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Effect of Supportive Periodontal Therapy on Tooth Loss in Regular and Irregular Compliant Smokers and Non-Smokers: A Retrospective Cohort Study with a Follow-up Up to 50 Years

Cover Page Footnote

Jean-Marie Megarbane and Roudy Khayat contributed equally to the making of this article. Special thanks to Dr Lara Nasr for the statistical work done for this article.

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ORIGINAL ARTICLE / *ARTICLE ORIGINAL*

Periodontology / *Parodontologie*

EFFECT OF SUPPORTIVE PERIODONTAL THERAPY ON TOOTH LOSS IN REGULAR AND IRREGULAR COMPLIANT SMOKERS AND NON-SMOKERS: A RETROSPECTIVE COHORT STUDY WITH A FOLLOW-UP UP TO 50 YEARS

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Introduction: The aim of this study is to compare retrospectively tooth loss (TL) rates in two cohorts, regular vs irregular compliant individuals, and smokers vs non-smokers, with a follow-up up to 50 years.

Methods: Chart data were collected from 192 patients undergoing supportive periodontal therapy (SPT) after non-surgical and/or surgical periodontal treatment for 10 - 50 (mean 24.89 ± 10.23) years. Patients were categorized as RC (attending regularly to their scheduled SPT with maximum delay of 6 months), and IC (patients missed at least one of the recall visits but continued to come on an irregular basis with a maximum delay of 18 months). Patients were then classified as smokers and non-smokers. Univariate comparisons between cohort groups were performed to assess significant differences at the level of baseline characteristics. Bivariate analyses were also performed between the main outcome variable (tooth loss) and baseline characteristics of the participants. Two negative binomial regression models were carried out in order to control confounding factors.

Results: A total of 4870 (25.36 ± 4.08) teeth were present at baseline. 423 (2.2 ± 3.44) teeth were lost during follow-up (SPT), corresponding to 0.07, 0.11, 0.08, and 0.09 TL annually among RC, IC, smokers, and non-smokers, respectively, with significant difference present only between RC and IC. Age > 40 years was found to increase TL rates.

Conclusions: Compliance with SPT affects TL rates after a mean of 24.89 years of follow-up. RC showed less TL than IC patients. Smoking did not reach statistical significance.

Keywords: Compliance, smoking, supportive periodontal therapy, tooth loss

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Conflicts of interest:
The authors declare no conflicts of interest.

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EFFET DE LA THÉRAPIE PARODONTALE DE SOUTIEN SUR LA PERTE DE DENTS CHEZ LES FUMEURS RÉGULIERS ET IRRÉGULIERS AINSI QUE CHEZ LES NON-FUMEURS: UNE ÉTUDE DE COHORTE RÉTROSPECTIVE AVEC UN SUIVI JUSQU'À 50 ANS

Introduction: Le but de cette étude est de comparer rétrospectivement les taux de perte de dents (TL) dans deux cohortes, individus conformes réguliers ou irréguliers, et fumeurs vs non-fumeurs, avec un suivi jusqu'à 50 ans.

Méthodes: Les données des dossiers ont été collectées auprès de 192 patients subissant un traitement parodontal de soutien (SPT) après un traitement parodontal non chirurgical et/ou chirurgical pendant 10 à 50 ans (moyenne 24,89 ± 10,23). Les patients ont été classés en RC (se présentant régulièrement à leur SPT programmé avec un délai maximum de 6 mois) et IC (les patients ont manqué au moins une des visites de rappel mais ont continué à venir de manière irrégulière avec un délai maximum de 18 mois). Les patients ont ensuite été classés en fumeurs et non-fumeurs. Des comparaisons univariées entre les groupes de cohortes ont été effectuées pour évaluer les différences significatives au niveau des caractéristiques de base. Des analyses bivariées ont également été réalisées entre la principale variable de résultat (perte de dents) et les caractéristiques de base des participants. Deux modèles de régression binomiale négative ont été réalisés afin de contrôler les facteurs de confusion.

Résultats: Au total, 4870 (25,36 ± 4,08) dents étaient présentes au départ. 423 (2,2 ± 3,44) dents ont été perdues au cours du suivi (SPT), correspondant à 0,07, 0,11, 0,08 et 0,09 TL par an chez les RC, les IC, les fumeurs et les non-fumeurs, respectivement, avec une différence significative présente uniquement entre les RC et IC. Il a été constaté qu'un âge supérieur à 40 ans augmentait les taux de TL.

Conclusions: Le respect du SPT affecte les taux de TL après une moyenne de 24,89 ans de suivi. RC a montré moins de TL que les patients IC. Le tabagisme n'a pas atteint une signification statistique.

Mots clés: Maintenance, tabagisme, thérapie parodontale de soutien, perte de dents.

