise adjacent teeth could help estimate whether tooth loss could be related to periodontitis.

The present study evaluated the correlations of periodontal parameters among 28 teeth after adjusting for potential confounders. It appeared that teeth have a higher correlation with their adjacent teeth than with other corresponding teeth. Notably, the PPD/CAL correlation coefficients of patients with severe periodontitis are significantly higher than those of individuals in the non-severe periodontitis group. Several possible explanations exist for the periodontal similarity of adjacent teeth. Teeth in poor condition result in a reduction of tooth-supporting soft tissue and bone loss at interproximal sites, which have an impact on adjacent teeth [23, 24]. The bone-loss vulnerable interproximal alveolar sites may lead to the higher PPD/CAL correlations compared with the other, more distant tooth-relationships [25, 26]. The periodontal similarity between the adjacent teeth also could be relative with similar occlusion force, and masticatory function.

We revealed robust correlations between adjacent teeth in the severe periodontitis patients and confirmed the relationship between TLPD tooth and the adjacent teeth. In the Java project, the teeth adjacent to TLPD tooth presented moderate periodontal compromise, although the ABL of the teeth rarely reached a severe degree (i.e., >50%). From these results, we can reasonably infer that the more periodontal severe destruction of the teeth adjacent to the lost tooth, the higher probability that the reason for extraction was of periodontal origin.

When tooth extraction reasons are unknown, it is difficult to ascertain the number of TLPD teeth and accurately classify patients into

