**Name of journal: *World Journal of Clinical Cases***

**ESPS Manuscript NO: 11949**

**Columns: MINIREVIEW**

**Prognostic factors in periodontal therapy and their association with treatment outcomes**

Ioannou AL *et al.* Prognostic factors in periodontal therapy

Andreas L Ioannou, Georgios A Kotsakis, James E Hinrichs

**Andreas L Ioannou, Georgios A Kotsakis, James E Hinrichs,** Advanced Education in Periodontology, Division of Periodontology, University of Minnesota, Minnesota, MN 55455, United States

**Author contributions:** All authors contributed to this paper.

**Correspondence to: George A Kotsakis, DDS, Dental Fellow,** Advanced Education Program in Periodontology, University of Minnesota, 515 Delaware Street SE, Minneapolis, MN 55455, United States. [kotsa001@umn.edu](mailto:kotsa001@umn.edu)

**Telephone:** +1-612-6255166

**Received:** June 13, 2014 **Revised:** August 22, 2014

**Accepted:** October 14, 2014

**Published online:**

**Abstract**

During the incipient steps of periodontal treatment, clinicians are usually asked to predict the prognosis of teeth with compromised periodontium. The aim of this literature review was to investigate the association between periodontal Prognosis, Tooth Loss and risk indicators, such as smoking and genetics. Results showed that the definition of good prognosis has much higher predictability than the one for questionable prognosis. Several risk indicators for periodontal prognosis and tooth loss are discussed as well as different definitions of questionable prognosis and their success in predicting tooth loss. In conclusion, the major focus of future studies should be to construct simplified prognostic models with high predictability that will increase the confidence of dentists and periodontists when assigning teeth prognosis.

© 2014 Baishideng Publishing Group Inc. All rights reserved.

**Key words:** Periodontal prognosis; Tooth loss; Risk indicators; Periodontitis

**Core tip:** During the incipient steps of periodontal treatment, clinicians are usually asked to predict the prognosis of teeth with compromised periodontium. Little advancements on this topic have been made in the periodontal literature during the last decade. Current evidence shows that except for good prognosis, the assignment of overall prognosis remains rather dicey. The major focus of future studies should be to construct simplified prognostic models with high predictability that will increase the confidence of Dentists and Periodontists when assigning teeth prognosis

Ioannou AL, Kotsakis GA, Hinrichs JE. Prognostic factors in periodontal therapy and their association with treatment outcomes. *World J Clin Cases* 2014; In press

**INTRODUCTION**

During the incipient phases of periodontal treatment, clinicians are usually asked to predict the prognosis of teeth with compromised periodontium[1]. To address this difficult and challenging task, Periodontists have introduced the term ‘’questionable’’ prognosis. In essence, this term means that a tooth may or may not respond well to treatment and many factors such as patient/host susceptibility, age, location of the tooth and degree of bone loss among others must be weighted to better determine its prognosis.

Scientific attempts to identify risk indicators for tooth loss that can help clarify and better define this term have been reported in the literature. Usually retrospective and cross-sectional studies are employed as these types of investigations allow for access to a large pool of data for analysis without the cost, or the ethical limitations that pertain to interventional studies[2]. The drawback is that it is uncertain whether an observational study can verify the causal role of a true risk factor, yet observational studies are valuable in identifying risk indicators[2].

The aim of this critical review was to investigate the association between periodontal Prognosis, Tooth Loss and risk indicators. This review paper will discuss how specific risk indicators affect periodontal prognosis and how accurate initial periodontal prognosis can be.

**CRITICAL REVIEW**

***The inceptive definition of questionable prognosis***

Hirschfeld *et al*[3] (1978)presented data of a cross-sectional study that included 600 patients with at least 15 years and up to 50 years of follow-up. This patient cohort was described by the authors as consisting of well-motivated middle-class patients that attended frequent (4-6 mo intervals) recalls.

The authors allocated the patients in three groups based on their response to treatment: well maintained (83.2%), downhill (12.6%), or extreme downhill (4.2%).

In the well-maintained group a mean of 0.68 teeth per patient were lost during the follow-up. The number of teeth lost in the downhill and extreme downhill groups were 5.7 and 13.3 per patient, respectively.

