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Case Report

Predictors of tooth loss due to periodontal disease in patients following long-term periodontal maintenance

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Abstract

Aim: To analyse patient-related factors (PRFs) and tooth-related factors (TRFs) associated with tooth loss due to periodontal disease (TLPD) in patients undergoing periodontal maintenance (PM).

Material and Methods: The sample consisted of 500 patients (mean follow-up of 20 years). The impact of PRFs on TLPD was analysed with Poisson regression and multivariate logistic regression. The simultaneous impact of PRFs and TRFs was analysed with multilevel logistic regression and Cox regression.

Results: Tooth loss due to periodontal disease was 515 (mean 0.05 patient/year). The significant PRFs were severe periodontitis ($p < 0.001$), aggressive periodontitis ($p < 0.001$), smoking ($p = 0.018$), bruxism ($p = 0.022$) and baseline number of teeth ($p = 0.001$). These PRFs allowed characterizing patients losing more teeth. The whole TRFs analysed were significant, depending on the type of tooth and the category of each factor (e.g. mobility 0, 1, 2, and 3). The significant PRFs increased the risk of TLPD by 2 to 3 times while TRFs increased the risk to a higher extent. Mobility was the main TRF.

Conclusions: Severe periodontitis, aggressive periodontitis, smoking, bruxism and baseline number of teeth, as well as the whole TRFs analysed, were associated with TLPD.

Key words: periodontal disease; periodontal maintenance; periodontal therapy; prognosis; tooth loss

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The pioneering attempt to characterize the response to periodontal treatment of patients undergoing periodontal maintenance (PM) (Wasserman & Hirschfeld 1988) was soon followed by the first studies on periodontal prognosis (McGuire 1991, McGuire & Nunn 1996a,b, McLeod et al. 1998). Two main conclusions were drawn, which remain generally accepted: establishing a periodontal prognosis is the basis of any treatment plan, and actual knowledge of the predictors of tooth loss (TL) is very limited. An extensive review on the subject noted the heterogeneity of the studies and the scarce information that could be drawn from them (Chambrone et al. 2010).

Several statistical models analysing the predictors of TL during PM were capable of explaining the variance in TL to a limited extent: 19% (Tonetti et al. 1998), 12% (König et al. 2002) and 14% (Faggion et al. 2007). The variances can be interpreted as the percentage of improvement in the prediction, compared to

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the alternative of not considering any information provided by prognostic variables (Faggion et al. 2007).

This lack of knowledge based on evidence is consistent with the discouraging observation that clinicians are able to predict good prognosis accurately (McGuire 1991). However, the accuracy of the remaining prognostic categories has been compared to a coin toss (McGuire & Nunn 1996a). Almost two decades after this illustrative comparison, we are far from improving on this scenario. Searching for additional information some authors wonder whether possible missing data on unknown or less studied prognostic factors could be involved (Tonetti et al. 1998, König et al. 2002).

The aim of explaining TL through the analysis of up to twenty patient-related factors (PRFs) and tooth-related factors (TRFs), as previously described (McGuire 1991), would require a strict study design. Insofar as analyses have been performed on overall tooth loss (OTL) we might obtain misleading results. OTL includes TL due to periodontal disease (TLPD) plus, as reviewed, a 35% (Al-Shammari et al. 2005) to 37% (Chambrone et al. 2010) rate of TL due to other reasons (TLOR) including caries, endodontic problems, root fractures and even strategic extractions, in some instances of periodontally stable teeth.

The main suspected PRFs (age, severity, smoking, and compliance with PM) have been found to be statistically associated with TL with rather low consistency, in 40% to 80% of trials (McGuire & Nunn 1996b, 1999, Tonetti et al. 1998, Matthews et al. 2001, Checchi et al. 2002, König et al. 2002, Fardal et al. 2004, Chambrone & Chambrone 2006, Miyamoyo et al. 2006 Muzzi et al. 2006, Carnevale et al. 2007, Faggion et al. 2007, Eickholz et al. 2008, Jansson & Lagervall 2008, Pretzl et al. 2008, Tsami et al. 2009, Leininger et al. 2010, Martin et al. 2010, Baümer et al. 2011a,b, Graetz et al. 2011, Ng et al. 2011, Lü et al. 2013, Costa et al. 2014, Kim et al. 2014, Salvi et al. 2014, Saminsky et al. 2015, Seirafi et al. 2014) and this association has occurred in a seemingly mutual exclusive pattern, so that, for instance, either age or severity is significant, but not both. The few studies identifying both variables simultaneously utilized different criteria: number of teeth lost (Eickholz et al. 2008) or TL > 2 teeth, in a subsample (Tonetti et al. 1998), rather than analysing TL as a dichotomous variable. Therefore, the statistical analysis may have influenced the results. In parallel, a masking or obscuring effect of some TRFs on PRFs has been described (McGuire & Nunn 1999, Pretzl et al. 2008).

The present research attempted to overcome some limitations of the previous research. This was a retrospective case series of 500 patients undergoing PM that aimed to assess the simultaneous impact of PRFs and TRFs on TLPD.

Material and Methods

Study population

The sample of the study consisted of 500 treated periodontal patients (12,830 teeth) attending a PM programme in a private periodontal practice in Valencia, Spain. These subjects were consecutively recruited from a baseline sample of 2975 patients, according to the following inclusion criteria: (1) age >20 years old; (2) compliance with PM for at least 17 years and at least every 12 months; (3) reliable and updated data on medical history, clinical and radiological parameters, smoking and bruxism, and the reason for TL, identified clinically and radiographically in all instances, and (4) diagnosis of periodontitis (Armitage 1999). In order to balance the sample towards moderate and severe forms, mild periodontitis was limited to 22% of the sample.

