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Ministry of Higher Education
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University of Baghdad
College of Dentistry

Smoking effects on Dental Implant and surrounding structures

A Project Submitted to
The College of Dentistry, University of Baghdad,
Department of Periodontology in Partial Fulfillment for the
Bachelor of Dental Surgery

By
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Certification of the Supervisor

I certify that this project entitled "Smoking effects on Dental Implant and surrounding structures " was prepared by the fifth-year student Ahmed Ali Abdulrazak under my supervision at the College of Dentistry/University of Baghdad in partial fulfilment of the graduation requirements for the Bachelor Degree in Dentistry.

Dedication

Thanks to God Almighty my creator, my strong pillar, my source of inspiration, wisdom, knowledge and understanding. He has been the source of my strength throughout this program and on His wings only have I soared. Thanks to my supervisor (Prof. Dr. Saif Sehaam Saliem) for his support and help to complete my graduation project. my beloved father, To the prayer of my sunshine, my superwoman, my model, My beloved Mother, To all my family member whom lived this long journey with me, To all teachers, and every person leaved impact in me, and especially, For all my friends, Whom where always there for me, I dedicate my graduation project.

Your sincere son, student and friend
Ahmed Ali Abdulrazak

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OR	odds ratio
Sa	arithmetic mean height
BC	British Columbia
SW	Sweden
N	number of patients entering the interval
ICC	intraclass correlation coefficient
SD	Standard deviation
CSR	cumulative survival rate
HR	hazard ratio
CI	confidence interval
P	probability for a given statistical model
BOP	bleeding on probing
PID	peri- implant disease
NS	Nonsmokers
S	Smokers
Y	Yes
N	No
MBL	marginal bone loss

Introduction:

One in five adults in the world smokes tobacco, despite the fact that negative effects on oral and general health are well known. Every seventh death in the world (13%) was the result of direct smoking in 2017; a further 2% was the result of secondhand smoke.
This means 15%—close to 1-in-6 deaths—was the result of tobacco. However, since 1990, there is a declining global trend in smoking reflected almost everywhere across the world **[Roser, M.; Ritchie, H. Smoking 2020].**

Smoking shows an overwhelmingly negative influence on oral health, affecting both soft and hard tissues. It is known as an important risk indicator for poor oral wound healing, dry socket, implant failure, and marginal bone loss around teeth and implants **[Millar, W.J.; Locker, D. Smoking and oral health status.2007].**

In regard to dental implants, a significant relationship has been shown between smoking and the risk of failure of osseointegrated implants, more particularly in the upper jaw **[Hinode, D.; Tanabe, S.; Yokoyama, 2006]**.

Smoking seems to have an early effect on osseointegration, dependent on the properties of the implant surface and local host genetic responses. It is also suggested that smokers, compared to non-smokers, have an altered bone structure and composition **[Sayardoust, S.; Omar, O.; Thomsen, 2017]**.

Using multilevel analysis, including early as well as late implant loss, smoking has been associated with a significantly higher percentage of early lost implants (2.2%) in comparison to non-smoking (0.9%). Late implant failure seems not to be affected by smoking habits **[Derks, J.; Hakansson, J.; Wennstrom, J.L.; M.; Berglundh, 2015]**.

A systematic review has shown a higher risk for implant failure in smokers with a patient-related odds ratio of 2.64 and an implant-related odds ratio of 2.25 **[Cochran, D.L.; Nummikoski, P., J.D.; Jones, 2009]**.

Another systematic review shows an average implant survival ranging between 65.3%–97% for smokers versus 82.7%–98.8% for non-smokers. A statistically significant difference in favor of non-smokers has also been found with an OR of 1.96 for implant failure **[Moraschini, V.; Barboza, 2016]**.

Cigarette smoking is associated with a reduction in bone mineral density in a dose-related and duration-related manner **[Yoon, V.; Maalouf, N.M.; Sakhaee, 2012]**.

A higher incidence of marginal bone loss is found for smokers with subsequent years.

Smokers show more than two times greater marginal bone loss and more than three times greater risk for implant loss in the maxilla **[Vervaeke, S.; Collaert, B.; Vandeweghe, E.; De Bruyn, 2012]**.

Vervaeke et al. (2015) showed an estimated additional bone loss of 1.18 mm for smokers vs. non-smokers **[Vervaeke, S., B.; Cosyn, J.; Deschepper, 2015]**.

A uni- and multivariate analysis has identified smoking as a significant factor affecting implant treatment outcomes, especially in the maxilla.

Over the last decade, implants surfaces have been modified from smooth/rough to moderately rough surface texture, expressed by an average Sa value of 1–2 μm **[Van de Velde, T.; Collaert, B.; Sennerby, L.; De Bruyn, 2010]**.

This evolution in surface topography has positively affected the bone-to-implant contact, even in smoking patients **[d'Avila, S., L.D.; Piattelli, A.; Aguiar, K.C.; de Faveri, 2010]**.

In 2004, a fluoride-modified surface was introduced (OsseospeedTM, Dentsply, Astra Tech, Mölndal, Sweden), with a moderately rough surface with nanoscale topography (Sa value of (1.32–1.82 μm)). A number of animal and human studies have been carried out to evaluate clinical performance.

The results have suggested that osseointegration has been enhanced (especially during the first weeks of healing), by enhanced osteoblast differentiation, platelet activation, and surface thrombogenic and osteoconductive properties **[Thor, A.; Rasmusson, L.; Wennerberg, P.; Hirsch, B.; Hong, 2007]**.

This attributes to improved survival rate, esthetic outcome, and marginal bone remodeling **[Collaert, B.; Wijnen, L.; De Bruyn, 2011]**.

Even more challenging situations show good short-term results with limited marginal bone loss and high implant survival like heavy alveolar atrophied ridges with augmentation **[Pieri, Bianchi, A.; Corinaldesi, G.; Marchetti, 2012]** and smoking patients **[d'Avila, S., L.D.; Piattelli, A.; Aguiar, K.C, M.; Borges, F.L.; Iezzi, 2010]**.

Aim of study:

The purpose of the present study was to evaluate the 10 years' survival and success of implants with a fluoride-modified surface in smokers and non-smokers treated under daily clinical and non-specifically selected conditions. **(Simon Windael, Stijn Vervaeke, Stefanie De Buyser, Hugo De Bruyn and Bruno Collaert,2020)**.

To analyze all pertinent literature, including systematic reviews, clinical trials, and long-term follow- up, to evaluate smoking as a real risk factor for periimplant diseases. **(Priscila Ladeira Casado, Telma Aguiar, Marina Prado Fernandes Pinheiro, 2022)**.

To describe the relationship between cigarette smoking and implant-related surgical procedures (i.e., sinus lift operations, bone grafts, and dental implantations), including the incidence of complications related to these procedures, and long- term survival and success rates of dental implants among smokers and nonsmokers. **(Liran Levin, Devorah Schwartz-Arad,2018)**.

To identify the risk of complications (eg, implant loss, infection, peri-implantitis, and mucositis) in a group of patients treated with osseointegrated implants and to assess the effect of smoking on this risk. **(Oscar Francisco Rodriguez-Argueta ,2011)**.

Chapter One

Review

1.1. The Long-Term Effect of Smoking on 10 Years Survival and Success of Dental Implants

1.1.1. Patient Selection and Clinical Procedure

All patients in need of implant placement between November 2004 and 2007 were evaluated. During intake and at the 10-year follow-up session, a medical history was taken, including self-reporting of smoking habits. The initial 2-years report was presented previously **[Vervaeke, S.; Collaert, B.; Vandeweghe, E.; De Bruyn, 2012]**.

The same surgeon (BC) placed all implants in healed ridges. No bone grafting, sinus lift, or guided bone regeneration procedures were used. Implants were placed using different surgical techniques (one-stage and two-stage surgery) and different loading protocols (immediate versus delayed loading). Hence, 3 types of protocols were performed: immediate loading, one-stage delayed loading, and two-stage delayed loading.

Surgery consisted of a crestal incision, followed by full mucoperiosteal flap elevation, implant installation (OsseospeedTM, Dentsply, Astra Tech, Mölndal, Sweden), following the manufacturer's guidelines and suturing. Implant installation was immediately followed by radiographs (baseline) with commercially available film-holders (Uni-Bite Film HolderTM, Dentsply, York, PA, USA) using the parallel long-cone technique to visualize marginal bone-to-implant contact points and implant threads. Care was taken to shoot

perpendicular on the implant axis. The individualization of standard film holders was not manageable in private practice.

