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Tooth loss in molars with and without furcation involvement- a systematic review and meta-analysis

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ABSTRACT

BACKGROUND: The aim of this study was to investigate risk of tooth loss in molars with furcation involvement (FI) based on initial diagnosis.

MATERIALS AND METHODS: A systematic search of the literature was conducted in Ovid Medline, Embase, LILACS and Cochrane Library for longitudinal studies with at least 3 years follow-up including measures of FI and data on tooth loss.

RESULTS: A total of 21 studies were included in the review, from an initial search of 1207 titles. The relative risk of tooth loss during maintenance therapy attributable to FI was 1.46 (95% CI= 0.99-2.15, p=0.06) for studies up to 10 years and 2.21 (95% C.I. = 1.79-2.74, p<0.0001) for studies with a follow-up of 10-15 years. A gradual increase in the risk of tooth loss was observed for molars with degree II and III FI.

CONCLUSIONS: The presence of FI approximately doubles the risk of tooth loss for molars maintained in supportive periodontal therapy for up to 10-15 years. However, most molars, even with grade III FI respond well to periodontal therapy, suggesting that every effort should be made to maintain these teeth when possible. Long-term studies reporting patient-reported outcomes are needed to substantiate this conclusion.

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CLINICAL RELEVANCE:

Scientific rationale for the study: Molars affected by furcation involvement are thought to have a high risk of tooth loss.

Principal findings: Molars with FI were found to have an increased relative risk of tooth loss compared with molars with no FI. However, even teeth with degree III furcation involvement have good survival rates in supportive periodontal care.

Accurate periodontal therapy and maintenance care should be planned for teeth even with severe furcation involvement, although recognizing their higher risk of long-term tooth loss.

BACKGROUND

Periodontitis affects the supporting apparatus of the teeth, leading to apical migration of the epithelial attachment and resorption of connective tissue and alveolar bone, often resulting in early tooth loss. In multi-rooted teeth, the bone destruction can reach the area of root separation, thus exposing it to microbial colonization. In this occurrence, a 'furcation involvement' is created. Furcation involvements or more simply 'furcations' are very common findings in periodontitis cases, with a reported prevalence of 13.7% in the general population in the U.S. (Albandar et al. 1999) and in about 30-50% of patients with periodontitis (Hirschfeld & Wasserman 1978, Svardstrom & Wennstrom 1996). Furcation defects are generally classified into degree I, II or III based on the horizontal component of the bony defect (Hamp et al. 1975), or in more complex diagnostic systems which take into account root morphology, horizontal and vertical bone loss (Müller & Eger 1999). As for any periodontal lesion, the treatment of furcation-involved teeth involves a non-specific reduction of the bacterial load below the gingival margin (Heitz-Mayfield et al. 2002), achieved by oral hygiene instructions and non-surgical periodontal therapy (NSPT), and aimed at removing calculus and disrupting the plaque biofilm from the affected root surfaces. However, teeth with furcation involvement (FI) have been shown not to respond as favourably to NSPT as teeth with no FI (Nordland et al. 1987, Loos et al. 1988), owing to difficulty in cleaning inside the furcation, both for clinician and patient (Lang et al. 1973, Fleischer et al. 1989). More advanced cases such as degree II and III FI may need surgical treatment or extractions. Overall, the evidence suggests that teeth with furcation involvement have a poorer long-term prognosis compared with single-rooted teeth and tooth with no furcation involvement (Hirschfeld & Wasserman 1978, Mc Fall 1982, Goodson 1994). However, the exact risk of tooth loss according to furcation diagnosis and treatment has not been previously assessed.

Tooth survival from resective studies (including hemisection and root amputation) varies according to different studies depending on operator, technique, patient and site factors (Buhler 1988, Carnevale et al. 1998, Huynh-Ba et al. 2009). More conservative surgical

techniques include the creation of a tunnel to facilitate self-performed oral hygiene inside the FI area (Hellden et al. 1989). With the emergence of implant therapy, often complex treatment of furcations is rejected in favour of extraction and placement of dental implants. However, there is a paucity of data on tooth survival in surgical furcation therapy vs. extraction and implant placement and there are no clear guidelines for furcation therapy (Huynh-Ba et al. 2009). The aim of this systematic review was to appraise the existing literature on periodontal furcation-involved teeth with respect to tooth loss based on initial diagnosis (no furcation/ furcation grade I, II or III) and treatment carried out and to identify areas needing further research.

MATERIALS AND METHODS

A systematic review protocol was written in the planning stages and the PRISMA checklist (Moher et al., 2009) was followed both in the planning and reporting of the review (checklist attached as supplemental material 1).

Focused question

The question addressed was the following: What is the risk of tooth loss in teeth with furcation involvement and which factors affect the outcome?

