THE EFFECT OF SMOKING ON SURVIVAL AND BONE LOSS OF IMPLANTS WITH A FLUORIDE-MODIFIED SURFACE: A 2-YEAR RETROSPECTIVE ANALYSIS OF 1106 IMPLANTS PLACED IN DAILY PRACTICE.

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ABSTRACT

Aim: To compare survival and peri-implant bone loss of implants with a fluoride-modified surface in smokers and nonsmokers.

Materials and Methods: Patient files of all patients referred for implant treatment from November 2004 to 2007 were scrutinized. All implants were placed by the same experienced surgeon (BC). The only inclusion criterion was a follow-up time of at least 2 years. Implant survival and bone loss were assessed by an external calibrated examiner (SV) comparing digital peri-apical radiographs taken during recall visits with the post-operative ones. Implant success was determined according to the international success criteria (Albrektsson et al. 1986). Survival of implants installed in smokers and nonsmokers were compared using the log-rank test. Both non-parametric tests and fixed model analysis were adopted to evaluate bone loss in smokers and nonsmokers.

Results: 1106 implants in 300 patients (186 females; 114 males) with a mean follow-up of 31 months (SD 7.15; range 24-58) were included. 19 implants in 17 patients failed, resulting in an overall survival rate of 98.3% on implant level and 94.6% on patient level. After a follow-up period of 2 years, the CSR was 96.7% and 99.1% with the patient and implant as statistical unit respectively. Implant survival was significantly higher for nonsmokers compared to smokers (implant level $p = 0.025$; patient level $p = 0.017$). The overall mean bone loss was 0.34 mm (n = 1076; SD 0.65; range 0.00-7.10). Smokers lost significantly more bone compared to nonsmokers in the maxilla (0.74 mm; SD 1.07 vs 0.33 mm; SD 0.65; $p < 0.001$), but not in the mandible (0.25mm; SD 0.65 vs 0.22mm; SD 0.50; $p = 0.298$).

Conclusion: The present study is the first to compare peri-implant bone loss in smokers and nonsmokers from the time of implant insertion (baseline) to at least 2 years of follow-up. Implants with a fluoride-modified surface demonstrated a high survival rate and limited bone loss. However, smokers are at higher risk to experience implant failure and more prone to show peri-implant bone loss in the maxilla. Whether this bone loss is predicting future biological complications remains to be evaluated.

INTRODUCTION

Smoking is harmful for general health and has been associated with various diseases, such as cardiovascular diseases, cancer and respiratory diseases (Fielding et al. 1985; La Vecchia et al. 1991; Peto et al. 1996; Millar & Locker 2007).
Also, the usage of tobacco has an overwhelming impact on oral health and is associated with tooth loss, loss of attachment, vertical bone loss, dry socket and impaired wound healing after surgery (Meechan et al. 1988; Johnson & Bain 2000; Kornman & Robertson 2000; Scabbia et al. 2001; Baljoon et al. 2004; Millar & Locker 2007; Warnakulasuriya et al. 2010). Although the mechanisms are not fully understood, wound healing is disturbed due to an impaired fibroblast function, less collagen production, an impaired vasculature affecting revascularization after surgery and an impaired polymorphonuclear neutrophilic and macrophagal function (Kenney et al. 1977; MacFarlane et al. 1992; Jorgensen et al. 1998; Lehr 2000; Palmer et al. 2005).

Smoking is also known to affect the outcome of implant treatment. Several studies reported lower survival rates for implants installed in smokers (Bain & Moy 1993; Schwartz-Arad et al. 2002; Nitzan et al. 2005; Moy et al. 2005; Strietzel et al. 2007; Koldsland et al. 2009; Anner et al. 2010). Some studies show that especially the maxilla is more prone to implant failure (De Bruyn & Collaert 1994). Most of these are early failures and occur before functional loading (De Bruyn & Collaert 1994; Gorman et al. 1994; Lambert et al. 2000).
Only a limited number of studies, summarized in Table 1, have compared peri-implant bone loss in smokers and nonsmokers. Only 1 study failed to show a significant difference (Aalam & Nowzari 2005). The other 15 reported significantly better peri-implant bone levels in nonsmokers compared to smokers (Haas et al. 1996; Lindquist et al. 1996; Lindquist et al. 1997; Carlsson et al 2000; Feloutzis et al. 2003; Karoussis et al. 2004; Penarrocha et al. 2004; Wennström et al. 2004a; Wennström et al. 2004b; Galindo-Moreno et al. 2005; Nitzan et al. 2005; Schwartz-Arad et al. 2005; DeLuca & Zarb 2006; Levin et al. 2008; Vandeweghe et al. 2009).
The last decade, most of the implant companies changed the implant surface to a moderately rough surface in order to enhance the osseointegration process. Fluoride-modified implants (Osseospeed™, Astra Tech®, Möldahl, Sweden) are grit-blasted with titanium dioxide particles followed by an additional treatment with diluted fluoride acid, which results in a nanoscale surface topography (Ellingsen et al. 2004). Results from

experimental studies suggest that osseointegration is enhanced around fluoride-modified implant surfaces, especially during the first weeks of healing (Ellingsen et al.2004; Cooper et al. 2006; Berglundh et al. 2007). Enhanced osteoblast differentiation (Masaki et al. 2005; Isa et al. 2006; Cooper et al. 2006; Stanford et al. 2006; Guo et al. 2007), platelet activation and thrombogenic properties (Stanford et al. 2006; Thor et al. 2007) of the fluoride-modified surface have been reported. A recent comparative study shows that, despite smoking having an adverse effect on peri-implant bone healing, surface topography changes may affect bone-to-implant contact (d'Avila et al. 2010). This might have an effect on peri-implant bone preservation and thus on the long-term success of dental implants.