Introduction

Periodontal disease is a bacterial-induced chronic inflammatory condition affecting the hard and soft tissue structures supporting the dentition. It ranges from mild inflammatory condition referring to gingivitis, to bone and attachment loss known as periodontitis [1]. Active periodontal treatment (APT) is implemented to reduce the inflammatory reactions through eliminating bacterial deposits, either surgically or non-surgically. Long-term effectiveness of APT depends on the maintenance of an ecosystem at the gingival sulcus, which must be compatible with a balanced host-parasite equilibrium. This balance mainly depends on daily elimination of dental plaque by the patient. Unfortunately, patient cooperation is difficult to maintain on the long run. Thus, professional aid is mostly needed [2]. Supportive periodontal therapy (SPT) is defined as procedures performed at selected intervals, aimed to assist the maintenance of periodontal health [3]. In general, SPT visits include update of medical and dental history, periodontal and implant evaluation, biofilm and calculus elimination, radiographic review if needed, oral hygiene assessment, occlusal control, and retreatment of recurrent sites. This will ensure the disruption of microbial colonies and minimize the inflammatory state. SPT therefore offers an opportunity for clinicians to promote periodontal health, rapidly detect and intercept recurrence or progression of periodontal disease [4]. If SPT is not properly delivered, progression of periodontal disease would occur despite the completion of APT [5].

The establishment of a criteria for interval time between SPT visits in attempt to classify individuals as regular compliers (RC) or irregular compliers (IC) were widely discussed and are still controversial. According to the literature, there is high degree of heterogenicity related to the definition of different compliant individuals, with no agreement regarding case definition of different compliant groups [6]. Demirel et al. in 1995 classified patients into RC who presented 100% of cooperation with SPT visits, erratic complaint (EC) who missed any scheduled SPT visits but continued to appear irregularly, and non-complaint (NC) who did not return for any maintenance visit [7]. While Renvert and Persson in 2004 classified their patients into RC who presented 100% compliant for SPT visits with a maximum interval of 6 months between consecutive visits and IC who missed any of the SPT visits but continued to appear on an irregular basis with a maximum interval of 18 months between consecutive visits [6].

Several factors are present which modify the outcome of SPT. Compliance is considered a critical factor for the maintenance of periodontal condition in SPT. Compliance refers to the extent to which a person's behavior coincides with medical or health advice. It is determined by factors related to both the patient and the provider [8]. A classic problem faced during SPT is patient compliance. A systematic review and meta-analyses, which included eight studies having at least 5 years of follow-up, evaluated patient compliance to SPT and TL. Only one study was prospective in nature while the others were retrospective. The rate of compliance was found to be heterogenous, with the most compliant group ranging between 11% and 88% of the sample. It should be noted that the definition of compliance was found to be heterogenous within the studies [5].

Several risk factors are present which modify the course of periodontal disease progression, one of these risk factors is tobacco smoking, which was first evaluated by Pindborg in 1947, and was considered a major modifiable risk factor which negatively affects periodontal disease progression [9]. Smokers show faster disease progression and recurrence [10], worse periodontal status, negative response to periodontal treatment [11], experience greater TL rates [12], and are associated with low level of compliance compared to non-smokers [13]. On the other hand, smokers show less gingival inflammatory status due to the vasoconstricting effect of nicotine [3].

TL is the most visible result of periodontal disease evolution which negatively affects the patient's physiological and psychological aspect. Many studies on TL during SPT report heterogenic, but in general low values of compliance with the scheduled appointments at different intervals. Many reasons contribute to this heterogenicity, (i) the duration of the study i.e. short-, medium-, and long-term studies, (ii) studies in countries with very high, high, and medium human development, and (iv) studies performed in university or private clinics also demonstrated different rates of compliance [14].

The aim of this study is to retrospectively compare TL rates in two cohorts, RC vs IC individuals, and smokers vs non-smokers, with a follow-up up to 50 years. The null hypothesis is that both RC and IC patients present equal rates of TL as well as smokers and non-smokers. While the alternative hypothesis is that RC present fewer rates of TL compared to IC, and non-smokers show fewer rates of TL compared to smokers.

The primary objective of this study is to determine TL rates in RC and IC patients, while the secondary objective is to determine TL rates in smokers and non-smokers over a period of follow-up up to 50 years.

Materials and Methods

Study Design and Patient Recruitment:

This retrospective cohort study investigated data retrieved from a Lebanese private dental clinic, by a specialist in the field of periodontology (JMM) between 1970 and 2020, who underwent supportive therapy in the same clinic. At initial examination (T0), full-mouth periapical

X-rays, periodontal examinations (periodontal pocket depth, clinical attachment level, percentage of bone loss), and case diagnosis was performed. According to the severity of each case, patients were enrolled into an APT program (T1) ranging from no therapy (NT) specifically for gingivitis patients comprising of oral hygiene encouragement and prophylaxis, non-surgical therapy (NST) defined as bacterial decontamination comprising of full-mouth ultrasonic debridement on a weekly or 15 days basis, removal of etiologic factors, and occlusal control, or surgical therapy (ST) which comprised of root resection and/or apical repositioning flap. After APT (T1), patients were enrolled into a maintenance program. The first SPT visit (T2) was considered as baseline evaluation for TL.

The maintenance protocol comprised periodical clinical examination, professional dental hygiene by eliminating supra- and subgingival plaque and calculus, and retreatment of recurrent sites with pocket depth > 5mm. Specific interventions, such as tooth extractions, restorations, and endodontic or prosthetic treatments, were performed during maintenance if deemed appropriate by the dentist. All patients were diagnosed, treated, and maintained accordingly by one specialized clinician at the same private practice for the course of this study.

The study was approved by the Ethical Committee of the Dental faculty of Saint-Joseph University of Beirut, (USJ-2021-35).