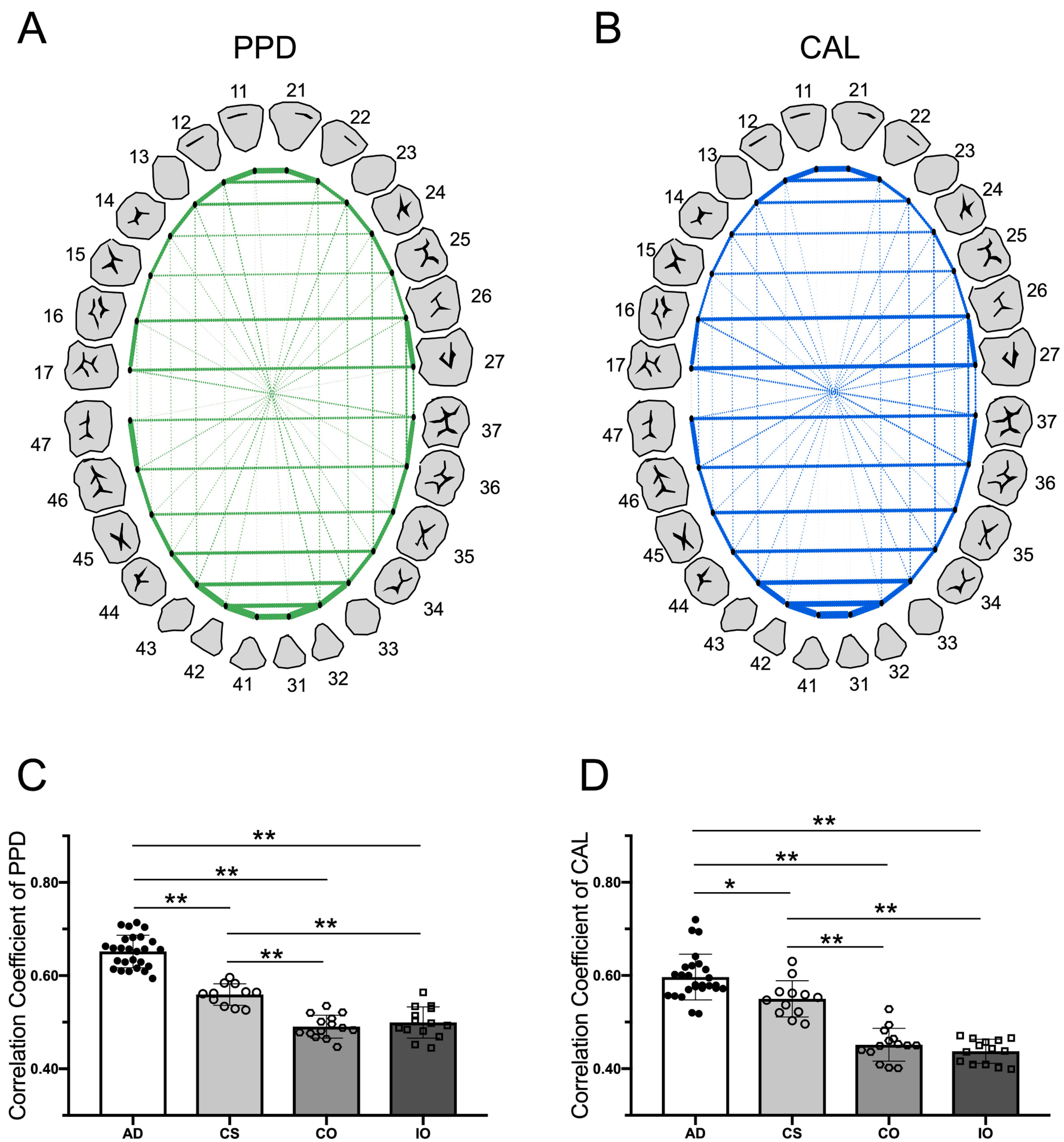

Fig. 3. Correlations of periodontal parameters among the tooth pairs were analyzed in the discovery dataset (NHANES 2009–2012). The tooth pairs in the four tooth-positions were shown in the tooth charts, with A for PPD and B for CAL. Teeth were identified using the FDI World Dental Federation notation. The correlation coefficients of PPD (C) and CAL (D) of tooth pairs in different positions were compared using a one-way analysis of variance. * $P < 0.01$, ** $P < 0.001$. Abbreviations: NHANES, National Health and Nutrition Examination Survey; PPD, probing pocket depth; CAL, clinical attachment loss; AD, adjacent teeth; CS, the contralateral teeth in the same jaw; IO, ipsilateral opposing teeth; CO, the contralateral teeth in the opposite jaw.

severe periodontitis (stage III or IV). A recent cohort study compared the 2018 and 1999 systems for classifying periodontitis [27]. As no reasons for tooth extraction were provided in the dataset, the investigators considered all lost teeth in periodontitis patients as TLPD. However, even in periodontitis patients, other factors such as caries, orthodontic interventions, or trauma could have caused tooth loss. It is anticipated that this method could result in overestimating the counts of TLPD. The overestimation of TLPD will be corrected if, for each lost tooth, it is possible to identify whether the loss was periodontitis-related or not. Furthermore, the Fourth National Oral Health Survey of China recently showed the periodontal status in Chinese adults using the case definitions of the 2018 classification [28]. Because the reason for tooth loss