In regards to risk indicators for post-treatment tooth loss, residual mobility was insignificant. The authors’ definition of questionable prognosis (furcation involvement, deep non-eradicable pocket, extensive bone loss and/or at least grade 2 mobility with active inflammation) was accurate in depicting clinical reality for the well-maintained group. In this group 80% of the teeth lost had been initially assigned a questionable prognosis. That percentage dropped to approximately 50% in the remaining groups. Almost all of the teeth with questionable prognosis were lost in the extreme downhill group. The authors concluded that tooth loss patterns were case-related and they noted a bilaterally symmetrical pattern. They found a predictable order of likelihood of tooth loss according to position in the arch. Mandibular cuspids and first bicuspids responded most favorable to treatment and maintenance, while maxillary second and first molars and mandibular second and first molars were more susceptible to loss. In this study the characteristics of the extreme downhill group were not identified, so the question of how to predict which patients will lose more teeth remains unanswered.

In a similar study McLeod *et al*[4] (1997) investigated the effectiveness of periodontal treatment in a cohort of patients with moderate to advanced periodontitis that were treated over a period of 29 years. Tooth loss was set as the primary outcome of treatment. The authors utilized the categorization to well-maintained (0-3 teeth lost), downhill (4-9 teeth lost) and extreme downhill (10-23 teeth lost) groups as suggested by Hirschfeld *et al*[3] (1978). The authors defined moderate disease as 4-7 mm of CAL loss and severe as greater than 7 mm of loss. It should be expected that this patient pool would be assigned a diagnosis of severe periodontitis based on contemporary definitions. All patients were treated by means of SRP followed by surgical treatment if indicated and were put on frequent (3-6 mo) recalls. Again, the definition of questionable prognosis was based on Hirschfeld’s definition[3]. A total of 2889 teeth were nested in the 114 patients included in this study. After a mean of 12.5 years post-treatment, 220 teeth were lost during maintenance. In agreement with the results of Hirschfeld *et al*[3] (1978), the authors noted a bilateral pattern of tooth loss. They also noted that maxillary and mandibular molars and maxillary first premolars had a higher incidence of extractions. The distribution of patients in the well-maintained, downhill and extreme downhill groups was 84.2%, 13.2% and 2.6%, respectively. Those findings are in remarkable agreement with results from the study of Hirschfeld *et al*[3] (1978).There was a higher rate of tooth loss in teeth with furcation involvement especially in the downhill groups. In regards to questionable prognosis accuracy, 529 teeth were initially assigned to this prognosis group. Sixty-eight of those teeth were lost (12.9%), while the remaining 152 teeth that were lost had not been assigned a questionable prognosis. Therefore, the negative predictive value of that definition of questionable prognosis is brought to question.

This study was novel in attempting to correlate the Hirschfeld *et al*[3] (1978) classification of response to periodontal treatment with the AAP-accepted terminology for periodontal disease. According to the authors: ‘’Nine of the 18 patients in the downhill and extreme-downhill groups had periodontal disease that would be classified as systemic-disease-associated or early-onset periodontitis, and the remaining patients would be classified as having refractory periodontitis’’. This statement is valuable as it provides an explanation for the response to treatment and maintenance, but does not yield information on how to predict which patients will have a downhill response.

McFall *et al*[5] (1982), replicated the study of Hirschfeld and Wasserman (1978)[3] in a faculty-practice based patient population (*n* = 100) that was followed up for at least 15 years. There results were in complete agreement with the previous studies. As in previous studies, maxillary 2nd molars were the most frequently lost teeth and mandibular cuspids and bicuspids were the less frequently lost ones. The definition of questionable prognosis that was utilized in this study predicted only 48.7% of the tooth loss in all groups. From the teeth that were initially assigned questionable prognosis, 62.3% were lost during the follow-up.

A question can be raised as to what benefit, other than a rough estimation of the percentage of poor responders, there is in categorizing patients in groups based on the outcome of treatment. Categorizing patients in a group prior to initiation of treatment, based on specific risk indicators and assessing the accuracy in predicting which patients will exhibit downhill response seems more reasonable.

