 doi:10.20944/preprints201902.0145.v1

Peer-reviewed version available at *Brazilian Oral Research* **2019**; doi:10.1590/1807-3107bor-2019.vol33.0081

Article type: Original Research

Research field focused on in the manuscript: Periodontics

Fine-tuning multilevel modeling of risk factors associated with nonsurgical periodontal treatment outcome

João Botelho[1] 0000-0002-1019-8263, jbotelho@egasmoniz.edu.pt,
Vanessa Machado[1] 0000-0003-2503-260X, vmachado@egasmoniz.edu.pt,
Paulo Mascarenhas[1] 0000-0002-6584-1199, pmascarenhas@egasmoniz.edu.pt,
Ricardo Alves[1] 0000-0001-7184-5965, ricardocastroalves@gmail.com,
Maria Alzira Cavacas[1] 0000-0002-1790-9646, mcavacas@egasmoniz.edu.pt,
José João Mendes[1] 0000-0003-0167-4077, jmendes@egasmoniz.edu.pt,

[1]Clinical Research Unit (CRU), Centro de Investigação Interdisciplinar Egas Moniz (CiiEM), Instituto Universitário Egas Moniz

Corresponding Author:

João Botelho

Periodontology Department

Clinical Research Unit (CRU), Centro de Investigação Interdisciplinar Egas Moniz (CiiEM)

Instituto Universitário Egas Moniz, Egas Moniz Cooperativa de Ensino Superior

Campus Universitário, Quinta da Granja, 2829 - 511, Almada, Portugal

Phone: +(351) 969 848 394

Fax: not available

E-mail: jbotelho@egasmoniz.edu.pt

Abstract

This retrospective study aimed to investigate the effect of known risk factors on nonsurgical periodontal treatment (NSPT) response using a pocket depth fine-tuning multilevel linear model (MLM). Thirty-seven patients (24 males and 13 females) with moderate to severe chronic periodontitis were treated with nonsurgical periodontal therapy. Follow-up visits at 3, 6, and 12 months included measurement of several clinical periodontal parameters. Data were extracted from a database system. Probing depth (PD) and Clinical Attachment Loss (CAL) reductions after NSPT in an overall of 1416 initially affected sites (baseline PD ≥ 4 mm), distributed on 536 teeth, were analyzed against known risk factors at three hierarchical levels (patient, tooth and site). The variance component models fitted to assess the three-level variance of PD and CAL decrease for each post-treatment follow-up showed that all levels contributed significantly to the overall variance ($P < 0.001$). Patients that underwent NSPT and were continually monitored had very curative results. All three hierarchical levels included risk factors who had impact on the to influence the magnitude of PD and CAL reduction. Specifically, the tooth's type, surfaces involved and teeth mobility site-level risk factors showed the highest influence on these reductions, being highly relevant factors for the NSPT success.

Keywords: multilevel analysis; periodontal disease; nonsurgical periodontal therapy; risk factor; modelling; periodontal healing

Introduction

Periodontitis is an inflammatory disease with progressive destruction of tooth-supporting structures and, according to the Global Burden of Disease Study (GBD, 1990–2010), its severe form is the sixth most prevalent disease worldwide, affecting 11% of the overall population [1–6]. Its bacterial biofilms complexity, "silent pattern" of progression and poor awareness of individuals for the periodontal health issue, hinders its treatment and demands a motivated patient and 'long-term' compliance for a successful treatment outcome [5–10].

Nowadays, periodontitis treatment approaches are sorted on nonsurgical periodontal treatment (NSPT) and surgical periodontal therapies (SPT) and should be patient-centered [11–13]. Conventional NSPT remains the mainstay of periodontitis treatment and has been demonstrated to diminish it meaningfully [7,12], but when residual pockets remain, they may endanger tooth survival [14,15], and nonsurgical retreatment or SPT may be undertaken [13].

Multilevel modeling (MLM) was proposed to periodontal research by Albandar & Goldstein [16] in an attempt to integrate explanatory variables in a hierarchical clustered data analysis. Since then, various articles validated the usefulness of that analysis, providing clear insights in

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 18 February 2019 doi:10.20944/preprints201902.0145.v1

Peer-reviewed version available at Brazilian Oral Research 2019; doi:10.1590/1807-3107bor-2019.vol33.0081

periodontal research, from disease onset and progression to risk factors on healing response [17–29].

Apart from the extensive literature of NSPT outcomes [11–13], MLM approaches to NSPT upshots are not so common but they have demonstrated that smoking habits, tooth type, antibiotherapy, baseline probing depth (PD), baseline clinical attachment loss (CAL), baseline teeth mobility, and frequency of periodontal maintenance are relevant factors for the NSPT success [21,23,24,28,29]. It is noteworthy that this is the first time a MLM analysis is applied to a Portuguese periodontitis patient's sample to highlight what factors have influenced the NSPT therapeutic result.

Therefore this retrospective study aimed to assess, through pocket depth fine-tuning multilevel modeling, the influence of defined risk factors that may affect NSPT of moderate to severe chronic periodontitis (CP) on Southern Portuguese patients. This study hypothesizes that, after NSPT, pocket depth and clinical attachment loss reduction are influenced by patient, tooth and site level factors, including age, gender, body mass index (BMI), education background, smoking, tooth type, some baseline clinical parameters and surfaces location.

