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PROGNOSTIC INDICATORS FOR SURGICAL PERI-IMPLANTITIS TREATMENT



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ABSTRACT

Objectives

Objective of this study was to identify prognostic indicators for the outcome of resective peri-implantitis treatment, by an analysis of the pooled data of two previously conducted randomized controlled trials.

Material and methods

Data of 74 patients with peri-implantitis (187 implants) who had received resective surgical treatment were available. Primary outcome variable was failure of peri-implantitis treatment after 12 months. Multilevel univariable and multiple logistic regression analyses were performed to evaluate the effect of various potentially prognostic indicators on the primary outcome.

Results

Peri-implantitis treatment was unsuccessful in 106 implants (57%) and 48 patients (67%) after 12 months. In the multiple regression analysis the variables order of inclusion ($p = 0.016$) and mean bone loss at baseline ($p = 0.030$) were significant prognostic indicators for treatment failure. To eliminate the effect of order of inclusion, post-hoc analyses were carried out in a subgroup of patients. The univariable post-hoc analysis showed a significant association for smoking ($p = 0.015$), maximum pocket depth at baseline ($p = 0.073$), mean bone loss at baseline ($p = 0.003$) and presence of plaque ($p = 0.100$). In the multiple regression post-hoc analysis only the variables smoking ($p = 0.044$) and mean bone loss ($p = 0.043$) remained statistically significant.

Conclusions

The outcome of surgical peri-implantitis treatment is influenced by the experience of the surgical team with the surgical procedure. The observed learning effect has consequences for clinical practice and for conducting and interpreting clinical trials on peri-implantitis treatment. Other prognostic indicators are amount of peri-implant bone loss at baseline and smoking, and to a lesser extent, probing pocket depth at baseline and presence of plaque during follow-up. Early diagnosis of peri-implantitis and control of behavioral factors are crucial in achieving peri-implantitis treatment success.

INTRODUCTION

Peri-implantitis is an infectious disease that resides in the mucosa surrounding dental implants and also affects the supporting bone (Lindhe et al. 2008). It is a common biological complication following implant therapy. The frequency of peri-implantitis on patient level ranges from 6 to 47% (mean 18.8%, 95% CI [16.8, 20.8]) and on implant level from 2 to 37% (mean 9.6%, 95% CI [8.8, 10.4]) after a mean observation period of approximately 10 years (Atieh et al. 2013). Higher prevalence figures are reported for smokers and patients with a history of periodontitis and with increasing implant function time (Atieh et al. 2013, De Waal et al. 2013b). Plaque has been identified as a major risk factor for development of peri-implantitis (Heitz-Mayfield 2008), which explains the observation that participation in a supportive maintenance program results in lower prevalence of peri-implantitis (Atieh et al. 2013). Once peri-implantitis has been diagnosed, it is essential to initiate a prompt curative intervention in order to resolve the inflammatory lesion and prevent further bone loss. Although some initial peri-implantitis lesions might be effectively treated by non-surgical treatment alone, more advanced peri-implantitis lesions require additional surgical intervention to achieve disease resolution (Lindhe et al. 2008). As of yet, the most effective intervention for treatment of peri-implantitis has not been identified and there is no validated treatment protocol available (Esposito et al. 2012).

It might be hypothesized that those patients who are at high risk for development of peri-implantitis, also run a higher risk for failure of peri-implantitis treatment once the disease has been diagnosed. Establishing such risk profiles for peri-implantitis treatment could expedite improvement of treatment protocols, assist in selection of the most effective individual treatment and could allow for optimal information and motivation of patients. Furthermore, it could be helpful in clinical decision making and would enable clinicians to estimate the chances on a successful treatment.