Eligibility criteria

Longitudinal human studies in patients with chronic periodontitis (CP) presenting data on furcation diagnosis and tooth loss were considered eligible. The inclusion criteria were:

- Study designs: longitudinal studies (retrospective or prospective)
- 'Secure' furcation diagnosis (clinical)
- Treatment of furcation involvement provided
- Reporting tooth loss data by furcation diagnosis (furcation vs. no furcation or different degrees of furcation involvement)
- With a follow-up of at least 3 years

The following study designs were excluded:

- Reviews
- Case reports
- Studies focused on aggressive periodontitis (AgP)
- Studies on animal models

Choice of main outcomes

Given the predictable heterogeneity of the studies to be included, we chose the most objective outcome 'tooth loss' as the most appropriate for this review. In an attempt to reduce risk of bias, although no clear evidence exist on the 'gold standard' for furcation diagnosis, for this review we categorized furcation diagnosis as 'secure' only if made through clinical measurement with Naber's probe or equivalent.

Information sources

The literature search for the present systematic review was conducted at Ovid Medline, Embase, LILACS and Cochrane Library up to 27 May 2014 and updated on 22 July 2015. The reference lists of included articles and relevant reviews were manually searched. The search was complemented by hand search of the journals most likely to publish studies on furcation involvement over the last 20 years (*Journal of Clinical Periodontology*, *Journal of Dental Research* and *Journal of Periodontology*). The Editors of the above-named journals were contacted to enquire about any papers in press on this topic.

Search strategy

The search strategy used a combination of MeSH terms and key words described in supplemental material 2.

Study selection

Studies were selected in two-stage screening and carried out by two independent reviewers (A.Z. and K.N. for the first stage and A.Z. and L.N. for the second stage). Disagreements about inclusion or exclusion of a study were resolved by consensus.

The first-stage screening of titles and abstracts was carried out in order to eliminate irrelevant articles and those that did not meet the inclusion criteria established by this study. At the second-stage screening, following proof reading of the full-texts, the study eligibility was verified independently by both reviewers and the data extraction and quality assessment were performed for the included studies. The level of agreement between the two reviewers was calculated using Kappa statistics for the first and second-stage screening.

Data collection process/ data items

Data were extracted based on the general study characteristics (authors and year of publication, country) and population characteristics (number of participants, age, gender, inclusion/exclusion criteria, diagnosis of periodontal status, method used for furcation diagnosis, degree of furcation involvement, treatment protocol, study timelines, outcomes described).

Risk of bias in individual studies

We aimed to assess the risk of bias of the included studies, defined as a systematic error or deviation from the truth, in results or inferences. Risk of bias/ quality assessment for the individual studies was performed using the Newcastle - Ottawa Quality Assessment Scale (http://www.ohri.ca/programs/clinical_epidemiology/oxford.htm, accessed 17 September 2014).

Summary measures/Synthesis of results/ Statistical methods

The primary outcome was tooth loss at various periods of follow-up years between groups with and without FI. For tooth loss, the total number of teeth lost and the patient-years for the length of follow-up were obtained from included studies. Further data were gathered on tooth loss based on furcation diagnosis (degree I, II or III) (Hamp et al. 1975) when available. The relative risk of tooth loss were estimated using a computer program (Review Manager Version 5.0. Copenhagen; The Nordic Cochrane Centre, The Cochrane Collaboration, 2008). The contribution of each article was weighed. Random effects meta-analyses of the selected studies were applied to allow for methodological differences among studies. Forest plots were produced to graphically represent the difference in outcomes of groups with and without FI for all included studies using tooth number as the analysis unit. Reported data did not permit accounting for clustering of teeth and therefore outcomes within individuals. A p value= 0.05 was used as the level of significance. Heterogeneity was assessed with chi-square test and I^2 test. The suggested interpretation of I^2 is; 0-40% might not be important, 30-60% may represent moderate heterogeneity, 50-90% may represent substantial heterogeneity and 75%-100% considerable heterogeneity (Higgins & Green 2011). To avoid the bias from data including third molars and different degrees of furcation involvement, meta-analyses with data of excluding third molars and comparing tooth loss of different degrees of furcation involvement were also performed. In addition, funnel plots were used to assess the presence of publication bias.

RESULTS

Study selection

Figure 1 reports the flowchart representing study selection and inclusion. The initial search resulted in 1207 articles at Ovid Medline, Embase, Cochrane Library and LILACS combined. Following first-stage screening of titles and abstracts, 41 articles qualified for full-text screening (considered potentially suitable by at least one reviewer). Four additional articles were identified by a manual search and one from editorial contacts (under review). After full text reading, 21 articles met the defined inclusion criteria and 25 were excluded (reported as supplemental material 3). The reasons for exclusion were as follow: 13 studies were excluded as they did not report reason for tooth loss separately for teeth with furcation involvement; 6 studies were excluded as they included some cases with follow-ups less than 3 years; 3 studies were excluded as they were book chapters, reviews or case reports; 2 studies were excluded because of non-secure furcation diagnosis (just radiographic analysis) and 1 because it was a duplicate report with a shorter follow-up on the same population of one of the included studies. Every effort was made to obtain any relevant missing data from the papers by contacting the authors by email.