To determine marginal bone levels correctly, the digital images were magnified by the software.
Hence, bone loss beyond the reference point was reported from the time of surgery, and initial bone remodeling was included in the total bone level changes over time. After the final restorations were made by the referring dentist, a professional maintenance schedule (including radiographic follow-up) was proposed to each patient, whereby the frequency was based on the clinical situation and individual needs. Given the fact that the patients were referred by and, therefore, returned to their original dentist, only patients that maintained their visits at the specialist clinic were included in the current study. These patients were prospectively followed up for at least 10 years. Briefly, this consisted of a recall interval of 6 or 12 months during the first 2 years and 12 or 24 months during the following years. All implants with at least 10 years of follow-up and part of the professional maintenance recall system of the specialist center were included to evaluate implant survival and peri-implant bone loss.

An independent external examiner (SW) from the University of Ghent performed the recall consultation at the 10 years' follow-up and had access to the patient files. All patients were thoroughly informed and signed a written consent form.

1.1.2. Examination Criteria

Smoking was defined as the smoking of at least 1 cigarette a day and was based on self-reporting. Ex-smokers and non-smokers were combined into the group of non-smokers. A history of periodontitis was based on the following criteria: (a) radiographic proof of bone loss extending 33% of the root length of residual teeth at the time of referral; (b) patients who were treated with (non)surgical periodontal treatment before implant therapy; (c) when before implant treatment, hopeless teeth were extracted due to periodontitis; (d) edentulous patients with evidence of periodontitis at the time of referral based on radiographs obtained in retrospect from the referring dentist.

Periapical radiographs were analyzed with the use of digital Software with an accuracy of 0.1 mm. These were taken from the day of surgery up to at least 10 years in function. The crestal bone level was calculated at both mesial and distal sites of each implant by measuring the distance between the reference point (lower border of the smooth implant collar) to the first marginal bone-to-implant contact (Figure 1).

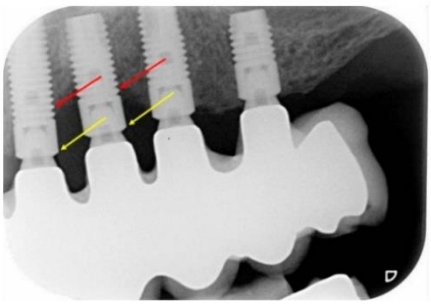


Figure 1. The yellow arrow points to the reference point (lower border of the smooth implant collar). The red arrow shows the first bone-to-implant contact. The distance in between was measured with digital software. **(J. .Clin. Med. 2020, 9, 1056)**

Bone loss beyond the reference point was calculated by comparing peri-apical radiographs taken during recall visits after 3 months, 1, 2, and 10 years with baseline (implant installation). The mean of both bone level readings (mesial and distal) was calculated to obtain a single value per implant. Plaque- and bleeding assessment was performed at six sites **[Mombelli, A.; Lang, 2000 1994]**.

Pocket probing was performed manually with a periodontal probe (CP 15 UNC, Hu-Friedy Mfg. Co. Inc, Chicago, IL, USA) at 6 sites of the implant, immediately followed by the scoring of bleeding on probing. An implant was considered as a failure when it was removed due to the following reasons: implant mobility, loss of integration, ongoing bone loss, infection, persistent pain, or patient discomfort **[Albrektsson, T.; Zarb, 1998]**.

An individual implant was considered a success when total bone loss beyond the reference point, from the placement of the implant to 10 years of follow-up, was less than 1 or 2 mm **[Sanz, M.; Chapple, 2012]**.

Incidence of peri-implantitis of the implants under maintenance after 10 years was calculated based on the Consensus report of the 4th workgroup of the 2017 World Workshop on the classification of periodontal and peri-implant diseases and conditions, by combining a total bone loss ≥3 mm with increasing probing depth ≥6 mm and bleeding/suppuration on location **[Berglundh, T.; Armitage, G.; Araujo, 2018]**.

The survival of the implant, the peri-implant bone loss, and the pocket probing depth were accounted as the dependent variable2.3

1.1.3 Implant Survival

For survival analysis at the patient level, we only included patients who had at least one implant with ≥ 10 year-follow-up (n = 121). For survival analysis at the implant level, we only included implants from patients who had at least one implant with ≥ 10 year-follow-up and with known observation time (n = 453). Kaplan–Meier estimates of implant survival at the patient level were compared between smokers and non-smokers with the log-rank test.

The estimated survival rates at 1, 2, 5, and 10 years were reported together with the 95% confidence intervals, which were calculated using the "log-log" approach.

Hazard estimates of implant loss at the implant level were compared between smokers and non-smokers, overall and per jaw using the Robust Score test for a simple Cox proportional hazards model. Robust standard errors were estimated to take into account the clustering of implants within patients.

The estimated survival rates at 1, 2, 5, and 10 years were reported together with the 95% confidence intervals—calculated using the "log-log" approach.

These confidence intervals didn't take into account the clustered design. A multiple Cox proportional hazards model—for smoking status, jaw, and their two-way interaction—was fitted with robust estimation of the standard error to take into account the clustering of implants within patients. Robust Wald 95% confidence intervals and corresponding p-values were reported.

Life tables (Tables 1-3) show the number of implant loss and the total number of implants at risk for implant loss as well as the cumulative survival rate for each year interval. Those were presented as overall, according to smoking status and according to both smoking status and jaw.

Table 1. Life table showing an overview of failures and the overall cumulative survival rate on the implant level.

Year Interval	Number of Implant Loss	Number of Implants Entering the Interval	Cumulative Proportion Surviving at the End of the Interval
0	8	453	0.98
1	0	445	0.98
2	2	445	0.98
3	1	443	0.98
4	2	442	0.97
5	2	440	0.97
6	6	438	0.95
7	2	432	0.95
8	3	429	0.94
9	1	421	0.94
10	6	397	0.91

Table 2. Life table showing an overview of failures and the overall cumulative survival rate on the patient level.

Year Interval	Number of Patients with Implant Loss	Number of Patients Entering the Interval	Cumulative Proportion Surviving at the End of the Interval
0	7	121	0.94
1	0	114	0.94
2	1	114	0.93
3	1	113	0.93
4	1	112	0.92
5	1	111	0.91
6	5	110	0.87
7	1	105	0.86
8	1	103	0.85
9	1	102	0.84
10	2	96	0.81

Table 3. Life table showing a summary of failures and the overall cumulative survival rate (CSR) in non-smokers and smokers with respect to the jaw (on the implant level).

Year Interval	Non-Smokers						Smokers					
	Mandible			Maxilla			Mandible			Maxilla		
	Number of Implant Loss	Number Entering Interval	CSR	Number of Implant Loss	Number Entering Interval	CSR	Number of Implant Loss	Number Entering Interval	CSR	Number of Implant Loss	Number Entering Interval	CSR
0	5	146	0.97	3	231	0.99	0	35	1	0	41	1
1	0	141	0.97	0	228	0.99	0	35	1	0	41	1
2	2	141	0.95	0	228	0.99	0	35	1	0	41	1
3	0	139	0.95	0	228	0.99	1	35	0.97	0	41	1
4	0	139	0.95	0	228	0.99	0	34	0.97	2	41	0.95
5	0	139	0.95	1	228	0.98	0	34	0.97	1	39	0.93
6	1	139	0.95	3	227	0.97	0	34	0.97	2	38	0.88
7	2	138	0.93	0	224	0.97	0	34	0.97	0	36	0.88
8	0	136	0.93	1	223	0.97	1	34	0.94	1	36	0.85
9	0	136	0.93	1	222	0.96	0	28	0.94	0	35	0.85
10	3	124	0.89	0	210	0.96	1	28	0.88	2	35	0.76

1.1.4 Peri-Implant Bone Loss (mm)

Intra- and inter-examiner reliability was evaluated using the intraclass correlation coefficient (ICC) based on a two-way random model with absolute agreement.

The observed mean, standard deviation, minimum, and maximum were used to describe bone loss beyond the reference point in several subgroups at different time points.

Cumulative frequencies of bone loss in mm were plotted for different time intervals. Lower curves would have a smaller proportion of bone loss <2 mm than higher curves and, hence, more bone loss. Cumulative frequencies of bone

loss in mm were plotted for smokers and non-smokers. For the analyses at the implant level, a linear mixed model for bone loss in mm was fitted with a random intercept for the patient to account for multiple implants within a patient and with smoking status, jaw, and their two-way interaction as fixed effects.