The aim of this study was to evaluate implant survival and peri-implant bone loss of implants with a fluoride-modified surface with respect to self-reported smoking habits.

MATERIALS & METHODS

Patient Selection and Clinical procedures

All patients referred for implant treatment between November 2004 and 2007 were scrutinized. Patients were asked for smoking habits as part of the medical anamnesis during intake. The only inclusion criterion was a follow-up time of at least 2 years. All implants were placed by the same experienced surgeon (BC) in healed ridges. In case of previous tooth extraction a healing time of at least 3 months was respected before implant insertion. A crestal incision was made in order to raise the flap and implants were installed according to the manufacturer's guidelines. Digital peri-apical radiographs were taken by the surgeon immediately after implant insertion (baseline) with commercially available filmholders using the parallel long-cone technique in order to visualize the implant threads and marginal bone-to-implant contact level. Hence bone loss is reported from the time of surgery. After implant treatment all patients were scheduled for professional maintenance including radiographic follow-up. The frequency and content of professional maintenance was based on the clinical situation and adapted to the individual needs of the patients. Basically this implies a recall interval of 6 or 12 months during the first years. The final restorations were made by the referring dentist.

All implants with at least 2 years of follow-up and thus participating in the professional maintenance recall system were included to evaluate implant survival and peri-implant bone

loss. An external examiner from the University of Ghent had access to the patient files. The study protocol was approved by the ethical committee of the Ghent University Hospital.

Examination Criteria and Statistical analysis

An Implant was considered a failure when it was removed because of implant mobility, loss of integration, ongoing bone loss, infection and/or persistent pain or patient discomfort (Zarb & Albrektsson 1998). An individual implant was dichotomized as either survival (value 0) or a failure (value 1) for Kaplan-Meier survival analysis. The log rank test was used to compare implant survival in smokers and nonsmokers both with the patient and the implant as statistical unit. Peri-implant bone loss was assessed by an external examiner (SV) comparing peri-apical radiographs, taken during recall visits, with the post-operative ones taken by the surgeon immediately after implant insertion using digital software (Visi-Quick®, Amsterdam, The Netherlands) with an accuracy of 0.1 mm (De Bruyn et al. 2008; Collaert & De Bruyn. 2008). Care was taken to visualize the implant threads clearly. Marginal bone level was determined both at the mesial and distal site of each implant by measuring the distance between the reference point (lower border of the smooth implant collar or the uppermost point of the microthreaded part) and the marginal bone-to-implant contact (Figure 1). These values were averaged to obtain a single value per implant (individual implant bone loss = IIBL). The reference point has been described by previous authors, using the same implant system (Åstrand et al. 2004, De Bruyn et al. 2008, Collaert & De Bruyn 2008, Van de Velde et al. 2010). The patient's bone loss (PBL) was calculated as the mean value of all IIBL's. Differences between smokers and nonsmokers were evaluated with the Mann-Whitney U-test. Moreover mixed model analysis was performed to analyze bone loss using PASW statistics 18 because of clustering of implants in patients and jaws. Therefore a logarithmic transformation of the data was performed to obtain linearity and homoskedasticity of the residuals. To evaluate the impact of time on bone loss, the Mann-Whitney U-test was adopted. Inter- and intra-examiner reliability was assessed using percent agreement within 0.2 mm deviation, Spearman correlation coefficient and the Wilcoxon signed ranks test. An individual implant was called a success when bone loss was ≤ 1.5 mm during the first year and ≤ 0.2 mm additionally per year (Albrektsson et al. 1986). The Fisher's exact test was used to compare success rates between smokers and nonsmokers.

RESULTS

IMPLANT SURVIVAL

In total 300 patients, 186 females and 114 males, with 1106 implants were evaluated (Table 2). The mean age was 56 years (SD 12.05; range 17-82). Hundred-fifty-seven patients received implants in the maxilla and 143 in the mandible. Twenty-six of them received implants in both jaws. Out of 1106 implants, 121 implants supported single crowns, 318 supported fixed partial dentures, 631 supported fixed cross-arch bridges and 18 supported overdentures. An overview of implant length and diameter is shown in table 3.

After a mean follow-up period of 31 months (SD 7.15; range 24-58), 19 implants failed (1.7%), resulting in an absolute survival rate of 98.3%. Nine failures occurred before prosthetic loading. In total, 17 patients out of 300 (5.6%) experienced implant failure. Table 4 shows cumulative survival rates (CSR). After a follow-up period of 2 years, the CSR was 96.7% and 99.1% with the patient and implant as statistical unit respectively.

Of 244 implants installed in 60 smokers, 8 implants (3.3 %) failed; of 849 implants installed in 235 nonsmokers, 11 implants failed (1.3 %) and of 5 patients with 13 implants, the smoking status was seemingly by mistake not registered into the patient record. In the smokers group, 1/139 (0.7%) implant failed in the maxilla, whereas 7/105 (6.7%) implants failed in the mandible. In the nonsmoking group, 4/502 (0.8%) implants failed in the maxilla and 7/347 (2.0%) in the mandible.

In smokers, the mandible was significantly more prone to implant loss compared to the maxilla ($p = 0.012$). This difference could not be found in nonsmokers ($p = 0.085$).

Seven out of 60 smokers (11.7%) and 10 out of 235 nonsmokers (4.3%) experienced implant failure. In detail analysis showed a significant difference comparing smokers and nonsmokers for cumulative failure rates both on patient ($p = 0.017$) (Figure 2) and implant level ($p = 0.025$) (Figure 3). Table 5 shows that individual cumulative implant failure rates in smokers affect only the maxilla. Patient cumulative failure rates were not affected by jaw location.