Methods

Ethical considerations

The data analyzed in this study was sourced from a database previously reported [30] regarding the effect of risk factors in a Portuguese cohort. This study was approved by the Egas Moniz Ethics Committee (IRB approval number: 595) and informed consent was obtained from all subjects. All data were registered on a database specifically created for this purpose, where a coded number was attributed to each participant. This was a retrospective cohort study, with periodontal intervention performed within the approved guidelines and regulations.

Patients selection

In this retrospective clinical study, we selected 37 patients from a total of 405 initial patients (Figure 1). The patients had been referred to the Department of Periodontology at the Egas Moniz Dental Clinic, Almada (Portugal), over the period of 2015-2017. The patients had moderate to severe periodontitis according to Page and Eke's case definitions (2012). Patients inclusion criteria were: (1) 35 to 60-years-old with no prior periodontal or orthodontic treatment; (2) at least 6 standing teeth (excluding third molars); (3) no serious mental illness or cognitive dysfunction. Exclusion criteria were: (1) do not consent to nonsurgical periodontal therapy or regular follow-up visits; (2) had a history of systemic antibiotic or periodontal treatment in the preceding 3 months; (3) pregnant or lactating females; (4) if failed the follow-up visits.

All eligible patients who agreed to participate had previously completed an in-person verbally administered survey.

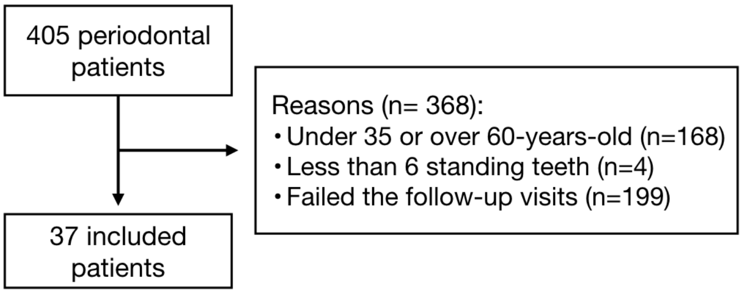

Figure 1. Flowchart of the included patients and reasons for exclusion.

Clinical procedures

The questionnaire included general information such as: gender (male/female), age, education level (elementary / middle / higher), and smoking history. The height of the participants was measured in centimeters, using a hard ruler installed vertically and secured with a stable base. Weight was assessed in kilograms using mechanical scales. BMI was calculated as the ratio of the individual's body weight to the square of their height. Self-reported hypertension and diabetes were collected from a medical questionnaire. All patients received the periodontal diagnosis, NSPT and follow-up from the same clinician, including oral hygiene instruction regarding brushing and interdental cleaning, and then regular follow-up visits at 3, 6, and 12 months. NSPT was performed by undergraduate students, under the supervision of Periodontists, following the protocol as in [31], on an average of four sessions. This was a 12-month retrospective study. The data collection was gathered at baseline and at 3, 6, and 12 months of nonsurgical periodontal treatment follow-up. Before periodontal evaluation, the number of absent teeth was recorded (excluding third molars). Plaque index was evaluated through plaque-control record (PCR) [32] in a six sites-based record (mesiobuccal, mid-buccal, distobuccal, mesiolingual, mid-lingual and distolingual). PD, Bleeding on Probing (BOP) and CAL were evaluated at six sites per tooth at baseline and follow-up visits using a manual periodontal probe (CP-12 SE Hu-Friedy,Chicago, IL, USA), circumferentially ((mesiobuccal, mid-buccal, distobuccal, mesiolingual, mid-lingual and distolingual). PD was measured as the distance from the cementoenamel junction (CEJ) to the bottom of the pocket and REC as the distance from the CEJ to the free gingival margin, and this assessment was assigned a negative sign if the gingival margin was located coronally to the CEJ. CAL was calculated as the algebraic sum of PD and REC. Presence of furcation involvement (FI) was assessed using a Nabers probe (2N Hu-Friedy, Chicago, IL, USA) following [33] in molars and upper first premolars and tooth mobility was appraised following [34]. At the follow-

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 18 February 2019 doi:10.20944/preprints201902.0145.v1

Peer-reviewed version available at Brazilian Oral Research 2019; doi:10.1590/1807-3107bor-2019.vol33.0081

up visit, all periodontal parameters above referred were repeated. Teeth that were extracted during the follow-up period were excluded from the multilevel analysis.

MLM Variables Assignment

At the Patient-level, age, BMI, number of missing teeth, percentage of sites with plaque at baseline, percentage of sites with BoP at baseline, percentage of sites with PD ≥ 5 mm at baseline were used as continuous variables, and gender (female = 0, male = 1), smoking habit (yes = 2, former smoker = 1, no = 0), Diabetes (yes = 1, no = 0), hypertension (yes = 1, no = 0) as categorical variables. At the Tooth-level, tooth-position (anterior = 1; premolar = 2; molar = 3) and mobility (physiologic mobility < 0.2 = 0; mobility ≤ 1 mm = 1; 1 mm < mobility ≤ 2 mm = 2; mobility > 2 mm = 3) and FI (no involvement = 0; degree I = 1; degree II = 2; degree III = 3) were used as categorical variables. At the Site-level, PD, CAL, Plaque and BoP values at baseline were used as continuous values, and Interproximal vs. mid surfaces (mesiobuccal/distobuccal/mesiolingual/distolingual = 1; mid-buccal/mid-lingual =2) and Buccal vs. Lingual surfaces (mesiobuccal/mid-buccal/distobuccal = 1; mesiolingual/mid-lingual/distolingual) as categorical variables.

