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30-years longevity of teeth

Longevity of teeth in patients susceptible to periodontitis. Clinical outcomes and risk factors associated with tooth loss after active therapy and 30 years of supportive periodontal care

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ABSTRACT

Aims:
i) to evaluate the efficacy of active periodontal therapy supplemented by supportive periodontal care (SPC) in retaining the dentition for a 30-year follow-up period in patients susceptible to periodontitis; and ii) to assess the prognostic factors associated with tooth loss.

Material and Methods:
154 patients with periodontitis, retrospectively classified as Stage I to IV and Grade B to C periodontitis, treated between 1984 and 1986 in a private practice, were enrolled in this study. After periodontal assessment patients received non-surgical treatment followed by surgical periodontal therapy, orthodontic treatment and tooth-splinting, where appropriate. SPC consisted of a strict recall programme every 3 to 6 months over a 30 years period. Recurrences were treated either with subgingival root planning or flap surgery. Dental and periodontal variables were measured at baseline (T0), end of active therapy (T1) and after 25 (T2) - 30 (T3) years. Generalized mixed models were performed to assess prognostic factors associated with tooth loss as well as survival analyses for tooth loss.

Results:
Data on 154 patients (4083 teeth) were available at baseline (T0). Teeth irrational to treat were extracted during active therapy (160, 3.9%) and at re-assessment (13, 0.3%) (T1). After 25 years of SPC, 140 teeth out of 3910 in 154 patients (3.6%) were lost (24 in 18 patients for periodontal reasons). Between 25 and 30 years, 20 patients (482 teeth) dropped out; 61 teeth (2%) were lost (15 in 14 patients for periodontal reasons). Overall, 201 teeth (5.1%) were lost (39 for periodontal reasons) in 30 years SPC.
Generalized mixed models showed that Stage III or IV periodontitis were associated with greater tooth loss during SPC compared to Stage I or II (OR = 2.10 P = 0.048). Generalized periodontitis showed a statistically significant OR = 3.24 (P = 0.016) compared to the localized one.
In SPC (T1-T3), age (P = 0.011), gender (male) (P = 0.038), molar teeth (P = < .001), T0 and T1 pocket depth (P = < .001), tooth mobility grade 2 (P = 0.018) and 3 (P = 0.050), T0 aand T1 bone loss (P = < .001), presence of a root canal treatment (P = < .001) and a crown (0.009) were statistically significantly associated with tooth loss.

Conclusion:
(I) Periodontal therapy and a stringent SPC are effective in maintaining most of the teeth in patients with moderate/advanced periodontitis for 30 years. (II) Age, gender, molar teeth, pocket depth, bone loss, presence of a root canal treatment and a crown are prognostic factors associated with tooth loss.

Key words: Periodontal disease, Periodontal therapy, Supportive periodontal therapy, Long term, Tooth survival

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Clinical Relevance

Scientific rationale for the study: Long-term retention of teeth in function is the ultimate goal of periodontal therapy. Very limited evidence exists on tooth retention above 20 years of follow up in patients with periodontitis

Principal findings: Patient- and tooth-related factors contribute to loss of teeth during active therapy and SPC. In this study, age, gender, molar teeth, pocket depth, bone loss, presence of a root canal treatment and a crown were shown to be prognostic factors associated with tooth loss

Practical implications: Dentists should enforce appropriate active periodontal therapy and a stringent SPC to maintain most of the teeth in patients with moderate/advanced periodontitis up to 30 years.

Introduction

Periodontitis is a chronic multifactorial inflammatory disease associated with accumulation of a dysbiotic plaque biofilm and characterized by progressive destruction of periodontal tissue support which may result in tooth loss. Periodontal diagnosis has been recently revised in the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions (Caton et al., 2018; Chapple et al., 2018; Jepsen et al., 2018; Papapanou et al., 2018). Treatment of periodontitis is based on various interventions delivered at different steps of therapy (Sanz et al 2020). The main goal of the first and second step is the establishment of adequate infection control by reducing the bacterial load below the individual threshold level of inflammation/disease. Health behavior strategies to facilitate patient motivation to reach high-levels of self-performed supragingival plaque control and management of lifestyle habits such as smoking are key in addressing the vital patient role in the treatment of periodontitis (Ramseier & Suvan, 2015). Supplemental to patient self-care, professional supragingival and subgingival instrumentation serves the purpose of altering the subgingival ecological environment through disruption of the microbial biofilm and removal of hard deposits thereby suppressing soft tissue inflammation (Heitz-Mayfield & Lang, 2013; Jepsen et al 2011). A re-evaluation after the second step will assess the need for additional surgical treatment (third step of therapy) or the initiation of a supportive periodontal care (SPC) program (fourth step of periodontal therapy).

SPC is the group of procedures performed at selected intervals to assist the periodontal patient in maintaining oral health (Sanz et al 2020). This periodic assessment is established following the initial active periodontal therapy (APT) and it includes an update of the medical and dental histories, extra-oral and intra-oral soft tissue examination, dental examination, periodontal evaluation, radiographic review, removal of the bacterial flora deposits from crevicular and pocket areas, scaling and root planning where indicated, polishing of the teeth and a review of the patient's plaque control efficacy (Cohen AAP position paper 2003). These procedures aim to prevent the recurrence and progression of periodontal disease and to prevent or reduce the incidence of tooth loss. Untreated or inadequately treated periodontitis will lead to progressive loss of tooth-supporting tissues and finally loss of teeth. Severe periodontitis, along with dental caries, is responsible for more years lost to disability than any other human disease (GBD 2017 Disease and Injury Incidence and Prevalence Collaborators, 2018). Reports from several studies showed the effectiveness of active periodontal treatment and long-term SPC in maintaining periodontal health and in preventing tooth loss in patients with periodontitis. A recent systematic review reported a weighted mean yearly rate of tooth loss of 0.15 and 0.09 for follow-up of 5 years or 12–14 years, respectively, and a mean clinical attachment loss lower than 1 mm at follow-up ranging from 5 to 12 years (Trombelli et al, 2015). Few studies have reported the clinical outcomes of periodontal therapy and loss of teeth up to 22 years of follow-up (Hirschfeld & Wasserman 1978, McFall 1982, Goldman et al 1986) and only one study to 30 years (Axelsson et al 2004).