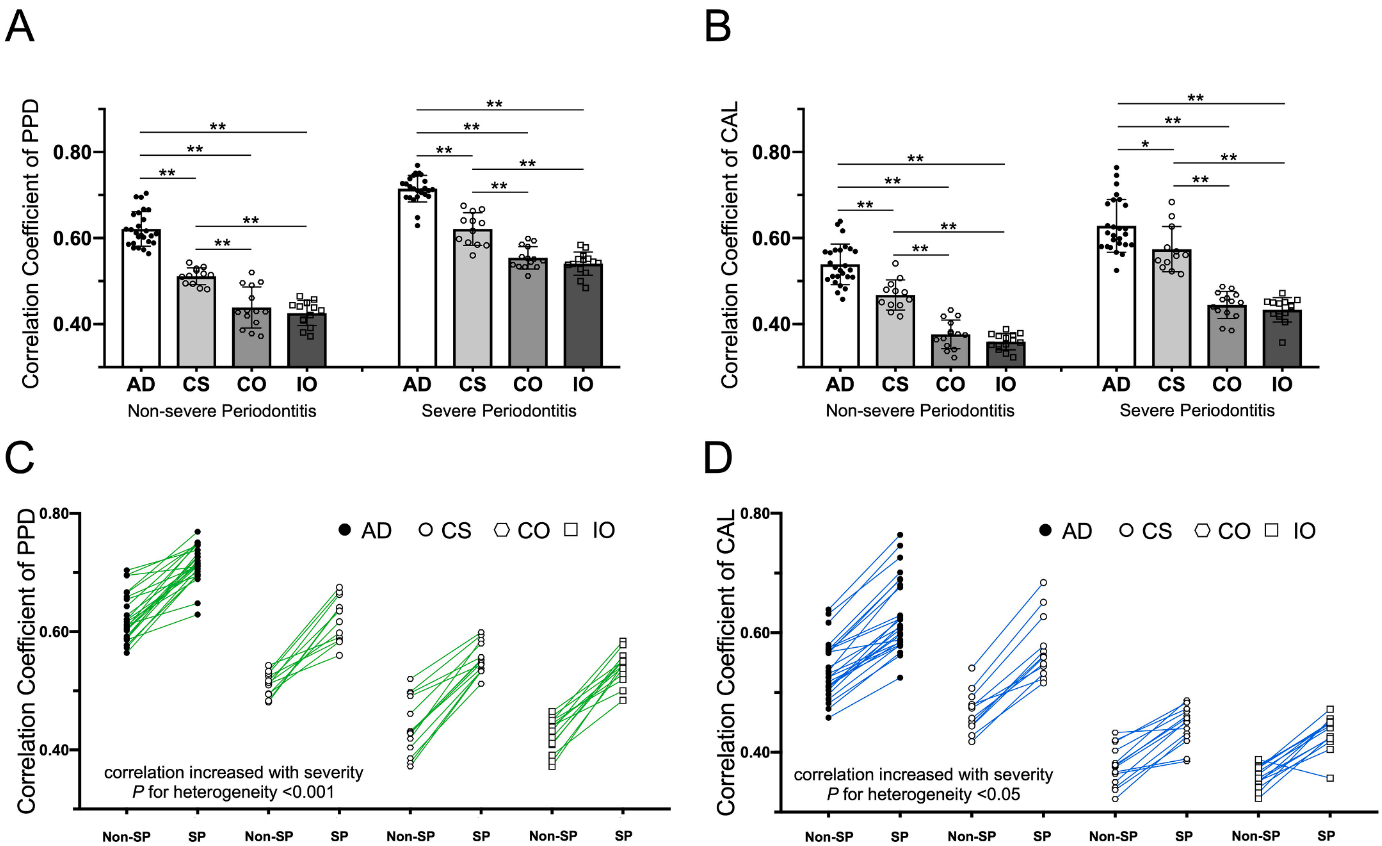

Fig. 4. Subgroup analyses were performed to assess the PPD/CAL correlation of the tooth pairs in different tooth-positions with periodontitis severity. Adjacent teeth have higher PPD (A) and CAL (B) correlation coefficients than the other teeth among participants with both non-severe and severe periodontitis. * $P<0.05$, ** $P<0.001$. Heterogeneity exists across two subgroups for each correlation coefficient, and the PPD (C) and CAL (D) correlations in severe periodontitis patients are stronger than those in the individuals with non-severe periodontitis. Circles represent tooth-position, and the lines indicate the different periodontitis severity of each tooth pair. Abbreviations: PPD, probing pocket depth; CAL, clinical attachment loss; AD, adjacent teeth; CS, the contralateral teeth in the same jaw; IO, ipsilateral opposing teeth; CO, the contralateral teeth in the opposite jaw; SP, severe periodontitis.

was not available, the authors staged periodontitis using the method proposed in the comparative study [27]. They regarded all lost teeth as TLPD and classified the patients with 1–4 missing teeth as stage IIII and ≥5 missing teeth as stage IV. The prevalence of subjects with stage IV periodontitis was 14.9% in the total population The prevalence of severe periodontitis (stage IV) was overestimated caused by neglecting other tooth loss reasons, compared with the age-standardized prevalence (9.8%) in the Global Burden of Disease 2017 Study [29]. From an epidemiological standpoint, the periodontal status of the adjacent teeth could be a reference indicator for estimating TLPD and a supportive tool for the 2017 World Workshop Classification System of periodontitis.