The exclusion criteria were: serious infectious diseases, type 1 diabetes and self-reported non-controlled type 2 diabetes, coronary heart diseases, immunodeficiency disorders, cancer, immunosuppressive drug use, radiation therapy, severe coagulation disorders, and anticonvulsant drug use. Smoking, pregnancy, controlled type 2 diabetes, anticoagulant use for prophylaxis and hypertension drugs without gingival overgrowth were allowed.

The baseline sample of 2975 patients was reduced to 500 patients mainly due to irregular or erratic compliance with PM and a lack of reliable data on the reasons for TL. All extractions performed either by the author (78%) or outside the office were accompanied by recent X-rays prior to extraction.

This study was approved by the Ethical Committee at Valencia: Comité Ético de la Dirección General de Salud Pública, Generalitat Valenciana. The patients provided their written informed consent. After pseudonymization of each patient′s chart, data were exported and compiled in an independent file for statistical analysis.

The author and sole investigator was responsible for the clinical and radiological examinations, data compilation, treatment and decision making during the entire follow-up period. Further treatment needs met outside the clinic were recorded, and the treatment rendered was updated during the next PM appointment. The routine clinical protocol of the dental hygienists was regularly supervised by the author, with calibration of the measurements registered at least once per year.

Treatment rendered

The APT was performed between July 1988 and February 1995, and it was similar for all the patients. It included oral hygiene instructions and reinforcement based on individual needs: scaling and root planning under local anaesthesia, and surgical treatment in 82% of the cases, depending on clinical judgment: modified Widman flap, osseous resective surgery, root resection and periodontal regeneration. Systemic antibiotic therapy with amoxicillin plus clavulanic acid, metronidazole or azitromycin was prescribed in 25% of the cases, corresponding to the most severe cases of periodontitis. Occlusal adjustment was performed in 65% of the cases. Retreatment during PM was performed in 20% of the patients due to increasing probing pocket depth (PPD) and/or alveolar bone loss.

PM and compliance

After APT, the PM appointments were scheduled at the following intervals: 4 months for aggressive periodontitis and moderate to severe chronic periodontitis; and 6 months

for mild periodontitis. Between one and two years later, the intervals were shortened by one or two months whenever increasing PPD and or signs of inflammation were present. The intervals were lengthened by one and two months for periodontally stable mild and moderate cases.

Periodontal maintenance included an update of the medical and dental histories, assessment of PPD and plaque score, reinforcement and reinstruction on oral hygiene, removal of plaque and calculus from *supra*- and subgingival sites, scaling and root planning when indicated, tooth cleaning and polishing, and application of fluoride gel or desensitizing agents.

Data collection

Medical history

The patients completed a medical history questionnaire at the baseline examination, and the health status was updated periodically during the follow-up period.

Bruxism and smoking habits

Bruxism or parafunctional grinding or clenching of the teeth (AASM, 2005) was diagnosed by anamnesis and clinical examination, using the Tooth Wear Index (Ekfeldt et al. 1990), associated with signs or symptoms of bruxism. This diagnosis was confirmed by anamnesis during the first years of PM. Of the patients with bruxism, 56% wore a bite guard but no distinction was made concerning its use because it varied during the follow-up.

Smoking habits were assigned to one of the following categories: non-smokers and former smokers (for more than 5 years); light smokers (<10 cigarettes per day) and heavy smokers (≥10). No significant differences were observed between non-smokers and light smokers with Poisson regression ($p = 0.260$) and logistic regression ($p = 0.279$). Therefore, for further statistical analysis light smokers were considered as non-smokers. Independent of the initial self-reported smoking habits, the actual habits was detailed and registered during the follow-up period.

Clinical findings

The following clinical parameters were obtained from the patients' charts. Third molars were excluded from the study.

- Baseline number of teeth after APT.
- Plaque-control record (PCR) (O'Leary et al. 1972): the mean value from the last two follow-up years.
- PPD: the deepest baseline value from the routinely measured six sites per tooth, using a manual periodontal probe (PCP 11, Hu-Friedy, Chicago, IL, USA) and assigning each PPD a value in one of these categories: < 5 mm, 5–6 mm, and > 6 mm.
- Gingival recession: the distance from the cemento–enamel junction to the gingival margin, measured with the periodontal probe.
- FI (Hamp et al. 1975): the most affected category from the routinely recorded extent of FI during either scaling and root planning or during open flap procedures. The manual periodontal probe was used. Furcation of the upper first premolars was excluded.
- Tooth mobility (Lindhe & Nyman, 1977).

Radiographic findings

A complete set of baseline periapical radiographs for each patient were examined by the author to measure the variables under study. A standardized radiographic protocol was applied to the film (Ultraspeed; Kodak, Rochester, NY, USA), including an XCP technique using film holders (54-2001 XCP, Dentsply Rinn, Elgin, IL, USA), an X-ray source (Trophy IRIX 70, 0459, Trophy España, Madrid), and a developing procedure (Periomat, Dürr dental, Bietigheim-Bissingen, Germany). Radiographs were examined in a darkened room using a radiographic screen (67-0442, Dentsply Rinn, Elgin, IL, USA).