Aims of this retrospective study were i) to evaluate the efficacy of active periodontal therapy supplemented by regular supportive periodontal care in retaining the dentition for a 30-year follow-up period in patients susceptible to periodontitis; and ii) to assess the prognostic factors associated with tooth loss.

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Material and Methods

Study population and experimental design

This is a retrospective analysis from a periodontal case registry cohort established at the private practice of the authors in Bergamo, Italy. Establishment of the case cohort was performed in accordance with the Helsinki Declaration on experimentation involving human subjects. The present retrospective analysis was approved by the local ethical committee for clinical research of the ASST Ospedale Papa Giovanni XXIII of Bergamo (Italy) (protocol ATRO2020BG, registration n° 039/21).

Study population is represented by a convenience sample collected during the supportive periodontal care program in the years 2009 – 2011, consisting of 154 consecutive patients with mild/moderate/advanced periodontitis, treated with non-surgical and surgical periodontal therapy in a time frame between 1984 and 1986 and participating in a stringent supportive periodontal care program (SPC) for at least 25 years.

A total of 642 patients were referred to the private practice of the authors for periodontal treatment in the period between 1984 and 1986. Many of these patients returned to the referral general practitioner after active periodontal therapy. Some patients were lost to SPC during 25 years; reasons were either severe systemic conditions or death, moving elsewhere, and other unspecified reasons. The study population is thereby represented by the 154 patients out of 642 complying with the SPC through 25 years.

These patients at baseline were 18 years or older, in good general health, highly motivated to participate into a stringent SPC, non-smokers or smokers ≤10 cigarettes/day and without dental implants or removable dentures.

Radiographic and clinical data of this group of patients were available at baseline (T0), at re-evaluation after active periodontal therapy (T1) and after 25 (T2) years of SPC. A large portion of this group of patients (134) was available for an additional clinical analysis after 30 (T3) years of SPC.

Patient intake and active periodontal therapy

At intake, general health and dental anamnestic data were collected and the oral cavity examined for recognition of the main oral pathologies. Patients received at least two sessions of professional oral hygiene including supragingival instrumentation, subgingival scaling and root planning, and motivation for home care, including the use of toothbrushes and interdental cleaning devices. Special care was devoted to quality of home care, through a meticulous individual program of oral hygiene instruction and motivation. After 2-4 weeks patients were examined with a full periodontal chart and periapical radiographs (Baseline examination, T0). Patients with probing depth (PD) at all teeth ≤ 4 mm were enrolled in the SPC recall program without any additional periodontal treatment. Patients presenting with residual PD ≥ 5 mm received additional therapy according to the following criteria:

- Sites with PD of 5 mm were treated with additional sessions of non-surgical periodontal therapy.
- Sites showing PD >5 mm were treated with flap surgery (Modified Widman flap, Ramfjord & Nissel 1974, Serino et al. 2001)

Some teeth were judged irrational to treat and extracted during the active treatment for one or more of the following reasons:

- Periodontal problems such as bone loss involving the apical third or the apex, furcation lesions not amenable for either treatment or maintenance, severe endo-perio lesions not amenable for treatment;
- Dental problems such as very severe fractures or loss of hard tooth substance, endodontic problems or root resorption not amenable for treatment;
- Severe uncontrollable tooth hypermobility not compatible with patient function;
- Strategic reasons including orthodontic and reconstructive plans

Dental splint was performed on maxillary or mandibular anterior sextants when at least 2 teeth presented with mobility > 1 and with a radiographic bone loss involving more than half of the root length. Splint consisted of a 0.5 mm braided metal wire positioned on the lingual surface of anterior teeth sealed with composite material.

Orthodontic fixed treatment was performed during active periodontal therapy and during SPC to solve misalignment in presence of crowded maxillary or mandibular anterior teeth followed by dental splint as retention (Papageorgiou et al 2001). Aim of orthodontic treatment was to favor stabilization of teeth, improve function, aesthetics and home care.

All the reported treatments were performed by the same clinician (G.A.).

Supportive Periodontal Care

SPC started 3 months after completion of active periodontal treatment and was scheduled every 3 to 6 months based on individual needs. Patients with more severe periodontal conditions were recalled more frequently. Every SPC session, performed by the same clinician (G.A.), consisted of a stringent programme including periodontal re-assessment of plaque control, PD and bleeding on probing (BOP), re-motivation and refinement/modification of oral hygiene instructions, full mouth supragingival debridement and prophylaxis. Non-surgical treatment consisting of subgingival scaling and root planning were performed at sites presenting with disease recurrences (PD ≥ 5 mm, BOP positive); flap surgery was preferred in sites with deeper pockets to improve soft and/or hard tissue morphology to facilitate home care. Periodontal chart and full periodontal status of periapical radiographs were repeated after 25-30 years of the follow-up period. Splinting was controlled at every visit and repaired or re-done when necessary.

Data collection

All measurements and data collection were performed at baseline and during the SPC by the same operator (G.A.).

Demographic Measurements

Age, gender and smoking habit were recorded. Smoker was defined as a patient smoking at least 1 cigarette per day.

Periodontal Variables

- Full mouth plaque score (FMPS): presence/absence of plaque on 4 sites per tooth. FMPS was calculated as percentage of positive sites with respect to the total number of tested sites (O'Leary et al. 1972)
- Full mouth bleeding score (FMBS): presence/absence of bleeding on probing detected on 4 sites per tooth with a periodontal probe (PWD William offset double hand, Hu-Friedy). FMBS was calculated as percentage of positive sites with respect to the total number of tested sites (Ainamo & Bay, 1975)
- PD was measured in mm on 4 sites per tooth with a periodontal probe rounded up to the nearest mm
- Furcation involvement was classified as Degree I, II, III (Hamp et al 1975) and further categorized as *Furcation Worst* to indicate the worst furcation degree per tooth
- Dental mobility: classified as grade I, II, III (Muhlemann 1954)
- Number of recall visits: calculated as total number of visits during SPC
- Type of tooth: categorized as molar *vs.* non-molar tooth
- Tooth Splinting: presence/absence of splint
- Periodontal Surgery: presence/absence of flap surgery at tooth level