PERI-IMPLANT BONE LOSS

Out of 1087 surviving implants, 1076 implants in 295 patients had readable radiographs and a follow-up of at least 2 years (Table 2). Intra-examiner repeatability on bone loss was high (95 % agreement within 0.2 mm deviation; Spearman correlation coefficient 0.925, $p < 0.05$;

Wilcoxon signed ranks test p = 0.673) as was the inter-examiner variability (90 % agreement within 0.2mm of deviation; Spearman correlation coefficient 0.912, p < 0.05; Wilcoxon signed ranks test p = 0.532). After a mean follow-up of 31 months, the overall mean bone loss was 0.34 mm (SD 0.65; range: 0.00 - 7.10) and 0.33 mm (SD 0.54; range: 0.00 – 4.90) with the implant and patient as statistical unit respectively. Follow-up time of the individual implants did not influence peri-implant bone level changes (p = 0.084). An overview of bone loss values is given in Table 6. Individual Implants installed in smokers are significantly more prone to experience peri-implant bone loss compared to nonsmokers (p < 0.001) (Figure 4) with a significant difference for the maxilla (p < 0.001), but not for the mandible (p = 0,298) (Figure 5).

Implants installed in the maxilla lost significantly more bone compared with those in the mandible both for smokers (p < 0.001) and non-smokers (p < 0.001). The same is valid when the patient's bone loss was considered as statistical unit (Table 6).

This was confirmed after a logarithmic transformation of the data and fixed model analysis to correct for clustering of implants in patients and jaws. Results are given in Table 7.

IMPLANT SUCCESS

Individual implant success was calculated with respect to the follow-up time. The overall success rate, based on radiographs taken between 24 and 58 months after implant insertion was 95.0 %. A significant difference was found between smokers (89.6 %) and nonsmokers (96.5 %) (p < 0.001). Table 8 gives an overview of success rates for smokers and nonsmokers with respect to the jaw. In the maxilla, the success rate was significantly higher for nonsmokers (96.8 %) compared to smokers (87.8 %) (p < 0.001). This difference could not be found in the mandible (96.2 % vs 92.2 %; p = 0.083).

If a threshold of < 1 mm or < 2 mm of bone loss is accepted as the criterion for success, an overall success rate of 90.6 % and 95.7 % was found respectively.

DISCUSSION

This study scrutinized implant outcome in relation to smoking. Given the retrospective study design it is based on patient's records. As such it relies upon the accuracy of the record and the self-reported smoking habits of the patients. It is known from clinical studies relating

general health issues with smoking, that patients cannot be considered truthful. Some patients considerably underreport their smoking behaviour (Kandell et al.2006; Attebring et al. 2001) and biochemical techniques are necessary to objectively quantify tobacco usage. Therefore a patient was called a smoker when it was written down in the patient file, irrespective of the amount of cigarettes consumed on a daily basis. As such, the study makes no distinction between heavy or light smokers. Also tobacco usage may change over time, but we consider smoking at the time of surgery as the decisive factor influencing peri-implant bone and soft tissue healing.

Only a few clinical studies (Donati et al. 2008; Stanford et al. 2008; Toljanic et al. 2008) or abstracts (Steveling et al. 2009; Roediger et al. 2009) are available on implants with a fluoride-modified surface, showing an implant survival of 94.5 % – 100 %. Grit-blasted implants without the additional fluoride modification (TiOblast^{TM}) are well documented and show good clinical results with survival rates from 89.7 % -100 % (Cooper et al. 2008; Collaert & De Bruyn. 2008; De Bruyn et al. 2008; Al-Nawas et al. 2010). The present study reports an absolute survival rate of 98.3% after 24-58 months of follow-up, confirming the good results of the aforementioned studies. The cumulative survival calculation shows that the majority of the failures occur prior to prosthetic loading, although additional failures do occur after 2 years. Controlled long-term clinical trials to give insight in stability and prognosis of these novel implant surfaces are still lacking. Additionally this study reflects the everyday clinical practice were all implants, placed by one experienced clinician, are included.

The present study shows that smokers are 2.5 times more likely to experience implant failure, both on implant and patient level when comparing absolute survival rates. This is in accordance with a previous meta-analysis showing a risk of implant failure for smokers of 2.4 considering all included studies on implant-related data and 2.6 considering all included studies on patient-related data (Strietzel et al. 2007). Cumulative survival rates reveal a 4.0 and 3.3 times higher failure rate for smokers compared to nonsmokers on patient level and implant level respectively. In our analysis smokers showed significantly more implant failures in the mandible compared with the maxilla ($p = 0.012$). All of the failures in the mandible occurred in the posterior region. One could speculate that this may be caused by the high

bone density and deficiency of vascularization known to occur in the posterior mandible, especially in elderly and edentulous patients. (Tolstunov 2007). This in combination with the negative effect of smoking on soft tissue healing due to an impaired revascularization may compromise bone healing after implant insertion, possibly increasing the number of early implant failures (Palmer et al. 2005). Additionally, negative effects of smoking on bone metabolism and delayed fracture healing are common sense in orthopaedics (Hoogendoorn et al. 2002). Smokers require a longer healing time after fractures and will have a higher incidence of non-union of broken bones, infection and/or flap necrosis.