The kappa value for inter-reviewer agreement was 0.89 at title and abstract screening and 0.82 at full text reading, showing good agreement between the reviewers.

Study characteristics

Table 1 reports the characteristics of the sample included in the reviewed studies. Of the 21 included studies, most articles were written in English (n=20) and 1 in German. The countries where the studies were conducted were United States (n=11), Germany (n=6), Sweden (n=2), Switzerland (n=1) and Italy (n=1). The patient sample ranged from 9 (Eickholz & Hausmann 2002) to 600 patients (Hirschfeld & Wasserman 1978). All studies were longitudinal, including both prospective and retrospective studies, although often it was difficult to distinguish the nature of the study as it was not always clearly stated. The 21 papers reviewed spanned across five decades, with 2 published in the 1970s (Lindhe & Nyman 1975, Hirschfeld & Wasserman 1978), 3 in the 1980s (McFall 1982, Goldman et al. 1986, Wood et al. 1989), 7 in the 1990s (Kuhrau et al. 1990, Wang et al. 1994, Little et al. 1995, McGuire & Nunn 1996, Yukna & Yukna 1997, Haney et al. 1997, McLeod et al. 1998), 5 in the 2000s (Eickholz & Hausmann 2002, Checchi et al. 2002, Dannewitz et al. 2006, Pretzl et al. 2008,

Zafiropoulos et al. 2009) and 4 in the 2010s (Johansson et al. 2013, Miller et al. 2014, Salvi et al. 2014, Graetz et al. 2015).

Table 2 summarises the interventions of the included studies. Five of the included papers focused on specific treatment for a specific group of furcation-involved teeth: 3 papers focused on regenerative treatment of grade II furcations (Haney et al. 1997, Yukna & Yukna 1997, Eickholz & Hausmann 2002), 1 on tunneling of grade II and III furcations (Little et al. 1995) and 1 on root resection or extraction and implant therapy in grade III furcations (Zafiropoulos et al. 2009). Two papers reported data for tooth loss in teeth with FI, but did not report data specifically on tooth loss ratio of molars without FI (Lindhe & Nyman 1975, McLeod et al. 1998). Fourteen papers assessed long-term tooth loss in cohorts of periodontitis patients during maintenance care (reporting breakdown of tooth loss by furcation degree), hence were suitable for meta-analysis. Supportive periodontal therapy (SPT) protocols had a wide range of frequency, while some were not clearly specified, and generally included periodic (3- to 6- to 12-monthly) periodontal clinical measurements, oral hygiene instructions and subgingival debridement and -when needed- periodontal surgeries.

Synthesis of results

The included studies generally reported clinical and occasionally radiographic outcomes. None of them reported patient-reported outcomes. As by study inclusion, all studies reported tooth loss data. In some cases, tooth loss data were reported for single-rooted teeth and for molars with and without FI in the patient cohort. Occasionally, only tooth loss data for molars were reported. Some studies reported data only on first and second molars, while other studies grouped third molars together as well. However, when possible an effort was made to extract data relative only to first and second molars. Studies focusing only AgP had been excluded. Some studies reported that the patient sample included both CP and AgP (Dannewitz et al. 2006, Pretzl et al. 2008, Salvi et al. 2014, Graetz et al. 2015). Authors were contacted to obtain data regarding only CP, but this was possible for only one study (Dannewitz et al. 2006). Hence, data including both CP and a smaller subset of AgP patients were included for Pretzl et al. 2008, Salvi et al. 2014 and Graetz et al. 2015. Considering that older studies may also have included subjects we now classify as AgP and that no differences in tooth loss rates between molars of AgP and CP patients had been reported (Graetz et al. 2015), we decided to include studies with mixed AgP-CP to avoid unnecessary exclusion of

relevant data. Only data on tooth loss following initial therapy (during maintenance care) were analysed.

Survival of molars with furcation involvement across all included studies

Grouping studies reporting data on tooth loss for molars with and without furcation involvement separately, a total of 8143 molars without furcation involvement and a total of 5772 molars with furcation involvement were included. Tooth survival ranged from 94 to 100% after 4 to 7.5 years in regeneration studies (Haney et al. 1997, Yukna & Yukna 1997, Eickholz & Hausmann 2002), 89% after 5.8 years in the study focusing on tunneling (Little et al. 1995), 79% after a minimum of 4 years for the study focusing on root resection (Zafiropoulos et al. 2009) and 43-100% after 5 to 53 years for studies including combined therapies (Hirschfeld & Wasserman 1978, McFall 1982, Goldman et al. 1986, Wood et al. 1989, Kuhrau et al. 1990, Wang et al. 1994, McGuire & Nunn 1996, Checchi et al. 2002, Dannewitz et al. 2006, Pretzl et al. 2008, Johansson et al. 2013, Miller et al. 2014, Salvi et al. 2014, Graetz et al. 2015). Among teeth reported in these studies, the average tooth loss/year was 0.01 and 0.02 respectively for molars without and with furcation involvement.

