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Early peri-implant bone loss as a predictor for peri-implantitis: A 10-year prospective cohort study

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Abstract

Purpose: To evaluate the effect of early bone loss (EBL), on long-term bone stability and future peri-implantitis development.

Materials and methods: Patients referred for implant placement between 2005 and 2009 were consecutively treated and followed for 10 years. After 10 years, patients were invited for a scientific diagnostic visit to evaluate implant survival and bone loss. Bone level changes were compared with baseline. Non-parametric testing was performed in cross-tabs (Pearson Chi-square and Fishers's exact test). Kaplan–Meier-estimated survival curves were plotted for different thresholds for EBL at different timepoints. Generalized linear mixed models with binomial distribution and logit link for peri-implantitis were fitted. An adjusted logistic mixed model was made to evaluate peri-implantitis, in relation with smoking status, history of periodontitis, and EBL > 0.5 mm.

Results: Four hundred and seven patients (mean age of 64.86 years [range 28–92, SD 10.11]), with 1482 implants, responded to the 10-year recall invitation. After an average follow-up time of 10.66 years (range 10–14, SD 0.87), implant survival was 94.74%. Mean crestal bone loss after 10 years was 0.81 mm (SD 1.58, range 0.00–17.00). One hundred and seventy five implants in 76 patients had peri-implantitis (11.8% on implant level, 18.7% on patient level). EBL of 0.5, 1, and 2 mm were significant predictors for peri-implantitis and implant loss after 10 years. Implants with EBL ≥0.5 mm during the first year of function showed a 5.43 times higher odds for future peri-implantitis development. Probability in developing peri-implantitis was 52.06% when smoking, Periodontal history and EBL of >0.5 mm was combined.

Conclusion: The present study suggests that EBL is a predictor for long-term peri-implant pathology, with a significant higher risk for peri-implantitis when early bone loss exceeds the thresholds of 0.5 and 1 mm, especially when additional risk factors such as smoking or susceptibility for periodontal disease prior to implant treatment are present. Clinical trial registration number B670201524796.

KEYWORDS
bone loss, early bone loss, implant, long term, peri-implantitis, predictor

1 | INTRODUCTION

Today, implantology offers a wide variety of treatment strategies in replacing missing teeth, even in complex or compromised cases. Over the past decade, an estimated 200 million implants have been installed worldwide.[1] This implies that simultaneously a rise in the prevalence of complications can be expected. On implant level, minor or major complications occur in the range of 34–50% during 5 years follow-up[2,3] and can be divided in biological and technical complications.[4] Biological complications refer mainly to inflammatory conditions induced by accumulated bacterial biofilm. The inflammatory response to the microbial challenge is patient specific[4,5] and can result in two distinct clinical conditions being either peri-implant mucositis or peri-implantitis.[5] It is anticipated that peri-implant mucositis (without bone loss) in some cases may lead to peri-implantitis with irreversible pathologic bone loss.[6,7]

It is widely perceived that following implant placement and abutment connection, a limited amount of bone loss (defined in literature as marginal bone loss, initial bone loss or initial bone remodeling) may occur. This is basically biologically driven as a result of the establishment of a biologic seal between soft tissues and implant components. Implants should be installed in an ideal surgical and prosthetic position, anticipating early bone remodeling and aiming to have the implant completely into the bone after the stage of biologic width formation.[8-10] Suboptimal implant positioning may result in crestal bone loss ranging from 0.5 to 2 mm.[11] The definition of early bone loss is controversial among studies: from implant placement to 2 months after abutment connection,[12] the first year since implant placement[13] or implant placement to 1 year after loading.[14]

Consequently, one may question whether early implant surface exposure could be predictive for further ongoing bone loss and the development of peri-implantitis, especially in patients with known risk factors for peri-implant pathology: A history of periodontitis, poor plaque control, and absence of regular maintenance care provide strong evidence for an increased risk for peri-implantitis, whereas smoking habits, excess cement, systemic diseases (e.g., diabetes), occlusal overload, implant position, supra-structure design, lack of keratinized mucosa, and genetic factors may be potential risk factors with limited evidence in the literature.[1,15] A recent study demonstrated that initial crestal bone loss of >0.44 mm was an indicator of peri-implant bone loss progression.[16] Windael and colleagues showed that bone loss above 0.5 mm after 2 years of function around immediately loaded implants in the mandible was predictive for ongoing bone loss up to 10 years.[17]

The aim of this study was to evaluate whether early bone loss including initial bone loss, can predict future development of peri-implantitis and implant loss.