Relative bone loss in per cent (BL) was assessed at the most affected site of each tooth, using a Schei ruler (Schei et al. 1959). The original categories of the index were modified, assigning BL to one of the following three groups: (1) BL < 30%; (2) BL 30 to 50%; and (3) BL > 50%. The ratio of crown height to root length (C/R) was classified into three categories: (1) C/R 1/2 (root length doubles, at least, crown height); (2) C/R 1/1.5; and (3) C/R 1/1. The root anatomy on multi-rooted teeth was classified as divergent or convergent.

Diagnosis and classification of periodontitis

Periodontitis was classified as ChP and AgP and was also classified according to severity (Armitage 1999). AgP was defined as patients younger than 36 years old with attachment loss (AL) ≥5 mm and bone loss >50% mm at more than two sites. Patients with moderate periodontitis (AL 3–4 mm and BL 30–50%) and <36 years of age were differentiated from AgP and ChP. At the tooth level, severe periodontitis was identified with PPD > 5 mm, BL > 50%, as well as FI II and III.

Assessment of TL

All teeth extracted either in the office (80%) or outside the office had a clinical and radiological evaluation immediately prior to the extraction. This protocol allowed ensuring as possible the reason for TL, either TLPD or TLOR: endodontic problems, root fractures and strategic extraction due to restorative and orthodontic considerations. Initial TL during APT was also assessed.

The criteria to define TLPR were as follows: spontaneous exfoliation; and BL > 75% with mobility of grade III, which caused pain under function or spontaneously. For molars BL > 50% associated to FI grade III and repeated abscesses. Teeth extracted for restorative purposes with BL > 75 and mobility grade III were considered TLPD. An effort was undertaken to differentiate the primary cause of combined endo-perio lesions. Endodontic complications with BL > 75% without caries or root fracture were considered TLPD.

Statistical analysis

Data entry and descriptive and analytical statistics were performed by independent statisticians (ERATEMA, I.A & L.D.). The SSPS software program (IBM, SPSS Statistics, V.19, Armonk, NY, USA) was utilized for Poisson regression, multivariate logistic regression and Cox regression. The STATA software

procedure xtmelogit (StataCorp. 2011. Stata Statistical Software: Release 12. College Station, TX: StataCorp LP) was used for multilevel logistic regression.

The patient was the unit of the analysis. Poisson regression assessed the associations of the independent variables PRFs with the main outcome, the dependent variable of the number of teeth lost. Multivariate binomial logistic regression analysis assessed the association of PRFs with the dependent dichotomous variable TLPD > 2 and TLPD > 3 teeth, to characterize patients with higher rates of TLPD.

The simultaneous analysis of the effects of PRFs and TRFs was performed by multilevel logistic regression. This generalized linear mixed regression was applied using a binomial distribution for the dichotomous-dependent variable TLPD and the logit as link function. For all analyses, the base-level tooth was nested into the upper-level patient. All patient effects were assumed to be random. These variables were entered into the model in a forward step-wise manner, based on the *p*-value. Statistical significance was set at $p < 0.05$ (Wald′s test). Factors with a *p*-value <0.05 were entered consecutively into the model, and those attaining a *p*-value of 0.5 were removed. Multicollinearity and interactions were also analysed.

Survival analysis was also performed with Cox regression, being the tooth the unit of the analysis. The multivariate approach allowed for the simultaneous analysis of PRFs and TRFs, quantifying the multiplicative increase or decrease in the risk for TLPD as a dichotomous variable. The least affected category was compared to each other category (e.g. mobility 0 versus mobility 1, 2 and 3), which were treated as dichotomous covariates. A more detailed description of the test may be found in Table S1.

The PRFs analysed were age, sex, AgP versus ChP, severity of the whole sample (mild, moderate and severe), bruxism, smoking habits, PCR, compliance with PM and baseline number of teeth. TRF analysed were type of tooth (molars versus non-molars), BL (<30%, 30–50% and >50%), PPD (<5, 5–6 and >6 mm), mobility (0, 1, 2, 3), FI (0, I, II, III), C/R ratio (1/2, 1/1.5 and 1/1) and root anatomy (convergent and divergent).

Comparison of results

The selection of the available literature to compare our results was compiled with the search strategy already utilized in two reviews of the subject (Chambrone et al. 2010, Faggion et al. 2014). Our criteria to select the publications were sample size ≥30 patients, at least 5 years of follow-up and reliable data on either TL or TLPD. The information provided by these studies is presented in two Tables (S1 and S2) and two Appendices (S1 and S2) as Supporting Information.

Results

Patients and PRF

The study population characteristics and PRFs under study are shown in Table 1. The sample consisted of 500 patients undergoing PM for a mean period of 20.2 years (±2.4), ranging from 17 to 25 years. The mean baseline age was 40.3 years old, ranging from 22 to 74 years. The subjects were mostly of Caucasian European origin (98%) and high to middle socio-economic level.

Baseline tooth sample and TRF

The baseline tooth sample was 12.830 teeth: 3.358 molars and 9.472 non-molars. The mean number of teeth per patient was 25.7 (±2.8) with a minimum of 10 and a maximum of 28. The distribution of TRFs in the sample is shown in Table 2.

TL: TLPD and TLOR

The baseline OTL was 875 teeth (6.8%). TLPD accounted for 515 teeth (4%): 300 (2.3%) molars and 215 (1.6%) non-molars. The mean TLPD per patient was 1 (mean 0.05 patient/year). The remaining 360 teeth (2.8%) were TLOR: non-restorable caries, 172 (1.3%); root and or crown fracture, 75 (0.6%); endodontic complication, 26 (0.2%) and strategic extraction due to orthodontic and prosthetic considerations, 85 (0.6%). During APT 235 teeth (1.8%) were extracted.

