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Peri-implantitis – onset and pattern of progression

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Abstract

Background: While information on the prevalence of peri-implantitis is available, data describing onset and progression of the disease are limited.

Material & Methods: A 9-year follow-up examination of 596 randomly selected implant-carrying individuals identified 62 patients with moderate/severe peri-implantitis. Longitudinal assessments of peri-implant marginal bone levels were used to construct a statistical model with bone loss as the dependent variable. A multilevel growth model estimated the pattern of bone loss for each implant/patient. Onset of peri-implantitis was determined by evaluating the cumulative percentage of implants/patients presenting with estimated bone loss at each year following prosthesis delivery.

Results: The analysis showed a non-linear, accelerating pattern of bone loss at the 105 affected implants. The onset of peri-implantitis occurred early, and 52% and 66% of implants presented with bone loss of >0.5 mm at years 2 and 3 respectively. A total of 70% and 81% of subjects presented with ≥1 implants with bone loss of >0.5 mm at years 2 and 3 respectively.

Conclusions: It is suggested that peri-implantitis progresses in a non-linear, accelerating pattern and that, for the majority of cases, the onset occurs within 3 years of function.

Key words: bone loss; complications; disease progression; onset; peri-implantitis

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Peri-implantitis is characterized by inflammation in peri-implant tissues and loss of supporting bone. While a meta-analysis performed in a systematic review on the epidemiology of peri-implant diseases estimated an overall prevalence of peri-implantitis of 14–30% (Derks & Tomasi 2015), reports from cross-sectional studies indicated that moderate and severe forms of peri-implantitis occurred in subgroups of 15–20% of implant-carrying subjects (Roos-Jansåker et al. 2006, Koldsland et al. 2010, Derks et al. 2016). In the light of the large number of subjects receiving implant-supported restorative therapy, peri-implantitis is a current and future challenge for patients and dental professionals. Prevention of peri-implantitis has therefore a high priority and was addressed at the 9th European Workshop on Periodontology (Jepsen et al. 2015). It was stated that peri-implant mucositis is the precursor to peri-implantitis, as is gingivitis for periodontitis, and that a continuum exists from healthy peri-implant mucosa to peri-implant mucositis and to peri-implantitis. Consequently, prevention and treatment of peri-implant mucositis may therefore prevent the conversion of peri-implant mucositis to peri-implantitis (Jepsen et al. 2015).

The shift from peri-implant mucositis to peri-implantitis thus

Conflict of interest and source of funding statement

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indicates the time of onset of peri-implantitis. The assessment of such a conversion, however, is difficult, as it requires the detection of early signs of loss of supporting bone. In addition, from a research perspective, the documentation of the onset of a disease requires a longitudinal approach. While a prospective outline may not be feasible from an ethical standpoint, a retrospective evaluation of peri-implant bone loss in radiographs in patients with severe forms of peri-implantitis is justified. Besides the detection of the time of onset of peri-implantitis, the progression pattern of the disease may also be evaluated in radiographs.

We assessed the occurrence of peri-implantitis in a large cohort of patients randomly selected from the national registry of the Swedish Social Insurance Agency (Derks et al. 2016). Thus, out of 596 patients who attended a 9-year follow-up examination, 14.5% exhibited moderate/severe peri-implantitis (bleeding/suppuration on probing and >2 mm bone loss) at ≥1 implants. Using radiographs collected from patient files and obtained at the 9-year examination in the group of patients presenting with moderate/severe peri-implantitis, we aimed to evaluate the onset and pattern of peri-implant bone loss during progression of disease.

Material and Methods

The research protocol was approved by the regional Ethical Committee, Gothenburg, Sweden (Dnr 290-10) and registered at ClinicalTrials.gov (NCT01825772). STROBE guidelines were followed.

Patient files of 2765 randomly selected implant-carrying individuals in two age groups (45–54 years and 65–74 years in 2003) were obtained. All had received implant-supported restorative therapy in Sweden in 2003. From this cohort, 596 individuals attended a 9-year clinical and radiographic examination, which included assessments of probing pocket depth and bleeding on probing. Radiographs of all relevant implant sites were obtained and compared with baseline radiographs retrieved from patient files. Peri-implant marginal bone loss was assessed from 1 year after prosthesis connection up to 9 years. Radiographs obtained during the 9 years of follow-up were categorized according to the time of examination and grouped by "year from prosthesis delivery". For more details on the patient sample, the clinical examination and the methodology of bone level measurements, including internal validity, see Derks et al. (2016).