Estimated marginal means at the original target scale for smoking status and for smoking status jaw was requested together with the pairwise comparisons. No test was performed to compare mean bone loss at the patient level between smokers and non-smokers because the residuals were not normally distributed, and, unlike with the analysis at the implant level, one could not solely rely on the central limit theorem due to the smaller sample size.

A non-parametric test would compare the mean rank between smokers and non-smokers, instead of comparing the actual mean.

1.1.5 Implant Success

Implant success was defined in two ways: Firstly, as ≤1 mm bone loss after 10 years, and, secondly, as ≤2 mm bone loss after 10 years.

For analysis at the implant level, a generalized linear mixed model with a binomial distribution and logit link for implant success was fitted with a random intercept for the patient and with smoking status, jaw, and their two-way interaction as fixed effects.

Estimated marginal means at the original target scale for smoking status and for smoking status jaw was requested together with the pairwise comparisons. For the analyses at the patient level, Fisher's exact test was used to test for a difference in the proportion of implant success between smokers and non-smokers.

1.1.6 Peri-Implant Health (Implant Level)

Mean bleeding on probing (at the time of recall visit) and mean probing pocket depth were calculated. The possibility of a statistically significant difference was examined by non-parametric testing (Mann–Whitney U test).

Peri-implant mucositis was identified as the presence of bleeding and/or suppuration on gentle probing with or without increased probing depth compared to previous examinations and absence of bone loss beyond crestal bone level changes resulting from initial bone remodeling.

Peri-implantitis was defined as loss of crestal bone with time ≥3 mm, suppuration, and/or bleeding on probing, with or without increasing probing pocket depth ≥6 mm **[Berglundh, T.; Armitage, P.M.; Chen, S.; Cochran, 2018]**.

A generalized linear mixed model with a binomial distribution and logit link for peri-implantitis was fitted with a random intercept for the patient and with smoking status, jaw, and their two-way interaction as fixed effects. Estimated marginal means at the original target scale for smoking status and for smoking status jaw was requested together with the pairwise comparisons.

1.1.7 Patient Population

Of the original 300 patients included in the previous report (Vervaeke et al 2012), 81 patients had never been maintained in the specialist clinic and had returned to their own dentist for regular maintenance, 6 maintained patients had passed away, and 72 had ignored maintenance over time at the specialty clinic

and returned to their referring dentist or indicated not to participate in the proposed recall program.

In total, 141 patients were cooperative and compliant with the maintenance program and were invited for the research assessment, and 121 responded positively (drop-out 14.2%). Forty-eight were male, and 73 were female, with a mean age of 65.2 years (SD 11; range 31–88). An overview of the distribution of implant length and diameter, with notification of implant loss, is shown in Table 4.

Table 4. Implant distribution according to implant diameter and length (implant failure is given between brackets).

Diameter (mm)	Length (mm)						
	8	9	11	13	15	17	Total
3.5	19 (3)	4 (0)	18 (2)	37 (0)	35 (1)	0 (0)	113 (6)
4	28 (3)	16 (1)	26 (0)	49 (8)	77 (4)	8 (3)	204 (19)
4.5	7 (0)	19 (4)	11 (0)	22 (0)	18 (1)	0 (0)	77 (5)
5	2 (0)	22 (1)	14 (2)	12 (0)	9 (0)	0 (0)	59 (3)
Total	56 (6)	61 (6)	69 (4)	120 (8)	139 (6)	8 (3)	453 (33)

J. Clin. Med. 2020,

Of the total of 121 patients, 43 had single crowns, 51 had fixed partial dentures, 24 had fixed cross-arch bridges, 2 had overdenture on locators, and 1 patient had an overdenture on a bar-structure.

On the implant level, 67 implants supported single crowns, 180 supported fixed partial dentures, 200 supported fixed cross-arch bridges, 4 supported overdentures on locators, and 2 implants supported an overdenture on a bar-structure.

Only one patient, a non-smoker, had diabetes (regulated with medication), and one patient started oral bisphosphonates during follow-up, several years after implant treatment.

Smokers showed significantly higher compliance compared to non-smokers (p = 0.001Clin

1.1.8 Implants Survival

After a mean follow-up time of 11.38 years (SD 0.78; range 10.00-13.65), 33 implants out of 453 initially placed had failed in 21 patients. An absolute survival rate of 92.7% and82.6% on the implant and patient levels was seen, respectively.

The cumulative 10 years survival rate (CSR) was 81% on the patient level and 91% on the implant level (figure 2 and 3, Table 1 and 2).

Eleven out of 76 implants failed in smokers, and 22/377 in non-smokers, resulting in absolute survival rates of 85.5% and 94.2% respectively. CSRs were 82% vs.75% on the patient level and 93% vs. 81% on the implant level for non-smokers and smokers, respectively. Eight implants failed before prosthetic loading, all in non-smokers.

Figure 2. Kaplan-Meier survival curve showing estimated implant failures in the function of time for smokers and non-smokers on the patient level. **(J. Clin.Med.2020)**.

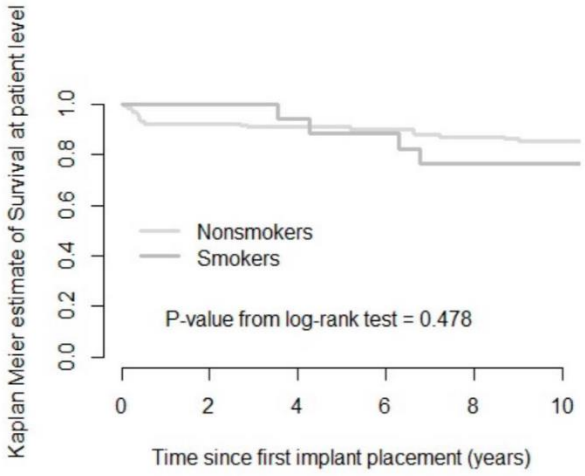
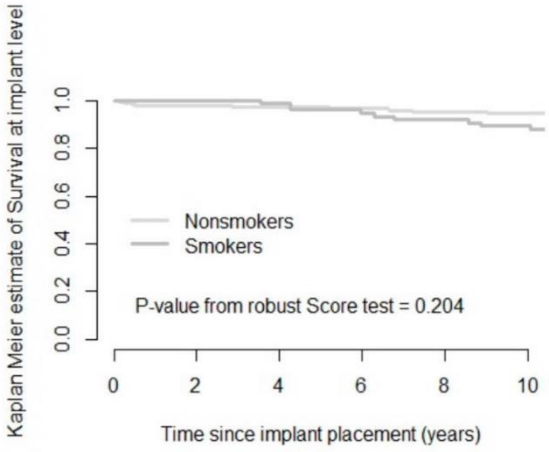


Figure 3. Kaplan-Meier survival curve showing estimated implant failures in the function of time for smokers and non-smokers on the implant level. **(J.Clin.Med.2020)**.



Regarding the jaw of treatment, 17/272 (6.25%) implants in the upper jaw and 16/181 (8.84%) implants in the lower jaw failed.
For smokers, 3/35 (8.57%) implants failed in the mandible and 8/41 (19.51%) in the maxilla.
For the non-smoking group, implant failure for the mandible was 13/146 (8.90%) and for the maxilla 9/231(3.9%).

CSRs in respect of smoking status and jaw are mentioned in Table 3. These were 89% vs. 96% for non-smokers and 88% vs. 76% for smokers, respectively, in the mandible and maxilla. No statistical differences were found between smokers and non-smokers regarding survival at the patient level, implant level, or regarding the type of jaw (based on Kaplan–Meier estimate of survival).

Only a significant difference was found in non-smokers with a higher survival rate for the maxilla (97% vs. 93% for the mandible, $p = 0.047$). However, the hazard of implant loss for implants of the maxilla was 5.64 times higher in smokers compared to non-smokers (95% CI for the HR went from 1.82 to 17.5) ($p = 0.003$).
The hazard of implant loss for implants of non-smokers was 2.92 times higher in the mandible compared to the maxilla (95% CI for the HR went from 1.29–6.62) ($p = 0.01$).

1.1.9 Peri-Implant Bone Loss

Regarding the different treatment protocols described, a separate analysis was not considered beneficial. This was to not decrease the power of the study, focusing on smoking habits on the long-term outcome. Another study by Vervaeke and coworkers (2015) found no statistical difference between the three treatment protocols **[Vervaeke, S.; Collaert, B.; Cosyn, E.; De Bruyn, 2015]**.