What is known:

- After implant placement and abutment connection, limited bone loss may occur. This biological process may surpass certain proposed criteria in defining peri-implantitis.
- This may lead to unwanted implant surface exposure and biofilm adherence.
- Early bone loss has been suggested as a possible risk factor for peri-implantitis, although this was based on small study samples.

What this study adds:

- Based on a large study population, early bone loss is a risk factor for peri-implantitis.
- The higher the amount of early bone loss, the higher the incidence of disease, especially in combination with other risk factors such as smoking.

2 | MATERIAL AND METHODS

2.1 | Study design

Five hundred and ninety four patients were initially referred by their general dentist to a private periodontal clinic for implant placement and were treated accordingly between 2005 and 2009. Treatment consisted of implant therapy for single and multiple tooth replacements in both jaws. Patients with periodontal or endodontic pathology were treated appropriately prior to implant installation to minimize the risk for biological complications. Radiographic presurgical planning was performed including CBCT analysis whenever required and left to the discretion of the treating surgeon.

All patients were treated by the same surgeon (B.C.) with the same implant system (Osseospeed, Astra Tech, Molndahl, Sweden). Introduced in 2004 as Osseospeed, the surface's predecessor (TiOblast, grade IV titanium and blasted with TiO_2 particles) underwent additional chemical modification in which fluoride-ions were attached to the titanium surface. This process yields a medium rough surface with nanoscale topography, having an S_a value of [1.32–1.82] and allowing potential for mechanical retention and biological reaction after placement.[18-21] This specific implant design was launched commercially in combination with the microthreads™. The implant has a conical connection and platform switch.

2.1.1 | Surgical and prosthetic treatment

The surgical and prosthetic treatment was extensively described previously.[17,22] Implants were placed using one-stage or two-stage surgery and loading was either immediate or delayed based on treatment decisions made by surgeon, dentist, and patient. Bone grafting, sinus lift, guided bone regeneration procedures or immediate placement were not performed. In case of multiple-unit restorations, abutments (uni-abutment, Astra Tech, Molndahl, Sweden) were placed at the time of implant surgery for the one-stage protocol or during second-stage surgery 3 months following implant placement. Peri-apical

radiographs were made immediately after implant placement (baseline) with commercially available film-holders (Uni-Bite Film Holder, Dentsply, York, PA) 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. Individualization of standard film holders and use of individual bite blocks was not manageable in a private practice setting. However, whenever implants threads were not clearly visible the radiograph was discarded and a new radiograph was taken. Final restorations were made by the general dentist after at least 3 months of healing. A professional maintenance schedule was proposed for all patients remaining at the periodontal clinic and not returning to their referring dentist for maintenance. Briefly, this consisted of a recall interval of 6 or 12 months during the first 2 years, and 12–24 month during the following years. During recall sessions, peri-apical radiographs were taken to evaluate peri-implant bone levels compared to baseline. All implants with at least 10 years of function were included to evaluate implant survival and peri-implant health. All types of prosthetic rehabilitation were included (single crown, partial bridge, full-arch bridge, and overdenture).