In the present study an overall mean bone loss of 0.34 mm was found with implant insertion as baseline value. Recent studies evaluating peri-implant bone level changes around implants with a fluoride-modified surface, reported mean bone level changes of 0.25 - 0.50 mm (Donati et al. 2008; Stanford et al. 2008; Toljanic et al. 2008). In a recent systematic review a mean value of 0.25 mm was found (Laurell & Lundgren. 2009) for grit-blasted implants without fluoride modification. The included studies reported on bone level changes from the time of prosthetic loading or second stage surgery, were the initial bone remodeling prior to prosthetic loading is not taken into account. As described by Åstrand and co-workers (2004) major changes in peri-implant bone level can take place between implant insertion and prosthetic loading. Additionally, Cooper and co-workers (2001) concluded that bone loss around early loaded implants amounted to 0.40 mm during the first six weeks of loading, while no further bone loss could be observed following the subsequent year. One could conclude that if the radiographic analysis is performed many months after implant insertion the total bone loss may be underestimated. Hence in the present study, a mean bone loss of 0.34 mm from time of implant insertion can be considered very successful.

As smoking is a systemic factor, peri-implant bone loss was analyzed on patient level. Moreover, calculation of peri-implant bone loss was also performed with the individual implant as statistical unit because a calculation on patient level may hide clinical complications when multiple implants are placed (De Bruyn & Collaert 2008; Misch et al. 2008). In the present study bone loss was 0.33 mm when calculated with the patient as statistical unit but the range decreased massively (0.00 – 7.10 mm vs 0.00 – 4.90 mm).

Indeed, one implant with extended bone loss can be masked when other implants in the same patient present no bone loss at all. Hence calculating individual peri-implant bone loss is an appropriate way to evaluate biological complications.

Findings from the present study show that the mean peri-implant bone loss is higher in smokers compared with nonsmokers. This is in accordance with other studies summarized in Table 1 whereby 15 out of 16 studies reported a significant difference. In 7 studies out of 16, separate values were not reported for smokers and nonsmokers but it was mentioned that a significant difference was observed. The difference in the present study was observed in the maxilla, but could not be found in the mandible. These results are in accordance with previous studies (Haas et al. 1996; Vandeweghe et al. 2009). This leads to the question what different effect cigarette smoking can have on the maxilla and the mandible. A possible explanation is that the mandible is partially protected by the tongue, preventing direct influences from tobacco smoke to the peri-implant tissues (Haas et al. 1996; Vandeweghe et al. 2009). This might explain the better results in the mandible, comparable to the results in nonsmokers. Moreover it is reasonable to believe, as bone quality is in generally more favorable in the mandible (Trulhar et al. 1997), that the maxilla is more subject to the pernicious effect of smoking over the years.

In the present paper an overall success rate of 95 % is found. Only 5 % of the implants lost > 1.5 mm during the first year of loading and additionally > 0.2 mm per year (Albrektsson et al. 1986). One should keep in mind that these criteria does not deal with bone remodeling before prosthetic loading, probably giving an underestimation of the success rate in this study. If we lower the threshold for success to < 1 mm of bone loss as proposed by De Bruyn & Collaert (2008), an overall success rate of 90.6 % is found. Recently, implant success was defined as < 2.0 mm of bone loss from the time of implant insertion (Misch et al. 2008). A success rate of 95.7 % was found according to the latter. Taken into account that different baseline values and different success criteria are used in literature, making a comparison between studies on implant success is extremely difficult.

Finally, surface modifications (Degidi et al. 2006; Fischer et al. 2008; Donati et al. 2008; Stanford et al. 2008; Toljanic et al. 2008) can influence bone preservation. Despite this enhanced outcome, smokers are more likely to experience implant failure and maxillary peri-

implant bone loss. A recent comparative, controlled, prospective study by Shibli and co-workers (2010) comparing bone healing in smokers and nonsmokers around implants with an anodized surface showed more marginal bone loss and fibrous tissue in smokers. Also bone-to-implant contact and bone density in the threaded area were significantly lower compared to nonsmokers. Randomized controlled trials are warranted to investigate the effect of surface modifications on long-term bone preservation in smokers.

CONCLUSION

The present study is the first to compare peri-implant bone loss in smokers and nonsmokers from the time of implant insertion (baseline) to at least 2 years of follow-up. Implants with a fluoride-modified surface demonstrated a high survival rate and limited bone loss. However, smokers are more prone to experience implant failure and show more peri-implant bone loss in the maxilla. Whether this bone loss is predicting future biological complications remains to be evaluated. Prospective studies are required to assess the dose-dependent effect of smoking on implant outcomes. In the mean time all patients should be informed about smoking cessation.

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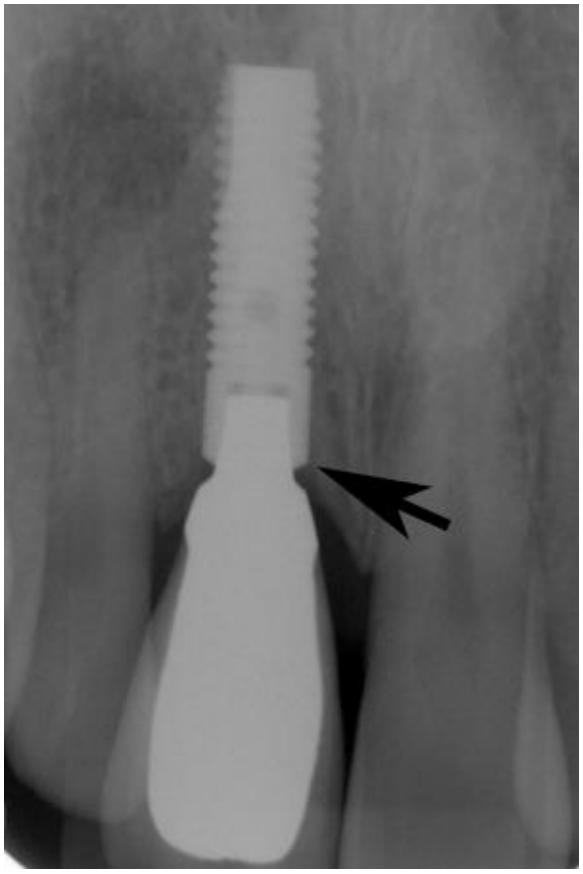

Figure 1. Reference point (lower border of the smooth implant collar or the uppermost point of the microthreaded part) indicated by black arrow.