The available evidence for the factor smoking as potential prognostic indicator for peri-implantitis treatment is limited and conflicting. From a large retrospective study it was suggested that smoking and smoking dose might be associated with failure of peri-implantitis treatment (Charalampakis et al. 2011), but this was not substantiated in prospective studies (Serino & Turri 2011, Heitz-Mayfield et al. 2012). The evidence on poor oral hygiene and history of periodontitis as potential prognostic indicators is scarce and available from only one retrospective study evaluating different treatment strategies with different follow-up periods (Lagervall & Jansson 2013). Other factors that have been suggested to influence results of peri-implantitis treatment include early disease development (Charalampakis et al. 2011), implant bone loss of more than 1/3 of the length of the implant (Lagervall & Jansson 2013), non-acceptable compliance (Lagervall & Jansson 2013), bone defect configuration (Schwarz et al. 2011), implant surface characteristics (Rocuzzo et al. 2011), amount of initial bone loss (Serino & Turri 2011), initial presence of pus (Thierbach & Eger 2013) and participation in a maintenance program (Serino et al. 2014). However, the evidence on all these factors is limited due to the small number of studies and small study groups.

The problem of small study groups can be overcome by pooling data of multiple

prospective studies and perform a meta-analysis. However, heterogeneity among study designs very often restricts the possibility of a meta-analysis.

Recently, two randomized controlled trials on resective surgical treatment of peri-implantitis were published, with almost identical study protocols (De Waal et al. 2013a, De Waal et al. 2014). The aim of the present study was to identify indicators that are prognostic for the outcome of resective surgical peri-implantitis treatment, by carrying out an analysis of the pooled data of these two previously conducted studies.

MATERIAL AND METHODS

This study was an analysis of the pooled datasets of two previously conducted randomized, double-blind, controlled trials evaluating the clinical, radiographic and microbiological outcomes of resective surgical treatment of peri-implantitis combined with mechanical debridement and chemical decontamination of the implant surface (De Waal et al. 2013a, De Waal et al. 2014). The research protocols of both studies were identical except for the method of chemical decontamination of the implant surface. The two studies were performed consecutively.

Intervention

Participants were consecutively recruited from patients referred for diagnosis and treatment of peri-implantitis to the University Medical Center Groningen, the Netherlands. Written informed consent was obtained from all participants before entering the study. The studies were approved by the Institutional Review Board of the University Medical Center Groningen (METc2009.172 and METc2010.028) and registered at ClinicalTrials.gov (NCT01521260 and NCT01852253).

Peri-implantitis was defined as bleeding and/or suppuration on probing combined with a peri-implant probing pocket depth (PPD) ≥ 5 mm and bone loss ≥ 2 mm. Patients were all surgically treated by one and the same oral and maxillofacial surgeon (G.R.).

Full thickness mucoperiosteal flaps were raised buccally and lingually. Granulation tissue was removed using curettes (Gracey, Hu-Friedy®, Chicago, IL, USA). Bone recontouring, aimed at eliminating angular bony defects, was performed using a rotating round bur under saline irrigation. The implant surfaces were mechanically cleaned using sterile surgical gauzes soaked in saline. After mechanical debridement, the implant surfaces were rinsed for 1 min with a placebo solution (De Waal et al. 2013a) 0.12% chlorhexidine (CHX) + 0.05% cetylpyridinium chloride (CPC) (De Waal et al. 2013a, De Waal et al. 2014) or a 2% chlorhexidine solution (De Waal et al. 2014). Subsequently, the implant surfaces were rinsed with abundant amounts of sterile saline for 1 min. Suprastructures were repositioned (if necessary) and mucosal flaps were apically positioned and firmly sutured (Vicryl Plus®, Ethicon Inc., Somerville, NJ, USA). For all patients, surgery was followed by two weeks of mouth rinsing with 0.12% CHX + 0.05% CPC without alcohol (PerioAid, Dentaaid SL, Cerdanyola, Spain) two times daily during 30 s. Sutures were removed after two weeks. During follow-up examinations, patients were re-instructed in oral hygiene measures and implants, and teeth

were cleaned as necessary. Use of topical or systemic antibiotic treatment was not part of the treatment protocol.

Follow-up visits were scheduled after 3, 6, and 12 months (T_3 , T_6 and T_{12}). At baseline (T_0) and during follow-up visits radiographs and microbiological samples were taken and clinical measurements were performed by one and the same examiner (Y.W.). Presence of plaque was assessed (present/absent) at four sites per implant (mesial, buccal, distal and lingual) by running a probe across the marginal surface of the implant/suprastructure. Peri-implant pocket probing was performed at four sites per implant using a pressure sensitive probe (probe force of 0.25 N; KerrHawe Click Probe®, Bioggo, Switzerland). PPD was scored to the nearest millimeter. Up to 30 s after pocket probing, the presence or absence of bleeding and suppuration were assessed. The width of keratinized mucosa was assessed at the mid-buccal position of the implant.