From the 453 initially placed implants in the followed population, 397 implants in 121 patients had readable radiographs. The intra-examiner repeatability for bone loss was high (ICC 0.99, 95% confidence interval (CI) (0.98–0.99)), as was the inter-examiner repeatability (ICC 0.84, 95% CI (0.76–0.89)). After a mean follow-up time of 11.38 years, mean bone loss beyond the reference point for all cases was 0.97 mm (SD 1.79, range 0–17) at the implant level and 0.90 mm (SD 1.39, range 0–7.85) at the patient level. When comparing smokers and non-smokers irrespective of jaw location, a mean bone loss of 1.93 mm (SE 0.57, 95% CI (0.811–3.047)) and 0.8 mm (SE 0.12, 95% CI (0.556–1.024)) on the implant level and 1.71 mm (SD 2.32, range 0.05–7.85) and 0.77 mm (SD 1.15, range 0–4.97) on the patient level was found, respectively. For mean bone loss according to smoking status adjusted for jaw, there was a significant difference in estimated mean bone loss at 10 year-follow-up between smokers and non-smokers ($p = 0.0031$) with smokers having a higher mean bone loss (1.9 mm versus 0.8 mm, estimated mean difference of 1.12 mm) (Figures 4 and 5).

Figure 4. cumulative percentage of individual peri-implant bone loss, smokers compared to non-smokers.

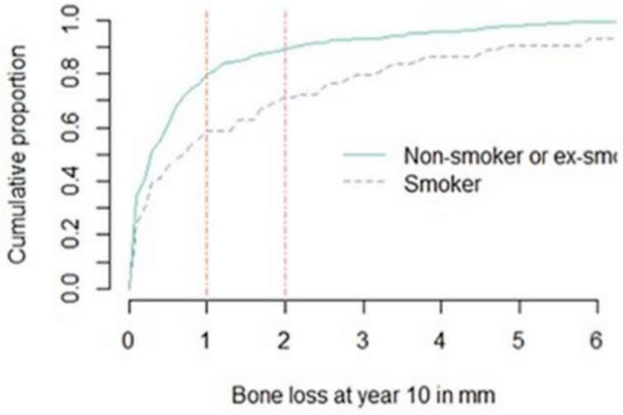
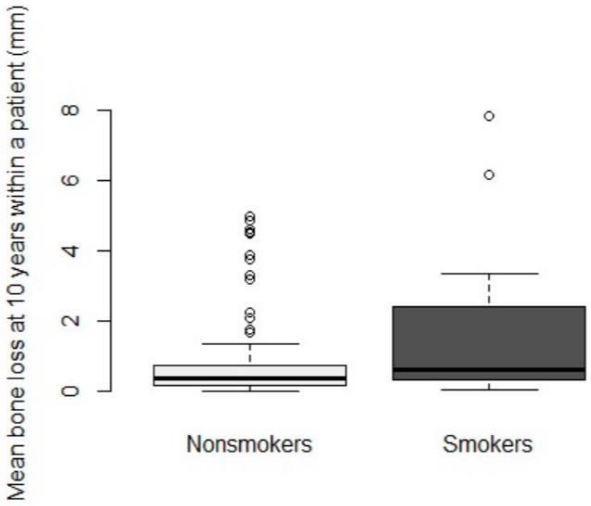
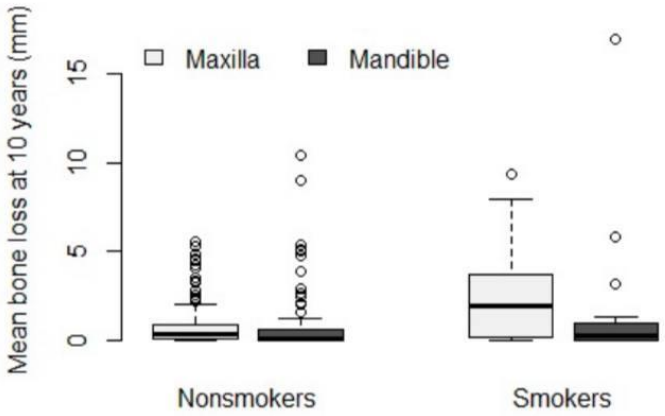


Figure 5. Boxplot reporting on mean peri-implant bone loss within each patient, comparing smokers and non-smokers after at least 10 years.



Considering the jaw of treatment in smokers versus non-smokers, mean bone loss of 2.46 mm (SE 0.721, 95% CI (1.043-3.877) versus 0.80 mm (SE 0.752 ,95% CI (-0.194-2.762) versus 0.78 mm (SE 0.206,95% CI (0.369-1.180)). Only for the maxilla, the difference of mean bone loss was significant between smokers and non-smokers (p=0.006). The difference in bone loss between maxilla and mandible was not significant within both groups (smoking p=0.47 and non-smoking p=1) (figure 6).

Figure 6. Boxplot reporting on individual peri-implant bone loss in smokers and non-smokers after a minimum of 10 years, comparing upper and lower jaw.



1.1.10 Implant Success

Implant success was calculated using a threshold for individual total bone loss arbitrary set at ≤1 mm and ≤2 mm changes. This was based on additional bone loss measured between 24 and 120 months. Table 5 gives a summary of the successful implants in smokers and non-smokers with respect to jaw location.

Table 5. Overview of the successful implants (with 1 mm and 2 mm marginal bone loss as success criterion) in smokers and non-smokers with respect to jaw location.

	Non-Smokers				Smokers			
	Bone Loss 10y Post-op ≤ 1 mm		Bone Loss 10y Post-op > 1 mm		Bone Loss 10y Post-op ≤ 1 mm		Bone Loss 10y Post-op > 1 mm	
Jaw of treatment	Count	%	Count	%	Count	%	Count	%
Total	272	81.2	63	18.8	37	59.7	25	40.3
Maxilla	165	78.9	44	21.1	14	41.2	20	58.8
Mandible	107	84.9	19	15.1	23	82.1	5	17.9
	Bone loss 10y post-op ≤ 2 mm		Bone loss 10y post-op > 2 mm		Bone loss 10y post-op ≤ 2 mm		Bone loss 10y post-op > 2 mm	
Jaw of treatment	Count	%	Count	%	Count	%	Count	%
Total	297	88.7	38	11.3	43	69.4	19	30.6
Maxilla	185	88.5	24	11.5	18	52.9	16	47.1
Mandible	112	88.9	14	11.1	25	89.3	3	10.7

With the success criterion of “bone loss ≤1 mm after 10 years of follow-up”, non-smokers showed 81.2% implant success versus 59.7% for smokers. This difference was significant (p = 0.049, adjusted for jaw).

There was a significant difference in the probability of implant success between smokers and non-smokers in the upper jaw (78.9% success in non-smokers versus 41.2% success in smokers, p = 0.003). In our sample, a significant difference in the probability of implant success between smokers and non-smokers in the lower jaw was absent (84.9% success in non-smokers versus 82.1% success in smokers, p = 0.761).

When the criterion was defined as “bone loss ≤2 mm after 10 years of follow-up”, non-smokers showed an overall success rate of 88.7% versus 69.4% for the smoking group, not statistically significant (p = 0.112, adjusted for jaw).

A significant difference in the probability of implant success was seen in the upper jaw (88.5% success in non-smokers versus 52.9% success in smokers, p = 0.007). In our sample, one could not find a significant difference in the probability of implant success in the lower jaw (88.9% success in non-smokers versus 89.3% success in smokers, p = 0.961).

Only the smoking group showed a significant difference in implant success between maxilla and mandible, with higher implant success in the mandible (1 mm criterion p = 0.004; 2 mm criterion p = 0.015). There was an indication of effect modification of smoking by the jaw, although not statistically significant (p-value Fixed effects = 0.081).

We found no difference in the proportion of implant success at the patient level between smokers and non-smokers (1 mm criterion p-value from Fisher’s exact test = 0.277 and 2 mm criterion p-value from Fisher’s exact test = 0.061).

1.1.11 Peri-Implant Health

The overall mean bleeding on probing was 0.30 (SD 0.38, range 0–1), with 30% of the implants showing bleeding on probing, 0.29 (SD 0.38, range 0–1) in non-smokers versus 0.35 (SD 0.41, range 0–1) in smokers (p = 0.332). Overall mean pocket probing depth was 4.25 mm (SD 1.26, range 2.83–17.00) being 4.69 mm (SD 2.09, range 3–17) for smokers versus 4.19 mm (SD 1.08, range 2.83–9.5) in non-smokers (p = 0.086). Table 6 gives an overview of the distribution of implants with peri-implantitis between smokers and non-smokers for both jaws.

Table 6. Distribution of implant with peri-implantitis in regard to jaw type and smoking status.