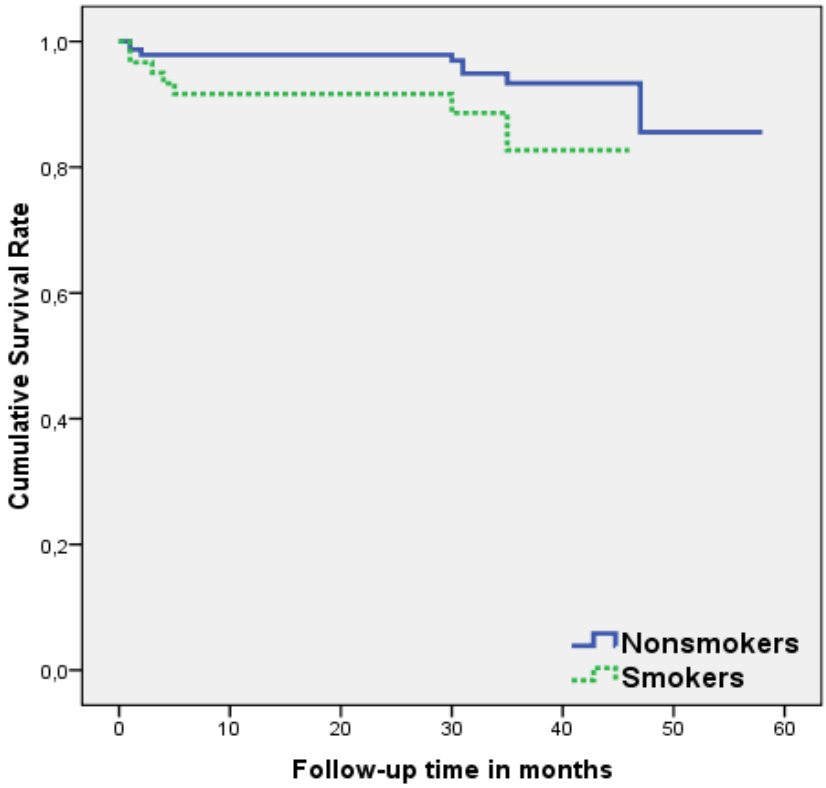

Figure 2. Kaplan-Meier Survival Curve showing estimated implant failures in function of time for smokers and nonsmokers with the patient as statistical unit.

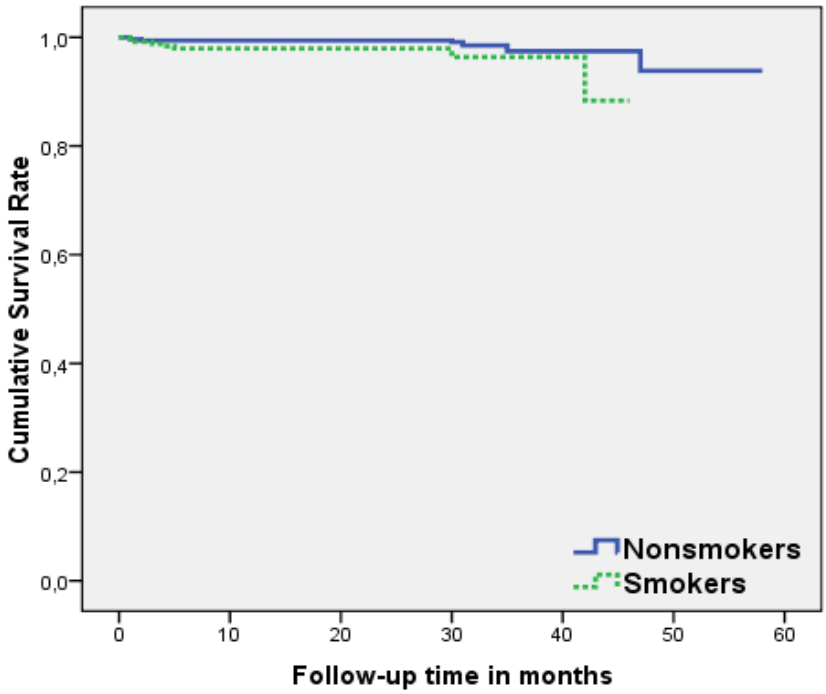

Figure 3. Kaplan-Meier Survival Curve showing estimated implant failures in function of time for smokers and nonsmokers with the implant as statistical unit.