Definition of Outcome and Compliance:

Annual TL rate is considered the primary outcome of this study. TL defined as a tooth that is lost during the course of the study. According to the pattern of compliance during SPT visits, as proposed by Renvert and Persson, patients were determined to be RC if they attended 100% of the recall visits with a maximum interval of 6 months, and irregular compliant (IC) if they missed at least one of the recall visits but continued to come back on an irregular basis with a maximum interval of 18 months [6]. According to the smoking status, non-smokers were defined subjects who never have smoked or subjects who have quit smoking, and smokers were defined as subjects consuming cigarettes regardless of the number.

Inclusion and Exclusion Criteria:

Subjects were included in the study if they met the following criteria: 1) age > 20 years, 2) at least 10 years of continued SPT, 3) diagnosis of generalized chronic periodontitis or gingivitis, and 4) patient who had undergone APT comprised of non-surgical and/or surgical therapy. Subjects were excluded from the study if they met one of the following criteria: 1) patients with bisphosphonate therapy, 2) patients with chemo or radiotherapy, 3) patients with hormonal therapy, and 4) patients with debilitating diseases that could impair the immune system (HIV/AIDS, cancer, or autoimmune diseases).

Evaluation of Patient's Charts:

The following patient- and tooth-related parameters were assessed by evaluating individual patient's chart:

- Age at T0: recorded in years.
- Gender: male or female.
- First and last visit: recorded the year from the first visit (T0) and last time the patient was seen.
- Duration of follow-up: determined by subtracting the first and last visit.
- Medical condition of patients.
- Smoking status: self-reported smoking status by the patient, categorized as non-smoker (subjects who never have smoked or subjects who have quit smoking), smoker (subjects consuming cigarettes regardless of the number).
- Initial number of teeth at the start of SPT (T2).
- Periodontal condition: gingivitis patient (PPD ≤ 3mm, BOP ≥10%), periodontitis patient (PPD > 3mm, CAL > 2mm, distance of CEJ and alveolar bone crest > 3mm) [15].
- Active periodontal therapy:
  - No therapy (NT): specifically for gingivitis patients comprising of hygiene encouragement and oral prophylaxis.
  - Non-surgical therapy (NST): defined as bacterial decontamination comprising of full-mouth ultrasonic debridement on a weekly or 15 days basis, removal of etiologic factors, and occlusal control.
  - Surgical therapy (ST): comprised of root resection and/or apical repositioning flap.
- Number of teeth lost during SPT.
- Location of teeth lost: recorded using the international numbering system.
- Endodontic treatment at T0: presence or absence of radicular filling material.
- Post and core at T0: presence or absence of post and core.
- Abutment teeth at T0: if lost teeth were supporting abutment for a removable or fixed prosthesis.
- Cause of extraction: caries, fracture, endodontic complication, periodontitis, root resorption, strategic (for prosthodontic purposes), iatrogenic, or any combination.
- Years in service of lost tooth: recorded from APT till extraction.
- SPT interval: recorded in months, ranged from 4, 6, and 12 months.
- Compliance: regular compliers (adhered to the suggested SPT intervals with maximum delay of 6 months), irregular compliers (missed at least one of the recall visits but continued to appear on an irregular basis with a maximum interval of 18 months) [6]. If patients exceeded the 18 months, they were excluded from the study.

Statistical Analysis:

Data analyses were carried out using IBM SPSS Statistics for Windows (Version 26) (IBM Corp., Armonk, NY, USA). All tests were two-tailed and a p-value of less than 0.05 was considered statistically significant. Number of lost teeth or tooth loss was defined as the main outcome variable of this study which was not normally distributed (Kolmogorov-Smirnov test for normal distribution, $p<0.001$), third molars were excluded from the analysis. Descriptive statistics were presented as frequency/percentage and mean ± standard deviation (SD) for categorical and continuous variables respectively. Univariate comparisons between cohort groups (regular compliance vs. irregular compliance, and smoking vs. non-smoking) were performed to assess significant differences at the level of baseline characteristics using chi-squared, Fisher's exact tests, and Spearman's correlation coefficient accordingly. Bivariate analyses were also performed between the main outcome variable (tooth loss) and baseline characteristics of the participants using Student t-test and Mann-Whitney U test accordingly.

In order to control for confounders, two negative binomial regression models were carried out (one for every exposure) based on the over-dispersed distribution of the dependent variable "tooth loss" (Kolmogorov-Smirnov test for Poisson distribution, $p<0.001$) where incidence rate ratio (IRR) values and their 95% confidence intervals (95% CI) were calculated. The models were established on significant bivariate correlations between tooth loss and baseline parameters (age groups, bruxism, cardiovascular disease, periodontal disease, and active periodontal therapy), in addition to the significant differences found between cohort groups in the bivariate comparisons (reflux between compliance cohorts, and sex, diabetes, and reflux between smoking cohorts). The first model was performed to identify factors related to tooth loss according to irregular and regular compliance groups; a possible collinearity was suspected with active periodontal therapy variable which was excluded from this model. The second model was performed to identify factors related to tooth loss according to smoking and non-smoking groups.

Results

A total of 192 participants were included in this study. Baseline characteristics of the total sample and the cohort groups are shown in Table 1; 91 participants belonged to the regular compliance cohort, and 77 to the smoking one. Bivariate comparisons of baseline parameters between cohort groups are also shown in Table 1. Participants having gastroesophageal reflux in the regular compliance group (12.1%) are significantly more frequent than those in the irregular compliance one (2%) ($p=0.005$); regular and irregular compliance groups are comparable regarding all other baseline parameters. On the other hand, significant smoking cohort-specific differences were revealed regarding sex, age groups at baseline, diabetes, cardiovascular disease, and gastroesophageal reflux. All participants were followed-up for a mean period of 24.89 ± 10.23 years (ranging from 10 to 50 years), and follow-up periods were similar between both cohort groups (Table 1).