Relative risk of Tooth Loss Based on Follow-Up Periods (3rd molars excluded)

Nine studies (Hirschfeld & Wasserman 1978, McFall 1982, Goldman et al. 1986, Wood et al. 1989, Dannewitz et al. 2006, Pretzl et al. 2008, Johansson et al. 2013, Miller et al. 2014, Graetz et al. 2015) reported data on tooth loss by furcation involvement excluding third molars. Meta-analysis for the comparison of tooth loss among selected studies presented an overall relative risk of 2.90 (95% CI= 2.01-4.18) for molars with furcation involvement ($p< 0.0001$) (Figure 2). For studies with a follow-up period of 5-10 years, 10-15 years, and >15 years, the relative risk of tooth loss between teeth with and without furcation involvement was 1.46 (95% CI= 0.99 to 2.15, p= 0.06), 2.21 (95% CI= 1.79 to 2.74, $p< 0.0001$), and 4.46 (95% CI= 2.62 to 7.62, $p< 0.0001$), respectively. The comparisons presented a low (p value for chi-square test= 0.40 and 0.56, and I^2 test = 0% and 0%, for follow-up period of 5-10 years and 10-15 years subgroup analyses, respectively) to high (p value for chi-square test <0.0001 and I^2 test = 96% for follow-up period of >15 years subgroup analysis) degree of heterogeneity among selected studies. The combined effect for all subgroups also showed a high heterogeneity among studies (p value for chi-square test <0.0001 and I^2 test= 93%).

Relative risk of Tooth Loss Based on Follow-Up Periods (3rd molars included)

Thirteen studies (Hirschfeld & Wasserman 1978, McFall 1982, Goldman et al. 1986, Wood et al. 1989, Kuhrau et al. 1990, Wang et al. 1994, Checchi et al. 2002, Dannewitz et al. 2006, Pretzl et al. 2008, Johansson et al. 2013, Miller et al. 2014, Salvi et al. 2014, Graetz et al. 2015) reported data on tooth loss with and without furcation involvement including all molars (only some studies reported both data relative to all molars and excluding third molars). Overall, only small changes to the summary estimate for risk of tooth loss by FI were detected when they were included, compared to when only first and second molars were included (Figure 3).

Relative risk of Tooth Loss Based on Degrees of Furcation Involvement (3rd molars excluded)

When studies reporting tooth loss by degree of FI were considered (McGuire & Nunn 1996, Dannewitz et al. 2006, Johansson et al. 2013, Salvi et al. 2014, Graetz et al. 2015), we observed that respectively 8%, 18% and 30% of teeth with furcation degree I, II and III were lost in the follow-up period (0.01, 0.02 and 0.03 teeth/patient/year). Meta-analysis for the comparison of tooth loss among included studies presented arelative risk of 1.67 (95% CI= 1.14 to 2.43, p= 0.008), 1.83 (95% CI= 1.37 to 2.45, p< 0.0001) and 3.13 (95% CI= 2.30 to 4.24, p< 0.0001) for furcation involvement degree II vs. I, degree III vs. II and degree III vs. I respectively (Figure 4). The comparisons presented a low to moderate degree of heterogeneity among selected studies (p value for chi-square test= 0.04, 0.20 and 0.26, and I^2 test = 61%, 33% and 25%, for degree II vs. I, degree III vs. II and degree III vs. I comparisons respectively).

Risk of bias assessment

Risk of bias analyses performed using the Newcastle Ottawa scale showed that study quality scores ranged from a total of 3 to a total of 5 (out of a maximum total of 9 stars) (table 3). Funnel plots of meta-analysis of relative risk for tooth loss based on follow-up periods and degrees of furcation involvement are reported in supplemental material 4, 5 and 6. These funnel plots were relatively asymmetrical, which implied potential publication bias. The asymmetrical result of the funnel plots might result from a lack of small sample studies included in the current systematic review since most of the selected studies were retrospective with a relatively large sample size.

DISCUSSION

This is the first systematic review, to our knowledge, to provide summary measures of risk of tooth loss in teeth with and without furcation involvement in chronic periodontitis. Acknowledging that it is difficult to summarise disease progression measured as PPD and CAL changes in studies in different settings and with different examiners and study protocols, we believed that the objective measure 'tooth loss' might be the best ultimate objective measure of disease progression reflecting different responses in teeth affected or not by furcation involvement. Although it is commonly thought that FI would affect tooth loss, no data so far were available for a direct comparison of this measure across different studies. This systematic review provides evidence to suggest that FI approximately doubles the risk of tooth loss for molars in supportive periodontal therapy for up to 10-15 years. In particular, first and second molars with furcation involvement had a relative risk (RR) of tooth loss of 1.46 ($p=0.06$) up to 10 years and of 2.21 from 10 to 15 years ($p<0.0001$) compared with molars with no furcation involvement (RR 1.69 and 2.06 respectively including third molars). A 3 to 4 times higher risk of tooth loss was observed for studies with longer follow-ups (>15 years, up to 53 years), although data relative to this outcome have to be interpreted cautiously due to high heterogeneity. Furthermore, this review provides evidence that the degree of FI (Hamp et al. 1975) is significantly associated with risk of tooth loss, increasing from furcation degree I to II to III. No data were available to assess risk of tooth loss by FI in the absence of periodontal therapy/maintenance.