2.2 | Dependent variables and covariates

All patients were invited for a diagnostic visit in order to scrutinize long-term follow-up outcome after at least 10 years of function. The scientific data collection was performed by an independent examiner of Ghent University (S.W.) not involved in previous initial treatment nor maintenance. Data collection consisted of registration of probing pocket depth with a manual periodontal probe (CP 15 UNC, Hu-Friedy Mfg. co. Inc), scoring of plaque and bleeding according to Mombelli and Lang at six sites.[23] Peri-apical radiographs were taken to evaluate the peri-implant bone levels. All patients were thoroughly informed and signed a written consent form. The study protocol was approved by the ethics committee of the Ghent University Hospital (Number B670201524796).

Mean values for pocket probing depth, bleeding on probing, and plaque were calculated per implant to obtain a single value per implant. Implant survival, interproximal bone loss, and pocket probing depth were considered the dependent variables. Smoking was assessed as either smoking at least 1 cigarette a day or non-smoking, based on self-reporting behavior registered at the time of implant placement. Patients were classified with a history of periodontitis based on the following preoperative conditions: (a) radiographic evidence of bone loss exceeding 1/3 of the root length of remaining teeth at time of referral, (b) patients treated before implant therapy with (non)surgical periodontal treatment, (c) patients with hopeless teeth, which were extracted due to periodontitis prior to implant placement, (d) edentulous patients at the time of referral with evidence of periodontitis based on radiographs obtained in retrospect from the referring dentist. Crestal bone levels were analyzed using digital software with an accuracy of 0.1 mm (Visi-Quick, Amsterdam, The Netherlands). Possible distortions were solved by calibration, based on the known implant diameter. Crestal bone levels were determined at both the mesial and distal sites of each implant by measuring the distance between the lower border of the smooth implant collar (the reference point) to the first bone-implant contact (Figure 1).

Bone loss was calculated comparing peri-apical radiographs taken during recall visits with the baseline radiograph taken at the moment of implant installation. The mean of the distal and mesial bone level on each implant was calculated to provide a single value per implant. Bone loss was evaluated at 3 months, 1 year, and 2 years and 10 years of function. In the present study, early bone loss was defined as the total sum of bone loss 1 year after implant installation according to Kang and colleagues.[13] Peri-implant mucositis was defined for each individual implant as bleeding and/or suppuration on gentle probing and in absence of bone loss. Peri-implantitis was defined as mucositis together with a probing pocket depth equal or above 6 mm and/or bone loss equal or above 3 mm.[24]

2.3 | Statistical Analysis

Descriptive statistics were performed to explore the study population. Paired samples *T*-tests were performed to assess differences in mean bone loss between different time points. Non-parametric testing was performed in cross-tabs using Pearson Chi-square test and Fishers's exact test on patient-level variables. Kaplan–Meier-estimated survival curves were plotted. For covariates that are measured at the level of the implant, the hazard of implant loss was compared between groups using the Robust Score test for a simple Cox proportional hazards model. The proportional hazards assumption was assessed graphically using the estimated log–log

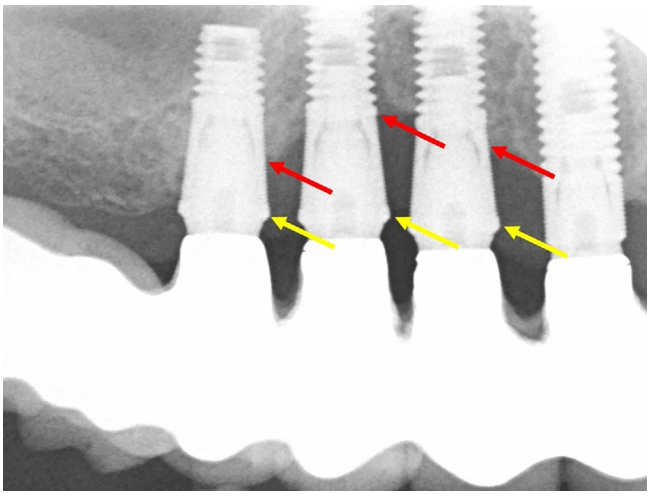

FIGURE 1 The yellow arrow points to the lower border of the smooth implant collar (reference point). The red arrow shows the first bone-to-implant contact. The distance between these two points was measured with digital software