Table 2 shows teeth-related characteristics for the total sample, as well as for the compliance and smoking cohort groups with bivariate comparisons. The mean of initial number of teeth per patient was similar between compliance groups ($p=0.949$) and between smoking groups ($p=0.140$). Regarding tooth loss per patient, the bivariate analysis revealed that it was significantly higher in irregular compliant patients (2.67 ± 3.71) than in regular compliant ones (1.68 ± 3.04) ($p=0.043$). However, tooth loss was similar between smokers (2.04 ± 3.38) and non-smokers (2.31 ± 3.48) ($p=0.589$).

Table 3 provides descriptive results on the distribution of extracted teeth according to cohort groups as well as the total sample. Maxillary molars were the most frequently extracted teeth (24.35%), followed by mandibular molars (24.11%) and maxillary premolars (20.8%).

Table 4 shows results of the bivariate analyses conducted between tooth loss and baseline parameters. Significant differences in tooth loss were noticed between age groups, bruxism, cardiovascular disease, periodontal disease, and active periodontal therapy. Patients aged more than forty years at baseline had significantly lost more teeth (2.81 ± 3.97) than those aged forty years and less (1.35 ± 2.27) ($p=0.022$). In addition, bruxers significantly lost more teeth (4.93 ± 4.75) than non-bruxers (1.76 ± 2.96) ($p<0.001$).

Based on the significant difference between irregular and regular compliance groups regarding gastroesophageal reflux as described in Table 1, and significant correlations between tooth loss and baseline parameters (age groups, bruxism, cardiovascular disease, periodontal disease, and active periodontal therapy) as described in Table 4, a negative binomial regression analysis was carried out (Table 5) which identified irregular compliance as a significant risk factor for tooth loss (IRR=0.604 for regular compliance; 95% CI: 0.380 – 0.959; $p=0.033$) while controlling for other risk factors.

Another binomial regression analysis was carried out (Table 6); it was based on significant differences found between smoking and non-smoking cohorts (sex, age groups at baseline, diabetes, cardiovascular disease, and gastroesophageal reflux) and the significant correlations described in Table 4. The relation between tooth loss and smokers/non-smokers turned out to be non-significant ($p=0.664$) while controlling for other risk factors (bruxism, cardiovascular disease, not having reflux, and not following any active periodontal therapy).

Table 1. Baseline characteristics of the study participants

	Regular compliance cohort (n=91)	Irregular compliance cohort (n=101)	p-value	Smoking cohort (n=77)	Non-smoking cohort (n=115)	p-value	Total sample (n=192)
Sex, n (%) *Males* *Females*	43 (47.3) 48 (52.7)	43 (42.6) 58 (57.4)	0.515	27 (35.1) 50 (64.9)	59 (51.3) 56 (48.7)	0.027*	86 (44.8) 106 (55.2)
Age groups, n (%) *≤40 years* *>40 years*	41 (45.1) 50 (54.9)	39 (38.6) 62 (61.4)	0.366	43 (55.8) 34 (44.2)	37 (32.2) 78 (67.8)	0.001*	80 (41.7) 112 (58.3)
Bruxism, n (%) *Yes* *No*	14 (15.4) 77 (84.6)	13 (12.9) 88 (87.1)	0.617	10 (13) 67 (87)	17 (14.8) 98 (85.2)	0.726	27 (14.1) 165 (85.9)
Diabetes, n (%) *Yes* *No*	11 (12.1) 80 (87.9)	11 (10.9) 90 (89.1)	0.795	4 (5.2) 73 (94.8)	18 (15.7) 97 (84.3)	0.026*	22 (11.5) 170 (88.5)
Cardiovascular disease, n (%) *Yes* *No*	8 (8.8) 83 (91.2)	11 (10.9) 90 (89.1)	0.627	2 (2.6) 75 (97.4)	17 (14.8) 98 (85.2)	0.006*	19 (9.9) 173 (90.1)
Reflux, n (%) *Yes* *No*	11 (12.1) 80 (87.9)	2 (2) 99 (98)	0.005*	1 (1.3) 76 (98.7)	12 (10.4) 103 (89.6)	0.014*	13 (6.8) 179 (93.2)
Nervous system disease, n (%) *Yes* *No*	2 (2.2) 89 (97.8)	7 (6.9) 94 (93.1)	0.175	3 (3.9) 74 (96.1)	6 (5.2) 109 (94.8)	0.743	9 (4.7) 183 (95.3)
Cholesterol, n (%) *Yes* *No*	1 (1.1) 90 (98.9)	2 (2) 99 (98)	-	1 (1.3] 76 (98.7]	2 (1.7] 113 (98.3]	-	3 (1.6) 189 (98.4)
Periodontal disease, n (%) *Periodontitis* *Gingivitis*	78 (85.7) 13 (14.3)	83 (82.2) 18 (17.8)	0.506	66 (85.1) 11 (14.3)	95 (82.6) 20 (17.4)	0.567	161 (83.9) 31 (16.1)
Active periodontal therapy, n (%) *Surgical* *Non-surgical* *No therapy*	46 (50.5) 45 (49.5) 0 (0)	41 (40.6) 53 (52.5) 7 (6.9)	-	30 (39) 44 (57.1) 3 (3.9)	57 (49.6) 54 (47) 4 (3.5)	-	87 (45.3) 98 (51) 7 (3.6)
Follow-up in years, mean (SD)	25.99 (10.98)	23.89 (9.45)	0.157	24.34 (10.36)	25.25 (10.17)	0.545	24.89 (10.23)