Outcomes

Primary outcome

The primary outcome of the present study was failure of peri-implantitis treatment after 12 months. Clinical and radiographic data collected during the last follow-up visit were combined to produce this outcome. Treatment was considered a failure if one or more of the following criteria were met:

- absence of the implant;
- progressive bone loss ≥ 1 mm during follow-up (between T_3 and T_{12}), on the mesial and/or distal side of the implant as assessed on radiographs;
- presence of suppuration on probing;
- bleeding on probing on 3 or 4 sites per implant;
- probing pocket depth of ≥ 5 mm in combination with bleeding;

Success was defined as the inverse of failure.

Predictors

Data on the following potential predictors were collected:

Patient characteristics (measured on patient level):

- Age at surgery;
- Gender;
- Daily medication intake;
- Use of systemic antibiotics during follow-up;
- Smoking;
- History of periodontitis;
- Dental status (fully edentulous versus partially edentulous);
- Number of implants with peri-implantitis;
- Order of inclusion (order in which patients were consecutively included and treated).

Clinical characteristics (measured on implant level):

- Removal of suprastructure during surgery;

- Use of surgical dressing;
- Presence of *Aggregatibacter actinomycetemcomitans* and/or *Porphyromonas gingivalis* in the oral cavity at baseline (measured on patient level);
- Presence of pus at baseline;
- Probing pocket depth (PPD) at baseline: highest value per implant (maximum PPD) and mean of four measurements per implant (mean PPD);
- Bone loss at baseline: highest value per implant (maximum bone loss) and mean of mesial and distal measurement per implant (mean bone loss);
- Bone defect configuration at baseline: angle between bone and implant in apical half of bone defect, lowest value of mesial and distal measurement;
- Presence of plaque at any moment during follow-up: yes/no and mean percentage of sites with plaque;
- Presence of keratinized mucosa at T₃.

Implant characteristics (measured on implant level):

- Implant function time: time between 2nd stage surgery and peri-implantitis surgery;
- Implant location: fully edentulous jaw versus partially edentulous jaw, maxilla versus mandibula, anterior region versus posterior region;
- Previous bone augmentation;
- Implant placement procedure: one-stage versus two-stage procedure;
- Implant length;
- Implant surface roughness: smooth/machined surface versus minimally/moderately rough versus rough.

Since it was shown that the method of surface decontamination did not have a significant effect on treatment outcome parameters (De Waal et al. 2013a, De Waal et al. 2014), this factor was not included in the present analysis.

Statistical analysis

To take into account the hierarchical structure of the data a two-level hierarchical random intercepts model was chosen, with two levels of analysis being implant-level and patient-level. Multilevel univariable logistic (logit) regression analyses were performed separately for all potential prognostic indicators with our primary outcome measure, *i.e.* failure of peri-implantitis treatment at 12 months after treatment. Parameters were estimated using the second order penalized quasi-likelihood (PQL) estimation procedure. The linearity of the associations of continuous variables with the outcome was examined by dividing the data into quartiles. Variables that did not show a continuous relationship were dichotomized or categorized, depending on the observed data structure. Variables with a statistically significant association with the outcome ($p \leq 0.10$) were selected for the multilevel multiple logistic (logit) regression analysis. Collinearity and multicollinearity between the selected variables were assessed by determining correlation coefficients and variance inflation factors (VIF). From variables that were strongly correlated (correlation coefficient > 0.70 or VIF > 5) only the variable that was most strongly associated with the outcome as observed from the univariable analyses was selected for the multiple regression analysis.

Multilevel models were analyzed using MLwiN version 2.12 (Centre for Multilevel Modeling, University of Bristol, Bristol, UK). For descriptive data and collinearity diagnostics Graphpad Prism 5 for Windows (version 5.04, Graphpad Software, San Diego, CA, USA) and IBM® SPSS® Statistics 22 (version 22.0.0.1, IBM, Armonk, NY, USA) were used.

