

Periodontal disease as a risk for dental implant failure over time: A long-term historical cohort study

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Abstract

Objectives: To evaluate the long-term survival rates of dental implants according to the patient's periodontal status, as well as to estimate if the effect of periodontal status regarding implant failure is constant throughout the long-term follow-up.

Materials and Methods: This was a historical prospective cohort study design of all consecutive patients operated from 1996 to 2006 at a periodontal clinic. The cohort consisted of 736 patients, with a total of 2336 dental implants. An extended Cox proportional hazards model, which includes interaction terms between survival time and variables of interest, was used.

Results: Patients' mean (SD) age was 51.13 (12.35). The follow-up time was up to 144 months, with a mean (SD) of 54.4 (35.6) months. The overall implant raw survival rate was 95.9%. The Kaplan–Meier estimates for the cumulative survival rate (CSR) at 108 months were 0.96 and 0.95 for implants inserted into healthy and moderate chronic periodontitis patients, respectively. The CSR declined to 0.88 at 108 months for the severe periodontitis group. The extended Cox model revealed that severe chronic status turned out to be a significant risk factor for implant failure after 50 months of follow-up [hazard ratio (HR) = 8.06; $p < 0.01$]. The extended Cox model for smoking indicates a near-significant effect after 50 months (HR = 2.76; $p = 0.061$).

Conclusions: Periodontal status and smoking are significant risk factors for late implant failures. The HR for periodontal and smoking status are not constant throughout the follow-up period.

Key words: cigarette; diabetes mellitus; implant failure; maintenance; periodontitis; smoking; supportive therapy

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Over the past decade, the use of osseointegrated implants as a foundation for prosthetic replacement of missing teeth has become widespread. Nowadays, implant therapy is highly predictable and successful (Berglundh et al. 2002, Pjetursson et al. 2004, Esposito et al. 2005, Levin et al. 2005, 2006a, b). However, certain risk factors might predispose individuals to lower success rates (Klokkevold & Han 2007) and to a

greater hazard for implant failure. There has been growing interest in identifying these factors but only a few studies have evaluated the long-term association between periodontal status and implant success and survival.

According to Klokkevold & Han (2007), a history of treated periodontitis does not appear to adversely affect implant survival rates but it could have a negative influence on implant success rates, particularly over longer periods.

Successful osseointegration has been shown in patients with different types of periodontitis (Nevins & Langer 1995, Ellegaard et al. 1997). However, these reports do not offer comparative data between periodontally compromised

patients who have been treated and periodontally healthy patients. Nevertheless, a systematic review by Van der Weijden et al. (2005) concluded that the outcome of implant therapy in periodontitis patients may be different compared with individuals without such a history in terms of loss of supporting bone and implant loss.

In a systematic review of implant outcomes in treated periodontitis subjects, Ong et al. (2008) concluded that there is some evidence that patients treated for periodontitis may experience more implant loss and complications around implants including higher bone loss and peri-implantitis than non-periodontitis patients. Evidence was

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stronger for implant survival than implant success.

A review by Renvert & Persson (2009) was aimed to assess whether individuals with a history of periodontitis are more likely to develop peri-implantitis compared with patients without such a history reported. This review was based on three studies with a limited number of patients and considerable variations in the study design, different definitions of periodontitis and confounding variables that had not been accounted for. They claimed that subjects with a history of periodontitis may be at a greater risk for peri-implant infections. However, they stressed that the data to support this conclusion are not very robust.

Recently, Simonis et al. (2010) stated that patients with a history of periodontitis may have lower implant survival rates than patients without a history of periodontitis and were more prone to biological complications such as peri-implant mucositis and peri-implantitis. The limited number of studies focusing on the effect of periodontal status on implant failure and the lack of evidence regarding changes of hazards for failure over time motivated us to perform the current study.

The objectives of the present study were

1. To estimate the correlation between periodontal status and other explanatory variables at the patient and the implant level.
2. To estimate the effect of periodontal status on hazard for implant failure.
3. To examine whether hazard ratios (HR) for variables of interest are constant throughout the long-term follow-up.