Moderate and/or severe peri-implantitis was defined as the presence of bleeding/suppuration on probing and >2 mm of bone loss at the 9-year examination. Sixty-two of 427 patients with available baseline radiographs presented with moderate/severe peri-implantitis at ≥1 implants and were included in this study.

A total of 126 implants in the 62 identified subjects exhibited moderate/severe peri-implantitis. For 21 of the implants, no additional radiographs beyond baseline and the 9-year examination were available, and hence, these implants were excluded from further analysis. The sample consisted of 53 patients and 105 implants presenting with moderate/severe peri-implantitis and ≥3 radiographic examinations over a 9-year period (mean years in function: 8.6 ± 0.7).

Data analysis

Continuous variables were recorded as mean ± standard deviation. A multilevel model was constructed with bone loss as the dependent variable (MLwiN 2.28; Center of Multilevel Modelling, University of Bristol, Bristol, UK) to analyse the pattern of progression of peri-implantitis. The hierarchical structure included the subject (n = 53), the implant (n = 105) and year of function (1–9 years). Year of function was entered as an explanatory variable with random effects for subject and implant levels. Following the modelling of a linear relation between year of function and bone loss, a curved relation growth model was built with a polynominal term showing an improved model fit as tested by reduction of the −2 log likelihood (chi-square distribution). In the final model, the intercept was forced through 0

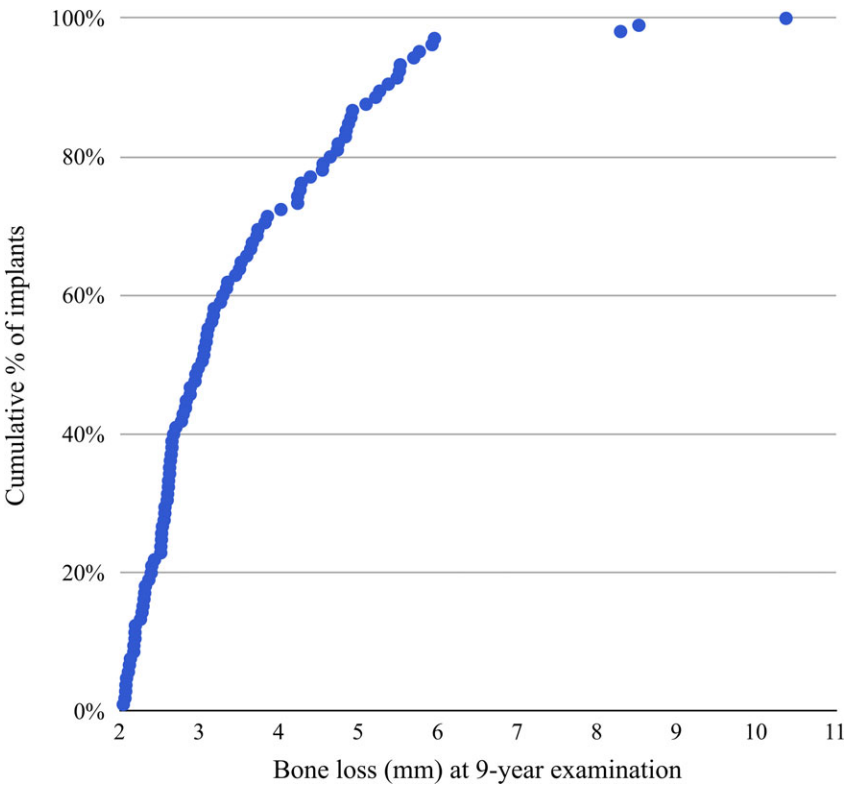

Fig. 1. Cumulative percentage of implants diagnosed with moderate/severe peri-implantitis at the 9-year examination: bone loss (n = 105).