Statistical Analysis

All statistical procedures were computed with SPSS Statistics 24 software (IBM Corp. 2011; Armonk, NY, USA). Data were filtered at the source to select only treated sites (baseline PD ≥ 4 mm). Means are reported with standard deviation (SD): mean (± SD). After the descriptive statistics, we confirmed the hierarchical structure of periodontal disease measurements by performing 3-level (tooth site, tooth, and patient) variance component model for both PD and CAL healing response to treatment. Because the treatment response at site-level turned out not being truly independent, we tested the data for other MLM assumptions and once met proceeded with MLM analysis [16,28,29] (Supplement 1). This type of analysis weights the influence of multilevel nested factors in the reduction of PD and CAL after nonsurgical periodontal treatment. To prevent over-fitness MLM was reduced from redundant variables through backward stepwise (p > 0.1, cutoff for removal). Furthermore, the treatment outcome at 3, 6 and 12-month follow-up visits were compared through nested design repeated-measures ANOVA with Greenhouse-Geisser correction. When differences were found, post-hoc pairwise multi-comparisons tests were performed with the conventional statistical significance of 5% modified through Bonferroni adjustment.

Peer-reviewed version available at Brazilian Oral Research 2019; doi:10.1590/1807-3107bor-2019.vol33.0081

Results

In this clinical study we assessed a total of 37 patients. The baseline clinical and periodontal parameters are described in Table 1. The mean age was 57.92 ± 10.87 years old, ranging from 36 to 75. This sample had higher prevalence of male patients (64.86%). Only seven patients were smokers. The mean BMI was 26.69 (± 3.97 kg/m2). In respect to the socio-economic background, there were 13 patients with a monthly income up to 580€ (national minimum wage), 11 patients with 581-900€ and 13 patients with more than 900€. The majority had high school education or below (78.38%). These patients had, in average, 7.24 (± 5.00) missing teeth. In terms of self-reported systemic diseases, diabetes and hypertension were reported in 11 (29.73%) and 17 patients (45.95%), respectively. The sample included a total of 758 teeth, with 366 anterior teeth, 221 premolars, and 171 molars. There were 574 teeth with physiologic mobility, 114 teeth with grade 1 mobility, 64 teeth with grade 2 mobility, and 6 teeth with grade 3 mobility. At baseline, plaque was present at 31.64 ± 20.43% of the sites. The mean percentage of sites with BOP at baseline was 10.56 ± 13.03. The mean percentage of sites with PD ≥ 5 mm at baseline was 8.18 ± 9.25.

In response to nonsurgical periodontal treatment, the full-mouth mean PD and CAL showed significant reductions from baseline to 3, 6, and 12 months' follow-up visits. The mean PD was 4.89 mm (± 1.19) at baseline, 3.61 mm (± 1.32) at 3 months, 3.14 mm (± 1.20) at 6 months, and 3.16 mm (± 1.21) at 12 months. The mean CAL was 5.84 mm (± 2.05) at baseline, 4.60 mm (± 2.16) at 3 months, 4.13 mm (± 2.13) at 6 months, and 4.14 mm (± 2.09) at 12 months.

The mean percentage of sites with plaque was 31.64 (± 20.43) at baseline, 21.20 (± 15.11) at 3 months, 21.02 (± 13.75) at 6 months, 20.60 (± 10.82) at 12 months. The mean percentage of sites with BoP was 10.56 (± 13.03) at baseline, 4.04 (± 5.81) at 3 months, 4.94 (± 5.70) at 6 months, 4.10 (± 5.48) at 12 months (Table 1).

Multilevel statistical analysis

To investigate the amount of variance associated with the reduction of PD and CAL allocated in each studied level we started the MLM analysis by fitting a variance componente model (Table 2). This model reported an unbalanced, though significant ($p < 0.001$), distribution of the variance across all three levels, with the major proportion being due to within tooth (site) variations. Furthermore, the marginal means output for PD and CAL reduction throughout the follow-up visits were all significantly positive, increasing within the follow-up visits time frame. Although the model results point out the major improvements occurring in the first 3 months after treatment, a smaller but still significant recovery is also shown to happen in the following 3- month period, until the 6-month checkup.

Peer-reviewed version available at Brazilian Oral Research 2019; doi:10.1590/1807-3107bor-2019.vol33.0081

Next, we fitted MLM including all our selected risk factor candidates for PD and CAL reductions (Supplement 1). In this crude models the continuous variables with significant positive coefficients were associated with recovery while those with significant negative coefficients represented an unfavorable prognostic. On the other hand, the categorical variables coefficients were relative to a reference category, with positive values meaning a better prognostic than the reference, and otherwise if negative. To prevent over-fitness this models were reduced through stepwise backwards ($p<0.10$ to remain in the model) and the final models variables and associated coefficients are shown in Table 3.