The null hypothesis was that there is no difference between periodontal disease groups with regard to long-term implant survival. In terms of HR, the null hypothesis states that $HR = 1$ for periodontal status.

Materials and Methods

This was a historical prospective cohort study. The cohort was created from all consecutive patients operated from 1996 to 2006, at a periodontal clinic, by a single surgeon (R. A.). The cohort consisted of 736 patients, with a total of 2336 dental implants.

The study variables

Dates of the following clinical events were recorded: implant placement,

implant loading and last follow-up visit or implant removal, where applicable. The major response variable was implant failure. Failure was defined as the removal of an implant for any reason. Early failures were defined as failures occurring before implant loading, while late failures occurred after loading. Survival time (T) was defined as the duration of time (months) from implant insertion to implant removal or to the last follow-up for surviving implants.

The main explanatory variable was periodontal status. Patients were divided into different periodontal groups according to their periodontal diagnosis that was based on the classification of periodontal diseases introduced by the 1999 International Workshop (Anon 1999). Patients were classified by a well-experienced periodontist (R. A.) with regard to the clinical attachment levels as recommended by the above-mentioned classification of periodontal diseases; the classification of patients who were examined before 1999 was adjusted to follow the updated current classifications. Patients diagnosed with aggressive periodontitis (19 patients with 77 implants) were excluded from the evaluation at the statistical analysis phase, as including them would have impaired the power of our statistical tests. More patients with aggressive periodontitis are needed in order to obtain a valid comparison with other periodontal groups. All periodontally involved patients had undergone cause-related as well as corrective-phase periodontal interventions (if indicated) before dental implant placement. Other explanatory variables of interest included:

Diabetic status: a binary variable (Yes/No).

Smoking status: a binary variable that describes whether the patient was a

smoker at the time of surgery. All smokers in the present study were heavy smokers, i.e. smoked more than 10 cigarettes per day.

Supportive periodontal therapy (SPT): a binary variable that assesses whether the patient attended at least twice a year supportive therapy. All patients were advised to attend a regular SPT programme; however, not all complied perfectly with and participated in all scheduled appointments.

Statistical methods

In periodontal studies, it is necessary to distinguish between patient- and site-level analysis as it is reasonable to assume that patients are independent from each other, but sites within patient mouth are correlated to some extent (Fleiss et al. 1988). In the current study, there were two levels for the units of statistical analysis. The primary units were 717 patients, while the elementary units were 2259 implants, with an average of 3.15 implants per patient. The Patient and implant units by periodontal status are described in Table 1. In the present study, the possibility for intra-class/patient correlation (ICC) was an important issue that was taken into consideration in the statistical analysis.

In order to compare between the three periodontal groups with regard to patient-level categorical variables (i.e. gender, smoking status), the Pearson χ^2 -test and a one-way ANOVA for patient-level scale variables (i.e. age) were performed.

Survival analysis methods were applied in order to estimate the cumulative survival rates (CSR) of our implants (life tables and Kaplan–Meier survival functions). These methods are useful to describe censored observations

Table 1. Statistical analysis units* at the patient and the implant level by periodontal diagnosis at surgery

	Periodontitis			Total
	No	moderate chronic	severe chronic	
Patient level				
No.	283	149	285	717
Percent	34.5	20.8	39.7	100
Implant level				
No.	747	447	1065	2259
Percent	33.1	19.8	47.1	100
Implants per patient				
Range	1–16	1–12	1–17	1–17
Mean	2.64	3	3.74	3.15

*19 Aggressive periodontitis patients with 77 implants were excluded from statistical analysis.

(implants for which we do not know the exact failure time). The main pitfall of these methods is the inability to take into account the within-mouth correlation (ICC) and therefore they can be treated as preliminary descriptive methods. In order to estimate HR, the Cox regression (with adjustment to possible confounders) combined with robust standard errors that accounts for ICC was utilized. The robust standard errors were obtained similar to GEE but with application to survival data. The method is described in the context of dental research by Chuang et al. (2002).