Chace *et al*[6] (1993) performed a cross-sectional study that specifically aimed to address the fate of teeth that were assigned a questionable prognosis. The authors’ definition of questionable prognosis slightly differed from the previous definitions, as it required that the teeth simultaneously exhibited pocket depth greater than 6 mm, mobility greater than 0.5 mm in buccal-lingual direction, poor root-crown ratio and at least class II furcation involvement. In this study 166 patients, lending 455 questionable teeth to the study, were followed up over up to 40 years. A total of 55 teeth were lost (12%), with an average survival period of 8.8 years. Half of the teeth were bilaterally symmetrical and as in the previous studies most frequently lost teeth mostly groups were maxillary second molars, first molars, first bicuspids, or mandibular molars[3-5]. Even though the accuracy of the assignment of ‘’questionable prognosis’’ could not be investigated with this study design, results of this study showed that teeth with significant loss of periodontal tissues could be functionally maintained. Yet, factors such as esthetics and patient satisfaction were not discussed.

In another study, Wilson *et al*[7] (1987) focused in investigating the effect of patient compliance on tooth loss. One hundred and sixty-two patients were followed up for at least 5 years and were categorized as ‘’compliant’’, or ‘’erratic’’. Results showed that completely compliant patients lost no teeth during the follow-up. Twenty-two patients in the erratic group lost a total 60 teeth, for an average of 0.06/patient/year in that group. The authors claimed a higher percentage of teeth with questionable to poor prognosis being lost, in comparison to teeth that were assigned good or fair prognosis, albeit no statistical test was performed.

**AN EVIDENCED-BASED ATTEMPT TO DEFINE PROGNOSIS: THE ‘’MCGUIRE AND NUNN’’ STUDIES**

In 1991 McGuire *et al*[1] evaluated the outcome of treatment in 100 patients that were followed up for a mean of 7 years following active treatment. All patients received standard of care non-surgical treatment and all of them received surgical treatment in areas with residual pockets. Patients underwent a stringent maintenance schedule with the first maintenance appointment scheduled at 1 mo post-surgery and at 1-3 mo intervals thereafter. Each tooth was assigned to one of the following five prognosis gradients: good, fair, poor, questionable, and hopeless. The author re-assigned prognosis to each tooth based on the clinical situation at 5 and 8 years post-active treatment. Results showed that the average prognosis of the teeth studied at each interval changed very little from initial to 5 to 8 years.

A 2.1% tooth loss (51/2484) was noted for the study population. The teeth with good prognosis remained relatively stable, while teeth in the fair and poor categories frequently improved. The questionable category generally got better, but a significant number of teeth were lost and teeth in the hopeless category were generally lost. Findings of interest were that prognosis was more accurate for single rooted teeth than multi-rooted, and that 3rd molars and mandibular molars tended to perform worse than expected. The author discussed that the criteria for assigning prognosis in this study were less lenient in downgrading a tooth to questionable prognosis in comparison to the criteria of Hirschfeld *et al*[3] (1978).

In the second part of this study the authors attempted to investigate the accuracy of a statistical model that would consider several explanatory variables such as, furcation involvement, pocket depth, percentage of bone loss, mobility, crown to root ratio and root proximity, based on the data published previously[8]. The model was very accurate in predicting prognosis (approximately 80%), especially in non-molar teeth. When scrutinizing the results, the authors found that the accuracy of the model was significantly compromised when teeth with good prognosis were excluded from the analysis (< 50%). The clinical repercussion of those findings is debatable. It may not be as crucial to determine if a tooth that was assigned questionable prognosis may move to fair, or vice versa. On the contrary it is very valuable the ability to foresee which teeth will shift from the fair, or questionable gradient to hopeless. That question was addressed in the third part of this study that was published later the same year[9].

In the third part of the study the authors extended the follow-up to 16 years. This extended observation time increased the number of teeth lost to 131 of the 2509 initially present. The average survival time for teeth that were lost was approximately 5years post treatment. In this publication a true endpoint[10] was chosen, tooth loss.

Results showed that both the sensitivity and specificity of the suggested prognosis classification increased when tooth loss was considered as the endpoint.

When questionable and hopeless prognoses were grouped together they were relatively accurate in predicting future tooth loss. The authors also constructed a proportional hazard model that identified initial probing depth, initial furcation involvement, initial mobility, initial percent bone loss, parafunctional habits with no biteguard, and smoking risk indicators for tooth loss.