RESULTS

The complete datasets of two randomized controlled trials were available for the current analysis (De Waal et al. 2013a, De Waal et al. 2014). A total of 74 patients presenting a total of 187 implants with peri-implantitis were previously included and had been treated according to the study protocols (respectively 30 patients with 79 implants in the first study and 44 patients with 108 implants in the second study). Two patients had their implant removed between T_3 and T_6 because of implant fracture and were excluded from the current analysis. The remaining patients attended all follow-up visits and no patient was lost to follow-up. Therefore, the current analysis is based on data from 72 patients and a total of 185 implants. Patient and implant characteristics are depicted in Table 1.

Five patients had one or more implants removed during follow-up because of persisting peri-implantitis. These implants were classified as failures (14 implants). An additional 92 implant were classified as failures based on the previously stated criteria on bone loss, suppuration, bleeding on probing, and/or probing pocket depth. In total, 106 implants (57%) in 48 patients (67%) showed failure of peri-implantitis treatment at T_{12} .

Prognostic indicators

Some of the continuous variables showed no linear association with the primary outcome and were either dichotomized (age, number of implants with peri-implantitis, mean plaque percentage after surgery, implant function time and implant length) or categorized (angle of bone defect). The results from the univariable and multiple regression analyses are presented in Table 1. Univariable analysis showed a significant association between the outcome for the potential prognostic indicators smoking, order of inclusion, maximum pocket depth at baseline, mean bone loss at baseline, presence of plaque after surgery, mean plaque percentage after surgery, implant length and implant surface roughness ($p \leq 0.10$). In the multiple regression analysis only the variables order of inclusion and mean bone loss at baseline were significant prognostic indicators for failure of peri-implantitis treatment ($p < 0.05$).

Post hoc analysis

Since order of inclusion was the strongest prognostic indicator for the primary outcome, the relationship between this variable and the outcome was examined in more detail. Implants were divided into deciles according to the order of inclusion and corresponding success percentages were calculated. The success percentages are graphically depicted in Figure 1, which may be interpreted as a graphical representation of the 'learning curve' of the treatment team.

Table 1. Univariable and multivariable associations with failure of peri-implantitis treatment after one year (study 1 and 2 combined)

Variable	n (%)	Univariable regression analysis			Multiple regression analysis		
		OR	95% CI	p*	OR	95% CI	p
<i>Patient characteristics</i>							
Age							
< 60 years [#]	32 (44)						
≥ 60 years	40 (56)	0.61	0.2 – 2.1	0.43			
Gender							
Female [#]	50 (69)						
Male	22 (31)	0.43	0.1 – 1.6	0.20			
Daily medication intake	37 (51)	0.86	0.3 – 2.9	0.80			
Smoking	24 (33)	3.40	1.0 – 11.8	0.054	2.12	0.5 – 9.0	0.31
History of periodontitis	32 (44)	1.44	0.4 – 4.9	0.56			
Dental status							
Fully edentulous [#]	39 (54)						
Partially edentulous	33 (46)	1.78	0.5 – 6.1	0.36			
# implant with peri-implantitis							
< 4 implants [#]	50 (69)						
≥ 4 implants	22 (31)	1.24	0.4 – 4.3	0.74			
Order of inclusion (range)	1-72	0.96	0.9 – 1.0	0.004	0.96	0.9 – 1.0	0.016**
<i>Treatment / clinical characteristics</i>							
Removal of suprastructure during surgery	116 (63)	0.97	0.3 – 3.4	0.96			
Use of surgical dressing	138 (75)	0.59	0.1 – 2.4	0.47			
Presence of Aa and/or Pg in the oral cavity at baseline	43 (23)	0.94	0.2 – 4.3	0.94			
Presence of pus at baseline	91 (49)	1.66	0.7 – 4.1	0.28			
Maximum pocket depth at baseline (mm; mean (SD))	6.5 (1.6)	1.73	1.2 – 2.5	0.003	1.22	0.8 – 1.8	0.32
Mean bone loss at baseline (mm; mean (SD))	4.0 (1.8)	1.61	1.2 – 2.2	0.003	1.48	1.0 – 2.1	0.030**
Angle of bone defect at baseline							
≤ 37.5° [#]	55 (30)						
> 37.5° and < 52.5°	63 (34)	0.52	0.2 – 1.5	0.24			
≥ 52.5°	67 (36)	0.84	0.3 – 2.5	0.75			
Presence of plaque after surgery	114 (62)	2.92	1.1 – 8.0	0.042	1.72	0.5 – 6.1	0.40
Mean plaque percentage after surgery							
< 25% [#]	117 (63)						
≥ 25%	68 (37)	2.92	1.0 – 8.6	0.051	1.62	0.4 – 6.1	0.48
Presence of keratinized mucosa after surgery	112 (61)	0.92	0.4 – 2.3	0.86			
<i>Implant characteristics</i>							
Implant function time							
< 6 years [#]	93 (50)						
≥ 6 years	92 (50)	0.73	0.2 – 2.5	0.61			
Implant location							
Fully edentulous jaw [#]	144 (78)						
Partially edentulous jaw	41 (22)	0.88	0.2 – 3.5	0.86			
Mandibula [#]	84 (45)						
Maxilla	101 (55)	1.19	0.4 – 3.5	0.75			
Anterior region [#]	96 (52)						
Posterior region	89 (48)	1.26	0.5 – 3.1	0.61			
Implant placed in bone augmented site	76 (41)	0.74	0.3 – 2.0	0.56			
Implant placement procedure							
Two stage procedure [#]	100 (54)						
One stage procedure	85 (46)	0.97	0.3 – 3.3	0.96			
Implant length							
< 13 mm [#]	81 (44)						
≥ 13 mm	104 (56)	3.17	1.0 – 9.9	0.048	2.38	0.7 – 8.0	0.16
Implant surface roughness							
Smooth	9 (5)	2.26	0.1 – 51.4	0.61	1.4	0.1 – 28.2	0.83
Minimally/moderately rough [#]	145 (78)						
Rough	31 (17)	0.22	0.1 – 1.1	0.063	0.22	0.1 – 1.2	0.09