The main assumption of the Cox regression is the proportional hazard (PH) assumption, which states that the HR is constant throughout the follow-up time. The validity of the results obtained from a Cox regression depends on the verity of the PH assumption, which was examined using the Grambsch–Therneau test. Violation of the PH assumption was graphically assessed by plots of the explanatory variable effects against the survival time. If the PH assumption is true, this plot will be a horizontal line. In case of violation of the PH assumption, an extended Cox model with an interaction term between the survival time and the problematic variable was applied (Tableman & Kim 2004). Statistical analysis was performed using SPSS (17.0 SPSS, Chicago, IL, USA) and R (R Foundation for Statistical Computing, Vienna, Austria) softwares.

Results

Overall, 717 patients (mean age = 51.13, 57.14% females) with a total of 2259 dental implants were included in the analysis. Table 1 presents the number of patients and implants according to the periodontal group. The follow-up time was up to 144 months, with a mean of 54.4 ± 35.6 months. Losses to follow-up were defined as patients with a follow-up < 18 months. Among the original cohort, 18.6% were classified as lost to follow-up. This group is not different with regard to gender and age. Smokers have a tendency towards loss to follow-up, while patients with a diagnosis of severe chronic periodontitis tend to attend more to follow-up ($p = 0.035$ and 0.027 , respectively).

Table 2 presents the cross tabulation of periodontal status by gender, diabetes status, smoking at surgery and SPT at least twice a year and reveals a significant

correlation ($p < 0.01$) between periodontal status with diabetes, smoking and SPT. A higher proportion of diabetic patients was observed among the severe chronic (16.5%) compared with moderate chronic periodontal patients (11.4%) and periodontally healthy patients (6.0%). According to Table 2, a significantly higher proportion of smokers was observed among the severe chronic group and SPT was more prominent among severe chronic periodontitis patients. Comparison of the three periodontal groups by age yielded significant differences; healthy periodontal patients tended to be younger (mean = 46.05 ± 8.4) compared with moderate chronic (mean = 53.77 ± 9.3) and severe chronic (mean = 54.93 ± 14.9 ; $p < 0.001$). No differences were observed with regard to the follow-up time.

During the follow-up period, a total of 43 (1.9%) implants failed at the surgical phase and 50 (2.2%) failed at the prosthetic phase. The raw distribution of failures by periodontal group is displayed in Table 3 and revealed 5.2% failures among the severe chronic periodontitis group, compared with only 3.3% and 3.0% among moderate chronic periodontitis and healthy patients,

respectively. During the prosthetic phase, we observed 3.2%, 2.1% and 0.9% failures within the severe, moderate and healthy groups.

The distribution of failures by periodontal group and smoking, accounting for the time to failure and censoring information, is displayed in the Kaplan–Meier survival functions (Fig. 1). Survival functions by periodontal status (left panel) seem to be similar until around 50 months but, afterwards, differences are apparent. A similar pattern is observed for smoking (right panel). Life table results (not shown) indicate that in healthy periodontal patients, the CSR stabilized around 60 months to a level of 0.96; for the moderate chronic periodontal patients, CSR stabilized around 72 months to a level of 0.95 while CSR continued to decline throughout the follow-up period for severe chronic periodontal patients and reached a level of 0.88 at 108 months.

The results of an initial naïve Cox regression model (main effects without interaction terms) indicate a violation of the PH assumption for smoking and periodontal group. The violation was detected by a significant Grambsch–Therneau test ($\chi^2 = 16.30$, $p < 0.01$). This result means that smoking and

Table 2. Cross tabulation of periodontal status by patient-level* categorical variables

Variable	Category	Periodontitis			p-value**
		No (n = 283)	moderate chronic (n = 149)	severe chronic (n = 285)	
Gender	Male	111 (39.2%)	50 (33.6%)	112 (39.3%)	0.443
	Female	172 (60.8%)	99 (66.4%)	173 (60.7%)	
Diabetes	No	266 (94.0%)	132 (88.6%)	238 (83.5%)	<0.001
	Yes	17 (6.0%)	17 (11.4%)	47 (16.5%)	
Smoking	No	251 (88.7%)	133 (89.3%)	230 (80.7%)	0.009
	Yes	32 (11.3%)	16 (10.7%)	55 (19.3%)	
SPT	No	231 (81.6%)	100 (67.1%)	143 (50.2%)	<0.001
	Yes	52 (18.4%)	49 (32.9%)	142 (49.8%)	

*N = 717.