Recent systematic reviews on furcations focused on short-term outcomes, concluding that degree II furcations show significant improvement 6 months after access flap surgery (Graziani et al. 2015) and could be successfully treated with regenerative surgery, especially with a combined regenerative approach (Reddy et al. 2015). The current review show that tooth survival ranged from 94 to 100% after 4 to 7.5 years in regeneration studies (Haney et al. 1997, Yukna & Yukna 1997, Eickholz & Hausmann 2002), 89% after 5.8 years in the study focusing on tunneling (Little et al. 1995), 79% after a minimum of 4 years for the study focusing on root resection (Zafiropoulos et al. 2009) and 43-100% after 5 to 53 years for studies including combined non-surgical and various surgical approaches (Hirschfeld & Wasserman 1978, McFall 1982, Goldman et al. 1986, Wood et al. 1989, Kuhrau et al. 1990, Wang et al. 1994, McGuire & Nunn 1996, Checchi et al. 2002, Dannewitz et al. 2006, Pretzl

et al. 2008, Johansson et al. 2013, Miller et al. 2014, Salvi et al. 2014, Graetz et al. 2015). It was not possible to sub-analyse risk of tooth loss based on treatment provided within each study, owing to lack of systematic data on tooth loss according to the various treatment approaches across different studies. Endodontic complications, caries, fractures were often reported as cause of tooth loss alongside periodontal disease progression (Kuhrau et al. 1990, McLeod et al. 1998, Haney et al. 1997, Yukna & Yukna 1997, Dannewitz et al. 2006). Only studies with 'secure' clinical diagnosis of furcation involvement were included in this review. Therefore, studies with radiographic measures of FI were excluded as considered less reliable (Ross & Thompson 1978, Bjorn & Hjort 1982).

A strength of the data included is that studies with shorter follow-up had consistent results and reported similar relative risk for tooth loss. This may be due to the fact that, although different operators and possibly different treatment strategies were used, all analysed studies had similar designs, consisting of initial periodontal therapy, surgical therapy when needed (including access flaps, osseous resective surgery, root resection, tunneling or regenerative surgery occasionally) and then supportive periodontal therapy (at regular intervals for most studies, generally every 3-4-6 up to 12 months). Limitations of the data include retrospective nature and lack of detailed data on degree of furcation involvement in most studies.

Strengths of this systematic review are a relatively high sample size and the small heterogeneity for most of the meta-analyses. Limitations are the residual heterogeneity for studies with over 15 years follow-up and the possible presence of publication bias, which means that the results of the current review should be interpreted cautiously. In summary, the data analysed in this review confirm that furcation involvement represents a risk of tooth loss. In patients undergoing cause-related periodontal therapy, surgical therapy if needed and supportive periodontal care, the risk of tooth loss is in the region of 1.5-2.2 (1.69-2.06 excluding third molars) up to 15 years in maintenance (only border-line significant for studies up to 10 years). Such risk seems to increase sharply after the 15-years time-point, although study heterogeneity does not allow clear conclusions on this. Great care is recommended in the diagnosis, treatment and supportive care of molars with FI. However, it must be emphasised that this review clearly shows that most molars affected by FI respond well to periodontal treatment and even in the presence of degree III furcations, only 30% of

molars were lost in a follow-up period of 5-15 years. Data on patient-related outcomes on survival of molars with FI are desperately needed. In light also of previous studies showing the cost-effectiveness of maintaining teeth with furcation involvement (Schwendicke et al. 2014) and their good survival rates even when compared with replacement dental implants (Fugazzotto 2001), we recommend that every effort is made to maintain teeth with FI whenever possible. Specific treatment protocols for molars with FI cannot be recommended based on this review owing to a paucity of data and lack of randomised controlled trials testing different treatment modalities according to FI.

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TABLE LEGENDS

Table 1: Summary of study procedures for all included studies (SRP= scaling and root planning; APT = active periodontal treatment; SPT= supportive periodontal therapy; PPD= probing pocket depth; al= attachment loss: OHI= oral hygiene instructions; OFD = Open Flap Debridement; CP= Chronic Periodontitis; AgP= Aggressive Periodontitis).

Table 2: Summary of study characteristics for included studies (SRP= scaling and root planning; APT = active periodontal treatment; SPT= supportive periodontal therapy; AB= antibiotic; PPD= probing pocket depth; OHI= oral hygiene instructions; OFD = Open Flap Debridement)

Table 3. Quality assessment of included studies.