Reference category

* Variables with a univariable p value ≤ 0.10 were selected for multiple regression analysis

** Statistically significant p < 0.05

Figure 1. Learning curve of the surgical team

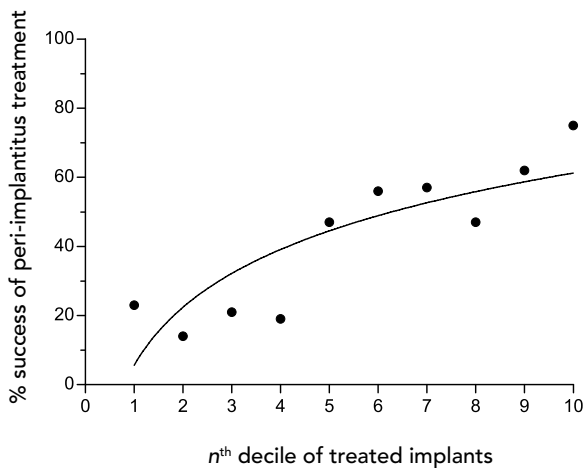


Figure 2. Success percentage of peri-implantitis treatment related to mean amount of bone loss at baseline (only study 2).

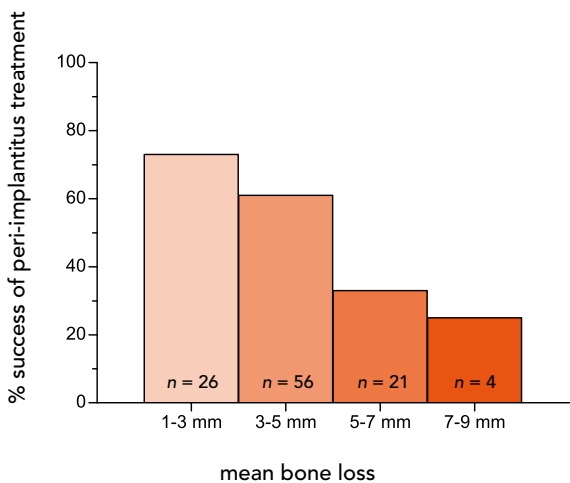
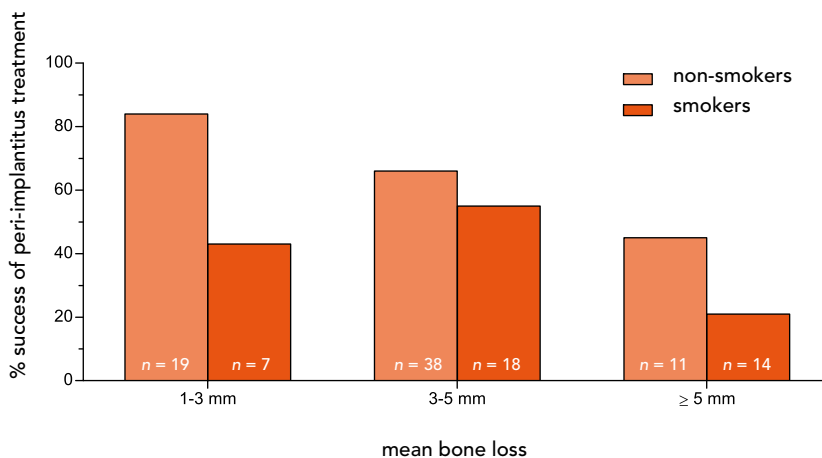