Differences in the prevalence of TLPD between molars (9%) and non-molars (2.2%) were statistically significant (X^2 $p < 0.05$). Therefore, the multilevel logistic regression analysis was performed independently for both groups of teeth. Only 7.6% of molars and 1.2% of non-molars with slight and moderate periodontitis were lost, while 36.6% of molars and 16.4% of non-molars with severe periodontitis (PPD > 5 mm, BL > 50%, as well as FI II and III) were lost.

A total of 292 patients (58.4%) did not lose any teeth; 159 patients (31.8%) lost 1 to 3 teeth (93 lost 1, 33 lost 2, and 33 lost 3) and 49 patients (9.8%) lost 4 to 9 teeth in the so-called D group. In the ED

Table 1. Study population characteristics and PRFs under study

Patients	500	Mean age 40.3 SD 9.07	Range 23–74
Gender		344 female (68.8%)	156 male (31.2%)
Classification			
ChP TOTAL	298 (59.6%)		
ChP mild	110 (22%)		
ChP moderate	66 (13.2%)		
ChP severe	122 (24.4%)		
Moderate < 36	102 (20.4%)		
AgP	100 (20%)		
PM years		Mean 20.2 SD 2.04	Range 16.7–26.1
Compliance		241 attending > 70%	259 failing > 30%
Smoking	276 no (55.2%)	81 light-s. (16.2%)	143 heavy-s. (28.6%)
Bruxism	264 no (53.1%)	233 yes (46.9%)	
PCR		281 < 30% (56.2%)	219 ≥ 30% (44.4%)

ChP, chronic periodontitis; AgP, aggressive periodontitis; ChP has been classified according to severity (Armitage 1999); moderate >36, patients under 36 years of age and moderate periodontitis; PRFs, patient-related factors; PM years, years under periodontal maintenance; PCR, plaque control record.

Table 2. Distribution of TRFs under study

	Total		Molar		Non-molar	
	Number	Percentage	Number	Percentage	Number	Percentage
Total	12,830	100	3358	100	9472	100
BL						
Total	12,803	100	3327	100	9442	100
<30%	7787	60.8	1854	57.4	5902	62.5
30–50%	3749	29.2	1030	31.9	2741	29.0
>50%	1267	9.8	443	13	799	8.4
PPD						
Total	12,850	100	3359	100	9472	100
<5 mm	6320	49.0	835	24.8	5457	57.6
5–6 mm	4749	37.0	1673	49.8	3085	32.5
>6 mm	1781	13.8	851	25.3	930	9.8
Mobility						
Total	12,756	100	3320	100	9432	100
0	8881	69.6	2343	70.5	6536	69.3
1	3494	27.3	857	25.8	2624	27.8
2	334	2.6	101	3.0	242	2.5
3	49	0.4	19	0.5	30	0.3
FI						
Total			3358	100		
0			2106	63.3		
I			824	24.5		
II			372	11.0		
III			56	1.6		
Root form						
Total			3358	100		
Convergent			1650	49.1		
Divergent			1708	50.8		
C/R ratio						
Total	12,830	100	3358	100	9472	100
1, 2	4314	33.6	776	23.1	3484	36.7
1, 1,5	7606	59.2	1867	55.5	5672	59.8
1, 1	910	7.1	715	21.2	316	3.3

TRFs, tooth-related factors; BL, bone loss; PPD, probing pocket depth; FI, furcation involvement; C/R, crown to root ratio. A reduced percentage (0.6%) of measurements on BL and mobility was not included, due to difficulties to measure interproximal BL or to clearly identify the extent of mobility. Note the lower percentages for the most affected category of each TRF.

group, only three patients (0.58%) lost 12, 13, and 16 teeth respectively.

Impact of PRFs on TLPD

Table 3 depicts how the presence of each PRF increased the TLPD rate per patient and the prevalence of patients with TLPD >2 and >3 teeth. Poisson regression analysis (Table 4) identified the following PRFs associated with the number of teeth lost: severe periodontitis ($p < 0.001$), AgP ($p < 0.001$), years under PM ($p < 0.001$), heavy smoking ($p = 0.018$), bruxism ($p = 0.022$) and baseline number of teeth ($p = 0.001$). PCR was close to statistical significance ($p = 0.053$). The quality of the model (Goodness-of-fit) was: Likelihood ratio Chi² 326.9 (p = 0.000) and Log-likelihood −646.5

Multivariate logistic regression (Table 5) to characterize TLPD > 2 teeth (85 patients) identified the following significant factors: severe periodontitis ($p < 0.001$) Exp.(B) 7.9, AgP ($p < 0.001$) Exp.(B) 3.1, heavy smoking with bruxism ($p = 0.001$) Exp.(B) 2.6, and years under PM ($p < 0.001$). For TLPD >3 teeth (52 patients) the significant PRFs were severe periodontitis ($p < 0.001$) Exp.(B) 3.8, AgP ($p < 0.001$) Exp.(B) 3.1, heavy smoking with bruxism ($p = 0.003$) Exp.(B) 3.7, baseline number of teeth ($p = 0.049$), and years under PM ($p = 0.002$). The isolated participation of either heavy smoking ($p = 0.450$) or bruxism ($p = 0.119$) did not show statistically significant differences for TLPD > 2 and > 3 teeth. No significant differences were found for the remaining variables.