Dental Variables

- Tooth Extraction (tooth extracted during active therapy), reported as dichotomous variable (extracted *vs.* retained tooth)
- Tooth Loss (tooth extracted during SPC), reported as dichotomous variable (lost *vs.* retained tooth)
- Restoration: presence/absence of a restoration at tooth level
- Root Canal Treatment: presence/absence of a root canal treatment at tooth level
- Crown: presence/absence of a crown at tooth level

Radiographic Variables

A retrospective evaluation of the radiographs was done by one experienced and calibrated operator (D.B.) and the following measurements were obtained at both the mesial and distal aspect of each tooth:

- CEJ-A: distance in mm between the cemento-enamel junction (CEJ) and the tooth apex (A)
- CEJ-C: distance in mm between the CEJ and the most coronal portion of the crestal bone (C)
- CEJ-D: distance in mm between the CEJ and the most apical portion of an intrabony defect (D)
- Worst Percentage of Bone Loss (%): worst measurement between mesial and distal site estimated as ratio between CEJ-D/CEJ-A
- Worst level of Bone Loss (categorized): worst bone level between mesial and distal site referred to the coronal, mid and apical third of the root length

The radiographs were measured with an electronic ruler at a 10x magnification (Sorriso, Ver. 13, Dental Trey, Italy) on a high-definition monitor at a resolution of 1600 X 1200 pixels. A calibration exercise was performed by the examiner of the radiographs (D.B.) on a set of 10 radiographs taken from patients with conditions and treatments similar to the ones of this case cohort. The clinical examiner carried out duplicate measurements (1 week apart) for

the variables: CEJ-A, CEJ-C and CEJ-D at mesial and distal aspects. The correlation coefficient for intra-examiner agreement for CEJ-A, CEJ-C and CEJ-D was 0.99 (P<0.001). The paired t-test showed no statistically significant difference between the 2 sets of measurements for CEJ-A (P = 0.168), CEJ-C (P = 1.000) and CEJ-D (P = 0.168).

Classification of periodontitis

The patient population was re-classified according to the 2018 classification of periodontitis as Stage I, II, III, and IV (Papapanou et al 2018). The parameters used were the following: interproximal radiographic bone loss at worst site (either mesial or distal) was considered at tooth level (Stage I < 15%; Stage II 15% to 33%; Stage III/IV > 33%); then pocket depth ≥ 6mm, presence of degree II or III furcation involvement, presence of ≥ 3mm deep intrabony defect were evaluated to adjust the diagnosis (i.e need of Stage shift due to complexity); the worst parameter/site per patient was then used to determine the Stage.

The Grade of periodontitis was also expressed as Grade A, B, and C based on the ratio between percentage (%) of radiographic bone loss and patient age (Grade A < 0.25; Grade B 0.25 to 1.0; Grade C > 1.0).

The disease extension was determined on the number of teeth showing clinical attachment loss over the total number of teeth (Generalized > 30%; Localized < 30%). No patients with molar/incisor pattern were part of this study.

Statistical Analysis

Descriptive statistics were expressed as mean and standard deviation for the quantitative variables and frequency and percentage for qualitative ones. Description of variables and unit of measurements are reported above.

Inferential statistics were conducted using generalized mixed models at 2 levels (patient and tooth); the dependent variable was the tooth loss and the explanatory variables were demographic, periodontal, dental and radiographic variables. The tooth was clustered within patient. Models were created for different time-points: T0-T3; T1-T3. Data measured at site level were averaged at tooth level. A survival analysis was also conducted using life distribution models of time-to-event data for tooth loss in SPC (T1-T3) incorporating multiple causes of failure.

The level of significance was $\alpha = 0.05$. The statistical analyses were carried out using JAMOVI Statistics Version 1.2.27.0.

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Results

DESCRIPTIVE STATISTIC

Baseline (T0) and active phase of periodontal therapy

Study population consisted of 154 patients (4083 teeth) with a diagnosis of periodontitis at baseline (T0), mean age 35.8 years (± 9.5; [21;67]), 36.4% male, and 7.9 % smokers.
Forty (25.9%) patients were re-classified with stage I/II periodontitis, 110 (72.4%) stage III and 4 (2.6%) stage IV; 132 (85.7%) patients presented with generalized and 22 (14.3%) with localized periodontitis; Grade A periodontitis was not assigned to any of the patients, while Grade B was assigned to 77 (50.0%), and Grade C to 77 (50.0%).
Baseline characteristics of the 4083 teeth are reported in Table 1. The baseline periodontal variables are reported in Table 2.
Out of the total population of 4083 teeth, 3241 (79.4%) received non-surgical treatment without any additional corrective surgery; 842 teeth (20.6%) received flap surgery; 16 teeth (0.3%) presenting with insufficient keratinized or attached gingiva were treated with a free gingival graft. A total of 625 (15.3%) teeth required splinting. 74 patients received orthodontic treatment.
During the active therapy, 160 teeth (3.9%) in 83 patients (53.9%) considered irrational to treat were extracted (Table 1).

Re-evaluation at the end of active phase of periodontal therapy (T1)

A total of 3923 (96.1%) teeth out of 4083 in 154 patients completed the active phase of periodontal therapy. Mean percentages of FMBS and FMPS were 3.8 ± 6.3 [range 0; 41] and 11.1 ± 2.7 [range 5; 17], respectively.
The mean PD was 2.6 ± 0.6 mm [0.5; 9]. The vast majority of teeth (3874, 98.8%) had no furcation involvement and 3763 teeth (95.9%) had no clinical signs of tooth mobility, (564 were splinted). Detailed periodontal parameters are reported in Table 2.
After re-evaluation, 13 teeth in 5 patients were extracted: 11 in 4 patients for periodontal reasons (poor response to active step of therapy) and 2 in 1 patient for orthodontic reasons. Therefore, 3910 teeth (95.8% of the baseline number of teeth) in 154 patients entered the supportive periodontal care program.

Supportive Periodontal Care (SPC) – 25 years follow-up (T2)

Patients and teeth survival

At T2 re-evaluation, 3770 teeth out of 3910 (96.4%) in 154 patients were maintained. One-hundred and forty (140) teeth (3.6%, Tab 1) were lost in 70 patients, of which only 24 in 18 patients for periodontal reasons (1 premolar and 23 molars). The reasons for tooth loss are listed in Table 3. During the routine anamnestic examination, none of the patients reported a systemic condition, diabetes in particular, that could have an impact on periodontitis.