**Pearson's χ^2 -test.

Table 3. Raw survival status by periodontal groups

Surviving status	Periodontitis			Total
	No	moderate chronic	severe chronic	
Surviving	724 96.9%	432 96.6%	1010 94.8%	2166 95.9%
Early failure*	16 2.1%	6 1.3%	21 2.0%	43 1.9%
Late failure†	7 0.9%	9 2.0%	34 3.2%	50 2.2%
Total	747	447	1065	2259

*At the surgical phase.

†At the prosthetic phase.

periodontal status effects (measured by HR) are not constant throughout the follow-up period and therefore the PH assumption is not true. Diagnostic plots for severe chronic periodontitis and smoking effects against survival time are displayed in Fig. 2. The positive slopes (non-horizontal line) seen in both figures support the finding of PH violation. According to these figures, the HR for both severe chronic and smoking are not constant with greater HR at a longer follow-up time. This finding is consistent with the non-parallelism of the survival functions displayed in Fig. 1.

In order to overcome this violation, the extended Cox PH model was constructed by including an interaction term between survival time (shorter or longer than 50 months) and periodontal status (Table 4) as well as interaction between survival time and smoking status (Table 5). The decision to split our survival

data at 50 months was motivated by Kaplan–Meier survival functions presented in Fig. 1. According to Table 4, it can be seen that moderate chronic periodontitis compared with healthy periodontal status is not a risk factor throughout the follow-up time. Severe chronic periodontitis does not relate to a greater hazard for implant failure up to 50 months, but turns out to be a strong significant risk factor at $T \geq 50$ with $HR = 8.06$ ($p < 0.01$). The right panel of Table 4 indicates that the extended model is not violating the PH assumption, which is further supported by Fig. 3. Notice the constant effect obtained from the extended model, seen as a horizontal line in Fig. 3.

The extended Cox PH model for smoking (Table 5) indicates a non-significant effect up to 50 months compared with non-smokers with $T < 50$ months. After 50 months, the smoking effect on implant survival is almost

significant, with $HR = 2.76$ ($p = 0.061$) and no violation of the PH assumption.

Discussion

An implant-supported restoration offers a predictable treatment for tooth replacement (Pjetursson et al. 2004, Esposito et al. 2005, Levin et al. 2005, 2006a, b, Anner et al. 2010). Nevertheless, failures that require immediate implant removal do occur (Duyck & Naert 1998, Esposito et al. 2005, Grossmann & Levin 2007, Jung et al. 2008, Schwartz-Arad et al. 2008). The consequences of implant removal jeopardize the clinician's efforts to accomplish satisfactory function and aesthetics. For the patient, this usually involves further cost and additional procedures (Levin 2008).

The null hypothesis of the present study was that the periodontal disease would have no effect on long-term implant survival. According to our findings, the null hypothesis was rejected as patients with severe periodontal disease presented a higher risk for long-term implant failures. Moreover, it was observed that the HR for both periodontal and smoking status were not constant throughout the follow-up period. Until around 50 months, periodontal status did not have a significant effect; however, following 50 months, the hazard for implant failure was eight times greater for the severe chronic periodontal patients. This could be attributed to the continuous and cumulative nature of periodontal disease.

Implant treatment in periodontitis-susceptible individuals is frequently debated. The outcome of implant treatment in terms of survival of supra-structures and implants as well as health status of the peri-implant tissues in individuals with and without a history of periodontitis-associated tooth loss has been studied in a few recently published papers and systematic reviews (Schou 2008, Renvert & Persson 2009, Greenstein et al. 2010, Brägger et al. 2011, Lang & Berglundh 2011), with conflicting results.