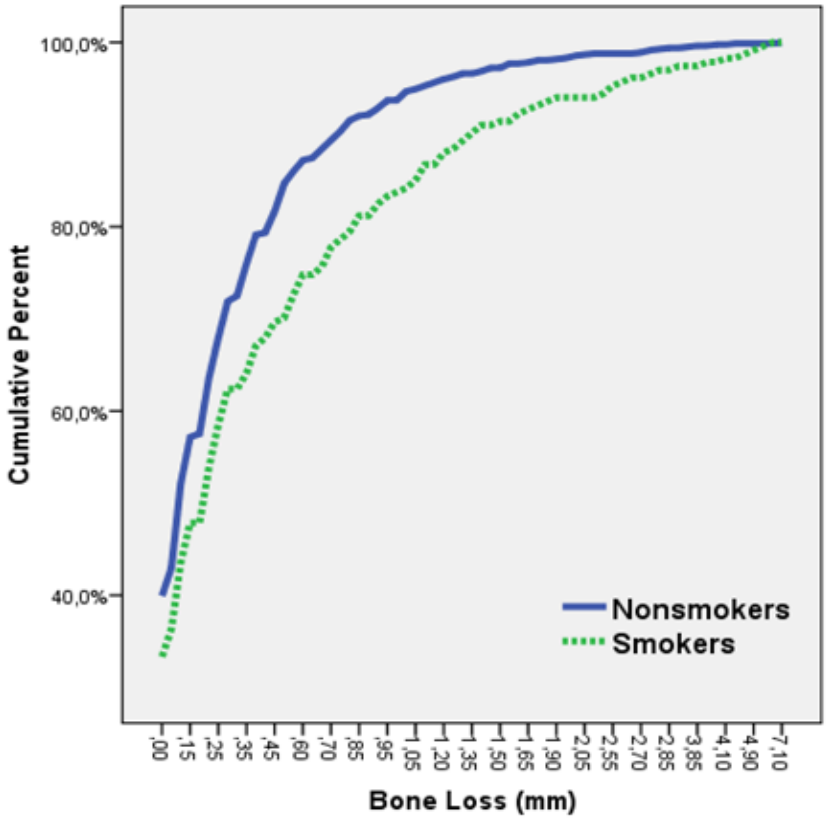

Figure 4. Cumulative percentage of individual peri-implant bone loss based on available radiographs (n=1076), smokers (n = 234) compared to nonsmokers (n = 829).

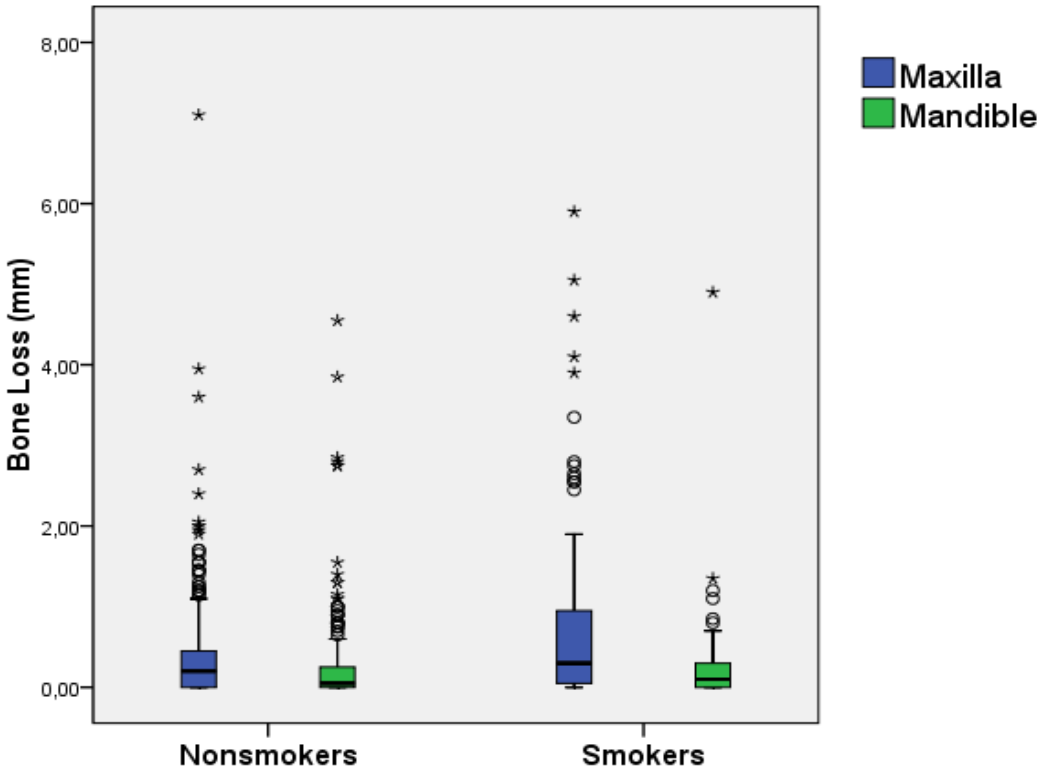

Figure 5. Boxplot presenting individual peri-implant bone loss in smokers and nonsmokers after at least 2 years, comparing maxilla (n = 492 in nonsmokers; n = 137 in smokers) and mandible (n = 337 in nonsmokers; n =97 in smokers).