**CONTEMPORARY VIEWS ON PERIODONTAL PROGNOSIS**

New data and studies have initiated a shift in the consideration of risk indicators for periodontal prognosis. A vastly increasing number of new studies are now focusing on risk indicators involving host susceptibility rather than local factors[11,12]. The genetic and host components of periodontal disease and their association with periodontal prognosis are magnetizing the interest of clinicians. The pathophysiologic cascade underlining this relationship has not been clearly elucidated. Yet, there are clear indications of this association. Fardal *et al*[13] (2004) investigated risk factors associated with tooth loss due to periodontal reasons during maintenance phase of treatment in a hundred patients in a Norwegian specialist periodontal practice. This study examined how initial prognosis related to actual outcome as measured by a true point, namely periodontal tooth loss. The patients included in this practice-based study, had comprehensive periodontal treatment and were followed for 9-11 years during maintenance care. The authors identified that only 36 (1.5%) of the 2436 teeth present at baseline were subsequently lost due to periodontal disease. The majority 27 (75%) of the teeth lost due to periodontal disease had been assigned an uncertain, poor or hopeless initial prognosis. Fardal *et al*[13] found that tooth loss was significantly associated with older age (> 60 years), male gender and smoking, but was not significantly associated with oral health status and family history, and that compliance with maintenance following active periodontal treatment was associated with low levels of tooth loss. Notably, even though the majority of teeth lost due periodontal disease had been initially assigned an uncertain, poor or hopeless prognosis, 9 of the teeth lost (25%) had been assigned a good prognosis at baseline. This indicates that it is not always possible to identify all teeth that are at risk of being lost during the progression of periodontitis. From the interpretation of results of Fardal *et al*[13] (2004) it is evident that risk indicators related with host and genetic components are more predictive of tooth loss, rather than those associated with clinical parameters and local factors. Age and gender were significantly associated with tooth loss in contrast with oral health status, indicating a strong association between tooth loss and the genetic-host component of periodontal disease[13].

A common finding in earlier studies on tooth survival following active treatment and maintenance has shown that furcation involvement is a risk indicator for future tooth loss[1,3-5] and makes assignment of accurate prognosis very challenging[9]. Svardstrom *et al*[14] (2000)evaluated 1313 molars in 222 patients in order to analyze the outcome of non-regenerative treatment. They found that from the 899 molars that were deemed maintainable, only 21 (3.5%) were extracted within a 10-year follow-up period. All molars in this group were treated with scaling and root planning followed by modified Widman flap surgery, if indicated. The authors concluded that molar teeth treated with non-resective, non-regenerative approaches have a good long-term prognosis if a frequent recall schedule is followed.

The potential prognostic value of clinical, genetic, and radiographic variables in predicting tooth loss in periodontal patients was assessed in a 10-year retrospective analysis[15].Sixty periodontal patients were treated according to the standard of care and were placed at 3-4 mo maintenance schedules. In addition to standard clinical and radiographic examination, the patient underwent interleukin-1 genotype assessment. The distance of the bottom of the bony defect to the root apex as well as molar teeth were significant predictors of tooth loss. On the contrary deep intrabony defects had a protective effect. Interleukin-1 test was not efficient as a predictor of tooth prognosis.

Faggion *et al*[16] (2007)also attempted to identify risk indicators to construct a prognostic model. In agreement with the previous studies, teeth with multiple roots were identified as a significant factor. The authors also identified diabetes mellitus, reduced bone levels at baseline, non-vital pulp and tooth mobility as risk indicators for future tooth loss.

A simplification of the McGuire *et al*[1] (1991)classification of periodontal prognosis was proposed by Checchi *et al*[17] (2002).This simplified classification includes three prognosis gradients: good, questionable, and hopeless. The authors elected to define prognosis based on residual bone levels and/or furcation involvement. Teeth with more than 75% per cent bone loss were assigned ‘’hopeless’’ prognosis and teeth that had between 50% to 75% bone loss, or furcation involvement were assigned ‘’questionable’’ prognosis. If a tooth exhibited both characteristics it was downgraded. Results showed that 0.07% of teeth with good prognosis were lost, 3.63% were lost from the questionable prognosis category and 11.34% were lost from the hopeless prognosis subgroup. While previous prognosis classifications were shown to be accurate for the ‘’good’’ and ‘’hopeless’’ prognosis, this simplified approach performed very well for ‘’good’’ and ‘’questionable’’ prognosis, but seemed to have been pessimistic in assigning ‘’hopeless’’ prognosis.