The limitations of the current study should be considered. Firstly, the high periodontal correlations between adjacent need to be interpreted cautiously. The cross-sectional design of the NHANES study restricts causal inference. Despite this study employed rigorous statistical analyses and observed significant and robust correlations, we cannot make the causal interpretation (e.g., the periodontally compromised tooth directly affects the neighboring ones), although it may seem reasonable. Secondly, there is no large-scale dataset for validation, in which reasons for teeth extraction are recorded. We do not have such a dataset to evaluate the method's accuracy regarding sensitivity and specificity. The Java study dataset was the best available data we were able to retrieve. However, the Java study consists of only five patients who were exclusively determined to have twelve TLPD teeth. Although the difference of ABL among AD, CS, CO, and IO did not reach statistical significance (probably given the small sample size), there was a tendency for the teeth adjacent to the TLPD tooth to show the most periodontal breakdown. This preliminarily supports our theoretical principle. Thirdly, the measurements used to describe periodontal compromise in NHANES and Java studies are inconsistent. The former measures the PPD and CAL by probing examination, but the latter assesses the ABL by means of radiography. And the exact cutoff values of measurements may be influenced by various confounders and therefore remains ambiguous. We restricted the periodontal breakdown of adjacent teeth as moderate to severe periodontitis instead of a mild one. In other words, the specific definition of moderate-severe periodontitis needs to be flexibly adjusted according to the type of periodontal measurement in the used datasets. On the other hand, when teeth adjacent to a lost tooth showed minimal or no periodontal breakdown, it is unlikely that periodontal disease is the cause of that tooth loss.

In conclusion, we proposed a reference indicator for estimating TLPD based on the robust and significant correlations of periodontal parameters between adjacent teeth. The presence of moderate-severe periodontally compromised adjacent to absent teeth might help estimate the reasons for tooth loss.

Declaration of Competing Interest

On behalf of all co-authors and myself, all institutional or corporate affiliations of mine and all funding sources supporting the study are acknowledged. Except as disclosed on a separate sheet, I certify that I have no commercial associations (eg, consultancies, patent-licensing arrangements, equity interests) that might represent a conflict of interest in connection with the submitted manuscript.

Authors' contributions

A. L., the first author, was responsible for study conception and design, data analysis and interpretation, statistical analysis, and drafted manuscript; L. C., a statistical consultant, contributed to the study design and statistical analysis; R. T. contributed to interpretation and critically reviewed the manuscript; U.v.d.V. provided data and critically reviewed the manuscript; A. A. provided data and critically reviewed the manuscript; L. S. contributed to interpretation and critically reviewed the manuscript; A. S. contributed to the study conception, interpretation, and critically reviewed the manuscript; G-H. T. contributed to the study conception and design, interpretation, and critically reviewed the manuscript. All authors gave final approval and agreed to be accountable for all aspects of work ensuring integrity and accuracy.

Funding

A.L. and L.C. are Ph.D. students conducting the research in the University Medical Center Groningen with funding from the China Scholarship Council (No. 201708440245 and No. 201708320268). The authors acknowledge funding support from the University of Groningen.

Acknowledgments

We thank the NHANES and Java study staff and investigators. A special thanks to all who participated in the studies for making this study possible through their participation.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jdent.2021.103755.