Authors	*Study Design*	*Observation period*	*Samples*	*Baseline/Reference Point*	*Bone Loss/Bone Level Changes*	*p-value*
Haas et al. (1996)	Retrospective	22 months	366 implants in 107 smokers 1000 implants in 314 nonsmokers	Prosthetic loading	Smokers maxilla: 3.95 mm mandible 1.47 mm Nonsmokers maxilla 1.65 mm mandible 1.53 mm	< 0.01*
Lindquist et al. (1996)	Prospective	15 years	278 implants in 47 patients	Prosthetic loading	Not reported separately	< 0.001*
Lindquist et al. (1997)	Prospective	10 years	266 implants in 45 patients	Prosthetic loading	Smokers 1.30 mm Nonsmokers 0.65 mm	< 0.001*
Carlsson et al.(2000)	Prospective	15 years	273 implants in 44 patients (21 smokers)	Prosthetic loading	Not reported separately	< 0.001*
Feloutzis et al. (2003)	Prospective	5.6 years	182 implants in 90 patients	Prosthetic loading	Nonsmokers 0.18 mm Smokers (heavy) 1.98 mm	< 0.02*
Karoussis et al. (2004)	Prospective	10 years	179 implants in 89 patients	1 year	Not reported separately	< 0.001*
Penarrocha et al. (2004)	Retrospective	1 year	47 implants in 16 smokers 61 implants in 26 nonsmokers	Prosthetic loading	Not reported separately	< 0.01*
Wennström et al. (2004)	Prospective	5 years	149 implants in 51 patients (34 nonsmokers, 17 smokers)	Prosthetic loading	Smokers 0.76 mm Nonsmokers 0.22mm	= 0.022*
Wennström et al. (2004)	Prospective	5 years	47 patients (15 smokers, 32 nonsmokers)	Prosthetic loading	Not reported separately	< 0.05*
Galindo-Moreno et al. (2005)	Prospective	3 years	514 implants in 185 patients (63 smokers)	Prosthetic loading	Smokers 1.36 mm Nonsmokers 1.25 mm	<0.02*
Nitzan et al. (2005)	Retrospective	42.9 months 48.4 months	271 implants in 59 smokers 375 implants in 102 nonsmokers	Implant exposure	Smokers 0.15 mm Nonsmokers 0.05 mm	= 0.001*
Aalam & Nowzari. (2005)	Retrospective	2 years	198 implants in 74 patients	Abutment-fixture interface	Not reported separately	> 0.05
Schwartz-Arad et al. (2005a)	Retrospective	37.9 months	50 implants in 8 smokers 227 implants in 53 nonsmokers	Implant exposure	Not reported separately	< 0.001*
DeLuca & Zarb. (2006)	Retrospective	1-20 years	767 implants in 235 patients	Prosthetic loading	Smokers 0.073 mm / year Nonsmokers 0.041 mm / year	= 0.010*
Levin et al. (2008)	Retrospective	1-14 years	64 implants in 64 patients	Implant exposure	Not reported separately	= 0.016*
Vandeweghe et al. (2009)	Retrospective	12 months	60 implants in 21 smokers 303 implants in 148 nonsmokers	Abutment-fixture interface	Smokers 1.56 mm Nonsmokers 1.32 mm	= 0.001*

*Table 1. Overview of studies comparing peri-implant bone loss is smokers and nonsmokers. * Statistically significant difference was found between smokers and nonsmokers.*

Implant Survival group			**Implant bone loss group**	
Implants	*Patients*		*Implants*	*Patients*
1106 (19)	300 (17)	***Total***	1076	295
244 (8)	60 (7)	***Smokers***	234	60
849 (11)	235 (10)	***Nonsmokers***	829	230
13	5	***Unknown smoking status***	13	5
648 (5)	170 (5)	***Maxilla***	636	168
458 (14)	156 (12)	***Mandible***	440	151

Table 2.Implant and patient distribution with respect to smoking status and jaw. Failures are given between brackets.

		Length (mm)					
		8.00	**9.00**	**11.00**	**13.00**	**15.00**	**17.00**
Diameter	**3.50**	37 (3)	24 (2)	26	110 (2)	87	0
(mm)	**4.00**	36 (2)	33 (1)	39 (1)	133 (1)	192 (1)	8 (1)
	4.50	0	30 (1)	12	67	48	0
	5.00	0	32	17 (2)	28 (1)	40	0

Table 3. Implant distribution according to implant length and diameter. Failed implants are given between brackets.

	IMPLANT						PATIENT					
	Smokers		Nonsmokers		Overall		Smokers		Nonsmokers		Overall	
	Failures	CSR	Failures	CSR	Failures	CSR	Failures	CSR	Failures	CSR	Failures	CSR
0-5m	5(244)	98,00%	5(849)	99,40%	10(1106)	99,10%	5(60)	91,70%	5(235)	97,90%	10(300)	96,70%
6-11m	0(239)	98,00%	0(844)	99,40%	0(1096)	99,10%	0(55)	91,70%	0(230)	97,90%	0(290)	96,70%
12-17m	0(239)	98,00%	0(844)	99,40%	0(1096)	99,10%	0(55)	91,70%	0(230)	97,90%	0(290)	96,70%
18-23m	0(239)	98,00%	0(844)	99,40%	0(1096)	99,10%	0(55)	91,70%	0(230)	97,90%	0(290)	96,70%
24-29m	0(239)	98,00%	0(844)	99,40%	0(1096)	99,10%	0(55)	91,70%	0(230)	97,90%	0(290)	96,70%
30-35m	2(124)	96,40%	5(364)	97,40%	7(499)	95,80%	1(30)	88,60%	4(108)	93,30%	5(142)	91,30%
36-41m	0(48)	96,40%	0(148)	97,40%	0(202)	95,80%	0(13)	88,60%	0(53)	93,30%	0(68)	91,30%
42-47m	1(12)	88,30%	1(51)	93,80%	2(67)	92,20%	1(4)	82,70%	1(21)	85,60%	2(26)	83,70%
48-53m	0(0)	88,30%	0(19)	93,80%	0(19)	92,20%	0(0)	82,70%	0(9)	85,60%	0(9)	83,70%
54-58m	0(0)	88,30%	0(2)	93,80%	0(2)	92,20%	0(0)	82,70%	0(2)	85,60%	0(2)	83,70%
	smokers vs nonsmokers: p = 0.025						smokers vs nonsmokers: p = 0.017					

Table 4. Overview of failures and cumulative survival rates in smokers and nonsmokers.
The total number of patients/implants at the start of the follow-up period is given between brackets.