The relationship of the risk factors and PD on healing response

A total of 1416 sites with baseline PD≥4mm (31.13% of all sites) from 536 teeth in 37 patients were included in this study (Table 4). The mean PD reduction from baseline at 3, 6 and 12 months were 1.29 mm (± 1.38), 1.75 mm (± 1.46) and 1.74 mm (± 1.49), respectively.

The selected site-level risk factor variables explained 30.3%, 42.3% and 45.9% of the total PD reduction site level variance at 3, 6, and 12 months. The mid surfaces showed the best prognostic in the reduction in PD at all follow-up visits ($p < 0.001$). Between buccal and lingual surfaces of teeth, buccal surfaces showed a significantly higher reduction at 6 and 12 months ($p < 0.01$).

The tooth level risk factor selected variables reduced the unexplained total variance of PD reduction at this intermediate level by 4.6% and 39.3% and 24.5%, at 3, 6 and 12 months, respectively. Tooth mobility enhanced the reduction in PD at 3 and 6 months ($p < 0.01$). Anterior teeth and premolars showed a significant decrease in PD at 3, 6 and 12 months ($p < 0.01$).

PD reduction unexplained variance on patient level decreased 19.3%, 29.5%, and 13.0%, at 3, 6, and 12 months, respectively, after the inclusion of selected patient-level risk factor variables in MLM. On the other hand, the number of missing teeth negatively influenced the decrease in PD at 6 months ($p = 0.024$).

There was a significant difference in PD reduction from baseline between the first follow-up (3 months) and both second and third follow-ups (6 and 12 months), but not between the second and third, even when adjusting for Patient and Tooth nested effects.

The relationship of the risk factors and CAL on healing response

The same 1416 sites were included in this analysis (Table 3). Compared with the baseline, CAL means reduction were 1.24 mm (± 1.34), 1.71 mm (± 1.43), 1.70 mm (± 1.46) at 3, 6, and 12 months, respectively.

Peer-reviewed version available at Brazilian Oral Research 2019; doi:10.1590/1807-3107bor-2019.vol33.0081

On the site level, there was an unexplained variance decrease of 30.1%, 42.0%, 46.2% of CAL reduction at 3, 6, and 12 months after including selected risk factors fixed-effects variables to MLM. At the site level, mid surfaces of teeth showed a significantly greater reduction in CAL at 3, 6, and 12 months ($p < 0.001$). When comparing buccal and lingual surfaces, buccal surfaces showed a significantly greater reduction at 6 and 12 months ($p < 0.01$). Baseline PD showed to be significant for CAL recovery at all follow-up visits ($p < 0.001$).

The variables on the tooth level reduced 27.5% and 15.0% the unexplained variance of this level regarding CAL reduction at 6 and 12 months. At the tooth level, teeth with mobility revealed greater reduction in CAL at 3 and 6 months ($p < 0.01$). Anterior teeth showed a significantly greater reduction in CAL at all follow-up visits, whereas premolars only revealed significant recoveries at 6 and 12 months ($p < 0.01$).

The unexplained CAL reduction variance on the patient level was reduced by 19.8%, 36.1%, and 23.3% at 3, 6, and 12 months. At the patient level, mean PD at baseline showed a significant positive effect in CAL reduction at 3, 6, and 12 months ($p < 0.001$), however, mean Rec at baseline showed no significant results. The number of missing teeth had significant impact in CAL reduction at 6 months ($p = 0.034$).

Discussion

The results of this retrospective study show that disdaining any level may lead to inaccurate conclusions, and is in agreement with previous research [19,20,29]. The variance component models were used to weigh and compare risk factors of moderate to severe forms of periodontitis after NSPT.

Since its proposal in periodontology research [16], multilevel analysis began to be employed to study periodontitis' onset risk factors [17,19,20,25,27], the effect of risk factors in nonsurgical and surgical periodontal therapies [21,23,24,28,29] and in the prediction of bone and tooth loss in maintained periodontal patients [18,22,26]. Though in periodontitis’ onset risk studies we reckon that all sites are potentially susceptible, in studies on periodontal therapies we should focus only in treated sites, and in this sense, the combination of initial sound and unsound locations may mislead and skew the results. Furthermore, Jiao et al. [28] assessed the NSPT outcomes in all sites against sites with baseline PD ≥ 5mm, and found significant differences in between. Ergo, in this study, we strictly confined our analyzes to baseline unsound PD (PD ≥ 4mm).

Patient-level showed that most of the covariates did not express any influence on post-NSPT recovery, namely age, gender, smoking, self-reported systemic diseases, education background and few clinical parameters. On the other hand, BMI and number of missing teeth showed irregular significance. Unlike previous studies, these patients presented decreased tendency for

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 18 February 2019 doi:10.20944/preprints201902.0145.v1

Peer-reviewed version available at *Brazilian Oral Research* **2019**; doi:10.1590/1807-3107bor-2019.vol33.0081

gingival bleeding. Mean baseline BoP was 10.56% and was much less than that of American (26.4–82.01%), Asian and European patients [23,24,28,35–39]. A possible explanation is the fact that all patients were referred by a Screening Department of our Clinic (Machado et al 2018). In this triage, patients are educated and instructed for oral hygiene. Therefore, the time between the Screening and the Periodontology appointments could have an influence on a hypothetical reduction of baseline BoP. This low tendency may explain why BoP percentage did not affect NSPT outcomes as previously reported [23,24,28,29].