Table 1. Multilevel model building with bone loss as the dependent variable

	Empty model	Standard error	Linear model	Standard error	Polynomial model	Standard error	Polynomial random	Standard error
Fixed part								
Intercept	−1.509	0.095	0.132	0.113	0.137	0.141	0.055	0.062
Year			−0.383	0.015				
$Year^1$					−0.485	0.129	−0.447	0.106
$Year^2$					0.04	0.035	0.03	0.03
$Year^3$					−0.003	0.002	−0.002	0.002
Random part								
Level: subject								
var (cons)	0.06	0.087	0.14	0.098	0.134	0.097		
var (y^1/y^1)							0.106	0.082
cov (y^2/y^1)							−0.027	0.021
var (y^2/y^2)							0.011	0.007
cov (y^3/y^1)							0.001	0.001
cov (y^3/y^2)							−0.001	0
var (y^3/y^3)							0	0
Level: implant								
var (cons)	0	0	0.287	0.11	0.287	0.109		
var (y^1/y^1)							0.243	0.055
cov (y^2/y^1)							−0.024	0.006
var (y^2/y^2)							0.003	0.001
Level: year of function								
var (cons)	3.207	0.232	1.15	0.091	1.144	0.09	0.301	0.03
−2*log likelihood	1708.716	*	1357.935	†	1355.333	‡	1127.788	

*The linear model is significantly different from the empty model ($p < 0.0001$).
†The polynomial model is not significantly different from the linear model ($p = 0.27$).
‡The polynomial model (random) is significantly different from the empty model, the linear model and the polynomial model.

at baseline by choosing fixed effects for subject and implant levels in the constant term. The pattern of bone loss was modelled for each implant and patient, and the overall mean estimated bone loss was calculated, including a 95% confidence interval.

To determine the time point of onset of peri-implantitis, the cumulative percentage of implants and patients presenting with estimated bone loss of >0.5, >1.0, >1.5 and >2.0 mm at each year following prosthesis delivery was calculated.

Results

The mean number of radiographic examinations for the 105 implants was 4.1 (range: 3–7) and the mean bone loss at the 9-year examination was 3.5 ± 1.5 mm. The cumulative percentage of implants in relation to bone loss is presented in Fig. 1. Bone loss of >3 mm occurred in 51% of implants, while 29% lost >4 mm.

Multilevel modelling

Results of the different steps of model building are illustrated in Table 1. The linear relationship between time and bone loss was significant and improved the model ($p < 0.0001$). The estimated annual bone loss was 0.38 mm, and year of function contributed with 73% to the total variance. Patient- and implant-related variance amounted to 9% and 18% respectively. The introduction of the polynomial term with fixed effects did not influence the model ($p = 0.27$). As time coefficients varied randomly over subjects and implants, the model improved significantly ($p < 0.0001$) and reduced the variance on the lowest level by 64% and 91% when compared to the linear and empty

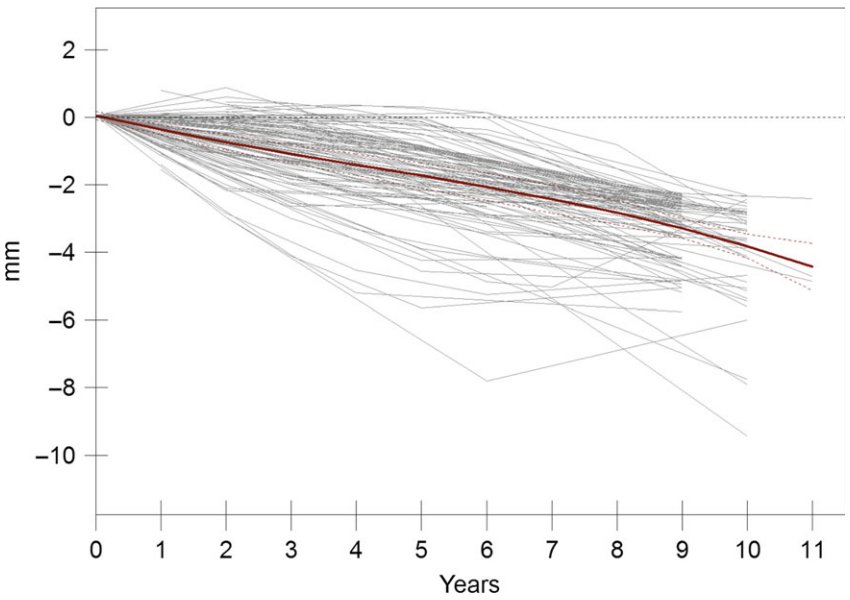

Fig. 2. Estimated pattern of bone loss for each implant diagnosed with moderate/severe peri-implantitis at the 9-year examination ($n = 105$). The red regression line indicates the mean estimated bone loss over time including the 95% confidence interval.