Jaw of Treatment	Non-Smokers		Smokers	
	Count	%	Count	%
Total	33	10.5	17	28.8
Maxilla	19	9.8	11	34.4
Mandible	14	11.6	6	22.2

When taken jaw into account, implants placed in patients with smoking habits experienced a 2.6 higher risk in developing peri-implantitis compared to the implants placed in non-smokers. This difference was borderline non-significant (p = 0.053). When comparing jaws, 22.2% and 11.6% of the implants placed in the mandible experienced peri-implantitis in smokers and non-smokers, respectively. Regarding the upper jaw, this was 34.4% versus 9.8%, respectively. These differences were found to be statistically non-significant (p = 0.228 and p = 0.127). Similarly, no statistically significant difference was present between maxilla and mandible in each group (p = 0.481 for smokers and p = 0.757 for non-smokers).

1.2 Smoking as a Risk Factor for the Development of Preimplant Diseases.

Nicotine is the main component of the cigarette, and it is frequently associated with bone- healing failures. Therefore, heavy smokers are nearly 7 times more prone to tooth loss, and increasing numbers of people are expected to require replacement of missing teeth. **(Tsigarida AA, Dabdoub SM, 2015)**.

Dental implants are widely used for rehabilitation of fully or partially edentulous ridges with high survival and success rates. **(Moraschini V, 2016)**

Inflammatory reactions around dental implants vary from periimplant mucositis to periimplantitis. Periimplantitis may disturb function of the implants, and progressive bone loss may eventually lead to implant loss. Smoking is an important risk factor not only for periodontitis-associated tooth loss, but also it has been related to periimplant bone loss and implant failure. **(Gurlek O, Gumus P, 2018)**

On the other hand, because life expectancy is increasing with the advent of better therapies and individualized medicine, an increasing number of patients who smoke or previously smoked may require dental implant treatment. **(Chen H, Liu N, Xu X, et al. 2013)**.

In this context, these individuals represent a high-need group for implant therapy, mainly due to cigarette consumption. **(Tsigarida AA, Dabdoub SM, 2015)**.

1.2.1 Preimplant Tissue Healing in Smoking

The mechanism in which the tobacco affects the osseointegration and the survival of implants remains partially unknown. However, implant failures generally occur due to the deposition of fibrous tissue at the bone-implant interface. **(Takamiya AS, Goiato MC, 2014)**

Immediately after implant placement, the coagulum is formed between the implant and bone tissue. Depending on the local conditions and the presence of primary stability of the implant, pluripotent mesenchymal cells differentiate into osteoblasts, and bone tissues are formed. The recruitment of pre-osteoblasts, their anchorage, adhesion, spreading, proliferation, and differentiation into osteo- blasts, which secrete extracellular matrix for calcification on the implant surface during osseointegration, is sensitive to the local and systemic effects of nicotine and other associated cigarette components. **(American academy of implant dentistry,2018)**.

Nitrosamines, aldehydes, carbon monoxide, carbon dioxide, ammonia, and benzene are components of the cigarette that may affect the bone- healing process. In addition, previous studies showed that the reactive oxygen associated with cigarette consumption correlates with bone resorption processes, which explains the negative effect of smoking in osseointegration. **(Takamiya AS, Goiato MC, 2014)**.

Carbon monoxide is an inhibitor of the oxygen and decreases the oxygen-carrying capacity of red blood cells; the hydrogen cyanide promotes hypoxia by inhibiting the enzyme systems necessary for metabolism oxidation. **(Balatsouka D, Gotfredsen K, Lindh CH, et al. 2005)**

The main component of cigarettes is nicotine, which can be detected in plasma (4–73 ng/mL), saliva (1.6–96 mg/mL) and in the gingival crevicular fluid (concentration nearly 300 times that which is found in plasma). **(RenvertS, QuirynenM. 2015)**

Nicotine reduces osteoblastic activity, affecting the amount of collagen available to form the extracellular matrix. The activation of voltage-dependent calcium channels by nicotine can modulate bone metabolism by changes in intracellular levels of calcium ions. **(Takamiya AS, Goiato MC, 2014)**

Nicotine may also induce microvascular obstruction, which results in ischemia. It also decreases the blood cell proliferation with direct reduction of blood flow and nutrients to the healing area after implant insertion. It was speculated that despite the fact that nicotine is only minimally expressed in the set- ting of dental implant surgery, its effect on early implant failure is possibly associated with this vasoconstrictive effect. **(Lambert PM, Morris HF, 2000)**

Depression of the immune system and the role in osteoclast genesis by nicotine action directly affect the immune response and cause increased susceptibility to infections in the peri- implant area. This consequence is probably due to inhibition of the proliferation and function of B and T cells. Some evidence also suggests a modified pattern of important modulators of inflammation and of bone tissue metabolism in smoking individuals when preimplant diseases are present **(Turri A, Rossetti PH, Canullo L, et al. 2016)** (Fig. 8).

Based on bioactive tissue effects in smoking, it has been related those patients with heavy smoking habits are under significantly increased risk of dental implant failure, not only by interfering with the tissue-healing process but also by increasing the susceptibility of the patient to other diseases. **(Chen H, Liu N, Xu X, et al. 2013)**.

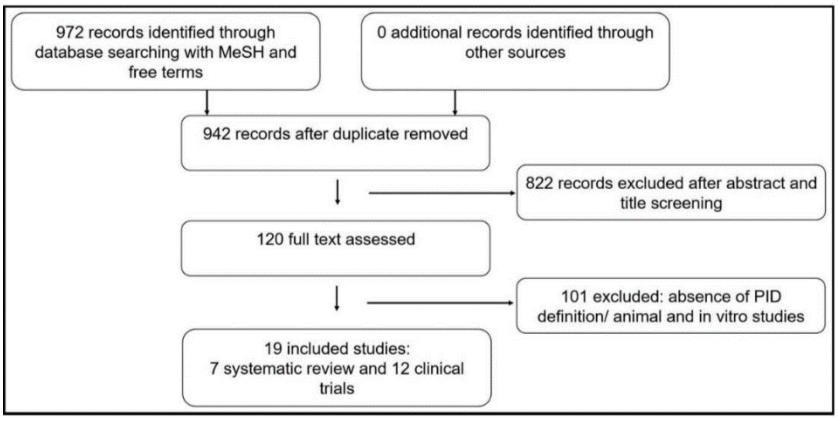


Figure 7. Study screening process. From 972 records identified, a total of 120 full texts were assessed after 942 duplicate records' exclusion. A total of 19 studies were included in this review. **(RenvertS,QuirynenM. 2015)**

1.2.2 Preimplant Core Microbiome in Smoking

The term "core microbiome" was introduced by the Human Microbiome Project to identify bacterial consortia that were present in most of the study population, implying that these species are best adapted to that particular microenvironment. The core preimplant microbiome was defined as that which is found in 75% or more of individuals. **(Tsigarida AA, Dabdoub SM, 2015)**

Based on these characteristics, studies **(Tsigarida AA, Dabdoub SM, 2015;94, Quaranta A, Assenza B, D Isidoro O, et al. 2015)** have demonstrated that although smokers and nonsmokers shared 34 species, they differed by 31

bacterial species. These data indicate that smoking can modify the core microbiome of the preimplant habitat. It was demonstrated that smoking negatively affects the subgingival microbiome, supporting the formation of pathogen-rich communities. **(Tsigarida AA, Dabdoub SM, 2015)**

In smokers, 2 important microbiological events are evident in the transition from health to disease. Not only did the process of pathogen enrichment observed in health continue into disease, but also the species that were being replaced were similar between individuals. Very few species were acquired between mucositis and periimplantitis, suggesting that the pathogen-rich state established in mucositis persists in periimplantitis in smoking individuals. **(Tsigarida AA, Dabdoub SM, 2015)**

In nonsmokers (but not smokers), the transition from health to mucositis and progression to periimplantitis resembles primary ecological succession, with acquisition of several species without replacement of pioneer organisms. Smoking shapes the preimplant microbiome even in states of clinical health, depleting commensals from this niche and enriching for pathogens. This effect seems to be a nonrandom event. **(Tsigarida AA, Dabdoub SM, 2015)**

Previous investigations support these findings on the impact of smoking on the preimplant microbiome in states of health and disease. They show that periimplantitis did not differ significantly from mucositis in species richness or evenness in smokers.

Quaranta et al (2015) evaluated the impact of smoking and previous periodontal disease on the peri implant microbiota on health in medium to long-term maintained patients, showing that smokers harbor significantly higher counts of pathogenic bacteria with clinical signs of inflammation, including deep pockets and slight bone compared with nonsmokers.