It has been reported that in partially edentulous patients, periodontal pathogens may be transmitted from teeth to implants, implying that periodontal pockets may serve as reservoirs for bacterial colonization around implants (Quirynen et al. 2006, Karoussis et al. 2007). The similarity in microbial flora

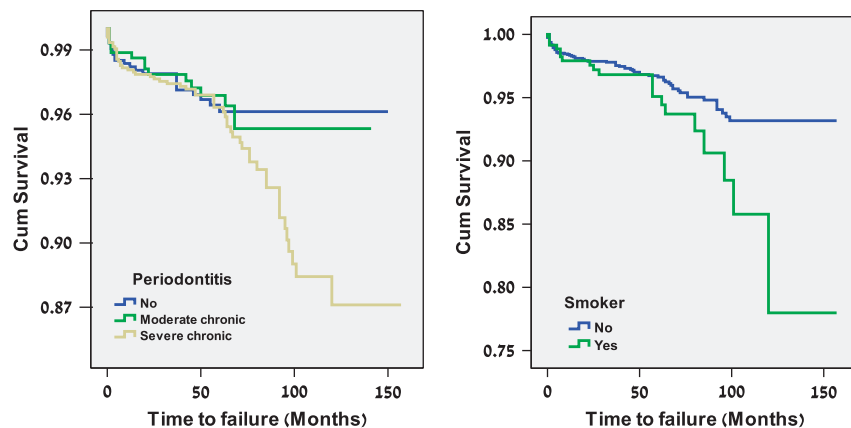


Fig. 1. Kaplan–Meier survival functions by periodontal status (left panel) and smoking status (right panel).

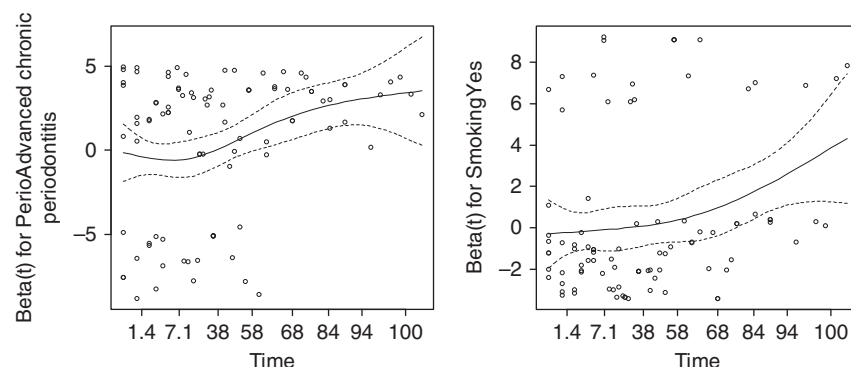


Fig. 2. Effect of advanced chronic periodontitis (left panel) and smoking (right panel) against survival time by fitting a naïve Cox regression model. The effect (Beta) is assumed to be constant in a Cox regression model (PH assumption). This should be reflected by a horizontal line. A non-horizontal line indicates a violation of the PH assumption and consequently a questionable validity for the naïve Cox regression model.

Table 4. Results of the extended Cox model* with interaction between the follow-up time at 50 months and periodontal status

Variable	Effect		PH assumption	
	hazard ratio	p-value	χ^2	p-value
Diabetes	0.85	0.66	0.45	0.50
Age(Years)	1.01	0.52	0.89	0.34
Jaw(mandible)	0.52	0.07	0.65	0.42
Moderate chronic				
$T < 50$	1.01 ⁽¹⁾	0.98	0.18	0.67
$T \geq 50$	2.43 ⁽²⁾	0.42	0.29	0.59
Severe chronic				
$T < 50$	0.93 ⁽¹⁾	0.84	0.02	0.90
$T \geq 50$	8.06 ⁽²⁾	<0.01	1.54	0.22
			Global = 3.96	0.86

*Adjustment for smoking status by stratification.

(1) Compared with the Healthy periodontal status with $T < 50$.

(2) Compared with the healthy periodontal status with $T \geq 50$.

Table 5. Results of the extended Cox model* with interaction between the follow-up time at 50 months and smoking status

Variable	Effect		PH assumption	
	hazard ratio	p-value	χ^2	p-value
Diabetes	0.853	0.670	1.1776	0.278
Age (Years)	1.006	0.540	0.8836	0.347
Jaw (mandible)	1.713	0.069	0.4323	0.511
Smoker				
$T < 50$	1.220 ⁽¹⁾	0.610	0.0339	0.854
$T \geq 50$	2.761 ⁽²⁾	0.061	0.1035	0.748
			Global = 2.4802	0.779

*Adjustment for periodontal status by stratification.