Periodontal parameters

Mean FMBS and FMPS percentages were 2.4 ± 4.5 [range 0; 32.3] and 12.4 ± 2.3 [range 8; 18], respectively.

The mean PD was of 2.5 ± 0.4 mm [range 2; 6.5]. A total of 3729 teeth (98.8%) had no furcation involvement, and 3719 teeth (98.5%) had no detectable tooth mobility.
Periodontal variables are reported in Table 2.

Supportive Periodontal Care (SPC) – 30 years follow-up (T3)

Patients and teeth survival

At T3, a population of 134 patients (3227 teeth) was available for re-evaluation. Between 25 and 30 years of SPC, 20 patients (482 teeth) dropped out; reasons were death (4), moving elsewhere (8), and other unspecified reasons (8). None of the patients reported a systemic condition, diabetes in particular, that could have an impact on periodontitis.
Between T2 and T3, 61 teeth (2%, Table 1) were lost of which only 15 in 14 patients for periodontal reasons: 1 incisor, 1 premolar and 13 molars. The reasons for tooth loss are listed in Table 3.
Between T1 and T3, 3227 teeth out of the T1 3910 (154 patients) were maintained: 482 (12.3%) were not available for examination belonging to the 20 drop-out patients, 201 teeth (5.1%) in 86 patients were lost, of which only 39 (1.0%) in 35 patients for periodontal reasons. Overall, 48 patients maintained all the teeth through the entire 30-year SPC (Table 1).

Periodontal parameters

Mean FMBS percentage was 4.7 ± 2.7 [range 0; 14]. The mean PD was of 2.4 ± 0.4 mm [range 1.5; 5.8]. A total of 3139 teeth (98%) had no furcation involvement and 3195 teeth (98.8%) had no clinical signs of tooth mobility. Radiographic bone loss and detailed periodontal parameters are reported in Table 2. Forty-three teeth (1.3%) had an intrabony defect either mesial or distal with a mean depth of 3.0 ± 1.4 mm.
Overall, the mean number of SPC recall visits was 82.7 ± 81.5 in 30 years.
Additional periodontal surgery was required to treat recurrences on 271 teeth (6.9%) in 58 patients (37.7%) during the 30-year SPC.
A restoration was detected in 1511 teeth (46.8%), a root canal treatment in 459 (14.2%) and a fixed prosthesis in 415 teeth (12.9%).

Replacement of extracted teeth

Some of the teeth extracted during all the follow up period were not replaced, while 6 patients received a tooth supported bridge, 3 patients a removable denture and 2 patients a Maryland bridge. None of the extracted teeth was replaced with an implant.

INFERENTIAL STATISTIC – Prognostic Factors for Tooth Loss

Tooth Loss from baseline (T0) up to 30 years of follow-up (T3)

When considering as dependent variable the total number of teeth extracted during the active phase of therapy (T0-T1) plus those lost during the 30 years of SPC, the generalized mixed effect model results showed that age (OR = 1.03; P = 0.011), tooth type = molar (OR = 9.53; P = < .001), baseline (T0) PD between 4-6 mm (OR = 2.76 compared to no pocket > 4; P = < .001), PD >6 mm (OR = 8.91 compared to no pocket > 4; P = < .001), baseline (T0) tooth mobility grade 1 (OR = 1.78; P = 0.077), tooth mobility grade 2 (OR = 2.32

compared to no mobility; P = 0.027), and tooth mobility grade 3 (OR = 34.67 compared to no mobility; P = < .001), bone loss to the mid third of the root at worst site (OR = 2.03 compared to bone loss not extending beyond the coronal third; P = 0.004), bone loss to the apical third of the root at worst site (OR = 6.26 compared to bone loss not extending beyond the coronal third; P = < .001), presence of a restoration, (OR = 0.63; P = 0.012), a root canal treatment (OR = 2.97; P = < .001) and a crown (OR = 1.83; P = 0.009) were statistically significantly associated with tooth loss after 30 years of follow-up (T3) (Table 4). Post-hoc pair-wise comparisons results for baseline PD, tooth mobility and bone loss are shown separately in supplementary material (Table S1, S2, S3).

A separate model was created to include the retrospective diagnosis performed according to the new classification of Periodontal Diseases (Papapanou et al. 2017) and evaluate the prognostic value of Stage, Grade and Extension on tooth loss. A periodontitis severity of Stage III or IV compared to Stage I or II was independently and statistically significantly associated with greater tooth loss (OR = 2.10 P = 0.048). A rate of periodontitis progression of Grade C compared to B was not found to be statistically significantly associated with tooth loss (P = 0.183). The generalized periodontitis showed a statistically significant OR = 3.24 (P = 0.016) compared to the localized one. (Table 5).

Tooth Loss from the end of active step of therapy (T1) to 30-years follow-up (T3)
When considering as dependent variable only the number of the teeth that were lost during the 30 years of SPC, the generalized mixed effect model results showed that age (OR = 1.04; P = 0.011), gender = male (OR = 1.77; P = 0.038), tooth type = molar (OR = 5.24; P = < .001), T1 PD between 4-6 mm (OR = 2.12 compared to no pocket > 4; P = < .001) PD >6 mm (OR = 9.73 compared to no pocket > 4; P = < .001), tooth mobility grade 2 (OR = 5.83 compared to no mobility; P = 0.018) and of grade 3 (OR = 6.03 compared to no mobility; P = 0.050), bone loss to the mid third of the root at worst site (OR = 2.68 compared to bone loss not extending beyond the coronal third; P = < .001), bone loss to the apical third of the root at worst site (OR = 16.84 compared to bone loss not extending beyond the coronal third; P = < .001), presence of a root canal treatment (OR = 2.67; P = < .001) and a crown (OR = 1.94=; P = 0.009) were statistically significantly associated with tooth loss after 30 years of follow-up (T3) (Table 6). Post-hoc pair-wise comparisons results for PD (T1), tooth mobility (T1) and bone loss are shown separately in supplementary material (Table S4, S5, S6).

Another generalized mixed model was created where only molar teeth were included to assess the impact of furcation involvement and bone loss over tooth loss in SPT, separately from the other covariates and factors included in the previous model. Molars with degree II furcation involvement were statistically significantly associated with higher tooth loss (OR = 8.78; P = 0.004) as well as those showing bone loss at mid (OR = 2.69; P = 0.015) and apical third (OR = 12.34; P < .001) compared to those where bone loss was limited to the coronal third. The fixed effects table and effects plot are reported in supplementary material (Table S7 and Figure S1).