The quality of the model (Goodness-of-fit) was $R^2 = 32\%$ (TLPD > 2) and 27% (TLPD > 3) with the log-likelihood ratio statistic decreasing on each step and the p value Hosmer–Lemeshow being >0.05 on the final step.

Impact of PRFs and TRFs simultaneously on TLPD

Results from multilevel logistic regression analysis for molars and non-molars (Table 6) revealed the simultaneous impact of PRFs and TRFs on TLPD.

Analysis for molars: significant PRFs were smoking ($p = 0.005$) Exp.(B) 3.2, bruxism ($p = 0.012$), Exp.(B) 2.3, and length of follow-up ($p = 0.010$), increasing the risk a 10% each additional year. Baseline number of teeth was also significant ($p = 0.017$), increasing the risk by 9.5% each absent tooth.

The type of tooth was significant ($p = 0.001$), so that lower first molar were 2.5 times less prone to be lost [Exp.(B) 2.5) than the remaining molars. With the exception of root anatomy and C/R ratio, the remaining TRFs were significant, although to an extent depending on the category of each TRF (e.g. mobility 0, 1, 2, and 3). Mobility grade 2 ($p < 0.001$) [Exp.(B) 4.7] and 3 ($p = 0.003$) [Exp.(B) 6.8] were the main factors, followed by FI, PPD and BL. The intermediate category of these factors doubled the risk for TLPD while for the extreme category the risk increased by three times (BL > 50%), to almost 4 times (PPD > 6 mm and FI III).

Analysis for non-molars: the only significant PRFs were length of follow-up ($p = 0.021$), increasing the risk by 19% each additional year, and baseline number of teeth ($p < 0.001$), increasing the risk by 28% each absent tooth. The whole TRFs analysed were significant. The type of tooth was clearly associated to TLPD ($p < 0.001$), increasing the risk by 2 (upper canines, upper incisors and lower lateral incisors) to 7 times (upper premolars and lower central incisors) as compared to lower canines and lower premolars. The increase in the risk according to the category of each TRF was similar to the model for molars, except for mobility II Exp.(B) 13 and III

Table 3. Mean TLPD/pt. and prevalence of patients with TLPD > 2 years >3 teeth according to PRF

PRF	*n* pts.	%	Mean	SD	TLPD > 2 (85 pts.)		TLPD > 3 (52 pts.)	
			TLPD/pt.		*n* pts.	%	*n* pts.	%
Total	500	100	1	1.7	85	17.0	52	10.4
Severity								
Mild	110	22	0.29	0.85	7	6.3	6	5.4
Moderate	178	35.6	0.60	1.10	13	7.3	8	4.4
Severe	222	40.4	1.77	2.19	65	29.2	38	17.1
Classification								
ChP	298	59.6	0.65	1.36	36	12	17	3.4
AgP & moderate < 36	202	40.4	1.30	1.93	49	24.2	35	17.3
AgP	100	20	2.3	2.47	32	32	25	25
PCR								
PCR < 30%	281	56.2	0.93	1.20				
PCR > 30%	219	44.4	1.20	1.96				
Smoking/Bruxism								
Smoking −	276	55.2	0.83	1.64				
Smoking < 10	81	16.2	1.12	1.78				
Smoking > 10	143	28.6	1.64	1.93				
Bruxism −	264	53.1	0.83	1.45				
Bruxism +	233	46.9	1.33	2.05				
Smoking − Bruxism −	203	40.6	0.69	1.45	15	7.3	10	4.9
Smoking − Bruxism +	151	30.2	1	1.86	15	9.9	10	6.6
Smoking + Bruxism −	62	12.4	1.23	1.33	15	24.2	8	12.9
Smoking + Bruxism +	84	16.8	1.89	2.23	40	47.6	24	28.5

TLPD, tooth loss due to periodontal disease, *n* pt., number of patients; PRFs, patient-related factors; ChP, chronic periodontitis; AgP, aggressive periodontitis; moderate < 36, patients under 36 years of age with moderate attachment loss and bone loss; PCR, Plaque control record.

Table 4. Poisson regression analysis: TLPD during PM

	Estimate	SE	Walds′Chi²	*p*	Risk ratio
Intercept	−3.486	0.7070	24.309	0.000	0.031
Severe perio.	1.289	0.2549	25.562	0.000	3.629
Smoking	0.527	0.2228	5.592	0.018	1.694
Bruxism	0.281	0.1225	5.253	0.022	1.324
AgP	0.624	0.1198	27.085	0.000	1.866
Baseline teeth	−0.046	0.0140	10.581	0.001	0.955
Years under PM	0.162	0.0234	48.347	0.000	1.176
Compliance with PM	0.002	0.0963	0.001	0.981	1.002
PCR > 30%	0.179	0.0921	3.760	0.053	1.196
Age	0.007	0.0065	1.157	0.282	1.007
Gender	−0.059	0.0979	0.365	0.546	0.943

Dependent variable: TLPD, tooth loss due to periodontal disease; PM, periodontal maintenance; AgP, aggressive periodontitis baseline teeth, baseline number of teet, PCR, plaque control record.

Exp.(B) 17. C/R ratio 1/1 was significant in this model (p = 0.007) Exp.(B) 3.1.

The quality of the model for molars and non-molars was, respectively, R^2: 30.9% and 24.4%, and AUC: 0.93 and 0.94. The variance partition coefficient (VPC) revealed that 26% (molars) and 42% (non-molars) of the variance was due to differences among patients. Multicollinearity and interactions were analysed and discharged.