References

[1] D.F. Kinane, P.G. Stathopoulou, P.N. Papapanou, Periodontal diseases, Nat. Rev. Dis. Primers 3 (2017) 17038.
[2] R.C. Oliver, L.J. Brown, Periodontal diseases and tooth loss, Periodontol 2000 2 (1993) 117–127.
[3] A. Wahlin, A. Papias, H. Jansson, O. Norderyd, Secular trends over 40 years of periodontal health and disease in individuals aged 20-80 years in Jonkoping, Sweden: Repeated cross-sectional studies, J. Clin. Periodontol. 45 (9) (2018) 1016–1024.
[4] A. Hugoson, T. Jordan, Frequency distribution of individuals aged 20-70 years according to severity of periodontal disease, Community Dent. Oral Epidemiol. 10 (4) (1982) 187–192.
[5] P.N. Papapanou, M. Sanz, N. Buduneli, T. Dietrich, M. Feres, D.H. Fine, T. F. Flemmig, R. Garcia, W.V. Giannobile, F. Graziani, H. Greenwell, D. Herrera, R. T. Kao, M. Kebschull, D.F. Kinane, K.L. Kirkwood, T. Kocher, K.S. Kornman, P. S. Kumar, B.G. Loos, E. Machtei, H. Meng, A. Mombelli, I. Needleman, S. Offenbacher, G.J. Seymour, R. Teles, M.S. Tonetti, Periodontitis: Consensus report of workgroup 2 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions, J. Periodontol. 89 (Suppl 1) (2018) S173–s182.
[6] J.M. Albandar, Underestimation of periodontitis in NHANES surveys, J. Periodontol. 82 (3) (2011) 337–341.
[7] C.E. Sung, C.Y. Chiang, H.C. Chiu, Y.S. Shieh, F.G. Lin, E. Fu, Periodontal status of tooth adjacent to implant with peri-implantitis, J. Dent. 70 (2018) 104–109.
[8] M. Aoki, K. Takanashi, T. Matsukubo, Y. Yajima, K. Okuda, T. Sato, K. Ishihara, Transmission of periodontopathic bacteria from natural teeth to implants, Clin. Implant Dent. Relat. Res. 14 (3) (2012) 406–411.
[9] C.L. Johnson, S.M. Dohrmann, V.L. Burt, L.K. Mohadjer, National health and nutrition examination survey: sample design, 2011-2014, Vital Health Stat. 2 (162) (2014) 1–33.
[10] E. Montero, D. Herrera, M. Sanz, S. Dhir, T. Van Dyke, C. Sima, Development and validation of a predictive model for periodontitis using NHANES 2011-2012 data, J. Clin. Periodontol. 46 (4) (2019) 420–429.
[11] U. van der Velden, A. Amaliya, B.G. Loos, M.F. Timmerman, F.A. van der Weijden, E.G. Winkel, F. Abbas, Java project on periodontal diseases: causes of tooth loss in a cohort of untreated individuals, J. Clin. Periodontol. 42 (9) (2015) 824–831.
[12] G.A. Kotsakis, V. Chrepa, N. Shivappa, M. Wirth, J. Hebert, A. Koyanagi, S. Tyrovolas, Diet-borne systemic inflammation is associated with prevalent tooth loss, Clin. Nutr. 37 (4) (2018) 1306–1312.
[13] E.A. Krall, C. Abreu Sosa, C. Garcia, M.E. Nunn, D.J. Caplan, R.I. Garcia, Cigarette smoking increases the risk of root canal treatment, J. Dent. Res. 85 (4) (2006) 313–317.
[14] J. Botelho, V. Machado, L. Proença, J.J. Mendes, The 2018 periodontitis case definition improves accuracy performance of full-mouth partial diagnostic protocols, Sci. Rep. 10 (1) (2020) 7093.
[15] M. Germen, U. Baser, C.C. Lacin, E. Fıratlı, H. İşsever, F. Yalcin, Periodontitis Prevalence, Severity, and Risk Factors: A Comparison of the AAP/CDC Case Definition and the EFP/AAP Classification, Int. J. Environ. Res. Public Health 18 (7) (2021).
[16] G.J. Linden, A. Lyons, F.A. Scannapieco, Periodontal systemic associations: review of the evidence, J. Clin. Periodontol. 40 (14) (2013) S8–19. Suppl.
[17] M.P. Cullinan, G.J. Seymour, Periodontal disease and systemic illness: will the evidence ever be enough? Periodontol 2000 62 (1) (2013) 271–286.
[18] L. Chen, I.C.L. van den Munckhof, K. Schraa, R. Ter Horst, M. Koehorst, M. van Faassen, C. van der Ley, M. Doestzada, D.V. Zhernakova, A. Kurilshikov, V. W. Bloks, A.K. Groen, N.P. Riksen, J.H.W. Rutten, L.A.B. Joosten, C. Wijmenga, A. Zhernakova, M.G. Netea, J. Fu, F. Kuipers, Genetic and microbial associations to plasma and fecal bile acids in obesity relate to plasma lipids and liver fat content, Cell Rep. 33 (1) (2020), 108212.