Most of the studies mentioned in this review evaluated the prognosis of teeth that had undergone periodontal treatment and went into a maintenance phase. Neely *et al*[18] (2001)looked into risk indicators for tooth loss in an untreated cohort of 154 Sri Lankan tea laborers. This patient cohort had no access to periodontal treatment and represented a population sample of untreated periodontal disease. Results were very interesting as they showed that plaque index and smoking were not associated with mean attachment loss. Age, gingival index, calculus index and time were associated with attachment loss over 20 years of follow-up.

The same group of researchers published a follow-up paper that evaluated a true endpoint (tooth loss) instead of a surrogate endpoint (attachment loss)[19].

Results were striking as they significantly differed from results of the previous study. In this second part, none of the individual risk indicators had a significant impact on tooth loss. Tooth loss was associated with increasing attachment loss in the presence of use of betel nut. Interestingly, betel nut (a nut containing substances with vasoconstricting properties) was found to be a poor predictor of increase in attachment loss in the first part of the study. These findings point out that even though attachment loss is a well-established surrogate for tooth loss in the treatment of periodontitis, studies that utilize surrogate endpoints should always be reviewed with that limitation in mind[20].

***Other risk indicators for tooth loss***

Several studies have investigated the effect of single risk indicators, or risk factors, depending on the definition, on tooth loss. Such ones are furcation involvement[21], retained ‘’hopeless’’ teeth[22], residual deep pockets[23] and maintenance schedule frequency[24].

Axelsson *et al*[24] (1981)assessed the efficacy of a stringent maintenance schedule in patients that had undergone surgical periodontal therapy. All patients were treated with modified widman flap surgery in all four quadrants. One third of the initial group of 90 patients was referred back to their general dentists for maintenance, while the remaining two thirds underwent a stringent maintenance schedule that included professional debridement once every two months for the first two years post-operatively and once every three months thereafter. Results showed that there was a significant difference in pocket depth maintenance and maintenance of attachment levels around treated teeth between the ‘’recall’’ and ‘’non-recall’’ groups. It should be noted that patients in the stringent maintenance group received subgingival scaling at their bimonthly, or trimonthly visits, when indicated. Results on tooth maintenance in each group were not at all that impressive. No significant difference was noted in the number of teeth lost between the two groups. No teeth were lost in the ‘’recall’’ group and only few teeth were lost in the ‘’non-recall’’ group. Numerical results were not published. The authors concluded that stringent maintenance is of paramount importance as it can prevent future attachment loss. One could argue that the authors overemphasized results of this study. It is more reasonable to evaluate a true endpoint, such as tooth loss as being more significant over a surrogate, such as attachment loss[10]. On the other hand the sample size on the non-recall group was smaller and as a result the study might have not been powered enough to identify a difference in the incidence of tooth loss, as this is a rare event.

Furcation involvement is another risk indicator that has been highlighted in several studies. Werhaug[21] (1980) investigated the anatomy and pathophysiology of furcation defects and concluded that if clinicians are aware of specific considerations when treating molar teeth with furcation defects, then their prognosis may be improved.

Interesting findings were that there is significantly increased attachment loss in the furcation area in comparison to the outer surfaces of the root and that the absence of bleeding on probing of the marginal gingiva is not associated with absence of inflammation, or progression of disease in the furcation area.