*Statistical significance $p<0.05$

Table 2. Teeth-related characteristics of the study participants

	Regular compliance cohort (n=91)	*Irregular compliance cohort (n=101)*	*p-value*	*Smoking cohort (n=77)*	*Non-smoking cohort (n=115)*	*p-value*	*Total sample (n=192)*
Initial number of teeth, n *Per patient, mean (SD)*	2310 25.38 (3.93)	2560 25.35 (4.23)	0.949	1994 25.9 (3.45)	2876 25.01 (4.44)	0.140	4870 25.36 (4.08)
Number of teeth at follow-up, n *Per patient, mean (SD)*	2157 23.7 (5.3)	2290 22.67 (6.64)	0.235	1837 23.86 (5.41)	2610 22.7 (6.42)	0.190	4447 23.16 (6.05)
Number of teeth lost, n *Per patient, mean (SD)* *Per patient/year, mean [SD)*	153 1.68 (3.04) 0.07 (0.12)	270 2.67 (3.71) 0.11 (0.17)	0.043* 0.043*	157 2.04 (3.38) 0.08 (0.15)	266 2.31 (3.48) 0.09 (0.15)	0.589 0.587	423 2.2 (3.44) 0.091 (0.15)

*Statistical significance $p<0.05$

Table 3. Distribution of lost teeth according to cohort groups

	Regular compliance cohort (n=91)	*Irregular compliance cohort (n=101)*	*Smoking cohort (n=77)*	*Non-smoking cohort (n=115)*	*Total sample (n=192)*
Maxillary anterior teeth, n (%)	14 (9.15)	31 (11.5)	12 (7.64)	33 (12.4)	45 (10.64)
Mandibular anterior teeth, n (%)	11 (7.19)	31 (11.48)	15 (9.55)	27 (10.15)	42 (9.93)
Maxillary premolars, n (%)	29 (18.95)	59 (21.85)	31 (19.74)	57 (21.43)	88 (20.8)
Mandibular premolars, n (%)	15 (9.8)	28 (10.37)	14 (8.92)	29 (10.9)	43 (10.16)
Maxillary molars, n (%)	39 (25.49)	64 (23.7)	39 (24.84)	64 (24.06)	103 (24.35)
Mandibular molars, n (%)	45 (29.41)	57 (21.11)	46 (29.30)	56 (21.05)	102 (24.11)

Table 4. Results of bivariate analyses between tooth loss (outcome variable) and baseline characteristics

	Tooth loss, mean (SD)	p-value
Sex		
Males (n=86)	2.71 (3.91)	0.221
Females (n=106)	1.79 (2.95)	
Age groups		
≤40 years (n=80)	1.35 (2.27)	0.022*
>40 years (n=112)	2.81 (3.97)	
Bruxism		
Yes (n=27)	4.93 (4.75)	<0.001*
No (n=165)	1.76 (2.96)	
Diabetes		
Yes (n=22)	2.05 (2.68)	0.350
No (n=177)	2.22 (3.53)	
Cardiovascular disease		
Yes (n=19)	1.89 (3.23)	<0.001*
No (n=173)	5.05 (3.98)	
Reflux		
Yes (n=13)	1.00 (2.27)	0.059
No (n=179)	2.29 (3.49)	
Nervous system disease		
Yes (n=9)	2.56 (2.92)	0.538
No (n=183)	2.19 (3.46)	
Cholesterol		
Yes (n=3)	2.33 (3.21)	0.729
No (n=198)	2.20 (3.45)	
Periodontal disease		
Periodontitis (n=161)	2.47 (3.58)	0.004*
Gingivitis (n=31)	0.84 (2.16)	
Active periodontal therapy ^		
Surgical (n=87)	2.72 (3.79)	
Non-surgical (n=98)	1.40 (2.48)	<0.001*
No therapy (n=7)	7.00 (5.38)	

*Statistical significance p<0.05 / ^ Bonferroni post-hoc test: significance between no therapy and non-surgical therapy (adjusted p=0.018) and between no therapy and surgical therapy (adjusted p=0.001)

Table 5. Negative binomial regression model showing predictors of tooth loss according to compliance groups

Parameter	*Regression coefficient*	*SE*	*p-value*	*Incidence rate ratio (IRR)*	*95% CI for ICC*	
					Lower limit	*Upper limit*
(Intercept)	-0.348	0.351	0.321	0.706	0.355	1.404
Compliance groups						
Regular	-0.505	0.236	0.033	0.604	0.380	0.959
Irregular (Ref.)	0	-	-	1	-	-
Bruxism						
Yes	1.202	0.328	<0.001	3.326	1.747	6.332
No (Ref.)	0	-	-	1	-	-
Cardiovascular disease						
Yes	0.955	0.362	0.008	2.598	1.276	5.288
No (Ref.)	0	-	-	1	-	-
Reflux						
Yes	-1.203	0.562	0.032	0.3	0.1	0.904
No (Ref.)	0	-	-	1	-	-
Periodontal disease						
Periodontitis	0.860	0.373	0.021	2.363	1.137	4.910
Gingivitis (Ref.)	0	-	-	1	-	-
(Negative binomial)	1.785	0.303	-	-	-	-