Results from Cox regression are presented in Table S3. The significant PRFs severe and AgP, as well as smoking and bruxism, increased the risk in a similar fashion as shown with multivariate logistic regression. In parallel, these factors decreased the expected survival time by 43–54%. The intermediate category of the whole TRFs decreased the survival time by 34–60%, while the extreme category decreased it by 79–95%.

Discussion

TLPD and OTL

Our study found a mean TLPD of 0.05 patient/year, consistent with the rates reported (Table S1) in studies of clearly defined TLPD samples, ranging from 0.04 to 0.08 (McGuire & Nunn 1999, Checchi et al. 2002, König et al. 2002, Fardal et al. 2004, Chambrone & Chambrone 2006, Muzzi et al. 2006). Even lower rates have been reported with a follow-up of 15 years (Lindhe & Nyman 1984).

As observed in Table S1, the mean TL rates patient/year reported in studies of patients undergoing PM, ranged from 0.02 (Lindhe & Nyman 1984, Chambrone & Chambrone 2006) to 1.17 (McFall 1982). The wide range of variation, as addressed in Appendix S1, is related to several aspects: The TL sample, either TLPD or OTL; the criteria to identify TLPD and to indicate the extraction; the treatment philosophy and the inclusion criteria of the sample. This may partially explain our TLPD rate.

Impact of PRFs

The extensive review of predictors of TL by Chambrone et al. (2010) noted that only age and smoking, in addition to periodontal prognosis, were clearly associated with TL. In parallel, downhill patients (D) and extreme downhill patients (ED) have been characterized to date by the number of teeth lost, instead of by actual PRFs. Our findings may contribute to identify PRFs clearly associated with TLPD and also could help to characterize patients losing more teeth. Severe periodontitis, AgP, smoking, bruxism and baseline number of teeth were significant PRFs associated with TLPD. Patients losing more teeth in our study (TLPD > 2 and > 3) were characterized by the above-mentioned PRFs, especially severe periodontitis and the combination of smoking and bruxism. These results are partially consistent with those initially reported from a sub-sample

Table 5. Variables PRF in the equation for TLPD >2 and TLPD >3. Multivariate logistic regression

	PRF	B	SE	Wald	*p*	Exp (B)	95% CI
TLPD >2	Severe period.	1.968	0.416	22,358	0.000	7.157	3.166–16.183
	Aggressive period.	0.909	0.334	7395	0.007	2.481	1.289–4.777
	Smoking + bruxism	1.326	0.335	15,695	0.000	3.768	1.955–7.262
	Years under PM	0.286	0.077	13,755	0.000	1.331	1.144–1.548
	Constant	−8.980	1.730	26,956	0.000	0.000	
TLPD >3	Severe period.	1.350	0.548	6066	0.014	3.857	1.317–11.294
	Aggressive period.	1.133	0.424	7135	0.008	3.104	1.352–7.126
	Smoking + bruxism	1.313	0.396	11,014	0.001	3.719	1.712–8.078
	Years under PM	0.275	0.091	9156	0.002	1.317	1.102–1.574
	Baseline *n* teeth	−0.134	0.053	6427	0.011	0.874	0.788–0.970
	Constant	−6.221	2.357	6969	0.008	0.002	

TLPD > 2 and >3, tooth loss due to periodontal disease >2 and >3 teeth; PRF, patient-related factor; PM, periodontal maintenance.

with TL > 2 teeth, in which 88.9% presented moderate to severe periodontitis, and 50% of patients were smokers (Tonetti et al. 1998).

The baseline number of teeth has rarely been analysed, yet the available information suggests its potential relevance (Tonetti et al. 1998, Ravald & Starkhammar Johanson 2012). Our study found this PRF clearly associated with TLPD.

There is only one study in which bruxism without the use of a bite guard was associated with TL (McGuire & Nunn 1996b) although lacking on details on the sample of patients. We found bruxism significant. However, in the models TLPD > 2 and > 3 teeth, bruxism required the presence of smoking to be significant.

Impact of TRFs

Our study found the whole TRFs associated. The type of tooth is a relevant factor, since differences were found between molars and non-molars, and even more, between different molars and non-molars. The category of each TRF clearly modifies its level of significance. We found differences between FI grade II and III, as other researchers recently showed (Salvi et al. 2014). The same would apply to the category of the remaining TRFs.

The statistical analysis of predictors of TL

Co-linearity and confounding effects, effect modification and statistical interaction could influence the results to a great extent. We searched for co-linearity among the variables under study, discharging any interaction. Adjusting for confounders is a routinely utilized procedure to control confounding effects. Ideally what would best ensure this control is a large sample, allowing for a more randomized distribution of variables under study. Unfortunately larger samples, with a balanced distribution of each variable, represent a major limitation.

The manner in which the significant PRFs associated with each other would enrich our understanding on predictors of TLPD. However, analysing several factors combined would face limitations of the complexity of the analysis and the sample size. It has been shown that heavy smoking increased the risk for TLPD by 2.9 times and IL-1 positive genotype raised it by 2.7 times, while both PRF combined increased the risk by 7.7 times (McGuire & Nunn 1999). We also found different TLPD rates in the subsamples, according to the presence or the absence of smoking and bruxism, either isolated or combined. The increase in the rate resulting from smoking combined with IL-1 positive genotype was our rationale to analyse the combined effect of smoking and bruxism (as an independent variable smoking*bruxism), finding that this combination was a stronger explanatory variable than isolated smoking, which was eliminated from the model TLPD > 2 and > 3 teeth.