Among tooth-level, anterior teeth (incisors and canines) had a more significant reduction of PD and CAL than molars throughout the follow-up time, but between molar and premolars, this significance was only expressed at 6 and 12 months. These results are in accordance with previous studies [21,23,28,29,40], although Jiao et al. [28] compared molar and non-molar teeth while Song et al. [29] did not show as much meaning in the reduction of PD. As is widely accepted, molars have the worse healing prognosis due to anatomic and morphologic characteristics such as furcations and size of entrance, root trunk length, bifurcation ridges, root concavities and cervical enamel projections [12,40,41]. Likewise, premolars have some peculiarities that decrease the prognosis, but far less sententious than molars [12,40,41]. Besides, initial hypermobility was more associated with lower treatment outcomes but only during the first six months after NSPT.

At site-level, the mid teeth surfaces showed more reduction both in PD and CAL at 3, 6, and 12 months. When opposing buccal and lingual surfaces, buccal teeth surfaces had a more significant decrease from the six months, expressing a significantly higher recovery. As in Song et al. [29], the interproximal surfaces had less recuperation than the mid ones, with more significant values for PD. Nevertheless, when comparing buccal and lingual surfaces, there was more substantial recovery on the buccal surfaces, only at 6 and 12 months, in contrast to the results of Wan et al. [23] that have observed a sounder improvement on the lingual sites. Although the reason for less recovery from the interproximal surfaces can be due to a marked history of less interproximal hygiene, the difference between buccal and lingual surfaces is not so easy to explain. In the future, further studies are needed to understand this matter thoroughly. Notwithstanding, baseline PD mainly influenced the efficacy of NSPT during the 3 follow-up periods in a growing manner, showing that the initial periodontal depth may guide the treatment outcome as previously demonstrated [21].

One limitation of this study is its that its limited sample size, may lead to unpowered analysis and test results, even though we have found the same limitation in other similar MLM studies [21,23,29]. We tried to overcome such issue by relaxing the model coefficients threshold for significance from $p<0.05$ to $p<0.10$ and also by fitting the model strictly with data from treated sites. The cost of NSPT is expensive and, for most, is not reimbursed. Moreover, our recent study highlighted the poor awareness of dental health and patient's consult neglect from this

Peer-reviewed version available at Brazilian Oral Research 2019; doi:10.1590/1807-3107bor-2019.vol33.0081

population [30]. On the other hand, the retrospective nature of the study and the fact that various clinicians treated and examined the participants can increase the probability of consistency fails.

Conclusion

In this study, pocket depth fine-tuning multilevel modelling showed that NSPT had a significant healing effect for moderate to severe CP with considerable PD and CAL reductions. Major recovery on PD and CAL were noticed to happen in the first 3 months after NSPT. The PD fine-tuning MLM analysis found that all three levels revealed to influence the reduction of PD and CAL levels. The largest effect on PD and CAL reductions was observed at the site-level.

Acknowledgements

None.

Funding information

None.

References

1. Pihlstrom BL, Michalowicz BS, Johnson NW: Periodontal diseases. Lancet 366: 1809, 2005.
2. Darveau RP: Periodontitis: a polymicrobial disruption of host homeostasis. Nat Rev Microbiol 8: 481, 2010.
3. Kassebaum NJ, Bernabé E, Dahiya M, Bhandari B, Murray CJL, Marcenes W: Global burden of severe periodontitis in 1990-2010: A systematic review and meta-regression. J Dent Res 93: 1045, 2014.
4. Richards D, Marcenes W, Kassebaum NJ, Bernabé E, Dahiya M, Bhandari B, Murray CJ: Review finds that severe periodontitis affects 11% of the world population. Evid Based Dent 15: 70, 2014.
5. Jin LJ, Lamster IB, Greenspan JS, Pitts NB, Scully C, Warnakulasuriya S: Global burden of oral diseases: emerging concepts, management and interplay with systemic health. Oral Dis 22: 609, 2016.
6. Tonetti MS, Jepsen S, Jin L, Otomo-Corgel J: Impact of the global burden of periodontal diseases on health, nutrition and wellbeing of mankind: A call for global action. J Clin Periodontol 44: 456, 2017.
7. Renvert S, Persson GR: Treatment of periodontal disease in older adults. Periodontol 2000 72: 108, 2016.
8. Arweiler NB, Auschill TM, Sculean A: Patient self-care of periodontal pocket infections. Periodontol 2000 76: 164, 2018.
9. Bosshardt DD: The periodontal pocket: pathogenesis, histopathology and consequences. Periodontol 2000 76: 43, 2018.
10. Donos N: The periodontal pocket. Periodontol 2000 76: 7, 2018.
11. Heitz-Mayfield LJA: How effective is surgical therapy compared with nonsurgical debridement? Periodontol 2000 37: 72, 2005.