Figure 3. Success percentage of peri-implantitis treatment related to mean amount of bone loss at baseline for non-smokers and smokers (only study 2).



An increase in success percentage and a flattening of the 'learning curve' was observed after treatment of about 40% of the implants. The highly significant effect of the variable order of inclusion on the outcome of peri-implantitis treatment might have blurred possible important effects of other potential prognostic indicators. Therefore, additional univariable and multiple regression analyses were carried out including only the patients from the second study, *i.e.* 107 implants in 43 patients. In this group, peri-implantitis treatment was unsuccessful in 26 of these 43 patients (60%) and in 46 of the 107 implants (43%).

Patient and implant characteristics and the results from the additional multilevel univariable and multiple logistic regression analyses are presented in Table 2. The variable order of inclusion no longer appeared to be statistically significant ($p = 0.26$). Variables that did show a significant univariable association with the primary outcome were smoking, maximum pocket depth at baseline, mean bone loss at baseline and presence of plaque ($p \leq 0.10$). In the multiple regression analysis only the predictors smoking and mean bone loss remained statistically significant ($p < 0.05$). The success percentages in different categories of bone loss and smoking are graphically depicted in Figure 2 and 3.

DISCUSSION

The present study was initiated with the aim to identify potential risk indicators for poor outcome of peri-implantitis treatment. It was shown that order of inclusion, mean amount of bone loss at baseline and smoking are strong prognostic indicators for the outcome of resective surgical peri-implantitis treatment. Less strong prognostic indicators were maximum pocket depth at baseline and presence of plaque during follow-up.

Table 2. Univariable and multivariable associations with failure of peri-implantitis treatment after one year (only study 2)