FIGURE LEGENDS

Figure 1. Flowchart of study inclusion

Figure 2. Forest plot presenting relative risk (risk ratio, RR) of tooth loss based on follow-up periods (3rd molars included). Meta-analysis for the comparison of tooth loss among selected studies presented an overall RR of 2.52 (95% CI= 1.85 to 3.42, p< 0.0001). For studies with a follow-up period of 5-10 years, 10-15 years, and >15 years, the RR of tooth loss between teeth with and without furcation involvement was 1.69 (95% CI= 1.11 to 2.56, p= 0.01), 2.06 (95% CI= 1.73 to 2.46, p< 0.0001), and 3.86 (95% CI= 2.34 to 6.39, p< 0.0001), respectively.

Figure 3. Forest plot presenting RR of tooth loss based on follow-up periods (3rd molars excluded). Meta-analysis for the comparison of tooth loss among selected studies presented an overall odds ratio of 2.90 (95% CI= 2.01 to 4.18, p< 0.0001). For studies with a follow-up period of 5-10 years, 10-15 years, and >15 years, the RR of tooth loss between teeth with and without furcation involvement was 1.46 (95% CI= 0.99 to 2.15, p= 0.06), 2.21 (95% CI= 1.79 to 2.74, p< 0.0001), and 4.46 (95% CI= 2.62 to 7.62, p< 0.0001), respectively.

Figure 4. Forest plot presenting risk ratio of tooth loss based on degrees of furcation involvement (3^{rd} molars excluded). Meta-analysis for the comparison of tooth loss among selected studies presented a RR of 1.67 (95% CI= 1.14 to 2.43), 1.83 (95% CI= 1.37 to 2.45) and 3.13 (95% CI= 2.30 to 4.24) with statistical significance (p= 0.008, p< 0.0001 and p< 0.0001) when comparing degree II to I, degree III to II, and degree III to I furcation involvement, respectively.

Author/ Year	Study design	Sample n=	Mean age	Follow-up years (range)	Inclusion/ disease classification	Country
Lindhe & Nyman (1975)	Prospective cohort	75	Range 26-79	5	≥50% loss of periodontal support and optimal oral hygiene	Sweden
Hirschfeld & Wasserman (1978)	Retrospective cohort	600	42	22 (15-53)	'Early': PPD of 4 mm or less, with gingival inflammation and subgingival calculus; 'Intermediate': PPD of 4 to 7 mm; 'Advanced': PPD >7 mm, furcation involvement	U.S.
McFall (1982)	Retrospective cohort	100	44	19 (15-29)	'Early': PPD ≤4mm (n=11); 'intermediate': PPD 4-7mm (n=53); 'advanced':PPD >7mm (n=36)	U.S.

Goldman et al. (1986)	Retrospective cohort	211	42	22.2 (15-34)	Chronic periodontitis	U.S.
Wood et al. (1989)	Retrospective cohort	63	45	13.6 (10-34)	Patients with moderate periodontitis treated and maintained by SRP for 10 years or longer	U.S.
Kuhrau et al. (1990)	Retrospective cohort	59	46	5.8 (4-8)	Patients with periodontitis with furcation-involved teeth treated surgically	Germany
Wang et al. (1994)	Prospective cohort	24	43	8	Patients with CP that had completed an 8-year clinical trial without missing appointments and had no more than 2 first or second molars missing at baseline.	U.S.
Little et al.(1995)	Prospective cohort	18	Not reported	4.6	Patient with periodontal disease with deep class Il or class III molar furcation invasion	U.S.
McGuire & Nunn (1996)	Retrospective cohort	100	46	10	Chronic generalized moderate to severe adult periodontitis	U.S.
Haney et al. (1997)	Retrospective controlled	13	Not reported	4-5	Chronic periodontitis	U.S.
Yukna & Yukna (1997)	Prospective cohort	13	51	6.7 (6-7.5)	Grade II molar furcation defects, with adjacent bone crest height >75% of the root length and coronal to the furcation bone level	U.S.
McLeod et al. (1998)	Retrospective cohort	114	53	12.5 (5-29)	Moderate to advanced periodontitis with 4 to 7 mm or greater AL	U.S.

Eickholz & Hausmann (2002)	Prospective controlled	9	48	5	Advanced periodontal disease	Germany
Checchi et al. (2002)	Retrospective cohort	92	45	6.7 (3-12)	Chronic adult periodontitis who completed APT and have been on a recall SPT schedule	Italy
Dannewitz et al. (2006)	Retrospective cohort	71	46	5	Chronic to aggressive periodontitis (≥ 50% bone loss in at least 2 permanent teeth)	Germany
Pretzl. et al. (2008)	Retrospective cohort	100	46	10	Generalised moderate chronic and generalized severe or aggressive periodontitis	Germany
Zafiropoulos et al. (2009)	Retrospective cohort	60	50	Min. 4	Chronic Periodontitis with a minimum of 4 sites with CAL loss < 4mm, radiographic evidence of bone loss and BOP in 4 sites	Germany
Johansson et al. (2013)	Retrospective cohort	64	Not reported	14.8 (13-16)	Patients referred to the Department of Periodontology	Sweden
Miller et al. (2014)	Retrospective cohort	106	42	15	Moderate to severe chronic periodontitis	U.S.
Salvi et al. (2014)	Retrospective cohort	199	45	11.5	Chronic or aggressive periodontitis (Level 1: proximal attachment loss of ≥ 3 mm at≥ 2 nonadjacent teeth; level 2: proximal attachment loss of ≥ 5 mm in≥ 30% of teeth)	Switzerland
Graetz et al. (2015)	Retrospective cohort	379	46	18.3	Chronic or aggressive periodontitis with at least one 1st or 2nd molar present, regular SPT and complete radiological documentation at	Germany