survival curves. Robust standard errors were estimated to take into account the clustering of implants within patients. Bone loss readings were calibrated by inter - and intra-examiner reliability assessment using the intra-class correlation coefficient (ICC) based on a two-way random model with absolute agreement. Simple generalized linear mixed models with binomial distribution and logit link for peri-implantitis were fitted. The fixed part of the model contained a binary indicator of bone loss (over 0.5 mm or 1 mm at 1 or 2 years). The random part of the model contained a random intercept for patient to allow for a correlation between bone losses for implants within the same patient. An adjusted logistic mixed model was made for peri-implantitis, with adjustment for smoking status, history of periodontitis, and initial bone loss 1 year 0.5 mm (full factorial). The threshold of 0.5 mm, 1 year after implant installation was used based on an earlier study by the same research group (65). Statistical descriptive analysis, non-parametric testing, and all generalized linear mixed models for peri-implantitis were fitted in SPSS version 25 (IBM, Armonk, NY). All survival analyses were made in R (R version 3.6.1 [05-07-2019]) using the survival package.

3 | RESULTS

3.1 | Overall

On a total of 594 initially treated patients, 407 patients (221 women and 186 men; mean age of 64.86 years [range 28–92, SD 10.11]), with 1482 implants, responded to the invitation for a clinical examination after 10 years. One hundred and eighty seven (31.5%) patients were considered dropout because they did not respond to the invitation, had passed away, or were untraceable. The average follow-up time in this study was 10.66 years (range 10–14, SD 0.87). Prosthetic rehabilitation consisted of 214 single crowns, 545 implants supporting partial bridges, 680 implants supporting full-arch bridges, and 43 implants supporting overdentures. Eight hundred and seventy one implants were placed in the maxilla and 611 in the mandible. Fifty patients with 206 implants were current smokers, while 66 patients with 275 implants ceased smoking at least 3 months prior to surgery. Two hundred patients (1002 implants) and 207 patients (480 implants) were respectively classified with and without a history of periodontitis. Thirty-five patients with 175 implants were smokers with a history of periodontitis.

Seventy eight implants in 52 patients failed, resulting in an absolute survival rate of 94.74%. Implant failure was experienced by 12.78% of the patients. Early implant failure prior to final restoration affected 20 implants (1.35%) in 19 patients (4.67%). A mean crestal bone loss of 0.22 mm (SD 0.60, range 0–9), 0.35 mm (SD 0.62, range 0–5.15), 0.42 mm (SD 0.76, range 0–6.35), 0.72 mm (SD 1.22, range 0–8.4), and 0.81 mm (SD 1.58, range 0.00–17.00) was observed after a follow-up of 3 months, 1, 2, 5, and 10 years, respectively. The differences in bone loss between all time-points were significant ($p < 0.001$). Intra-examiner repeatability on bone loss was high (ICC 0.989, 95% confidence interval [CI] 0.983–0.992), as was the inter-examiner repeatability (ICC 0.837, 95% CI 0.758–0.890). After 10 years, the mean pocket probing depth on implant level was 4.31 mm (SD 1.11, range 2.83–17.00) The mean bleeding on probing and plaque was 0.26 (SD 0.36, range 0–1) and 0.18 (SD 0.31, range 0–1) respectively, both on implant level. Fifty six implants (3.8%) in 18 patients (4.4%) were diagnosed with peri-implant mucositis and 175 implants (11.8%) in 76 patients (18.7%) were diagnosed with peri-implantitis based on the composite criteria. Implants diagnosed with peri-implantitis had a mean probing pocket depth of 6.5 mm (SD 2.15) versus 4.1 mm (SD 0.66) for implants without peri-implantitis.

3.2 | Early bone loss

When looking at the different bone loss thresholds (0.5, 1 and 2 mm) at 3 months, 1 year, and 2 years, the difference between groups for each early bone loss threshold was statistically significant for both peri-implantitis and implant loss (Table 1). For all time points, the proportion of peri-implantitis positive implants increased when the early bone loss was higher.