Strengths and limitations of the study

The sample of this study was compiled retrospectively, according to previously defined inclusion and exclusion criteria. It was necessary to count on a baseline sample six-fold larger (2975 patients) to gather the final sample of 500 patients. Therefore, this study had the inherent limitations of a retrospective case-series study, but it also counts on a well documented sample in the long-term, ensuring reliable data on the variables registered and the reasons for TL. Great care was taken to ascertain the reason for TL. It was also attempted to have an even distribution of the main suspected PRFs within the sample. This feature allowed for the controlling of the confounding effect due to a more randomized distribution of the variables.

The long and close relationship with the patients during the long-term follow-up allowed for the obtaining of reliable information about smoking habits and bruxism. In many instances, the self-reported habits registered in the initial health questionnaire differed from those recognized by the patient years later.

A limitation of our study results from the lack of a clear-cut method to differentiate ChP and AgP in certain circumstances. Some studies identify AgP with BL ≥ 50% (Baümer et al. 2011a,b, Graetz et al. 2011) while others considered BL > 33% (Lü et al. 2013). The form of periodontitis commonly found in adults can also be seen in adolescents (Papapanou 1996) and in parallel, patients being 36–40 years old, for instance, with severe BL, might have presented a comparable extent of BL a few years before. As it has been pointed out, some patients formerly classified as having generalized juvenile periodontitis in the older literature might appropriately be placed in either the

Table 6. Multilevel logistic regression analysis for molars and non-molars

	B	SE	*t*	*p*	Exp (B)	95% CI
Molars						
Constant	−5.884	1.524	−3.861	0.000	0.003	0.000–0.056
Age	−0.006	0.012	−0.463	0.643	0.994	0.971–1.019
Gender	−0.029	0.217	−0.134	0.893	0.971	0.635–1.486
Smoking	1.186	0.424	2.794	0.005	3.272	1.424–7.521
Bruxism	0.872	0.345	2.528	0.012	2.392	1.216–4.705
Severe	0.570	0.421	1.352	0.177	1.768	0.774–4.039
AgP	0.041	0.418	0.098	0.922	1.042	0.459–2.364
Compliance PM	−0.198	0.212	−1	0.350	0.820	0.542–1.242
PCR > 30%	0.046	0.201	0.230	0.818	1.047	0.706–1.553
Length on follow-up	0.096	0.037	2.584	0.010	1.101	1.023–1.184
Lower firs molar (ref.)						
Remaining molars	0.898	0.262	3.427	0.001	2.455	1.468–4.103
Baseline *n* teeth	−0.091	0.038	−2.391	0.017	0.913	0.847–0.984
Mobility 0 (reference)						
Mobility 1	0.538	0.188	2.861	0.004	1.713	1.184–2.476
Mobility 2	1.548	0.319	4.847	0.000	4.701	2.514–8.793
Mobility 3	1.930	0.646	2.988	0.003	6.890	1.941–24.448
FI 0 (reference)						
FI I	0.325	0.209	1.556	0.120	1.384	0.919–2.084
FI II	0.800	0.246	3.253	0.001	2.225	1.374–3.603
FI III	1.273	0.410	3.103	0.002	3.573	1.589–7.988
BL > 30% (reference)						
BL 30–50%	0.540	0.234	2.305	0.021	1.716	1.084–2.718
BL > 50%	1.177	0.276	4.267	0.000	3.244	1.889–5.571
PPD < 5 (reference)						
PPD 5–6	0.771	0.346	2.227	0.026	2.163	1.096–4.265
PPD > 6	1.349	0.366	3.692	0.000	3.855	1.883–7.894
Root anatomy	0.107	0.178	0.598	0.550	1.113	0.784–1.579
C/R 1/2 (reference)						
C/R 1/1.5	0.306	0.242	1.258	0.209	1.358	0.843–2.189
C/R 1/1.5	0.255	0.259	0.986	0.324	1.291	0.777–2.144
Non-molars						
Constant	−6.249	2.186	−2.086	0.004	0.002	0.140–0.349
Age	−0.006	0.017	0.36	0.719	1.006	0.973–1.040
Gender	0.12	0.313	0.38	0.703	1.127	0.610–2.082
Smoking	0.397	0.692	0.570	0.556	1.487	1.424–7.521
Bruxism	0.454	0.542	0.840	0.402	1.575	0.544–4.556
Severe	1.002	0.600	1.067	0.095	2.725	0.840–8.841
AgP	0.023	0.566	0.040	0.967	1.042	0.338–3.102
Compliance PM	0.193	0.307	0.630	0.529	1.213	0.665–2.212
PCR > 30%	−0.167	0.296	0.560	0.846	0.846	0.474–1.513
Length on follow-up	0.176	0.076	2.030	0.021	1.193	1.027–1.385
Teeth A (reference)						
Teeth B	0.705	0.031	2.013	0.033	2.024	1.058–3.875
Teeth C	1.991	0.319	6.024	0.000	7.320	3.915–13.685
Baseline *n* teeth	−0.249	0.050	−4.097	0.000	0.779	0.706–0.860
Mobility 0 (reference)					1.000	
Mobility 1	0.672	0.253	2.065	0.008	1.958	1.192–3.216
Mobility 2	2.584	0.350	7.039	0.000	13.245	6.673–26.289
Mobility 3	2.879	0.744	3.087	0.000	17.803	4.144–76.481
BL > 30% (reference)					1.000	
BL 30–50%	−0.028	0.287	−0.1	0.924	0.973	0.554–1.708
BL > 50%	1.116	0.325	3.043	0.001	3.053	1.615–5.772
PPD < 5 (reference)					1.000	
PPD 5–6	0.705	0.272	2.060	0.009	2.024	1.189–3.447
PPD > 6	1.349	0.366	3.692	0.000	3.855	2.826–10.278
C/R 1/2 (reference)					1.000	
C/R 1/1.5	0.470	0.257	1.083	0.067	1.601	0.968–2.647
C/R 1/1	1.137	0.419	2.071	0.007	3.116	1.370–7.089