In a different study, researchers attempted to evaluate the retention of ‘’hopeless’’ teeth as an indicator for future progression of disease in neighboring sites[22].In order to define ‘’hopeless’ the authors employed a combination of risk indicators such as at least 75% of bone loss, class 3 furcation defect, residual 8mm pocket depth, or repeated periodontal abscesses. Results showed no significant effect of the hopeless teeth on the ‘’adjacent’’ surfaces of the neighboring teeth in comparison to the ‘’non-adjacent’’ ones. Pocket depth post-treatment averaged at approximately 3.5 mm around the teeth that were in the vicinity of retained ‘’hopeless’’ teeth, which indicates that even though no significant increase in surrogate markers for progression of disease was noted, many of the teeth had residual pockets greater than 3 mm. The authors concluded that retained “hopeless’’ teeth do not affect the periodontium of neighboring teeth as long as patients undergo frequent maintenance.

The influence of residual pockets in the prognosis of teeth has also been a matter of interest. Matuliene *et al*[23] (2008)followed 172 patients with residual pockets after the active phase of treatment for 3-27 years. Progression of disease was defined as at least 3 mm of proximal attachment loss in at least two teeth. During the maintenance phase of treatment the percentage of pocket depths that were less than 5 mm did not change significantly. On the other hand, the percentage of pockets that had an initial depth of at least 5 mm increased from 2.9% to 4.3%. Increased pocket depth was found to be strongly associated with tooth loss in multilevel logistic regression analysis. During the follow-up 1.7 teeth were lost per patient. Residual pockets of at least 6 mm that were left untreated were a significant factor for tooth loss. During the maintenance phase, 43% of all cases were identified as progressing cases based on the definition mentioned above. The authors concluded that residual pockets with depth greater or equal to 6 mm represent incomplete periodontal treatment and are a risk indicator for tooth loss.

**CONCLUSION**

Even though this topic has been extensively discussed in the literature a solid definition of questionable prognosis has not been yet established. The importance of assigning an accurate prognosis for teeth prior to initiation of treatment cannot be emphasized enough. Not only it sets the foundation of trust between the therapist and the patient but also prevents legal implications from arising after the treatment process.

The major focus of future studies should be to construct simplified prognostic models with high predictability that will increase the confidence of dentists and periodontists when assigning teeth prognosis.

**REFERENCES**

1 **McGuire MK**. Prognosis versus actual outcome: a long-term survey of 100 treated periodontal patients under maintenance care. *J Periodontol* 1991; **62**: 51-58 [PMID: 2002432 DOI: 10.1902/jop.1991.62.1.51]

2 **Hulley SB**. Designing Clinical Research. Lippincott Williams & Wilkins; 2007 [DOI: 10.1097/OPX.0b013e3181b2fb29]

3 **Hirschfeld L**, Wasserman B. A long-term survey of tooth loss in 600 treated periodontal patients. *J Periodontol* 1978; **49**: 225-237 [PMID: 277674 DOI: 10.1902/jop.1978.49.5.225]

4 **McLeod DE**, Lainson PA, Spivey JD. The effectiveness of periodontal treatment as measured by tooth loss. *J Am Dent Assoc* 1997; **128**: 316-324 [PMID: 9066216 DOI: 10.14219/jada.archive.1997.0195]

5 **McFall WT**. Tooth loss in 100 treated patients with periodontal disease. A long-term study. *J Periodontol* 1982; **53**: 539-549 [PMID: 6957591 DOI: 10.1902/jop.1982.53.9.539]

6 **Chace R**, Low SB. Survival characteristics of periodontally-involved teeth: a 40-year study. *J Periodontol* 1993; **64**: 701-705 [PMID: 8410607 DOI: 10.1902/jop.1993.64.8.701]

7 **Wilson TG**, Glover ME, Malik AK, Schoen JA, Dorsett D. Tooth loss in maintenance patients in a private periodontal practice. *J Periodontol* 1987; **58**: 231-235 [PMID: 3295181 DOI: 10.1902/jop.1987.58.4.231]

8 **McGuire MK**, Nunn ME. Prognosis versus actual outcome. II. The effectiveness of clinical parameters in developing an accurate prognosis. *J Periodontol* 1996; **67**: 658-665 [PMID: 8832476 DOI: 10.1902/jop.1996.67.7.658]

9 **McGuire MK**, Nunn ME. Prognosis versus actual outcome. III. The effectiveness of clinical parameters in accurately predicting tooth survival. *J Periodontol* 1996; **67**: 666-674 [PMID: 8832477 DOI: 10.1902/jop.1996.67.7.666]