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The life distribution model of time-to-event data for tooth loss in SPC (T1-T3) incorporating multiple causes of failure is reported in Figure 1.

Discussion

This is a unique 30-years long-term analysis of a group of patients affected by periodontal disease, treated with non-surgical and surgical periodontal therapy in a time frame between 1984 and 1986 and monitored within a supportive periodontal care program (SPC) until 2016. Only another study of comparative longevity (Axelsson et al 2004) focused on the efficacy of a plaque control program on tooth mortality, caries and periodontal disease including in the experimental population patients presenting with oral health, gingivitis and periodontitis.

Tooth loss

Tooth loss can be considered as the final outcome of disease progression or the result of the occurrence of adverse events, unless case specific considerations and prognostic or strategic evaluations may lead dentists to extract teeth following a discussion with the patient. In the present study, 154 patients were on regular care after 25 years. In this period 140 teeth were lost (97 molars) in 70 patients, only 24 for periodontal reasons (23 molars). The loss of teeth represented 3.6% of the total number entered in the SPC program, definitely much lower than the percentage reported by Eickholz (6.7%, Eickholz et al 2008) and by Matuliene (7.2%, Matuliene et al 2010) in studies with a duration up to 10 years. The cited studies showed that irregular compliance with SPC is correlated with higher incidence of tooth loss (Eickholz et al 2008, Matuliene et al 2010). The importance and effectiveness of SPC has been recently evaluated in a systematic review (Trombelli et al 2015). These authors concluded that appropriate SPC may limit the incidence of tooth loss in patients treated for periodontitis. A recent systematic review reported that patients with lower compliance showed significantly increased odds of tooth loss (Helal et al JCP 2019). Patient compliance with SPC in the present study was excellent with a mean 82.7 ± 31.5 SPC recall visits over the 30 years follow-up period (2.8 ± 1 per year on average), that might explain at least in part the high percentage of teeth maintained over such a long period of time. The issue of time is not irrelevant, because the progression of periodontal destruction and the consequent potential loss of teeth is a function of time (Matuliene et al 2008) and very few studies overcome the 10-year follow-up period, making the outcomes of the present study even more relevant.

Between 25 and 30-year examination, 20 patients dropped and 61 teeth were lost, only 15 for periodontal reasons (13 molars).

Overall, 201 teeth were extracted during the SPC program with a mean yearly tooth loss/patient of 0.04 This favorably compares with a recent systematic review (Helal et al JCP 2019) reporting a mean yearly tooth loss/patient of 0.12 (min 0.01 – max 0.36) out of a group of studies with a mean follow-up period of 12 years. In the present study the 201 teeth were lost in 86 patients, while the remaining 48 maintained all the dentition for 30 years. These data do not confirm the evidence of a cluster of patients responsible for the majority of tooth extraction during SPC (Chambrone et al 2010). In fact, in the present study, the number of lost teeth was distributed within two thirds of the population. A possible explanation might be the selection of a population with very low levels of systemic and behavioral risk factors, such as diabetes and smoking, and the treatment approach aiming at a careful elimination/control of local risk factors during the active phase of therapy and SPC. Table 3 shows the number and the reason for tooth loss during SPC. Main reason was the clinical decision to extract teeth for orthodontic/prosthodontic/aesthetic needs occurring mostly during the first 25 years of follow up (46 out of 55 total extractions). In other words, these teeth were extracted in accordance with the patient for strategic reasons and as part of an overall treatment plan, not as a consequence of a pathology/adverse event. When we exclude the teeth extracted for strategic reasons, the total number of teeth lost for a negative

event drops to 146 with a mean yearly tooth loss per patient of 0.03, while a mean yearly tooth loss per patient of 0.01 can be calculated considering only the 39 teeth lost for periodontal breakdown. Figure 1 shows the life distribution model of time-to-event data for tooth loss in SPC highlighting a correlation between probability and time.

The successful outcomes in terms of very limited incidence of tooth loss, in particular for periodontal reasons, during the SPC reported in this study is explained not only by the quality of the SPC, but also by the very high standard of plaque control and the very low levels of residual bleeding at all the re-evaluation points, and by the clinical strategy undertaken during the active phase of therapy aimed at reducing/eliminating factors that could have negatively affected long-term tooth retention. Teeth with very deep pockets and very severe bone loss to the apical third of the root, especially when associated to furcation involvement and not amenable to the treatment modalities available at the time of study initiation, were extracted during active treatment. This clinical decision taken 30 years ago has been recently confirmed in 2 studies showing a stringent correlation between severity of vertical bone destruction of furcated molars and their prognosis (Tonetti et al 2017, Nibali et al 2018). As a result, 160 teeth deemed as irrational to treat were extracted during the active phase of therapy of which - not by chance - 132 were molars. It is well known that teeth with the characteristics mentioned above have very high chances of disease recurrences during SPC and the highest probability to be lost (Chambrone et al 2010, Helal et al JCP 2019). The clinical challenge is to take decisions on either to perform a treatment able to modify the prognosis of such teeth, or to extract or to enroll them into the SPC phase accepting very high odds of tooth loss over time. Modern periodontal therapy is enriched with treatment approaches, regenerative in particular, that may help clinicians to preserve more teeth during active phase as highlighted by the Guidelines of the European Federation of Periodontology (Sanz et al 2020). Regenerative surgery reportedly may improve the long-term prognosis of teeth with furcation involvement (Huynh-Ba et al 2009, Dannewitz et al 2016, Nibali et al 2020), of teeth with furcation involvement associated with deep intrabony defects (Cortellini et al 2020), of teeth with deep intrabony defects (Nibali et al 2020, Cortellini et al 2017, 2022), and even of teeth with a baseline “hopeless” prognosis (Cortellini et al 2011, 2020).

Replacement of the teeth extracted during active therapy and SPC was done according to the functional or aesthetic requirements of the patients. Some of the teeth were not replaced, especially molars, when function with a reduced number of teeth was considered acceptable by the patients. Six patients received a tooth supported bridge, 2 patients a Maryland bridge, and 3 patients a removable denture. None of the extracted teeth was replaced with an implant, even when implants were suggested as preferred option (5 patients).