TLPD, tooth loss due to periodontal disease; AgP, aggressive periodontitisPM, periodonta maintenance; PCR, plaque control record; lower first molar (ref.), lower first molar as a reference category versus the remaining molars; Baseline *n* teeth, baseline number of teeth; FI, furcation involvement; Teeth A, lower canines and lower premolars, Teeth B, upper canines, upper incisors and lower lateral incisors, Teeth C, upper premolars and lower central incisors; BL, bone loss; PPD, probing pocket depth; C/R, crown to root ratio.

ChP or AgP in the following classification system, depending on a variety of primary and secondary characteristics (Armitage 1999). However, neither age nor knowledge of the rate of progression seems to be reliable parameters to differentiate both forms in some instances (Armitage 1999), so a more precise distinction might require bacteriological and histopathological analysis. Alternatively a more practical approach has been, for instance, the exclusion of patients 36–39 years old (Graetz et al. 2011). The variable AgP in our analysis was identified with patients being ≤36 years old and having BL ≥ 50%. Patients ≤36 years old and moderate BL <50%, were classified as such, without labelling them as ChP or AgP."

On the other hand, AgP, with a characteristic bacteriological and histopathological profile (Gajardo et al. 2005, Lafaurie et al. 2007, Armitage 2010, Smith et al. 2010) has been shown to be a clear risk factor. However, it still has to be elucidated whether it is a significant prognostic factor, in patients under PM. There is a unique research complying with high standards of experimental design, analysing matched samples of 34 ChP and 34 AgP patients under PM. No differences were found for TL and PPD (Graetz et al. 2011). Other authors have found TL rates in AgP comparable to the rates found in ChP patients (Baümer et al. 2011a,b, Lü et al. 2013). Although we found AgP to be a significant factor, perhaps by analysing a sample with and without AgP, it still has to be elucidated whether the actual significant factor is the severe stage of the disease or the type of periodontitis by itself. In our multilevel analysis, TRFs associated to severity of disease were significant while AgP was not.

The rather common use of the term risk factor in studies on predictors of tooth loss during PM might be revisited, since results from research on prognostic factors may substantially differ from results of risk factors in the untreated population.

Another limitation of the study was the lack of intra-examiner calibration for extracting and managing the data. However, for all the patients with TL > 2 teeth, either TLPD or TLOR, the database was compared to the original records to search for any discrepancy.

Compliance with the use of the bite-guard varied among patients and within the patient during the entire follow-up. Therefore, the analysis was done without considering the use of the appliance. This represents a limitation, lacking on information on the actual benefit of wearing the bite-guard.

As it was noted in the introduction, several statistical models have explained the variance of TL (R^2 values) to a limited extent, between 14 to 19%. Our results may contribute to a better understanding of predictors of TLPD, having obtained R^2 values of 24–31% with four PRFs and the whole TRFs (multilevel logistic regression). It should also be pointed out the consistency of our results, obtained with several statistical methods. This may get us slightly closer to a theoretical complete explanation of TLPD. That is to say, the whole significant factors, explaining a 100% of the variance of TLPD ($R^2 = 1$). This does not seem an attainable objective.

Conclusions

Within the limitations of our study, the following conclusions can be drawn.

- The main patient-related factors associated with TLPD were severe periodontitis and aggressive peridontitis, followed by heavy smoking, bruxism and fewer baseline teeth.
- Patients losing more teeth, in the models TLPD > 2 and > 3 teeth, were characterized by severe periodontitis, lower number of baseline teeth and the combination of smoking with bruxism. Isolated smoking and isolated bruxism did not characterize these patients.
- Tooth-related factors analysed were all significant, depending on the type of tooth and the category of each factor. The intermediate category of FI, BL, PPD and C/R ratio duplicated the risk of TLPD, while the extreme category increased the risk by 3 to 4 times. Mobility was the main factor, increasing the risk between 2 to 4 times more than the remaining TRFs.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Comments to data shown in Table S1.
Appendix S2. Comments to data shown in Table S2: comparison of results and statistical considerations.
Table S1. Studies on tooth loss during periodontal maintenance (PM).
Table S2. Statistically significant differences for PRFs and TRFs on tooth loss.
Table S3. Cox regression: PRFs and TRFs associated with TLPD.

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Clinical Relevance

Scientific rationale for the study: Very few patient-related factors (PRFs) have been clearly shown to be associated with tooth loss due to periodontal disease (TLPD). There is also limited knowledge on the impact of tooth-related factors (TRFs) on TLPD.

Principal findings: The significant PRFs were severe periodontitis, aggressive periodontitis, smoking, bruxism and baseline number of teeth. These factors were useful to characterize patients losing more teeth. TRFs were all significant although to an extent depending on the type of tooth and the category of each TRF (e.g. mobility 0, 1, 2, and 3).

Practical implications: A better understanding on the impact of PRFs and TRFs may contribute to establish a more accurate periodontal prognosis.