When looking at the estimated implant survival on implant level for implants with the bone loss threshold of 0.5 mm 1 year after implantation, a statistical significant difference is found ($p = 0.021$), showing lower implant survival when this threshold is exceeded (Figure 2). A similar, statistical significant result ($p = 0.036$) can be found when the threshold is raised to 1 mm bone loss 1 year after implantation (Figure 3). When increasing the time period after implant installation to 2 years, again a statistical significant difference can be found of $p = 0.003$ and $p = 0.002$ for the same thresholds of 0.5 and 1 mm of bone loss, respectively, (Figures 4 and 5). When comparing Figures 2 and 3 or similar 4 and 5, the incidence of implant failure increases when the higher threshold is exceeded. For every mm increase in bone loss at 1 year, the estimated hazard of implant loss increases by a factor 1.98 (95% CI goes from 1.47 to 2.66, $p = 0.013$).

The odds for developing peri-implantitis are significantly higher when each bone loss threshold is exceeded at every time point (Table 2). For example, the odds for peri-implantitis in implants with >0.5 mm of bone loss after the first year of function, are 5.43 times the odds for peri-implantitis in implants with ≤0.5 mm bone loss at the first year, or the odds for peri-implantitis are 443% higher in implants with >0.5 mm bone loss. Similar to implant survival, the odds for peri-implantitis increase when a greater threshold is exceeded.

When combining the risk factors 'smoking and history of periodontitis with the proposed risk factor of early bone loss, a 'traffic light' distribution can be made dividing implants in three categories: low (green), medium (orange), and high (red) risk for peri-implantitis and implant loss (Tables 3 and 4). When comparing both tables, representing implants with >0.5 mm and ≤ 0.5 mm early bone loss, respectively, it is shown that exceeding the bone loss threshold of 0.5 mm results in higher prevalence of peri-implantitis and implant loss, especially in combination with smoking and/or a history of periodontitis.

TABLE 1 Overview of the distribution of implants grouped per initial bone loss of 0.5, 1, and 2 mm, respectively, at the 3 months, 1 year, and 2 years post-operative assessment

Amount of early bone loss at time point		No. implants	No. PI (10 years)	% PI (10 years)	*p* Value	No. implant loss (10 years)	% Implant loss (10 years)	*p* Value
3 months	≤0.5 mm	1187	119	10.0%	$p < 0.001$	36	3.0%	$p < 0.001$
	> 0.5 mm	165	45	27.3%		30	18.2%	
	Total	1352	164	12.1%		66	4.9%	
3 months	≤1.0 mm	1284	143	11.1%	$p < 0.001$	47	3.6%	$p < 0.001$
	>1.0 mm	68	21	30.9%		19	27.9%	
	Total	1352	164	12.1%		66	4.9%	
3 months	≤2.0 mm	1330	155	11.7%	$p < 0.001$	54	4.1%	$p < 0.001$
	>2.0 mm	22	9	40.9%		12	54.5%	
	Total	1352	164	12.1%		66	4.9%	
1 year	≤0.5 mm	739	63	8.5%	$p < 0.001$	20	2.7%	$p < 0.001$
	>0.5 mm	186	47	25.3%		22	11.8%	
	Total	925	110	11.9%		42	4.5%	
1 year	≤1.0 mm	843	77	9.1%	$p < 0.001$	28	3.3%	$p < 0.001$
	>1.0 mm	82	33	40.2%		14	17.1%	
	Total	925	110	11.9%		42	4.5%	
1 year	≤2.0 mm	898	92	10.2%	$p < 0.001$	34	3.8%	$p < 0.001$
	>2.0 mm	27	18	66.7%		8	29.6%	
	Total	925	110	11.9%		42	4.5%	
2 years	≤0.5 mm	590	35	5.9%	$p < 0.001$	13	2.2%	$p < 0.001$
	>0.5 mm	177	59	33.3%		23	13%	
	Total	767	94	12.3%		36	4.7%	
2 years	≤1.0 mm	688	54	7.8%	$p < 0.001$	16	2.3%	$p < 0.001$
	>1.0 mm	79	40	50.6%		20	25.3%	
	Total	767	94	12.3%		36	4.7%	
2 years	≤2.0 mm	738	70	9.5%	$p < 0.001$	24	3.2%	$p < 0.001$
	>2.0 mm	29	24	82.8%		12	41.4%	
	Total	767	94	12.3%		36	4.7%	