12. Heitz-Mayfield LJA, Lang NP: Surgical and nonsurgical periodontal therapy. Learned and unlearned concepts. Periodontol 2000 62: 218, 2013.
13. Graziani F, Karapetsa D, Mardas N, Leow N, Donos N: Surgical treatment of the residual periodontal pocket. Periodontol 2000 76: 150, 2018.
14. Fardal Ø, Johannessen AC, Linden GJ: Tooth loss during maintenance following periodontal treatment in a periodontal practice in Norway. J Clin Periodontol 31: 550, 2004.
15. Matuliene G, Pjetursson BE, Salvi GE, Schmidlin K, Brägger U, Zwahlen M, Lang NP: Influence of residual pockets on progression of periodontitis and tooth loss: Results after 11 years of maintenance. J Clin Periodontol 35: 685, 2008.
16. Albandar JM, Goldstein H: Multi-Level Statistical Models in Studies of Periodontal Diseases. J Periodontol 63: 690, 1992.
17. Axtelius B, Söderfeldt B, Attström R: A multilevel analysis of factors affecting pocket probing depth in patients responding differently to periodontal treatment. J Clin Periodontol 26: 67, 1999.
18. Nieri M, Muzzi L, Cattabriga M, Rotundo R, Cairo F, Prato GPP: The Prognostic Value of Several Periodontal Factors Measured as Radiographic Bone Level Variation: A 10-Year Retrospective Multilevel Analysis of Treated and Maintained Periodontal Patients. J Periodontol 73: 1485, 2002.
19. Tu Y-K, Gilthorpe MS, Griffiths GS, Maddick IH, Eaton K a, Johnson NW: The Application of Multilevel Modeling in the Analysis of Longitudinal Periodontal Data – Part I: Absolute Levels of Disease. J Periodontol 75: 127, 2004.
20. Tu Y-K, Gilthorpe MS, Griffiths GS, Maddick IH, Eaton K a, Johnson NW: The Application of Multilevel Modeling in the Analysis of lLongitudinal Periodontal Data – Part II: Changes in Disease Levels over Time. J Periodontol 75: 137, 2004.
21. Tomasi C, Leyland AH, Wennström JL: Factors influencing the outcome of non-surgical periodontal treatment: a multilevel approach. J Clin Periodontol 34: 682, 2007.
22. Muzzi L, Nieri M, Cattabriga M, Rotundo R, Cairo F, Pini Prato GP: The Potential Prognostic Value of Some Periodontal Factors for Tooth Loss: A Retrospective Multilevel Analysis on Periodontal Patients Treated and Maintained Over 10 Years. J Periodontol 77: 2084, 2006.
23. Wan CP, Leung WK, Wong MCM, Wong RMS, Wan P, Lo ECM, Corbet EF: Effects of smoking on healing response to non-surgical periodontal therapy: A multilevel modelling analysis. J Clin Periodontol 36: 229, 2009.
24. Mdala I, Haffajee AD, Socransky SS, Blasio BF de, Thoresen M, Olsen I, Goodson JM: Multilevel analysis of clinical parameters in chronic periodontitis after root planing/scaling, surgery, and systemic and local antibiotics: 2-year results. J Oral Microbiol 4: 17535, 2012.
25. Zeng J, Williams SM, Fletcher DJ, Cameron CM, Broadbent JM, Shearer DM, Thomson WM: Reexamining the Association Between Smoking and Periodontitis in the Dunedin Study With an Enhanced Analytical Approach. J Periodontol 85: 1390, 2014.
26. Martinez-Canut P: Predictors of tooth loss due to periodontal disease in patients following long-term periodontal maintenance. J Clin Periodontol 42: 1115, 2015.
27. Dalazen CE, Carli AD De, Bomfim RA, Santos MLM Dos: Contextual and individual factors influencing periodontal treatment needs by elderly brazilians: A multilevel analysis. PLoS One 11: 1, 2016.
28. Jiao J, Shi D, Cao Z, Meng H, Lu R, Zhang L, Song Y, Zhao J: Effectiveness of non-surgical periodontal therapy in a large Chinese population with chronic periodontitis. J Clin Periodontol 44: 42, 2017.
29. Song J, Zhao H, Pan C, Li C, Liu J, Pan Y: Risk factors of chronic periodontitis on healing response: A multilevel modelling analysis. BMC Med Inform Decis Mak 17: 1, 2017.
30. Machado V, Botelho J, Amaral A, Proença L, Alves R, Rua J, Cavacas MA, Delgado AS, Mendes JJ: Prevalence and extent of chronic periodontitis and its risk factors in a Portuguese subpopulation: a retrospective cross-sectional study and analysis of Clinical Attachment Loss. PeerJ, 2018.
31. Lang NP, Lindhe J: Clinical Periodontology and Implant Dentistry. In: Chichester: John Wiley & Sons Ltd., 2015.