baseline and last visit

Table 1

Author/ Year	Initial therapy (active periodontal therapy, APT)	Supportive periodontal therapy (SPT)
Lindhe & Nyman (1975)	OHI, SRP, restorative therapy if needed, periodontal surgery in PPDs>4mm (gingivectomy, Widman flaps, bone recontouring, furcation plasty, tunneling, root resection as indicated)	3-6 monthly OHI and prophylaxis by hygienist, yearly periodontal examinations and radiographs
Hirschfeld & Wasserman (1978)	Subgingival scaling with or without surgery (additional surgical procedure or non-surgical procedure performed depending on tooth diagnosis)	Deep scaling + 'problem areas' retreated when necessary, occlusion was checked and adjusted as indicated, OHI
McFall (1982)	Supragingival and subgingival scaling, polishing, OHI, occlusal adjustment and biteguards if needed, gingival curettage, gingivectomy, gingivoplasty, ostectomy, osteoplasty	Generally every 3-4 to 6 months (including curettage, muco-periosteal flaps, osseous surgery, root resection if needed)
Goldman et al. (1986)	Oral physiotherapy, supragingival and subgingival scaling, OHI	3-6 months recalls (selective grinding and coronal re-shaping, adjunct restorative treatment if needed)
Wood et al. (1989)	OHI+ non-surgical (SRP, curettage, occlusal adjustment) and surgical treatment (gingivectomy, flap surgery, flap curettage, osseous contouring, osseous grafting, root	Not reported

	amputation)	
Kuhrau et al. (1990)	Surgical therapy (modified Widman flap, root resection, tunneling)	'Regular'
Wang et al. (1994)	SRP followed by one of three procedures: pocket elimination surgery, modified Widman flap surgery or gingival curettage	3-month recall interval for maintenance prophylaxis and yearly examinations
Little et al.(1995)	Surgical therapy consisting of osseous resectioning and/or recontouring to the adjacent mesial tooth and tunneling	3- monthly following surgery to control plaque and potential bacterial pathogens
McGuire & Nunn (1996)	SRP, OHI, removal of fremitus, surgery if indicated (osseous surgery, open SRP, rarely bone grafts	2- or 3-month intervals (majority under a 3-month interval) (SRP, polishing, minor occlusal adjustments)
Haney et al. (1997)	Coronally-advanced flap procedures and citric acid root treatment with or without adjunctive implantation of freeze-dried, demineralized allogeneic bone	6-monthly for 5 years
Yukna & Yukna (1997)	Regenerative surgery with bone grafts and coronally-advanced flaps.	Weekly, then monthly deplaquing until surgical re-entry at 6-12 months, then 3-month recalls
McLeod et al. (1998)	Non-surgical therapy (OHI, SRP, occlusal adjustment, occasional use of systemic AB and antibacterial mouthrinses) followed by surgical treatment (pocket reduction and pocket elimination procedures and occasional regeneration procedures)	6-monthly

Eickholz & Hausmann (2002)	Guided tissue regeneration	3-monthly for the first 2 years (OHI and professional tooth cleaning), then 3–6-monthly maintenance visits according to individual periodontal risk.
Checchi et al. (2002)	OHI, SRP, re-evaluation and periodontal surgery	3-4 monthly hygienist appointment recall
Dannewitz et al. (2006)	OHI, professional tooth cleaning, SRP Surgical intervention included access flap surgery, GTR, tunneling, resective procedures or tooth extraction	Generally 3- to 6- or 12-monthly (clinical measurements, plaque score and if necessary re-instrumentation of sites with PPD of 4mm and BOP or ≥ 5mm
Pretzl. et al. (2008)	Subgingival debridement under local anaesthesia and periodontal surgery if required	Patints with and without SPT (3 to 6-monthly including OHI, professional tooth cleaning, polishing, application of a fluoridegel)
Zafiropoluos et al. (2009)	56 mandibular first or first and second molars were treated by hemisection (Group H, n=32). 36 implants in the mandible to replace periodontally involved first or first and second molars (Group I, n=28).	6-monthly (OHI, supra- and subgingival debridement, polishing)
Johansson et al. (2013)	OH, supra- and sub-gingival scaling, selective periodontal surgeries (occasionally regenerative)	3- to 4-monthly for 2 years by dental hygienists (then referred back to general dentist/hygienist for supportive care)
Miller et al. (2014)	Non-surgical and surgical periodontal treatment	Lasted for as long as the patient continued to be seen (periodontal health and oral hygiene assessment, retreatment and surgery when necessary)