10 **Greenstein G**. The use of surrogate variables to reflect long-term tooth survivability. *J Periodontol* 2005; **76**: 1398-1402 [PMID: 16101375 DOI: 10.1902/jop.2005.76.8.1398]

11 **Volzing K**, Biliouris K, Kaznessis YN. proTeOn and proTeOff, new protein devices that inducibly activate bacterial gene expression. *ACS Chem Biol* 2011; **6**: 1107-1116 [PMID: 21819083 DOI: 10.1021/cb200168y]

12 **Miao D**, Godovikova V, Qian X, Seshadrinathan S, Kapila YL, Fenno JC. Treponema denticola upregulates MMP-2 activation in periodontal ligament cells: interplay between epigenetics and periodontal infection. *Arch Oral Biol* 2014; **59**: 1056-1064 [PMID: 24973519 DOI: 10.1016/j.archoralbio.2014.06.003]

13 **Fardal Ø**, Johannessen AC, Linden GJ. Tooth loss during maintenance following periodontal treatment in a periodontal practice in Norway. *J Clin Periodontol* 2004; **31**: 550-555 [PMID: 15191591 DOI: 10.1111/j.1600-051X.2004.00519.x]

14 **Svärdström G**, Wennström JL. Periodontal treatment decisions for molars: an analysis of influencing factors and long-term outcome. *J Periodontol* 2000; **71**: 579-585 [PMID: 10807122 DOI: 10.1902/jop.2000.71.4.579]

15 **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* 2006; **77**: 2084-2089 [PMID: 17209795 DOI: 10.1902/jop.2006.050227]

16 **Faggion CM**, Petersilka G, Lange DE, Gerss J, Flemmig TF. Prognostic model for tooth survival in patients treated for periodontitis. *J Clin Periodontol* 2007; **34**: 226-231 [PMID: 17257157 DOI: 10.1111/j.1600-051X.2006.01045.x]

17 **Checchi L**, Montevecchi M, Gatto MR, Trombelli L. Retrospective study of tooth loss in 92 treated periodontal patients. *J Clin Periodontol* 2002; **29**: 651-656 [PMID: 12354091 DOI: 10.1034/j.1600-051X.2002.290710.x]

18 **Neely AL**, Holford TR, Löe H, Anerud A, Boysen H. The natural history of periodontal disease in man. Risk factors for progression of attachment loss in individuals receiving no oral health care. *J Periodontol* 2001; **72**: 1006-1015 [PMID: 11525431 DOI: 10.1902/jop.2001.72.8.1006]

19 **Neely AL**, Holford TR, Löe H, Anerud A, Boysen H. The natural history of periodontal disease in humans: risk factors for tooth loss in caries-free subjects receiving no oral health care. *J Clin Periodontol* 2005; **32**: 984-993 [PMID: 16104963 DOI: 10.1111/j.1600-051X.2005.00797.x]

20 **Kotsakis GA**, Kher, U. A critical review of periodontal prognosis and tooth loss. *J Dental Res Rev* 2014; **1**: 32-36 [DOI: 10.4103/2348-3172.126164]

21 **Waerhaug J**. The furcation problem. Etiology, pathogenesis, diagnosis, therapy and prognosis. *J Clin Periodontol* 1980; **7**: 73-95 [PMID: 6929794 DOI: 10.1111/j.1600-051X.1980.tb01951.x]

22 **Wojcik MS**, DeVore CH, Beck FM, Horton JE. Retained "hopeless" teeth: lack of effect periodontally-treated teeth have on the proximal periodontium of adjacent teeth 8-years later. *J Periodontol* 1992; **63**: 663-666 [PMID: 1507046 DOI: 10.1902/jop.1992.63.8.663]

23 **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* 2008; **35**: 685-695 [PMID: 18549447 DOI: 10.1111/j.1600-051X.2008.01245.x]

24 **Axelsson P**, Lindhe J. The significance of maintenance care in the treatment of periodontal disease. *J Clin Periodontol* 1981; **8**: 281-294 [PMID: 6947992 DOI: 10.1111/j.1600-051X.1981.tb02039.x]

**P-Reviewer:** Arabaci T, Bartold PM,Shimauchi H **S-Editor:** Ji FF **L-Editor: E-Editor:**