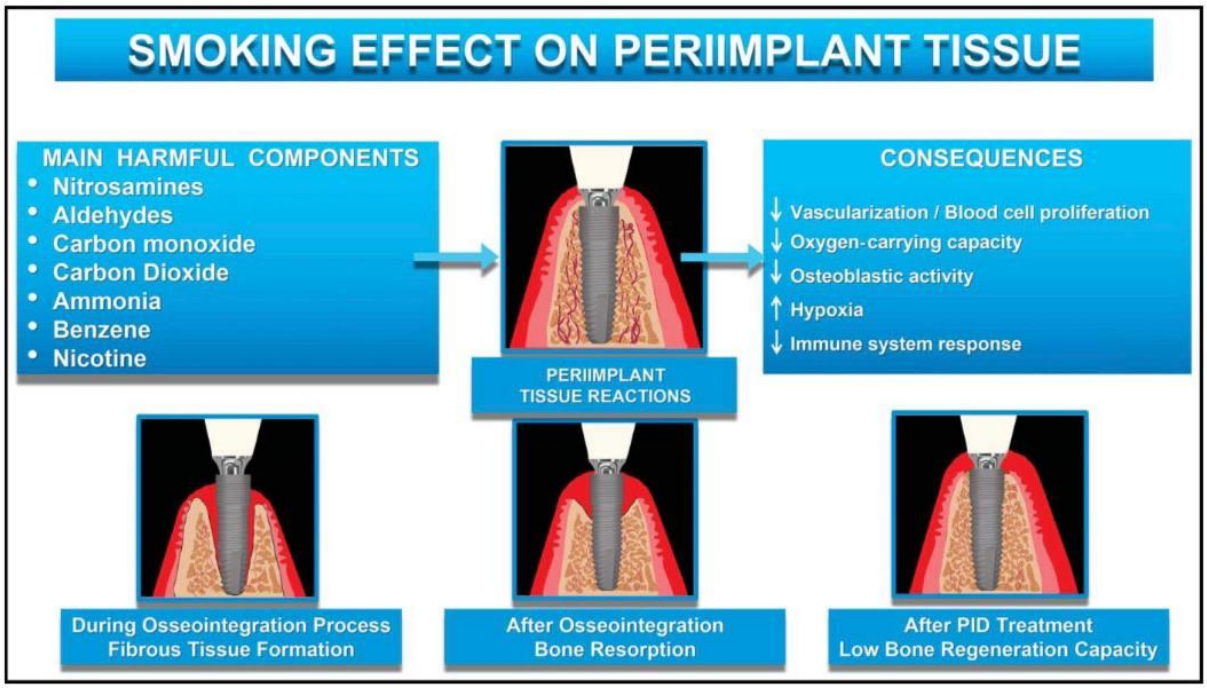


Figure 8. Description of the main harmful chemicals components that affect preimplant tissues, causing depletion of vascularization, oxygen-carrying capacity, osteoblastic activity, and immune system response, during and after osseo integration and in cases of preimplant disease treatment. **(Quaranta A, Assenza B, D Isidoro O, et al. 2015)**

1.2.3 Clinical Effects of Smoking: Main Findings Associated with Preimplant Disease

Preimplant mucositis has been defined as “a reversible inflammatory change in the preimplant soft tissue without bone loss,” It usually presents as inflammation with erythema, swelling, and bleeding on probing (BOP) around the head of the dental implant. **(Lindhe J, Meyle J. 2008)**

Dental implants with periimplantitis must have evidence of >2-mm bone loss from the expected marginal bone at implant installation and with concurrent BOP and/or suppuration. Implants with a distance ,2.0 mm between bone level

and implant platform level or other reference point and with no BOP or suppuration represent healthy conditions. **(Lindhe J, Meyle J. 2008)**

Clinically, research has found that, compared with nonsmokers, smokers present greater probing depths, increased plaque scores, suppuration, and BOP values around dental implants, increasing clinical signs of inflammation, probably associated with the negative effects in healing process. **(Ata-Ali J, Flichy-Fernandez AJ, Alegre-Domingo T, et al. 2016)**

Other important aspects are the association between smoking habits and delayed bone healing, reduced bone height, increased rate of bone loss, formation of poor-quality bone, as well as increased incidence of periimplantitis and implant loss (bone loss greater than 50% compared with nonsmokers). **(RenvertS, QuirynenM. 2015)**

(Clementini et al) in a systematic review confirmed previous studies showing that bone loss in smokers was 1.98 versus 0.20 mm in nonsmokers, with smokers presenting a higher amount of preimplant bone loss (0.164 mm/y) than non- smokers. **(Clementini M, Rossetti PHO, Penarrocha D, et al. 2014)**

A recent meta-analysis evaluating 7 studies indicated that the marginal bone loss in smokers ranged between 0.07 and 2.7 mm, while it varied between 0.04 and 3.13 mm in non- smokers, in a period from 12- to 24- month follow-up. **(Moraschini V, Porto Barboza E. 2016)**

The preimplant tissue responses to:

smoking can also be responsible for the adverse effects on implant survival before prosthesis insertion in smokers. In general, smokers present a 1.69 times higher chance of implant failures than nonsmokers during the first implant surgical stage (before prosthesis insertion). **(Moraschini V, Porto Barboza E. 2016)**

Follow-up data for the implants, over an observational period of 36 months, showed that smokers experience more overall implant failures than nonsmokers (8.9% vs 6.0%). **(Lambert PM, Morris HF, Ochi S. 2000)**

It has also been reported that the duration and number of cigarettes smoked can affect the preimplant bone tissue. The survival rate of dental implants in 464 patients over 10 years was 92.28%. Patients who were smokers at the time of implant surgery had a significantly higher implant failure rate (23.08%) than nonsmokers (13.33%). **(Takamiya AS, Filho HG. 2014)**

A different meta-analysis by (Sgolastra et al) showed that smokers have a significantly higher risk of periimplantitis compared with nonsmokers. It has also been demonstrated that between the time of surgical uncovering (stage 2) and insertion of the prosthesis (stage 3), smokers have more failures than nonsmokers. **(Sgolastra F, Petrucci A, Severino M, et al. 2015)**

However, most of the studies do not associate smoking habits with preimplant disease. Instead, there is an association with implant failure, which has many descriptions according to the research from preimplant mucosal inflammation to implant loss. Table 1 describes the incidence of preimplant disease in smokers compared with nonsmokers, considering clinical studies. The relationship between smoking and preimplant disease is described in Table 2.

Periimplant Disease	Authors	N patients (NS/S)	Type of Study	Follow-up	PID Percentage (NS/S)	PID Association With Smoking* (Y/N)
Mucositis	Rodriguez et al[18]	295 (182/113)	Retrospective	—	9.2%/11.8%	Yes
	Gurlek et al [6]	142 (74/68)	Prospective	1 y	25.7%/32.4%	Yes
Periimplantitis	Lambert et al[11]	2887 implants (1928/959)	Prospective	3 y	6%/8.9%	Yes
	Karoussis et al[19]	53 (41/12)	Prospective	10 y	9.5%/17.9%	Yes
	Roos-Jansåker et al[7]	218 (161/57)	Prospective	9–14 y	2.8%/15.5%	Yes
	Rodriguez et al[18]	295 (182/113)	Retrospective	—	5.3%/9.3%	Yes
	Alissa and Oliver[20]	83	Prospective	6 y	—	Yes
	Swierkot et al[21]	53 (39/14)	Prospective	8.2 y	S > NS	Yes
	Stoker et al[22]	94 (59/34)	Prospective	8.3 y	1.7%/11.4%	Yes
	Casado et al[23]	215 (194/21)	Prospective	1–8 y	40.2%/38.1%	No
	Marrone et al[24]	103 (83/20)	Prospective	8.5 y	30.3%/38.5%	Yes
	Ata-Ali et al[15]	29 (22/7)	Prospective	>2 y	—	No
	Gurlek et al[5]	142 implants; 43 participants (74/68)	Prospective	1 y	17.6%/41.2%	Yes

Table 7. Only 2 clinical studies showed no association between smoking and PID development.

*It was considered association with smoking when the incidence of PID in smoking was higher than in nonsmoker. NS indicates nonsmoker; S, smoker. **(Priscila Ladeira Casado,2019)**.