Prognostic factors associated with tooth loss

The second aim of this study was to assess the prognostic factors associated with tooth loss. A series of demographic, periodontal, dental and radiographic variables were included into generalized mixed effect models for tooth loss from baseline to 30 years (Table 4) and from the beginning of SPC up to 30 years of follow-up (Table 6). Among patient-level variables, age resulted to be significantly associated to tooth loss, while smoking did not. This is apparently in contrast with other studies showing a negative impact of smoking on tooth retention over time (Chambrone et al 2010, Helal et al JCP 2019). However, it should be noted that the number of smokers in the present study was very low (7.9%) mostly being “light smokers”. In other words, this population represented by a vast majority of non-

smokers does not allow any conclusion about the impact of smoking on tooth retention over time.

Among the tooth-level periodontal variables, the severity of bone destruction at baseline, together with presence of tooth mobility, and the persistence of ecological niches favoring the formation of a subgingival biofilm like deep pockets and furcations was statistically significantly associated to tooth loss, in agreement with outcomes from previous analyses (Chambrone et al 2010, Helal et al JCP 2019). Baseline radiographic bone levels (Table 2) indicate that a minority of teeth had severe (5%) or very severe (2%) bone destruction. After 30 years of follow-up, the distribution of bone loss severity remained substantially stable. Conversely, the number of deep pockets were dramatically reduced with active treatment and remained stable during the SPC period. These data along with the low number of teeth lost over time for periodontal reasons support the success of the treatment strategy reported in this study.
It is worth mentioning that most of the teeth lost for periodontal reasons were molars. A separate analysis on molars showed that the presence of a degree II furcation and bone loss at the mid or apical third of the roots were associated with higher tooth loss (Table S7 and Fig S1). These data support the conclusions of two recent studies showing the combined negative effect of severe vertical destruction of bone and furcation involvement on tooth survival (Tonetti et al 2017, Nibali et al 2018). In the present study the odds of losing a tooth were greater in teeth with degree II than with degree III furcation involvement. This "unexpected" outcome can be explained by the fact that only 4 teeth with degree III furcations were enrolled into the SPC. Molars with furcation involvement are a problem that should be carefully considered during active therapy and monitored during SPC for the high chances of disease progression. Table 2 clearly shows a trend for a tiny but constant deterioration of the furcation condition over time with an increasing number of teeth showing a furcation involvement. Considering that some teeth with furcation involvement were extracted during SPC, it is apparent that some molars developed/progressed a furcation involvement in the same period of time.

Among the dental variables, the presence of a root canal treatment, of a restoration or a crown was associated with greater probability to lose teeth. Teeth that underwent such restorative treatments are not infrequently associated to biological and mechanical complications including fractures, endodontic complications or technical failures (Tonetti et al. 2000, Axelsson et al. 2004 Carnevale et al. 2007b; Pretzl et al. 2016), with a tendency to increase over time as demonstrated in Figure 1.

The present patient population was also challenged with the new classification of periodontitis (Papapanou et al 2018) and re-classified in terms of Stage, Grade, and disease extension. Interestingly, the model reported in Table 5 shows a statistically significant correlation between tooth loss and periodontitis severity. Patients with periodontitis Stage III or IV have greater probability to lose teeth than patients with Stage I or II (OR = 2.10 P = 0.048). In addition, the generalized periodontitis showed a statistically significant OR of 3.24 (P = 0.016) compared to the localized one. Unexpectedly, grading was not found to be a statistically significant variable. A possible explanation might be the limited number of grade C periodontitis patients along with the baseline exclusion of heavy smokers and patients with diabetes. It should be noted that the predictive value of future tooth loss of reported odds ratios should be considered carefully, particularly for estimates below 3, in view of the risks of false positives which may negatively impact the clinical validity of results. Within the limitations of a retrospective diagnosis based on the new classification, these data provide a unique long-term evaluation of the prognostic value of the new staging and grading system

on tooth loss. This information enforces the need to allocate patients into subgroups according to the type of periodontitis to allow more accurate evaluations and comparisons among studies. In addition, it indicates the absolute need for early diagnosis that will render treatment and maintenance much easier and successful over time.

Conclusion

In conclusion this study on patients susceptible to periodontitis demonstrates that the vast majority of teeth can be maintained over a period up to 30 years. Both the strategy of active therapy and the effective enforcement of a supportive periodontal care program are key to success. Clinicians should be aware of the need to consider relevant variables that can inform long-term tooth retention; in particular age at patient level, severe bone destruction, deep pockets and furcation involvement at periodontal level, and presence of endodontic treatment and restorations at tooth level. Both in the active phase of therapy and during SPC, clinicians should focus on the control/elimination of these conditions in order to improve the tooth prognosis and long-term retention.

The excellent clinical outcomes and their long-term stability should be considered in the light of the patient population selection, including highly motivated, mostly non-smoking and systemically healthy subjects, treated by an expert clinician in a private clinical setting providing high standards of periodontal care. Therefore, external validity of the reported results and their applicability to a wider population of clinicians and patients should be taken with caution.

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Table 1 – Baseline characteristics of included teeth and number of teeth extracted and lost during the full period of active treatment and SPC. The teeth of patients that dropped out of the study are reported as “drop-outs T2-T3

	Baseline		**Extracted Teeth T0**	**Lost Teeth T1-T2**	**Lost Teeth T2-T3**	**Drop-outs T2-T3**	**Lost Teeth T1-T3**
	N	%	N	N	N	N	
Total number of teeth	4083	-	160/4083	140/3910	61/3428	482/3910	201/3910
Molars	1162	28.5%	132	97	34	117	131
Premolars	1115	27.3%	20	33	17	133	50
Canines	608	14.9%	-	-	1	80	1
Incisors	1198	29.3%	8	10	9	152	19
Maxillary Teeth	2041	49.9%	94	76	31	244	107
Restorations	1629	39.9%	74	107	39	177	146
Root Canal Treatments	428	10.4%	27	43	16	44	59
Crowns	409	10%	19	47	16	28	63

Table 2 - Periodontal variables at different time-points.