Variables entered originally were: compliance, bruxism, cardiovascular disease, reflux, periodontal disease, and age groups (p=0.189). AIC= 700.9 / Omnibus test: Likelihood ratio chi-square=39.457, p<0.001. Abbreviations: SE = standard error of the mean, 95% CI = 95% confidence interval

Table 6. Negative binomial regression model showing predictors of tooth loss according to smoking groups

Parameter	*Regression coefficient*	*SE*	*p-value*	*Incidence rate ratio (IRR)*	*95% CI for ICC* *Lower limit*	*Upper limit*
(Intercept)	-0.348	0.351	0.321	0.706	0.355	1.404
Smoking groups						
Smoker	0.111	0.256	0.664	1.118	0.677	1.847
Non-smoker (Ref.)	0	-	-	1	-	-
Bruxism						
Yes	1.339	0.338	<0.001	3.813	1.967	7.392
No (Ref.)	0	-	-	1	-	-
Cardiovascular disease						
Yes	1.046	0.366	0.004	2.847	1.391	5.828
No (Ref.)	0	-	-	1	-	-
Reflux						
Yes	-1.185	0.562	0.032	0.306	0.104	0.901
No (Ref.)	0	-	-	1	-	-
Active periodontal therapy						
Surgical	-1.161	0.536	0.030	0.313	0.109	0.896
Non-surgical	-1.651	0.536	0.002	0.192	0.067	0.549
No therapy (Ref.)	0	-		1	-	-
(Negative binomial)	1.583	0.282	-	-	-	-

Variables entered originally were: smoking, bruxism, cardiovascular disease, reflux, periodontal disease (p=0.173), diabetes (p=0.299), sex (p=0.573), and age groups (p=0.145). AIC= 699.05 / Omnibus test: Likelihood ratio chi-square=49.393, p<0.001. Abbreviations: SE = standard error of the mean, 95% CI = 95% confidence interval

Discussion

The aim of this retrospective study is to compare TL rates during SPT between two cohorts, the compliance cohort (RC vs IC patients), and the smoking cohort (smoker vs non-smokers patients), over a follow-up period up to 50 years. All patients were treated and followed by a specialist in the field of periodontology (JMM) in a private dental practice. After APT (T1) all patients were enrolled into an individualized SPT program (T2) according to the severity of each case.

The primary outcome of this study was TL since it represents the end point of periodontal disease, a result of irreversible and progressive attachment loss if not treated. Because periodontal disease is chronic in nature, SPT program must be implemented after APT. SPT is defined as procedures performed at selected intervals to assist the periodontal patient in maintaining oral health and stabilize the remaining periodontal condition as much as possible. On the other hand, neglecting the enrollment into a SPT has been proven to increase the risk of reinfection and progression of periodontal disease, as well as TL. However, this program requires long-lasting patient cooperation, which is easy to accept, but difficult to maintain. Many studies on TL during SPT report heterogenic, but in general low values of compliance with the scheduled appointments at different intervals [5].

As stated by Ramseier et al, "even although all authors consistently agree that increased compliance with SPT intervals results in improved periodontal health, no standard for the definition of compliance has been established yet" [16]. According to the literature, compliance classification and definition is wildly heterogenous, each with different advantageous and disadvantageous. In this retrospective cohort RC were defined as patients who adhered to the suggested SPT intervals with maximum delay of 6 months, while IC were defined as patients who missed at least one of the recall visits but continued to appear on an irregular basis with a maximum interval of 18 months) [6]. This classification was chosen because it best suits our patient's data.

Another problem faced by SPT is the frequency of the scheduled appointments. According to the literature, intervals vary from 3, 4, 6, 12, 18 months, or "as necessary" as needed according to the severity and risk factors in each case. However, there is no strong evidence regarding the efficacy, as well as appropriateness and cost-effective-

ness of a specific time interval for SPT [17]original data on the relevance of residual diseased sites (ie, bleeding pockets. Farooqi et al. in 2015 conducted a systematic review to evaluate the evidence regarding the most appropriate time interval for SPT in patients previously treated for chronic periodontitis. Because no randomized controlled trials (RCT) or cohort studies directly comparing different time intervals between SPT visits could be found, the effect of patient compliance with the suggested SPT regimen on tooth retention was analyzed. Although more frequent SPT recall visits were associated with fewer TL in some studies, other reports showed no statistically significant differences in TL in cohorts with SPT intervals of less than or more than 6 months [18]. Miyamoto et al. in 2006 reported that patients who attended at least 70% of 3 to 4 monthly SPT visits were significantly more likely to lose teeth than those attending less than 70% of visits. This could be attributed to the fact that patients who are highly compliant to the prescribed SPT are also likely to have a more severely diseased condition and a higher rate of acceptance with regard to the proposed dental treatment [19]. On the other hand, it is logical to say that if the extraction strategy was conservative during APT, i.e., retaining teeth with poor prognosis, then TL rates would likely increase during SPT and vice versa [20]. This concludes that although the available evidence appears to favor more frequent SPT recall visits, the optimum frequency is unclear and a "one size fits all" type of recommendation seems to be questionable. In this cohort study, the recall interval for compliant patient was varied between 4 to 12 months according to the severity of each case.