(1) Compared with a non-smoker with $T < 50$.

(2) Compared with a non-smoker with $T \geq 50$.

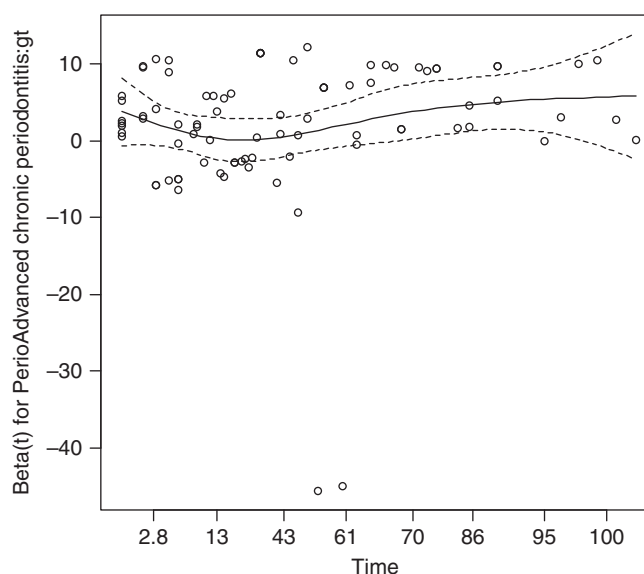


Fig. 3. Effect of advanced chronic periodontitis against survival time by fitting an extended Cox regression model. The extended Cox model include an interaction term between survival time (shorter or longer than 50 months) and periodontal status.

responsible for periodontitis and peri-implantitis supports the concept that periodontal pathogens may be associated with periimplant infections and failing implants (Karoussis et al. 2007).

The results of the present study support the evidence that long-term dental implant success might be jeopardized in patients with periodontal disease in the long run. The periodontal-associated bacteria might be related to this prolonged process of implant loss during a long-term follow-up.

There are other environmental- and patient-related factors that contribute to implant failures. Nitzan et al. (2005) reported a relationship between marginal implant bone loss and smoking habits. A higher incidence of marginal implant bone loss was found in the smoking group, which was more pronounced in the maxilla. A higher degree of complications, or implant failure rates, was found in smokers with and without bone grafts (Levin & Schwartz-Arad 2005). However, in an 18-month study of 1183 implants, Kumar et al. (2002) reported similar survival rates (97% and 94.4%) for smokers and non-smokers. In the present study, smokers exhibited a lower long-term survival rate than non-smokers. A longer follow-up time is needed in order to further assess the effect of smoking as a risk factor for implant failure. Smokers undergoing both implant-related surgical procedures and dental implantation should be encouraged by their dentists, oral and maxillofacial surgeons, or treating physicians to cease smoking, emphasizing that smoking can increase complications and reduce the success rate of these procedures.

Last but not the least, the current study demonstrates the use of advanced statistical methods in order to obtain statistically valid and efficient estimates. In the setting of oral health research, ignoring the correlation of multiple observations taken within a patient might end with wrong conclusions. The use of the Cox PH model is recommended only after ensuring that the PH assumption is not violated; otherwise, the validity of the results is questionable.

Conclusions

Periodontal status and smoking are significant risk factors for late implant failures. The HR for periodontal and smoking status are not constant through-

out the follow-up period. After 50 months, the hazard for implant failure is eight times greater for the severe periodontitis patients.

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Clinical Relevance

Scientific rationale for the study: The purpose of the present study was to compare the long-term survival rates of dental implants according to the patient's periodontal status as well as to estimate changes of hazards for failure over time.

Principal findings: This prospective cohort study design consisted of 736 patients with a total of 2336 dental implants. The overall implant success was 95.9%. Severe periodontitis patients showed higher rates of late implant failures. Until around 50 months, periodontal status is not a significant factor but after 50 months

the hazard for implant failure is eight times greater for the severe periodontitis group.

Practical implications: Periodontal status and smoking are significant risk factors for late implant failures. The HR for periodontal and smoking status are not constant throughout the follow-up period.

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