	Time Point							
Variable								
	T0		T1		T2		T3	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Bone Loss (% at worst site per tooth)	19.12	10.84	N/A	N/A	N/A	N/A	20.58	10.22
Pocket Depth (mm)	3.08	0.94	2.58	0.61	2.52	0.44	2.42	0.36
FMBS (%)	14.60	14.25	3.82	6.27	2.36	4.54	4.70	2.69
	N (Teeth)	%	N (Teeth)	%	N (Teeth)	%	N (Teeth)	%
Bone Loss at coronal third (at worst site per tooth)	3795	92.9%	N/A	N/A	N/A	N/A	2947	91.3%
Bone Loss at mid third (at worst site per tooth)	219	5.4%	N/A	N/A	N/A	N/A	225	6.9%
Bone Loss at apical third (at worst site per tooth)	69	1.7%	N/A	N/A	N/A	N/A	55	1.7%
No Furcation Involvement	3993	97.8%	3874	99.1%	3729	98.9%	3139	97.3%
Furcation Involvement I (at worst site)	43	1.1%	30	0.8%	25	0.7%	32	0.9%
Furcation Involvement II (at worst site)	26	0.6%	15	0.4%	11	0.3%	21	0.7%
Furcation Involvement III (at worst site)	21	0.5%	4	0.1%	9	0.2%	11	0.3%
No Tooth Mobility	3799	93.0%	3763	96.2%	3719	98.6%	3195	99.0%
Tooth Mobility I	158	3.9%	125	3.2%	23	0.6%	4	0.1%
Tooth Mobility II	91	2.2%	24	0.6%	30	0.8%	3	0.1%
Tooth Mobility III	35	0.8%	11	0.3%	2	0.1%	1	0.0%
Pocket Depth < 4mm	1972	48.3%	3010	76.9%	3206	85.0%	2810	87.1%
Pocket Depth = 4-6 mm	1753	42.9%	847	21.7%	530	14.1%	381	11.8%
Pocket Depth > 6 mm	358	8.8%	66	1.7%	38	1.0%	10	0.3%

Table 3 – Number of teeth lost during SPC.

		Periodontal reasons	Endodontic reasons	Dental trauma	Tooth fracture	Root resorption	Dental caries	Orthodontic/Prosthodontic/Aesthetic reasons	Increased mobility
T1-T2	Total	24	13	5	33	6	12	46	1
	Molars	23	11	1	24	4	8	25	1
	Premolars	1	2	0	9	2	4	16	0
	Canines	0	0	0	0	0	0	0	0
	Incisors	0	0	4	0	0	0	5	0
aT2-T3	Total	15	7	2	20	5	3	9	0
	Molars	13	4	0	11	1	3	2	0
	Premolars	1	2	0	7	0	0	7	0
	Canines	0	0	0	1	0	0	0	0
	Incisors	1	1	2	1	4	0	0	0
T1-T3	Total	39	20	7	53	11	15	55	1
	Molars	36	15	1	35	5	11	27	1
	Premolars	2	4	0	16	2	4	23	0
	Canines	0	0	0	1	0	0	0	0
	Incisors	1	1	6	1	4	0	5	0

Table 4. Generalized mixed effect model for Tooth Loss T0-T3

Names	Effect		Estimate	SE	OR	95% OR Confidence Interval		z	p
						Lower	Upper		
(Intercept)		(Intercept)	-0.90	0.35	0.41	0.21	0.81	-2.57	0.010
T0 - Bone Loss - Worst (1=Apical; 2=Mid; 3=Coronal)		2 - 3	0.71	0.25	2.03	1.25	3.29	2.88	0.004
T0 - Bone Loss - Worst (1=Apical; 2=Mid; 3=Coronal)		1 - 3	1.83	0.40	6.26	2.88	13.62	4.63	< .001
T0 - PD Range (0=<4; 1=4-6; 2=>6)		1 - 0	1.02	0.22	2.76	1.78	4.29	4.51	< .001
T0 - PD Range (0=<4; 1=4-6; 2=>6)		2 - 0	2.19	0.29	8.91	5.03	15.78	7.50	< .001
T0 – Mobility		1 - 0	0.57	0.32	1.78	0.94	3.36	1.77	0.077
T0 – Mobility		2 - 0	0.84	0.38	2.32	1.10	4.88	2.22	0.027
T0 – Mobility		3 - 0	3.55	0.67	34.67	9.29	129.46	5.28	< .001
T0 - Furcation Worst		1 - 0	-0.03	0.42	0.97	0.42	2.24	-0.06	0.951
T0 - Furcation Worst		2 - 0	1.06	0.60	2.88	0.89	9.28	1.77	0.076
T0 - Furcation Worst		3 - 0	-0.75	0.64	0.47	0.13	1.66	-1.17	0.242
Age		Age	0.03	0.01	1.03	1.01	1.06	2.55	0.011
Gender (1=Male)		Gender (1=Male)	0.38	0.24	1.46	0.91	2.34	1.56	0.118
T0 - Tooth Type (1=Molar)		T0 - Tooth Type (1=Molar)	2.25	0.18	9.53	6.65	13.66	12.27	< .001
T0 - Restoration		T0 - Restoration	-0.47	0.19	0.63	0.43	0.90	-2.52	0.012
T0 - Crown		T0 - Crown	0.61	0.23	1.83	1.16	2.89	2.61	0.009
T0 - Root Canal Treatment		T0 - Root Canal Treatment	1.09	0.22	2.97	1.92	4.60	4.89	< .001
T0 - FMBS (%)		T0 - FMBS (%)	-0.00	0.01	1.00	0.98	1.02	-0.19	0.848