The results of this study have shown that RC patients presented significantly less TL rates than IC ones (0.07 ± 0.12 and 0.11 ± 0.17 per patient per year) respectively. In order to control confounding factors, such as and the nature of APT, a negative binomial regression analysis was carried out. The result of this analysis revealed that IC presents a significant risk factor for TL [IRR=0.604 for regular compliance; 95% CI: 0.380 – 0.959; p= 0.033) after a mean follow-up of 25.99 ± 10.98 years. In the systematic review by Trombelli et al. in 2015, the long-term clinical effect of routine professional mechanical plaque removal, as an essential part of a SPT regimen, was assessed in patients previously treated for varying severities of periodontitis. The SPT regimen was based on 1-6 month recalls, with the majority of reports following a 2-4 month recall frequency in the included prospective studies (n= 19). Studies having a short follow-up (5 years) had a mean TL rate ranging from 0 to 0.36 with a weighted mean TL rate of 0.15 ± 0.14 teeth per year. For studies with a longer follow- up (12-14 years), the mean TL rate ranged from 0.025 to 0.225 with a weighted mean tooth loss rate of 0.09 ± 0.08 teeth per year [21]. These findings coincide with the results of our study and reinforce the well-documented concept that patients treated for moderate to advanced periodontitis can maintain their dentition over the long term when regularly complying with a SPT regimen. The results can be explained by the fact that IC patients present with increased plaque index, BOP, PPD, and re-establishment of a periodontal microbiome, due to lack of oral hygiene monitoring and motivation. Additionally, IC patients do not have the opportunity to re-assess their periodontal risk, hence lose the chance to retreat diseased sites, eventually leading to TL. All in all, these facts could explain the increased TL rates in IC patient [22].

Cigarette smoking, which is the source of more than 4000 toxins, such as carbon monoxide, oxidizing radicals, and carcinogens such as nitrosamine and nicotine, is considered a major modifiable risk factors for the development of periodontal disease and subsequent TL with an attributed risk ranging from 2.5 to 7 as reviewed by Tonetti [23]. The effects of cigarette smoking on periodontal status are independent of the plaque index and oral hygiene of the patient, due to the direct influence of tobacco on periodontal tissues, which means that smokers have increased risk to develop periodontal disease, even if plaque and calculus indices are minimal [24]. Hanioka et al. in 2007 assessed the link between smoking and tooth loss in 3999 Japanese individuals. By using logistic regression models, a positive relation was found between TL and smokers but not in former smokers [25]999 subjects aged older than 40 years were analyzed using logistic regression models, controlling for confounding factors, such as age, frequency of tooth brushing, body mass index, alcohol consumption, and intakes of vitamin C and E.\n\nResults\nPrevalence of tooth loss in terms of having less than 19 existing teeth was 37.3% overall. Smoking rates differed in males (45.6%. Similarly, the association between tobacco smoking and TL was confirmed by Ojima et al. in 2007 where smokers had 40.6% more chance for TL than non-smokers (27.9%) [26].

Several possible explanations could justify the increased TL rates in smokers, these include, dysfunction of gingival fibroblasts, decrease in microcirculatory function and immune system deficiency. Additionally, overproduction of inflammatory molecules and suppression of anti-inflammatory molecules could lead to inflammatory destruction of connective tissue and alveolar bone. Interestingly, periodontal tissue destruction in smokers may be modulated by an impaired ability to repair damaged tissue rather than by direct tissue damage. Furthermore, smokers showed change in the microbial profile, leaning towards a more destructive microbiome. The microbial profile of disease-associated and health-compatible organisms in smokers was significantly

different from that in non-smokers. Lastly, several chemicals in tobacco could alter the immune system and tissue repair. Nicotine, benzo(a) pyrene and benzo(a)anthracene are immunosuppressive, whereas tobacco glycoprotein and metals are immunostimulatory. Nicotine, acrolein and acetaldehyde inhibit the function of gingival fibroblasts, including proliferation, collagen production, adhesion to root surfaces, and induce cytotoxicity. Together, the substantive evidence strongly supports the biological plausibility of the adverse effect of smoking on the periodontium [12].