models respectively. The final model demonstrated that bone loss was not linear and accelerated over time. In addition, the residual variance at implant level and year in function increased over time (Figs. S1 and S2).

Estimated bone loss

Results from the estimation of bone loss are illustrated in Fig. 2. Each line represents one implant diagnosed with moderate/severe peri-implantitis at the 9-year examination. The regression line indicates the mean estimated bone loss over time including the 95% confidence interval. In Fig. 3, the pattern of bone loss over time is illustrated for each subject, including only implants diagnosed with moderate/severe peri-implantitis at the 9-year examination.

Onset of peri-implantitis

Different levels of bone loss expressed as cumulative percentages of implants diagnosed with moderate/severe peri-implantitis at the 9-year examination are illustrated in Fig. 4. For estimated bone loss of >0.5 mm, 52% and 66% of implants were identified at year 2 and year 3 respectively. At year 5, 89% of implants presented with estimated bone loss of >0.5 mm. Using the >1 mm threshold for estimated bone loss, the proportions of implants detected at years 2, 3 and 5 were 31%, 47% and 73% respectively. The corresponding calculations for patients diagnosed with moderate/severe peri-implantitis at the 9-year examination are illustrated in Fig. 5. A total of 70%, 81% and 96% of subjects presented with ≥1 implants with estimated bone loss of >0.5 mm at years 2, 3 and 5 respectively. Estimated bone loss of >1 mm was calculated for 57% of patients at year 3 and 81% at year 5.

Figure 6 illustrates one of the included cases demonstrating progressive and accelerating marginal bone loss over time.

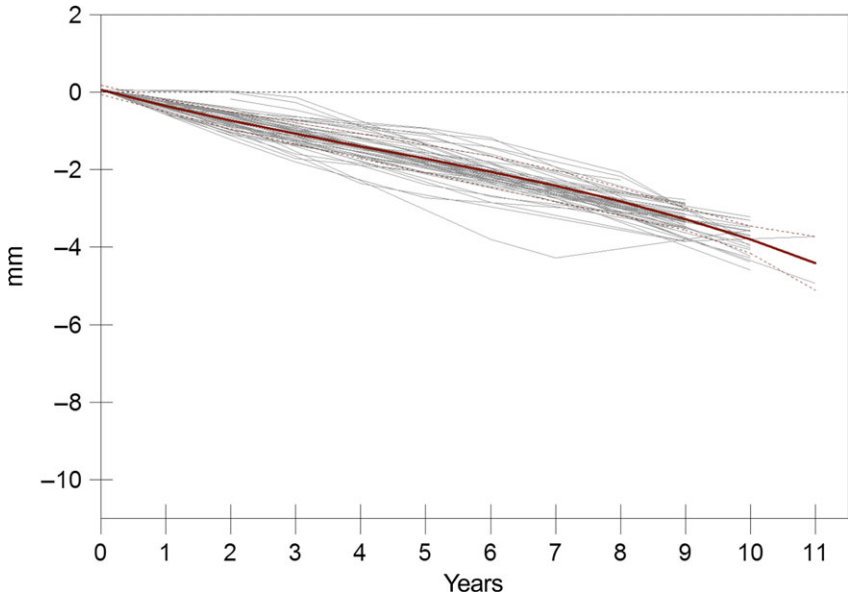

Fig. 3. Estimated pattern of bone loss for each subject diagnosed with moderate/severe peri-implantitis at the 9-year examination (n = 53); only implants diagnosed with moderate/severe peri-implantitis are included (n = 105). The red regression line indicates the mean estimated bone loss over time including the 95% confidence interval.