Variable	n (%)	Univariable regression analysis			Multiple regression analysis		
		OR	95% CI	p*	OR	95% CI	p
<i>Patient characteristics</i>							
Age							
< 60 years [#]	21 (49)						
≥ 60 years	22 (51)	1.00	0.3 – 3.2	1.00			
Gender							
Female [#]	30 (70)						
Male	13 (30)	0.37	0.1 – 1.3	0.11			
Daily medication intake	22 (51)	0.91	0.3 – 2.9	0.87			
Smoking	13 (30)	3.70	1.3 – 10.6	0.015	3.82	1.0 – 14.1	0.044**
History of periodontitis	19 (44)	0.85	0.3 – 2.7	0.79			
Dental status							
Fully edentulous [#]	21 (49)						
Partially edentulous	22 (51)	0.78	0.2 – 2.5	0.68			
# implant with peri-implantitis							
< 4 implants [#]	30 (70)						
≥ 4 implants	13 (30)	0.65	0.2 – 2.1	0.47			
Order of inclusion (range)	30-72	0.97	0.9 – 1.0	0.26			
<i>Treatment / clinical characteristics</i>							
Removal of suprastructure during surgery	77 (72)	2.01	0.6 – 7.0	0.24			
Use of surgical dressing	69 (65)	0.56	0.2 – 1.9	0.35			
Presence of Aa and/or Pg in the oral cavity at baseline	30 (28)	1.91	0.5 – 7.0	0.33			
Presence of pus at baseline	57 (53)	1.73	0.7 – 4.5	0.26			
Maximum pocket depth at baseline (mm; mean (SD))	6.0 (1.1)	1.49	1.0 – 2.3	0.073	1.27	0.8 – 2.0	0.31
Mean bone loss at baseline (mm; mean (SD))	4.1 (1.6)	1.73	1.2 – 2.5	0.003	1.46	1.0 – 2.1	0.043**
Angle of bone defect at baseline							
≤ 37.5° [#]	29 (27)						
> 37.5° and < 52.5°	35 (33)	0.43	0.1 – 1.5	0.18			
≥ 52.5°	43 (40)	1.23	0.4 – 4.1	0.74			
Presence of plaque after surgery	56 (52)	2.55	0.8 – 7.8	0.100	2.59	0.8 – 8.3	0.11
Mean plaque percentage after surgery							
< 25% [#]	73 (68)						
≥ 25%	34 (32)	1.88	0.6 – 6.2	0.30			
Presence of keratinized mucosa after surgery	70 (65)	0.81	0.3 – 2.2	0.67			
<i>Implant characteristics</i>							
Implant function time							
< 6 years [#]	61 (57)						
≥ 6 years	46 (43)	0.70	0.2 – 2.3	0.55			
Implant location							
Fully edentulous jaw [#]	77 (72)						
Partially edentulous jaw	30 (28)	0.48	0.1 – 1.6	0.24			
Mandibula [#]	50 (47)						
Maxilla	57 (53)	1.17	0.4 – 3.3	0.77			
Anterior region [#]	50 (47)						
Posterior region	57 (53)	1.31	0.5 – 3.4	0.57			
Implant placed in bone augmented site	40 (37)	0.70	0.2 – 2.0	0.50			
Implant placement procedure							
Two stage procedure [#]	60 (56)						
One stage procedure	47 (44)	1.07	0.3 – 3.4	0.91			
Implant length							
< 13 mm [#]	44 (41)						
≥ 13 mm	63 (59)	2.47	0.8 – 7.4	0.11			
Implant surface roughness							
Smooth	5 (5)						
Minimally/moderately rough [#]	85 (80)	2.60	0.2 – 35.9	0.48			
Rough	17 (16)	0.34	0.1 – 1.7	0.18			

[#] Reference category

* Variables with a univariable p value ≤ 0.10 were selected for multiple regression analysis

** Statistically significant p < 0.05

All patients included in the present study were treated by the same surgical team. This team has great experience in oral- and maxillofacial surgery, including implant dentistry, but the experience with the specific resective surgical peri-implantitis treatment was relatively limited prior to the start of the study. The variable 'order of inclusion' was included in the current analysis to explore a possible learning effect of the surgical team with the specific procedure. This variable appeared to be a strong prognostic indicator for the outcome of peri-implantitis treatment. The first treated patients showed significantly higher failure rates than the patients that were treated later in the study. This holds true even when other factors such as amount of bone loss and probing pocket depth at baseline are taken into account, as can be observed from the multiple regression analysis. This 'learning effect' or phenomenon of improvements in performance over time when adopting a 'new' technique is well-known in medicine, psychology and engineering (Ramsay et al. 2000, Ramsay et al. 2002). Factors that influence individual learning curves include: experience and type of people in the surgical team, facilities provided by the institution, individual patient and clinical characteristics in the population undergoing the procedure and characteristics of the surgeon such as attitude, natural abilities, capacity for acquiring new skills and previous experience (Cook et al. 2004). As learning effects are present in many surgical procedures, including implant dentistry (Geckili et al. 2014), they form an obstacle to undertaking and interpreting clinical trials (Cook et al. 2004). It is therefore important to statistically consider learning effects in clinical studies (Ramsay et al. 2000). This has been done in the present study by carrying out a post-hoc analysis including only patients that were treated after fading of the learning effect.