Despite the adverse effect of smoking on the periodontium and its effect on TL, the results of this cohort proved otherwise. There was no statistical significance in TL rates between smokers and non-smokers (0.08 ± 0.15 and 0.09 ± 0.15 mean per patient respectively). The results are in agreement with Fisher et al. in 2008, where a total of 108 patients diagnosed with chronic periodontitis, underwent regular maintenance for a period of 3 years. Smoking status was confirmed by analysis of exhaled carbon monoxide concentrations. At the end of the 3-year period, no statistical significance was present between the smoking and non-smoking group regarding disease progression, which has been assessed by mean CAL, PPD and TL [27]the effect of cigarette smoking on the recurrence of disease in patients undergoing regular maintenance therapy is less understood. Therefore, we set out to assess disease progression longitudinally in smoking and non-smoking subjects with chronic periodontitis undergoing periodontal maintenance therapy every 3 to 4 months.\nMETHODS: A total of 108 subjects undergoing regular maintenance therapy for chronic periodontitis were followed over a 3-year period. Self-reports of smoking status were confirmed by analysis of exhaled carbon monoxide concentrations. Clinical parameters (plaque index [PI], bleeding on probing [BOP], clinical attachment loss [CAL], probing depth [PD], and tooth loss. Additionally, Papantonopoulos in 2004 evaluated radiographic bone loss and PPD in 29 (15 self-reported smokers and 14 non-smokers) compliant patients diagnosed with advanced periodontitis (50% bone loss on 50% of teeth). All patients received surgical and non-surgical therapy for pocket elimination and were followed for 5 to 8 years. At the end of the follow-up period smokers had higher mean of radiographic bone loss and PPD compared to non-smokers, and only one tooth in a non-smoker and three teeth in two smokers were lost. The differences were not statistically significant [28] the longitudinal effect of smoking on treatment results in patients who undergo long-term maintenance therapy has not been extensively investigated. This study clinically and radiographically compared smoking and non-smoking patients who had been treated for advanced periodontal disease and who received maintenance therapy for a minimum of 5 years.\nMETHODS: Twenty-nine patients were selected over a 6-month period when they presented for a regularly scheduled visit in a private office. Patients were selected on the basis of initially having lost 50% of bone support on 50% of their teeth; had received follow-up therapy for at least 5 years; were compliant at 75% of the appointments; and had plaque scores < 20% in 75% of the visits. All patients had received non-surgical and surgical therapy as required for pocket elimination. Fourteen were active smokers during the entire maintenance period. Clinical measurements of probing depths and presence of plaque and gingivitis and a new set of standardized radiographs were taken.\nRESULTS: Smokers had higher mean radiographic bone loss values prior to treatment (7.52 +/- 1.39 versus 6.65 +/- 1.39. Hirata et al. in 2019 conducted a multicenter joint retrospective cohort study to assess risk of TL due to periodontitis. A total of 82 patients diagnosed with severe periodontitis were recruited from 11 dental institutions who continued SPT for at least 1 year and a mean follow-up of 4.9 years. At the end of the follow-up, compliant patient had a 0.04 TL/patient/year with smoking not being statistically significant in increasing TL ratios [29].

The result of this study could be attributed to the self-reported smoking status of the patient, which could often be unreliable, and the misclassification of smoking habit as “smoker” and “non-smoker”, which ideally should take into account the intensity of smoking (cigarettes per day), and hence classify smokers into mild, moderate, and heavy smokers. A recent retrospective cohort study by Ravidà et al. in 2020, investigated the effects of smoking on TL due to periodontitis in long-term compliant patients after 47 years of follow-up. A total of 258 periodontal patients were enrolled in a SPT program (at least 1 visit per year) for a mean of 24.2 years. Patients were grouped as never smokers, former smokers, current light smokers (<10 cigarettes/day), and current heavy smokers (≥10 cigarettes/day). TL due to periodontitis accounted for 0.03, 0.05, 0.08 and 0.11 amongst never smokers, former smokers, current light smokers, and current heavy smokers, respectively. Heavy smokers had 4.4-fold, 2.7-fold, and 2.6-fold increased risk of TL compared to never smoker, current light smoker, and former smoker, respectively. Hence, a dose-response pattern of TL could be present, where heavy smokers present increased TL rates than light smokers [30].

Another possible reason for our non-significant result is probably that some of the patients classified as non-smoker had been smoking for a period of time in the past and hence should be considered as “former smokers”. Dietrich and colleagues demonstrated that quitters among male US health professionals had a significantly lower risk for TL compared with current smokers. Although this risk decreased gradu-

ally over time, it did not reach the level of never smokers until after 10–20 years after cessation [30],[31]. On the other hand, smoking cessation significantly benefits an individual's likelihood of tooth retention, but it may take decades for the individual to return to the rate of TL observed in non-smokers [32]. These results demonstrate that former smokers have a residually elevated risk for TL compared to non-smokers for a substantial duration of time immediately after quitting.

Strengths

To the best of our knowledge, this study is one of the largest studies of its kind, as the 192 participants underwent SPT for an unusually extended follow-up period [mean 24.89 ± 10.23 years) ranging from 10 to 50 years. Only one specialist performed case diagnosis, APT, and SPT. Due to the high number of patients available, we could exclude those with less than 10 years of SPT. To avoid bias in results due to confounding factors, two negative binomial statistical tests were performed in order to determine TL ratios in both cohorts.

Limitations

The inclusion of data over many years could lead to some systematic bias caused by changing treatment plans and trends on the possibility of tooth retention (vs. extraction and replacement by implants) and periodontal practice protocols for SPT over time. Moreover, the clinical judgement of the clinician may play a role and may also change over time as well as differ between operators. Additionally, the attitude, motivation and financial circumstances of each patient also influence the decision to extract a tooth.

Conclusion

The literature explored in this study showed that supportive treatment after active therapy can successfully maintain teeth in RC subjects when compared to IC ones. This cohort proved that periodontally affected patients could maintain their dentition after up to 50 years of follow-up. Different reasons could lead to the increase TL rates in IC subjects, among them, lack of oral hygiene reinforcement during recall visits, leading to higher plaque and bleeding scores causing an imbalanced periodontal microbiome. Conversely, smoking habit did not show any statistical significance in TL rates in this cohort, this can be explained by the smoking classification adopted in this study. One final result showed that subjects older than 40 years had a higher risk of TL during the follow-up period analyzed.

Author Contributions

Jean-Marie Megarbane and Roudy Khayat contributed equally to the making of this article. Special thanks to Dr Lara Nasr for the statistical work done for this article.

Conflict of Interest

All authors declared they have no conflict of interest related to this report.

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