Note: For each group and time period the number of assessed implants, the percentage of implants diagnosed with peri-implantitis (PI) at the 10 year's assessment as well as the corresponding total number of implants loss as well as proportion of implant loss during the total 10 years period is given. The difference between groups for each bone loss threshold was tested with Pearson Chi-square and Fishers's exact test.

When looking at the probability of peri-implantitis of different subgroups of patients based on smoking, history of periodontitis, and early bone loss threshold of 0.5 mm, only non-smokers with less than 0.5 mm early bone loss, with or without a history of periodontitis, show a statistical significant lower probability in developing peri-implantitis ($p = 0.013$ and $p = 0.024$ respectively), compared with the 'worst case' group (smokers with history of periodontitis and early bone loss >0.5 mm) (Table 5).

A clinical example of a patient with early bone loss evolving in peri-implantitis on the long term is given in Figure 6. This was a smoker with a history of periodontitis. One year after loading, there are several implants with early bone loss exceeding the 0.5 and 1.0 mm threshold, representing implants at risk following the red "traffic light" from Table 3. This resulted in time in the development of peri-implantitis.

4 | DISCUSSION

Long-term studies indicate that crestal bone loss occurs mainly during the first year of function and is a multifactorial phenomenon.[9,10,25-29] However, it has been suggested that early bone loss and consequently exposure of the implant surface may increase the risk for peri-implantitis.[9,10,16,30,31] The current study describes more than 400 patients and nearly 1500 implants followed over 10 years and is one of the first studies on a large population evaluating the influence of early implant exposure on peri-implantitis development.

Research evidence indicates that more early bone loss may lead to increased future bone loss[16,17], although this is debated by some authors.[30] The present study shows that early bone loss resulting in implant surface exposure of 0.5 and 1 mm significantly affects implant survival. Early bone loss beyond these threshold values increases the

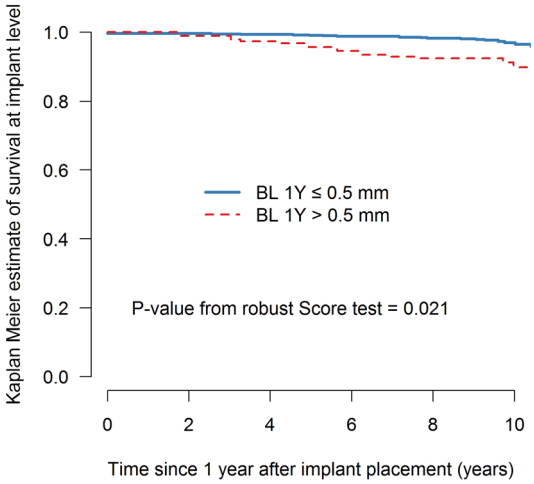

FIGURE 2 Implant survival curve comparing implants with early bone loss ≤0.5 mm and >0.5 mm after the first year of function, showing significant more implant failures after 10 years of function for implants with >0.5 mm bone loss after 1 year (p = 0.023)