The amount of bone loss was the only statistically significant prognostic indicator in both the first evaluation as well as the post-hoc evaluation. Increasing amounts of bone loss at baseline were associated with decreasing success percentages. Specifically smokers with peri-implant bone loss exceeding 5 mm were extremely difficult to treat successfully, resulting in a success percentage of only 32%. The factor bone loss has been identified by others as a determining factor for peri-implantitis treatment outcome. Serino & Turri (2011) found that the proportion of implants that showed healthy peri-implant conditions following resective peri-implantitis treatment was higher for those with minor initial bone loss (2–4 mm bone loss as assessed during surgery) compared to implants with bone loss of ≥ 5 mm (74% vs. 40%). The retrospective study of Lagervall & Jansson (2013) showed that implants with bone loss exceeding 1/3 of the length of the implant were significantly associated with failure of peri-implantitis treatment. Amount of bone loss and pocket depth at baseline can be seen as representatives for disease severity. Implants with large amounts of bone loss and with deep peri-implant pockets are generally associated with large inflammatory lesions. If the bone and attachment loss have occurred in a relatively short period of time, the disease process may be viewed as an 'aggressive' or 'rapidly progressing' form of peri-implantitis. In line with what seems to be true for treatment of aggressive and chronic periodontitis (Teughels et al. 2014), aggressive peri-implantitis might be more difficult to treat than 'slowly progressing' peri-implantitis. In implants with large amounts of bone loss a substantial part of the rough, screw-shaped implant surface becomes exposed to the oral environment and is covered with a biofilm. In these

cases, complete biofilm removal, by the surgeon during surgery and by the patient after surgery, might be more difficult to achieve than in cases with only minor bone loss and mainly smooth surfaces to be cleaned. In addition, the unfavorable configurations with regard to neighboring teeth that can develop as a result of substantial bone loss (angular defects and deflecting gingival/mucosal margin) might hinder proper cleaning of the implant and may hamper treatment success. Early diagnosis of peri-implantitis seems crucial for achieving a successful peri-implantitis treatment outcome.

Two out of the three major risk factors for development of peri-implantitis (Heitz-Mayfield 2008), were also identified as prognostic indicators for peri-implantitis treatment outcome, being smoking and, to a lesser extent, presence of plaque. A history of periodontitis could not be identified as prognostic indicator, which might be due to the fact that a substantial proportion of patients was fully edentulous and data on history of periodontitis was mainly based on self-reported information. Smoking, a known risk factor for peri-implantitis (Heitz-Mayfield 2008), is also a major risk factor for periodontitis (Bergström 2006). It has been shown that smoking negatively influences periodontitis treatment outcomes (Bergström 2006, Labriola et al. 2005) and that smoking cessation results in better treatment results (Chambrone et al. 2013). The results of the present study are in line with this observation and the findings of Charalampakis et al. (2011), who also showed an association between smoking and poor peri-implantitis treatment outcomes. Although this association could not be established in prospective studies up to now (Serino & Turri 2011, Heitz-Mayfield et al. 2012), it seems advisable to encourage smokers with peri-implantitis to abandon smoking as part of their peri-implantitis treatment strategy.

The variable presence of plaque after surgery was not statistically significant ($p = 0.11$ in multiple regression analysis), but may still be considered a relevant prognostic indicator for peri-implantitis treatment. Patients with plaque at their implants at any moment during the follow-up period (at T_3 , T_6 and T_{12}) showed higher failure rates than patients with good oral hygiene, which is in line with observations made by others (Lagervall & Jansson 2013). A high standard of oral hygiene and participation in a recall system seem important, both for prevention of peri-implant disease (Anner et al. 2010, Costa et al. 2012) as well as maintenance of stable peri-implant conditions after peri-implantitis surgery (Serino et al. 2014).

In conclusion, the present study is an analysis of the pooled data of two previously conducted studies. The data sets of the two studies could be meaningfully combined because the research protocols were almost identical, patient groups were similar and treatments were performed by the same surgical team. The outcome of a surgical peri-implantitis treatment is most significantly influenced by the amount of experience of the surgical team with that specific procedure. The observed learning effect has consequences for clinical practice and for conducting and interpreting clinical trials on treatment of peri-implantitis. Other factors that influence the treatment outcome are amount of peri-implant bone loss at baseline and smoking, and to a lesser extent, probing pocket depth at baseline and presence of plaque during follow-up. Early diagnosis of peri-implantitis and control of behavioral factors are crucial in achieving peri-implantitis treatment success.

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