	Included Studies (n)	Periimplant Disease	PID Association With Smoking* (Y/N)
Chen et al[6]	33	Bone loss (periimplantitis)	Yes
Clementini et al[16]	13 (478 smokers/1207 nonsmokers)	Periimplantitis	Yes
Sgolastra et al[17]	7	Periimplantitis	Yes
Renvert and Quirynem[10]	28	Periimplantitis	No
Chrcanovic et al[25]	107	Periimplantitis/mucositis	Yes
Turri et al[12]	6	Periimplantitis	Yes
Ting et al[26]	33	Periimplantitis	Yes

Table 8. All information from meta-analysis and review articles, 1 article showed no association between PID and smoking. *Y is YES and N is NO.

(Priscila Ladeira Casado,2019).

1.3 The Effect of Cigarette Smoking on Dental Implants and Related Surgery

1.3.1 THE Oral Cavity, Periodontium, And Dental Implants

Of smokers, an increase in plaque accumulation, a higher incidence of gingivitis and periodontitis, a higher rate of tooth loss, and an increased resorption of the alveolar ridge have been found in the oral cavity. The exact mechanisms in which tobacco exerts its influence on periodontal tis- sues are not completely known. It is likely that smoking primarily has a systemic influence by altering the host response and/or by directly damaging the periodontal cells. **(Scabbia A, Cho KS, Sigurdsson TJ, et al. 2001)**

The use of endosseous implants has increased over the past decade in certain edentulous situations. Bain and Moy assessed the various factors that predispose implants to failure in a group of 540 patients who received 2194 Brånemark System implants (Nobel Biocare USA Inc., Yorba Linda, CA). **(Bain CA, Moy PK. 1993)**

The most significant factor was smoking. (De Bruyn and Collaert) found that smokers have a significantly higher failure rate before functional loading of implants than nonsmokers. **(De Bruyn H, Collaert B. 1994)**

Lindquist et al compared marginal bone loss (MBL) around osseointegrated dental implants among smokers and nonsmokers. Of smokers who also had poor oral hygiene, MBL was nearly 3 times as high as that in nonsmokers. **(Lindquist et al ,1996-1997)**

According to (Haas et al), smokers can have detrimental effects around successfully integrated maxillary implants, with a significantly higher bleeding index, higher mean peri-implant pocket depth, more frequent peri- implant inflammation, and radiographically higher mesial and distal bone loss. It is difficult to assess adverse effects of smoking on the prognosis of implants on the basis of implant failure alone. Specific factors, such as type (e.g., coating, design) of implant and immediate versus late implantation, can also be assessed and compared between smokers and nonsmokers. These factors, related to clinical complications, enable the evaluation of the survival rate of the implants. **(HaasR, HaimbockW,MailathG,et al. 1996)**

Our observations revealed a significantly higher incidence of complications following dental implantation among smokers. When the number of cigarettes/day and smoking years were considered, a significantly higher incidence of complications was found in relation to quantity and duration of smoking. In the smoker's group, there were more complications, regardless of the time of implantation (immediate vs. nonimmediate) (Table 9). **(Schwartz-AradD, YanivY,LevinL, et al. (1999-2004))**.

Procedure	Criteria	Smokers	Non-Smokers	P value
Dental implants	*Marginal Bone Loss*	0.15 mm	0.04 mm	0.001
	5-Year Cumulative Survival Rate	87.8%	97.1%	0.001
	Complications	46%	31%	0.05
Onlay Bone Graft	*Complications*	50.0%	23.1%	0.05
	Graft exposure and graft mobility (Graft Failure)	33.3%	7.7%	0.05
Sinus Lift Operation	*Complications*	66.7%	63.3%	NS

Table 9. Study results on the relationship between cigarette smoking and implant-related surgical procedures. These are findings of the authors' recent studies concerning the influence of cigarette smoking on cumulative survival rate, MBL, and the prevalence of complications, as well as smoking influence on implant-related surgical procedures (i.e., sinus lift and bone graft procedures).

In a subsequent study, the influence of smoking on MBL around im- plants was examined. In the maxilla, heavy smokers (>10 cigarettes/day) had the highest amount of bone loss, followed by mild smokers (<10 cigarettes/day) and nonsmokers. In the mandible, there was no distinction be- tween heavy and mild smokers, and both had higher MBL than nonsmokers. Overall success rate for all implants was 93.2%. Nonsmokers had a higher success rate (97.1%) than smokers (87.8%) ($P < 0.001$) (Fig. 1)

1.3.2 Wound Healing

Cigarette smoking has long been suspected as adversely affecting wound healing. Arteriolar vasoconstriction and decreased blood flow are seen in response to smoking. **(De Bruyn H, Collaert B. 1994)**

Toxic by-products, such as nicotine, carbon monoxide, and hydrogen cyanide, have been implicated as risk factors for impaired healing. **(Silverstein P. 1992)**

Smoking impairs wound healing in various surgical operations, such as orthopedic (hip or knee arthroplasty, open tibial fractures) and plastic surgery (elective facial esthetic procedures, cosmetic and reconstructive breast operations, abdominoplasty, free-tissue transfer, and replantation procedures). **(Muller AM, Pedersen T, Villebro N, et al. 2003)**

Smoking also compromises healing after various mucogingival surgeries. **(Krall EA, Dawson-Hughes B, Garvey AJ, et al. 1997)**

1.3.3 Implant-Related Surgeries

The most common augmentation procedures for dental implants include guided bone regeneration, sinus lift operation, and bone grafting. Guided bone regeneration is a common and well described procedure for augmentation, with considerable long-term results. **(Zitzmann NU, Scharer P, Marinello CP.1999)**

Sinus lift surgery has a predictable outcome as well, with an implant survival rate >90% for 3–5 years. **(Hurzeler MB, Kirsch A, Ackermann KL, et al.1996)**

It is considered a safe treatment modality, with only minor complications. **(Ziccardi VB, Betts NJ.1999)**

The use of autologous bone grafts with dental implants was originally described by Brånemark et al in 1975, and is now a well-accepted procedure in oral and maxillofacial rehabilitation. **(Brånemark PI, Lindstrom J, Hallen O, et al. 1975)**

It is noteworthy that smoking is considered a contraindication for protocols, such as bone regeneration and bone grafting. **(Renouard F, Rangert B.1999)**

The predictability and extent of periodontal regeneration are associated with cigarette smoking. **(Reynolds MA, Bowers GM.1996)**

Smoking adversely affects treatment outcome, as measured by gains in clinical attachment levels of intrabody defects treated by regenerative therapy. **(Rosen PS, Marks MH, Reynolds MA.1996)**

An association between dental implants placed in augmented maxillary sinuses and history of smoking has been reported. **(Olson JW, Dent CD, Morris HF, et al. 2000)**

Smokers, after rehabilitation of severely resorbed maxillae with and without bone grafts, have a higher implant failure rate. **(Misch CE, Scortecci GM, Benner KU. 2003)**

Cigarette smoking is detrimental to implant osseointegration in grafted maxillary sinuses, regardless of the amount of cigarettes consumed. **(Kan JY, Rungcharassaeng K, Lozada JL, et al. 1999)**

Our observations found a complication rate of 23.1% following onlaybone grafts in nonsmokers, compared to a complication rate of 50% in smokers. Major complications were found in one third of the operations in smokers, compared to 7.7% in the nonsmokers (P 0.04). There was also a relationship between complications and past smoking, al- though not statistically significant (P 0.06). There was no relationship between sinus lift operation complications and smoking habits, including intraoperative and postoperative complications (Fig. 1). **(Schwartz-Arad D, Herzberg R, Dolev E. 2004)**.

1.4 Postoperative Complications in Smoking Patients Treated With Implants

Smoking has been associated with a greater risk of postoperative complications in many surgical fields. Reports have shown the negative effects of this habit in areas well beyond dentistry, including abdominal, orthopedic, and oncologic surgery. **(Lindström D, Sadr-Azodi O, Wladis A, et al,2008)**

As a general rule, surgeons ask their patients to stop smoking before any surgical procedure. Nevertheless, short-term smoking cessation does not seem to decrease the rate of complications in colorectal surgery, because it seems to reduce the altered chemotaxis of macro- phages and neutrophils only marginally. **(Sørensen LT, Nielsen HB, Kharazmi A, et al,2004)**

However, a recent systematic review of randomized controlled trials on smoking cessation showed that intensive programs performed at least 4 weeks before surgery seemed to improve the results and increase the cessation rates. **(Thomsen T, Tønnesen H, Møller AM,2009)**.

Smoking is also associated with healing complications in oral surgery and periodontology, such as dry socket, slow epithelization in free gingival graft donor sites, and a poor prognosis for periodontal treatment. **(Wan CP, Leung WK, Wong MC, et al:2009)**.

The use of Osseointegrated implants for tooth replacement has become a highly predictable treatment, with success rates usually greater than 90% for different implants systems, although these data depend much on the criteria used by researchers to assess implant success. **(Baig MR, Rajan M,2007)**.