	IMPLANT								PATIENT							
	Smokers				Nonsmokers				Smokers				Nonsmokers			
	Maxilla		Mandible		Maxilla		Mandible		Maxilla		Mandible		Maxilla		Mandible	
	Failures	CSR	Failures	CSR	Failures	CSR	Failures	CSR	Failures	CSR	Failures	CSR	Failures	CSR	Failures	CSR
0-5m	1(139)	99,30%	4(105)	96,20%	3(502)	99,40%	2(347)	99,40%	3(31)	90,30%	5(35)	85,70%	3(136)	97,80%	2(118)	98,30%
6-11m	0(138)	99,30%	0(101)	96,20%	0(499)	99,40%	0(345)	99,40%	0(28)	90,30%	0(30)	85,70%	0(133)	97,80%	0(116)	98,30%
12-17m	0(138)	99,30%	0(101)	96,20%	0(499)	99,40%	0(345)	99,40%	0(28)	90,30%	0(30)	85,70%	0(133)	97,80%	0(116)	98,30%
18-23m	0(138)	99,30%	0(101)	96,20%	0(499)	99,40%	0(345)	99,40%	0(28)	90,30%	0(30)	85,70%	0(133)	97,80%	0(116)	98,30%
24-29m	0(138)	99,30%	0(101)	96,20%	0(499)	99,40%	0(345)	99,40%	0(28)	90,30%	0(30)	85,70%	0(133)	97,80%	0(116)	98,30%
30-35m	0(65)	99,30%	2(59)	92,90%	0(224)	99,40%	5(140)	94,20%	0(13)	90,30%	1(19)	77,90%	3(63)	91,70%	4(55)	89,30%
36-41m	0(17)	99,30%	0(31)	92,90%	0(93)	99,40%	0(55)	94,20%	0(4)	90,30%	0(9)	77,90%	0(30)	91,70%	0(26)	89,30%
42-47m	0(7)	99,30%	1(5)	74,30%	1(36)	93,90%	0(15)	94,20%	0(1)	90,30%	0(2)	77,90%	1(14)	80,30%	0(7)	89,30%
48-53m	0(0)	99,30%	0(0)	74,30%	0(14)	93,90%	0(5)	94,20%	0(0)	90,30%	0(0)	77,90%	0(7)	80,30%	0(2)	89,30%
54-58m	0(0)	99,30%	0(0)	74,30%	0(2)	93,90%	0(0)	94,20%	0(0)	90,30%	0(0)	77,90%	0(2)	80,30%	0(0)	89,30%
	p = 0.012				p = 0,085				p = 0,447				p = 0,929			

Table 5. Overview of failures and cumulative survival rates in smokers and nonsmokers with respect to the jaw.
The total number of patients/implants at the start of the follow-up period is given between brackets.

IMPLANT	***nonsmoker***	***smoker***	***p value***
Maxilla + Mandible	0,29 mm n=829 (SD 0.54) range: 0.00 - 7.10	0,53 mm n = 234 (SD 0.92) range: 0.00 - 5.90	p < 0.001*
Maxilla	0,33 mm n=492 (SD 0.65) range: 0.00 - 7.10	0,74 mm n = 137 (SD 1.07) range: 0.00 - 5.90	p < 0.001*
Mandible	0,22 mm n=337 (SD 0.50) range: 0.00 - 4.55	0,25 mm n = 97 (SD 0.56) range: 0.00 - 4.90	p = 0.298
p value	p < 0.001*	p < 0.001*	
PATIENT			
Maxilla + Mandible	0,30 mm n = 235 (SD 0.65) range: 0.00 - 4.90	0.46 mm n = 65 (SD 0.56) range: 0.00 - 2.80	p = 0.009*
Maxilla	0,33 mm n = 135 (SD 0.53) range: 0.00 - 4.90	0.61 mm n = 31 (SD 0.66) range 0.00 - 2.80	p = 0.008*
Mandible	0,27 mm n = 117 (SD 0,58) range 0.00 - 4,20	0.32 mm n = 34 (SD 0.43) range 0.00 - 1.58	P = 0.097
p value	p < 0.001*	p = 0.020*	

Table 6. Overview of individual peri-implant bone loss values and patient's bone loss values in smokers and nonsmokers with respect to the jaw.
* Statistically significant at 0.05 level with Mann-Whitney U-test.

	Value	95 % CI	SE	p-value		Value	95 % CI	SE	p-value
Intercept	-1.90		0.15			-1.60	-1.74 /-1.45	0.07	
Maxilla	0.83	0.45/1.20	0.19	0.000		0[a]		0	
Mandible	0[a]		0			-0.45	-0.65/-0.24		0.000
Nonsmoker	-0.15	-0.49/0.18	0.17	0.378		0[a]		0	
Smoker	0[a]		0			0.52	0.20/0.85		0.001
Maxilla * Nonsmoker	-0.37	-0.80/-0.05	0.22	0.84		0[a]		0	
Maxilla * Smoker	0[a]		0			0[a]		0	
Mandible * Nonsmoker	0[a]		0			0[a]		0	
Mandible * Smoker	0[a]		0			-0.37	-0.80/-0.05	0.22	0.084

Table 7. Fixed model analysis after logarithmic transformation of the bone loss data. Parameters set to zero as reference (a).

	Nonsmoker	Smoker	p-value
Maxilla + Mandible	96,50%	89,60%	< 0.001*
Maxilla	96,80%	87,80%	< 0.001*
Mandible	96,20%	92,20%	= 0.083
p-value	= 0.402	= 0.181	

Table 8. Overview of implant success rates in smokers and nonsmokers with respect to the jaw.

*Statistically significant at 0.05 level with the Fisher's Exact Test