32. O'Leary J, Drake B, Naylor JE: The Plaque Control Record. J Periodontol 43: 38, 1972.
33. Hamp S-E, Nyman S, Lindhe J: Periodontal treatment of multi rooted teeth. Results after 5 years. J Clin Periodontol 2: 126, 1975.
34. Lindhe J, Nyman S: The role of occlusion in periodontal disease and the biological rationale for splinting in treatment of periodontitis. Oral Sci Rev 10: 11, 1977.
35. Sculean A, Schwarz F, Berakdar M, Romanos GE, Brecx M, Willershausen B, Becker J: Non-surgical periodontal treatment with a new ultrasonic device (Vector^{TM}-ultrasonic system) or hand instruments a prospective, controlled clinical study. J Clin Periodontol 31: 428, 2004.
36. Trombelli L, Rizzi A, Simonelli A, Scapoli C, Carrieri A, Farina R: Age-related treatment response following non-surgical periodontal therapy. J Clin Periodontol 37: 346, 2010.
37. Shiloah J, Bland PS, Scarbecz M, Patters MR, Stein SH, Tipton DA: The effect of long-term aspirin intake on the outcome of non-surgical periodontal therapy in smokers: A double-blind, randomized pilot study. J Periodontal Res 49: 102, 2014.
38. Costa FO, Cota LOM, Cortelli JR, Cortelli SC, Cyrino RM, Lages EJP, Oliveira APL: Surgical and non-surgical procedures associated with recurrence of periodontitis in periodontal maintenance therapy: 5-year prospective study. PLoS One 10: 1, 2015.
39. Baelum V, López R: Defining and predicting outcomes of non-surgical periodontal treatment: A 1-yr follow-up study. Eur J Oral Sci 124: 33, 2016.
40. Angst PDM, Piccinin FB, Oppermann RV, Marcantonio RAC, Gomes SC: Response of molars and non-molars to a strict supragingival control in periodontal patients. Braz Oral Res 27: 55, 2013.
41. Matthews DC, Tabesh M: Detection of localized tooth-related factors that predispose to periodontal infections. Periodontol 2000 34: 136, 2004.

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 18 February 2019 doi:10.20944/preprints201902.0145.v1

Peer-reviewed version available at Brazilian Oral Research 2019; doi:10.1590/1807-3107bor-2019.vol33.0081

Table Legends

Table 1. Baseline clinical and periodontal parameters by variables

Table 1. Baseline clinical and periodontal parameters by variables

Variable	
Patient-level (*N* = 37)	**Mean (SD)**
Age	57.92 (10.87)
BMI (kg/m2)	26.69 (3.97)
Number of missing teeth (N)	7.24 (5.00)
% of sites with plaque at baseline	31.64 (20.43)
%of sites with plaque at 3-month Follow-up	21.20 (15.11)
%of sites with plaque at 6-month Follow-up	21.02 (13.75)
%of sites with plaque at 12-month Follow-up	20.60 (10.82)
%of sites with BoP at baseline	10.56 (13.03)
%of sites with BoP at 3-month Follow-up	4.04 (5.81)
%of sites with BoP at 6-month Follow-up	4.94 (5.70)
%of sites with BoP at 12-month Follow-up	4.10 (5.48)
%of sites with PD ≥ 5mm at baseline	8.18 (9.25)
Variable	
Patient-level (N = 37)	**N (%)**
Gender	
Male	24 (64.86%)
Female	13 (35,14%)
Education	
Elementary School	21 (56.76%)
High School	8 (21.62%)
Higher	8 (21.62%)
Hypertension	
Yes	17 (45.95%)
No	20 (54.05%)
Diabetes	
Yes	11 (29.73%)
No	26 (70.27%)

Peer-reviewed version available at *Brazilian Oral Research* **2019**; doi:10.1590/1807-3107bor-2019.vol33.0081

Smokers	
Yes	7 (18.92%)
Former smokers	0 (0.00%)
No	30 (81.08%)
Tooth position-level (N = 758)	
Tooth position	
Anterior	366 (48.28%)
Premolar	221 (29.16%)
Molar	171 (22.56%)
Mobility	
Do not have mobility	574 (75.73%)
Mobility ≤ 1 mm	114 (15.04%)
1 mm < Mobility ≤ 2 mm	64 (8.44%)
Mobility > 2 mm	6 (0.79%)
FI (first premolars and molars) (n=122)	
No involvement	209 (91.14%)
Degree I	9 (4.05%)
Degree II	2 (0.90%)
Degree III	2 (0.90%)
Site-level (N = 1416)	
Surface of tooth	
buccal / lingual	640 (45.2%) / 776 (54.8%)
interproximal (mesiocclusion/distocclusion) / mid	1218 (86.0%) / 198 (14.0%)

BMI – Body Mass Index, BoP – Bleeding on Probing, FI – Furcation Involvement, PD – Pocket Depth, Rec – Recession

Peer-reviewed version available at *Brazilian Oral Research* **2019**; doi:10.1590/1807-3107bor-2019.vol33.0081

Table 2: Variance Components models for PD and CAL reduction

Table 2: Variance Components models for reduction in PD and CAL

Variance	Variance Components (%)	SE	*P*	Marginal Mean values (SE)
The reduction in 3-month PD				
Patient (level-3)	0.465 (24.4%)	0.128	*<0.001	1.14 (0.12) [a]
Tooth (level-2)	0.220 (11.5%)	0.043		
Site (level-1)	1.220 (64.0%)	0.054		
The reduction in 6-month PD				
Patient (level-3)	0.525 (26.3%)	0.139		1.51 (0.13) [b]
Tooth (level-2)	0.280 (14.0%)	0.047		
Site (level-1)	1.195 (59.8%)	0.054		
The reduction in 12-month PD				
Patient (level-3)	0.506 (24.2%)	0.138		1.56 (0.13) [b]
Tooth (level-2)	0.331 (15.8%)	0.052		
Site (level-1)	1.257 (60.0%)	0.057		
The reduction in 3-month CAL			*<0.001	
Patient (level-3)	0.324 (18.5%)	0.093		1.10 (0,10) [c]
Tooth (level-2)	0.229 (13.0%)	0.043		
Site (level-1)	1.202 (68.5%)	0.054		
The reduction in 6-month CAL				
Patient (level-3)	0.438 (23.2%)	0.117		1.46 (0.12) [d]
Tooth (level-2)	0.276 (14.6%)	0.046		
Site (level-1)	1.172 (62.1%)	0.053		
The reduction in 12-month CAL				
Patient (level-3)	0.417 (21.0%)	0.116		1.52 (0.12) [d]
Tooth (level-2)	0.341 (17.2%)	0.052		
Site (level-1)	1.227 (61.8%)	0.055		