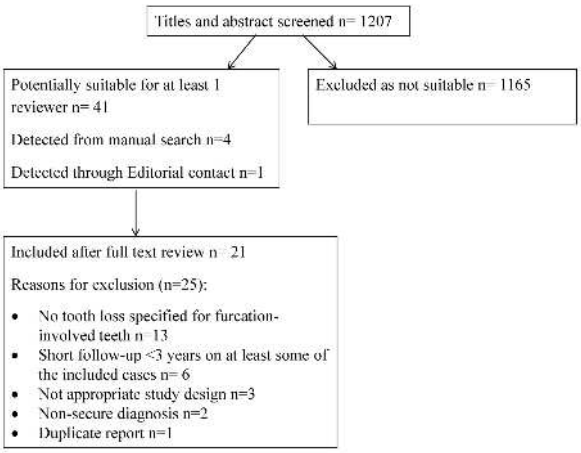
Salvi et al. (2014)	OHI, SRP, surgery if needed (OFD, regeneration, tunneling or resective surgery)	SPT at Department of Periodontology or private practice according to needs (some patients were 'non-compliers')
Graetz et al. (2015)	Subgingival debridement with manual and power-driven instruments, OFD in case of PPD ≥ 5mm with BOP or PPD≥ 6mm (tunneling or root resection when needed)	3- to 12-monthly (non-surgical or surgical subgingival debridement with or without antibiotic therapy)

Table 2

Study	Selection	Comparison	Outcome
Lindhe & Nyman (1975)	★★	★	★★
Hirschfeld & Wasserman (1978)	★★	★	★★
McFall (1982)	★★	★	★★
Goldman et al. (1986)	★★	★	★
Wood et al. (1989)	★★	★	★
Kuhrau et al. (1990)	★★	★	★★
Wang et al. (1994)	★★	★	★★
Little et al.(1995)	★★	-	★★
McGuire & Nunn (1996)	★★	-	★★★

Haney et al. (1997)	★★	★	★★
Yukna & Yukna (1997)	★★	-	★★
McLeod et al. (1998)	★★	★	★★
Eickholz & Hausmann (2002)	★★	★	★★
Checchi et al. (2002)	★★	★	★★
Dannewitz et al. (2006)	★★	★	★★
Pretzl. et al. (2008)	★★	★	★
Zafiropoulos et al. (2009)	★★	-	★
Johansson et al. (2013)	★★	★	★
Miller et al. (2014)	★★	★	★★
Salvi et al. (2014)	★★	★	★★
Graetz et al. (2015)	★★	★	★★

Table 3



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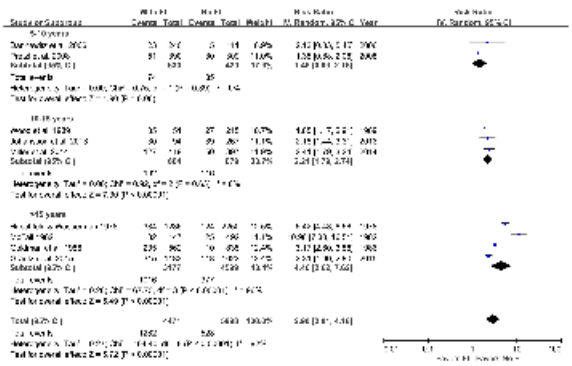

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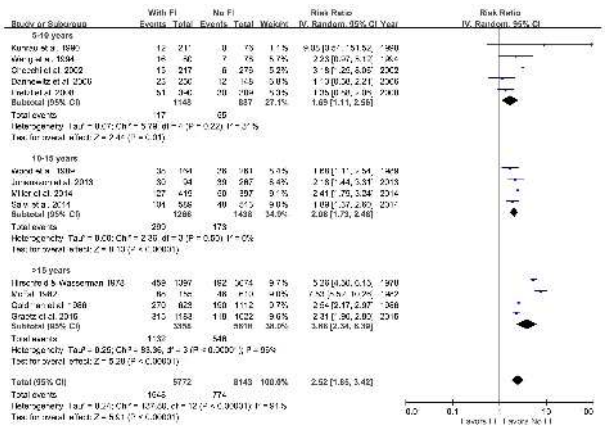

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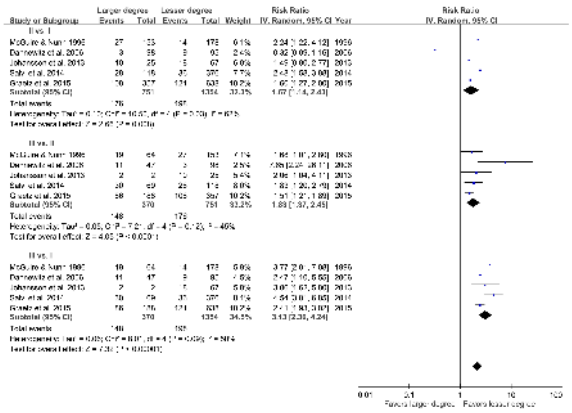

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