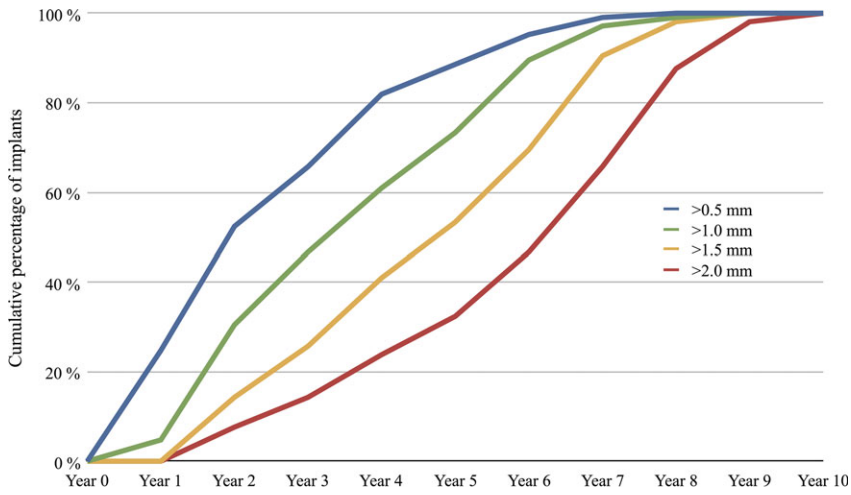

Fig. 4. Cumulative percentage of implants diagnosed with moderate/severe peri-implantitis at the 9-year examination: different levels of bone loss by year (n = 105). Blue line: >0.5 mm; green line: >1.0 mm; yellow line: >1.5 mm; red line: >2.0 mm.

Discussion

In this study, we evaluated the pattern of progression and the onset of disease at implants diagnosed with moderate/severe peri-implantitis 9 years after treatment. Multilevel analysis showed a non-linear, accelerating pattern of bone loss at affected implants. The onset of peri-implantitis occurred early as 70% and 81% of subjects presented with ≥1 implants with bone loss of >0.5 mm at years 2 and 3 respectively.

Previous reports on the epidemiology of peri-implantitis have focused on the prevalence of the disease. In a review on the epidemiology of peri-implantitis, Derks & Tomasi (2015) noted that longitudinal data, allowing inferences on disease development, were rarely reported. In this context, the data on onset and pattern of progression of peri-implantitis presented in this study provide novel information to the understanding of the disease. Results from this study suggest that the onset of peri-implantitis occurred early, as the majority of subjects (81%) presented with signs of detectable bone loss at year 3. Only a subgroup of patients (4%) experienced the onset of peri-implantitis after

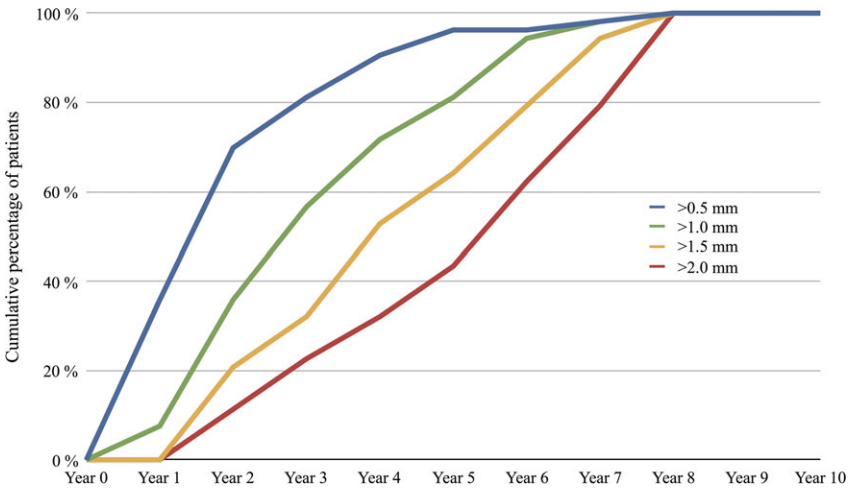

Fig. 5. Cumulative percentage of subjects diagnosed with moderate/severe peri-implantitis at the 9-year examination: different levels of bone loss by year (n = 53). Blue line: >0.5 mm; green line: >1.0 mm; yellow line: >1.5 mm; red line: >2.0 mm.

year 5. In the systematic review by Derks & Tomasi (2015), a positive correlation between the prevalence of peri-implantitis and the time of follow-up of implants was observed, suggesting peri-implant bone loss to be time dependent.