*Nested ANOVA repeated measures, *P* < 0.05

[a,c] *Post-hoc* test, *different letters mean Bonferroni adjusted significant differences*, *P* < 0.001

Peer-reviewed version available at Brazilian Oral Research 2019; doi:10.1590/1807-3107bor-2019.vol33.0081

Table 3. Adjusted intercept models for PD and CAL reduction

	3-month Estimate (SE)	*p*	6-month Estimate (SE)	*p*	12-month Estimate (SE)	*p*	3-month Estimate (SE)	*p*	6-month Estimate (SE)	*p*	12-month Estimate (SE)	*p*
Patient-level												
BMI	0.05 (0.03)	0.055	-	-	-	-	-	-	-	-	-	-
Number of missing teeth	-	-	-0.05 (0.02)	0.024*	-	-	-	-	-0.04 (0.02)	0.034*	-	-
Tooth-level												
Molars (reference)												
Anteriors	0.27 (0.08)	0.002*	0.35 (0.08)	<0.001***	0.30 (0.08)	<0.001***	0.02 (0.09)	0.023*	0.30 (0.08)	<0.001***	0.28 (0.09)	0.001**
Premolars	0.19 (0.09)	0.040*	0.23 (0.08)	0.005**	0.24 (0.09)	0.008**	0.15 (0.09)	0.119	0.20 (0.08)	0.019*	0.24 (0.09)	0.010*
Degree III (reference)												
Degree 0	1.18 (0.35)	0.001**	0.96 (0.31)	0.002**	0.61 (0.34)	0.069	1.17 (0.35)	0.001**	0.95 (0.32)	0.003**	0.62 (0.35)	0.074
Degree I	0.99 (0.35)	0.005**	0.88 (0.31)	0.005**	0.40 (0.34)	0.233	0.92 (0.35)	0.010*	0.81 (0.32)	0.011*	0.34 (0.35)	0.331
Degree II	0.84 (0.35)	0.018*	0.68 (0.32)	0.033*	0.31 (0.34)	0.362	0.83 (0.36)	0.020*	0.67 (0.32)	0.038*	0.30 (0.35)	0.400
Site-level												
Surface (Interproximal vs. Center)	-0.30 (0.08)	<0.001***	-0.43 (0.07)	<0.001***	-0.46 (0.07)	<0.001***	-0.29 (0.08)	<0.001***	-0.42 (0.07)	<0.001***	-0.44 (0.07)	<0.001***
Surface (B vs. L)	0.09 (0.05)	0.074	0.16 (0.05)	<0.001***	0.17 (0.05)	<0.001***	-	-	0.15 (0.05)	0.001**	0.15 (0.05)	0.002**
Baseline PD	0.60 (0.03)	<0.001***	0.74 (0.02)	<0.001***	0.84 (0.03)	<0.001***	0.59 (0.03)	<0.001***	0.73 (0.02)	<0.001***	0.76 (0.02)	<0.001***
Baseline CAL	-	-	-	-	-0.06 (0.02)	0.010*	-	-	-	-	-	
Variance												
Patient	0.38 (0.11)	<0.001***	0.37 (0.10)	<0.001***	0.44 (0.12)	<0.001***	0.26 (0.08)	<0.001***	0.28 (0.08)	<0.001***	0.32 (0.09)	<0.001***
Tooth	0.21 (0.04)	<0.001***	0.17 (0.03)	<0.001***	0.25 (0.03)	<0.001***	0.24 (0.04)	0.001**	0.20 (0.03)	<0.001***	0.29 (0.04)	<0.001***
Site	0.85 (0.04)	<0.001***	0.69 (0.03)	<0.001***	0.68 (0.03)	<0.001***	0.84 (0.04)	<0.001***	0.68 (0.03)	<0.001***	0.66 (0.03)	<0.001***
Total variance % change in variance												
Patient	-18.3%	-	-29.5%	-	-13.0%	-	-19.8%	-	-36.1%	-	-23.3%	-
Tooth	-4.6%		-39.3%		-24.5%		4.8%		-27.5%		-15.0%	
Site	-30.3%		-42.3%		-45.9%		-30.1%		-42.0%		-46.2%	

 doi:10.20944/preprints201902.0145.v1

Peer-reviewed version available at *Brazilian Oral Research* **2019**; doi:10.1590/1807-3107bor-2019.vol33.0081

BMI – Body Mass Index, PD – Pocket Depth, B - Buccal. L – Lingual, SE – Standard Error, CAL – Clinical Attachment Loss

*bold face representative *P* < 0.05. **bold face representative *P* < 0.01. ***bold face representative *P* < 0.001