Implant loss, infection, and inflammation of the peri-implant mucosa, with or without bone loss, are among the most common complications of

implant treatment. These complications are associated with different risk factors, both implants related (e.g., surgical procedure, implant surface, number and position of the implants, and loading protocol, among others) and patient related (eg, hygiene, uncontrolled diabetes, alcohol abuse, and smoking). **(Weyant RJ,1994)**.

These complications (i.e., implant loss, infection, mucositis, and periimplantitis) can be divided into immediate, early, and late and, in turn, can be reversible or irreversible, depending on the type and extent of the complication. **(Bain CA, Moy PK,1993)**.

Although tobacco has been reported as a risk factor for implant failure and bone loss around implants, few reports have addressed the risk of complications in smoking patients. Therefore, the purpose of the present study was to identify the risk factors of several complications (i.e., implant loss, infection, peri-implantitis, and mucositis) in a group of patients treated with Osseointegrated implants and to assess the effect of smoking on this risk. **(Heitz-Mayfield LJ, Huynh-Ba G: 2009)**.

All implants had been placed according to the manufacturer's instructions under sterile conditions by fellows of the Master Degree Program in Oral Surgery and Orofacial Implantology under direct supervision of clinical assistant professors. After the operation, an antibiotic (usually amoxicillin 750 mg every 8 hours for 4 to 7 days [Clamoxyl 750; GlaxoSmithKline, Ma- drid, Spain]), a nonsteroidal anti-inflammatory drug (usually ibuprofen 600 mg every 8 hours for 4 to 5 days [Algiasdin 600; Esteve, Barcelona, Spain]), and a mouthrinse (0.12% chlorhexidine digluconate every 12 hours for 15 days [Clorhexidina Lacer; Lacer, Bar- celona, Spain]) were prescribed.

The following variables were collected: age, gender, number and position of the implants, implant manufacturer and system, length and diameter of each

implant, and follow-up time. The smoking habit was recorded as smoker or nonsmoker. The postoperative complications were classified per implant as follows: failure to achieve osseointegration, when the implant was lost before loading; mucositis, when the mucosa surrounding the implant had inflammatory signs (i.e., redness, swelling, or bleeding) but no objective bone loss had occurred; peri-implantitis, when the mucosa surrounding the implant had inflammatory signs and bone loss of more than 1 thread had occurred compared with the initial situation; and postoperative infection, when swelling and suppuration followed the insertion of the Osseointegrated implants.(table 10)

Variable	No Complications	Implant Loss	Peri-Implantitis	Mucositis	Postoperative Infection	Total
Smoking	291 (74.8)	14 (3.6)	36 (9.3)	46 (11.8)	2 (0.5)	389 (100)
Nonsmoking	533 (82.8)	18 (2.8)	34 (5.3)	59 (9.2)	0 (0)	644 (100)
Total	824 (79.8)	32 (3.1)	70 (6.8)	105 (10.2)	2 (0.2)	1,033 (100)

Table 10. COMPLICATIONS IN SMOKING AND NONSMOKING PATIENTS

(Rodriguez-Argueta et al. Smoking and Dental Implants. J Oral Maxillofac Surg 2011.)

Chapter Two

Discussion

The pathogenic mechanisms of smoking on wound healing seem to be quite complex. Cigarette smoke contains more than 4,000 toxins, including nicotine, carbon monoxide, nitrosamines, benzenes, aldehydes, and hydrogen cyanide.

Nicotine is a potent vasoconstrictor that reduces blood flow and nutrient delivery to healing sites, causing tissue glucose reduction and acidosis. However, nicotine does not seem to be the only factor responsible for the dramatic decrease in blood flow and oxygen tension in the skin and mucosa observed in smokers. **(Sørensen LT, Jørgensen S, Petersen LJ, et al,2009)**.

Carbon monoxide also reduces the oxygen-carrying capacity of erythrocytes, and hydrogen cyanide causes tissue hypoxia. An experimental work with rats has shown that nicotine does not seem to affect bone development, but it might inhibit the bone matrix-related gene expressions required for wound healing and thereby diminish implant osseo integration at a late stage. **(Yamano S, Berley JA, Kuo WP, et al: 2010)**.

In contrast, smokers' fibroblast activity and collagen metabolism are affected by a lack of vitamin C and by a change in the inflammatory cell response. **(Sørensen LT, Toft BG, Rygaard J, et al,2010)**.

Smokers have a vitamin C deficiency, probably owing to the greater turnover caused by the smoke-derived oxidant products and because of a dietary deficit of fruit and vegetables. **(Hampl JS, Taylor CA, Johnston CS,2004)**.

Moreover, some compounds of tobacco also act as chemotactic substances, which enhance tissue destruction by enzymes released by

neutrophils and macrophages, such as matrix metalloproteinases. **(Perlstein TS, Lee RT,2006)**.

The most common complication encountered in our series was mucositis (11.8% for smoker's vs 9.2 for nonsmokers). Peri-implantitis was also more common in smokers (9.2% vs 5.3%). The reason for this could be multifactorial, because the tobacco toxic effects are multiple, including blood flow, chemotactic activity of leukocytes or collagen synthesis, among others. (table2.)

Table 2. OCCURRENCE OF COMPLICATIONS ACCORDING TO IMPLANT MANUFACTURER

Manufacturer	No Complications	Implant Loss	Peri-Implantitis	Mucositis	Postoperative Infection	Total
AstraTech						
Smoking	21 (95.5)	1 (4.5)	0 (0)	0 (0)	0 (0)	22
Nonsmoking	24 (100)	0 (0)	0 (0)	0 (0)	0 (0)	24
Nobel Biocare						
Smoking	174 (80.6)	9 (4.2)	23 (10.6)	9 (4.2)	1 (0.5)	216
Nonsmoking	378 (84.0)	10 (2.2)	17 (3.8)	45 (10.0)	0 (0)	450
Impladent Defcon						
Smoking	90 (62.1)	4 (2.8)	13 (9.1)	37 (25.5)	1 (0.7)	145
Nonsmoking	115 (74.7)	8 (5.2)	17 (11.0)	14 (9.1)	0 (0)	154

Table 11. Occurrence of Complications According to Implant Manufacturer. **(Rodriguez-Argueta et al. Smoking and Dental Implants. J Oral Maxillofac Surg 2011.)**

The implant size was related to complications. A possible explanation is that long implants could heat the bone, making the loss of osseointegration more likely, and short implants are usually placed in sites with considerable resorption, which could interfere with oral hygiene. This last consideration could also explain why thinner implants were more prone to infectious complications. (table 11).

An association was recorded between the risk of complications and older patients, although this relation might have been from other age-related factors such as systemic diseases (e.g., diabetes), bone type, and difficulty in oral hygiene. The number of implants placed is also greater in older patients, and we found an association between this variable and the occurrence of complications.

Smokers had an increased risk of complications (i.e., infection, implant loss, mucositis, and peri-implantitis) compared with nonsmoking patients. Although implant therapy can be applied to smokers, these patients should be encouraged to cease this habit or decrease its intensity, otherwise complications could occur.

Location	No Complications	Implant Loss	Peri-Implantitis	Mucositis	Postoperative Infection	Total
Incisors	255 (83.6)	10 (3.3)	16 (5.2)	23 (7.5)	1 (0.3)	305 (100)
Canine	9 (75)	0 (0)	0 (0)	3 (25)	0 (0)	12 (100)
Premolar	334 (78.2)	13 (3)	32 (7.5)	48 (11.2)	0 (0)	427 (100)
Molar	226 (78.2)	9 (3.1)	22 (7.6)	31 (10.7)	1 (0.3)	289 (100)
Total	824 (79.8)	32 (3.1)	70 (6.8)	105 (10.2)	2 (0.2)	1,033 (100)

Table 12. Complications and Implant Location. **(Rodriguez-Argueta et al. Smoking and Dental Implants. J Oral Maxillofac Surg 2011.)**

Chapter Three

Conclusion

Based on current scientific evidence, smoking can have negative effects on dental implant success rates and overall implant health.

Smoking can increase the risk of implant failure, implant loss, and implant-related complications such as peri-implantitis (inflammation and bone loss around the implant). Smoking can also impair the healing process after implant surgery and compromise the integration of the implant with the surrounding bone.

Therefore, if you are a smoker and considering getting dental implants, it is recommended to quit smoking or at least reduce smoking as much as possible before and after the implant surgery. This will not only improve the success rates of your implants but also benefit your overall health.

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