[19] Y. Benjamini, D. Drai, G. Elmer, N. Kafkafi, I. Golani, Controlling the false discovery rate in behavior genetics research, Behav. Brain Res. 125 (1–2) (2001) 279–284.
[20] L. Chen, V. Collij, M. Jaeger, I.C.L. van den Munckhof, A. Vich Vila, A. Kurilshikov, R. Gacesa, T. Sinha, M. Oosting, L.A.B. Joosten, J.H.W. Rutten, N.P. Riksen, R. J. Xavier, F. Kuipers, C. Wijmenga, A. Zhernakova, M.G. Netea, R.K. Weersma, J. Fu, Gut microbial co-abundance networks show specificity in inflammatory bowel disease and obesity, Nat. Commun. 11 (1) (2020) 4018.
[21] S. Yamazaki, H. Arakawa, K. Maekawa, E.S. Hara, K. Noda, H. Minakuchi, W. Sonoyama, Y. Matsuka, T. Kuboki, Retrospective investigation of the remaining teeth status of patients with implant-supported fixed partial dentures in unilateral free-end edentulism, J. Prosthodont. Res. 57 (4) (2013) 262–267.
[22] A. Amaliya, M.L. Laine, J.R. Delanghe, B.G. Loos, A.J. Van Wijk, U. Van der Velden, Java project on periodontal diseases: periodontal bone loss in relation to environmental and systemic conditions, J. Clin. Periodontol. 42 (4) (2015) 325–332.
[23] J.H. Lin, C.C. Tu, Y.W. Chen, C.Y. Wang, C.M. Liu, M.Y. Kuo, P.C. Chang, Influence of Adjacent Teeth Absence or Extraction on the Outcome of Non-Surgical Periodontal Therapy, Int. J. Environ. Res. Public Health 16 (22) (2019).
[24] E.E. Machtei, Y. Zubrey, A. Ben Yehuda, W.A. Soskolne, Proximal bone loss adjacent to periodontally "hopeless" teeth with and without extraction, J. Periodontol. 60 (9) (1989) 512–515.
[25] P.N. Papapanou, J.L. Wennström, K. Gröndahl, Periodontal status in relation to age and tooth type. A cross-sectional radiographic study, J. Clin. Periodontol. 15 (7) (1988) 469–478.
[26] I.M. Nielsen, L. Glavind, T. Karring, Interproximal periodontal intrabony defects. Prevalence, localization and etiological factors, J. Clin. Periodontol. 7 (3) (1980) 187–198.
[27] C. Graetz, L. Mann, J. Krois, S. Salzer, M. Kahl, C. Springer, F. Schwendicke, Comparison of periodontitis patients' classification in the 2018 versus 1999 classification, J. Clin. Periodont. 46 (9) (2019) 908–917.
[28] J. Jiao, W. Jing, Y. Si, X. Feng, B. Tai, D. Hu, H. Lin, B. Wang, C. Wang, S. Zheng, X. Liu, W. Rong, W. Wang, W. Li, H. Meng, X. Wang, The prevalence and severity of periodontal disease in Mainland China: data from the Fourth National Oral Health Survey (2015-2016), J. Clin. Periodontol. 48 (2) (2021) 168–179.
[29] E. Bernabe, W. Marcenes, C.R. Hernandez, J. Bailey, L.G. Abreu, V. Alipour, S. Amini, J. Arabloo, Z. Arefi, A. Arora, M.A. Ayanore, T.W. Bärnighausen, A. Bijani, D.Y. Cho, D.T. Chu, C.S. Crowe, G.T. Demoz, D.G. Demsie, Z.S. Dibaji Forooshani, M. Du, M. El Tantawi, F. Fischer, M.O. Folayan, N.D. Futran, Y.C. D. Geramo, A. Haj-Mirzaian, N. Hariyani, A. Hasanzadeh, S. Hassanipour, S.I. Hay, M.K. Hole, S. Hostiuc, M.D. Ilic, S.L. James, R. Kalhor, L. Kemmer, M. Keramati, Y. S. Khader, S. Kisa, A. Kisa, A. Koyanagi, R. Lalloo, Q.Le Nguyen, S.D. London, N. D. Manohar, B.B. Massenburg, M.R. Mathur, H.G. Meles, T. Mestrovic, A. Mohammadian-Hafshejani, R. Mohammadpourhodki, A.H. Mokdad, S. D. Morrison, J. Nazari, T.H. Nguyen, C.T. Nguyen, M.R. Nixon, T.O. Olagunju, K. Pakshir, M. Pathak, N. Rabiee, A. Rafiei, K. Ramezanzadeh, M.J. Rios-Blancas, E. M. Roro, S. Sabour, A.M. Samy, M. Sawhney, F. Schwendicke, F. Shaahmadi, M. A. Shaikh, C. Stein, M.R. Tovani-Palone, B.X. Tran, B. Unnikrishnan, G.T. Vu, A. Vukovic, T.S.S. Warouw, Z. Zaidi, Z.J. Zhang, N.J. Kassebaum, Global, Regional, and National Levels and Trends in Burden of Oral Conditions from 1990 to 2017: a Systematic Analysis for the Global Burden of Disease 2017 Study, J. Dent. Res. 99 (4) (2020) 362–373.