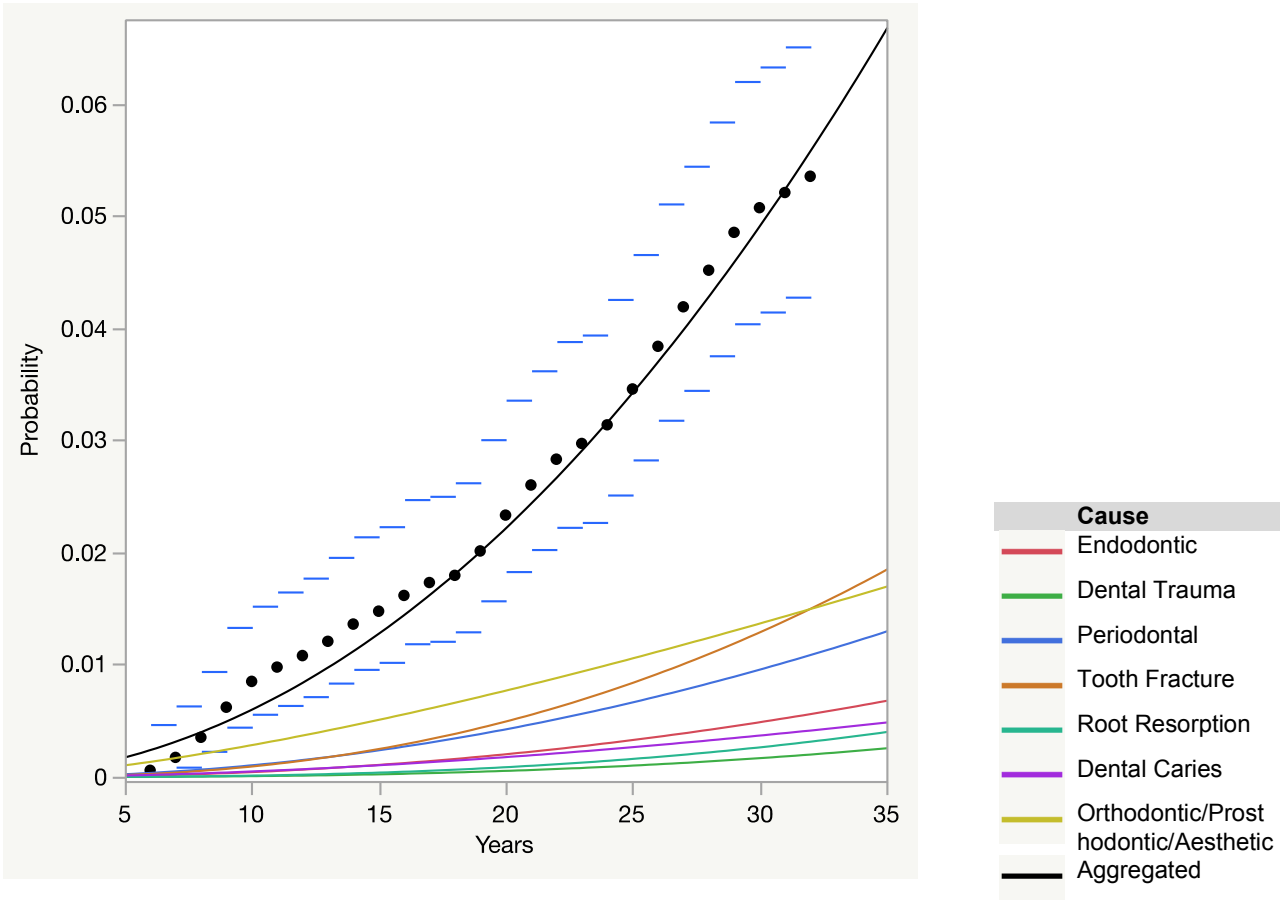
Table 5. Generalized mixed effect model for Tooth Loss T0-T3 based on the 2018 classification of periodontal diseases (Papapanou et al. 2018).

Names	Effect	Estimate	SE	OR	95% OR Confidence Interval		z	p
					Lower	Upper		
(Intercept)	(Intercept)	-3.07	0.21	0.05	0.03	0.07	-14.68	< .001
T0 - Stage (2=I or II; 3=III or IV)	3 - 2	0.74	0.37	2.10	1.01	4.36	1.98	0.048
T0 - GRADE (1=A; 2=B; 3=C)	3 - 2	0.33	0.24	1.39	0.86	2.24	1.33	0.183
T0 - Extent (1=Gen; 2 = Loc)	1 - 2	1.18	0.49	3.24	1.24	8.46	2.40	0.016

Table 6. Generalized mixed effect model for Tooth Loss T1-T3.

Names	Effect	Estimate	SE	OR	95% OR Confidence Interval		z	p
					Lower	Upper		
(Intercept)	(Intercept)	-1.20	0.55	0.30	0.10	0.89	-2.17	0.030
T0 - Bone Loss - Worst (1=Apical; 2=Mid; 3=Coronal)1	2 - 3	0.98	0.30	2.68	1.49	4.80	3.29	< .001
T0 - Bone Loss - Worst (1=Apical; 2=Mid; 3=Coronal)2	1 - 3	2.82	0.47	16.84	6.70	42.36	6.00	< .001
T1 - PD Range (0=<4; 1=4-6; 2=>6)1	1 - 0	0.75	0.21	2.12	1.41	3.18	3.62	< .001
T1 - PD Range (0=<4; 1=4-6; 2=>6)2	2 - 0	2.28	0.41	9.73	4.34	21.84	5.52	< .001
T1 - Mobility1	1 - 0	0.50	0.42	1.65	0.73	3.76	1.20	0.231
T1 - Mobility2	2 - 0	1.76	0.75	5.83	1.34	25.29	2.36	0.018
T1 - Mobility3	3 - 0	1.80	0.92	6.03	1.00	36.50	1.96	0.050
T1 - Furcation Worst1	1 - 0	-0.30	0.68	0.74	0.20	2.79	-0.44	0.658
T1 - Furcation Worst2	2 - 0	0.51	0.73	1.67	0.40	6.99	0.70	0.486
T1 - Furcation Worst3	3 - 0	-0.85	1.40	0.43	0.03	6.64	-0.61	0.545
Age	Age	0.04	0.02	1.04	1.01	1.07	2.55	0.011
Gender (1=Male)	Gender (1=Male)	0.57	0.27	1.77	1.03	3.02	2.07	0.038
T0 - Restoration	T0 - Restoration	0.46	0.25	1.58	0.98	2.55	1.86	0.063
T0 - Root Canal Treatment	T0 - Root Canal Treatment	0.98	0.25	2.67	1.63	4.38	3.90	< .001
T0 - Crown	T0 - Crown	0.66	0.26	1.94	1.18	3.21	2.60	0.009
T0 - Tooth Type (1=Molar)	T0 - Tooth Type (1=Molar)	1.66	0.22	5.24	3.43	8.01	7.64	< .001
1 - FMBS (%)	T1 - FMBS (%)	0.02	0.02	1.03	0.98	1.07	1.17	0.242

Figure 1. Life distribution model of time-to-event data for tooth loss in SPC (T1-T3).



Tooth mobility was not estimated as less than 2 events in the data.