While comprehensive information is available on the prevalence of periodontitis around teeth, the time of onset of the disease is not fully understood. In a systematic review on prevalence and incidence of severe periodontitis, Kassebaum et al. (2014) reported that severe periodontitis was the sixth most common disease in man. It was also reported that the overall prevalence of the condition was about 11% in the period 1990–2010 and that the incidence rate increased rapidly between 20 and 40 years of age, peaking at the age of 38. Few cases had their onset beyond the age of 50. The findings presented by Kassebaum et al. (2014) do not indicate a general onset of periodontitis as the target of the study was the severe form of the disease. Nevertheless, it may be assumed that severe periodontitis commonly commences after 20 years of age. Thus, peri-implantitis, as demonstrated by data in this study, appears to be an early occurring disease and is different in terms of onset when compared to severe forms of periodontitis. It should be noted that the assessment of the onset of peri-implantitis in this study was solely based on radiographic signs of marginal bone loss. This presents an obvious limitation as information on the presence/absence of inflammation at the time of onset was lacking. In this context, it should be kept in mind that similar limitations need to be considered in studies on periodontitis.

The pattern of peri-implant bone loss has been described previously. Fransson et al. (2010) identified progressive bone loss at 419 implants in 182 patients and demonstrated in a multilevel analysis that bone loss occurred in a non-linear pattern and that the rate of bone loss increased over time. The findings reported by Fransson et al. (2010) are in agreement with results presented in this study. While many methodological features of analysis were similar in the two studies, the function time of implants differed. In the study by Fransson et al. (2010), it varied between 5 and 20 years, while this study included patients with a defined follow-up time of 9 years. In addition, the patients in the study by Fransson et al. (2010) were treated at one single specialist centre and provided with implants from one implant system. In contrast, the patients in the present cohort represented different clinical settings and different implant systems.

The implants included in this study demonstrated a mean marginal bone loss of 3.5 ±1.5 mm during a mean follow-up period of 8.6 ±0.7 years. This corresponds to an annual rate of bone loss of about 0.4 mm. As previously reported, the average bone loss of 3.5 mm corresponded to about 30% of the intraosseous portion of the affected implants (Derks et al. 2016). The significance of annual bone loss assessments, however, is difficult to interpret. Periodontitis is characterized by marginal bone loss, and different population studies have presented a range of annual bone loss extending from 0.05 to 0.30 mm (e.g. Axelsson & Lindhe 1978, Löe et al. 1978, Schätzle et al. 2003). Thus, calculated data on annual bone loss may be misleading, as pattern of bone loss during progression of disease is not always linear. Data from this study revealed that the progression pattern of peri-implantitis is not linear.

Author contributions

J. Derks, T. Berglundh and J. L. Wennström contributed to concep-

Fig. 6. Seveny-nine-year old woman diagnosed with moderate/severe peri-implantitis at the 9-year examination (2013). The radiographs indicate progressive and accelerating marginal bone loss at the distal implant site.

tion, design and data analysis, drafted the manuscript; J. Håkansson contributed to conception and design, critically revised the manuscript; D. Schaller and T. Tomasi contributed to data analysis, critically revised the manuscript. All authors gave final approval and agreed to be accountable for all aspects of the work.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Fig. S1 Total variance in growth model over time (the dotted lines indicate the 95% confidence interval).

Fig. S2 Variance in growth model by level over time. Yellow line: patient level; brown line: implant level; red line: time level.

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Clinical Relevance

Scientific rationale for the study: While information on the prevalence of peri-implantitis is available, data describing onset and progression of the disease are limited.

Principal findings: Data from the present study revealed that the progression of peri-implantitis occurred in a non-linear, accelerating pattern and that onset occurred early.

Clinical implications: The present findings highlight the importance of early diagnosis and adequate therapy of peri-implantitis.