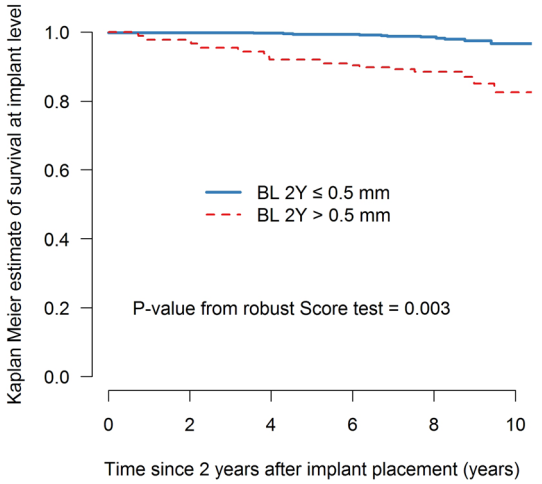

FIGURE 4 Implant survival curve comparing implants with early bone loss ≤0.5 mm and >0.5 mm after 2 years of function, showing significant more implant failures after 10 years of function for implants with >0.5 mm bone loss after 2 years (p = 0.003)

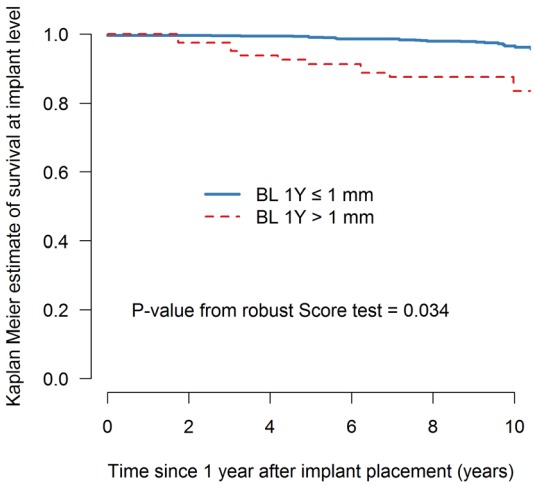

FIGURE 3 Implant survival curve comparing implants with early bone loss ≤1 mm and >1 mm after the first year of function, showing significant more implant failures after 10 years of function for implants with >1 mm bone loss after 1 year (p = 0.036)

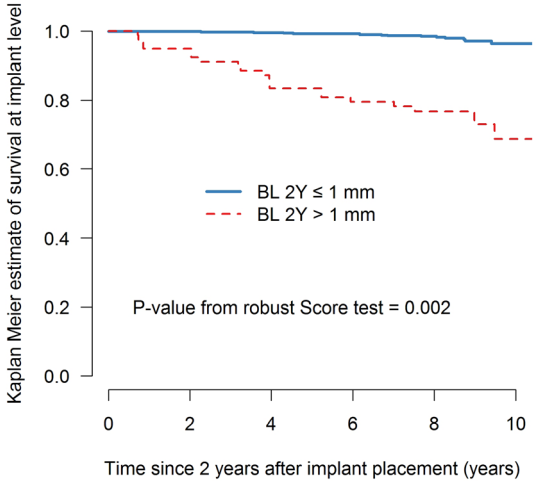

FIGURE 5 Implant survival curve comparing implants with early bone loss ≤1 mm and >1 mm after 2 years of function, showing significant more implant failures after 10 years of function for implants with >1 mm bone loss after 2 years (p = 0.002)

risk for implant failure as well as peri-implantitis development. Furthermore, the higher the exceeded threshold, the lower implant survival and the higher the odds for peri-implantitis. In a previous study, early bone loss exceeding 0.5 mm was identified as a risk factor in developing peri-implantitis.[17] However, this involved a small patient group, including 21 patients (105 implants), with immediate loading in the edentulous mandible. The reported survival rate was 100% and only 4.8% of the implants were diagnosed with peri-implantitis. The present study includes a much larger patient population treated with different surgical and prosthetic protocols, showing the daily reality in a referring clinical practice. No distinction was made between immediate loading and the one- or two-staged delayed loading. The literature reports comparable results of marginal bone loss for both immediate and delayed loading protocols.[32-38] On the other hand, a higher incidence of (early) implant failure has been reported for immediate loaded implants.[38]

The present study confirms that early bone loss is a predictor for ongoing bone loss, leading to the development of peri-implant pathology and resulting in implant failure. The importance of evaluating early bone loss in relation to peri-implant bone loss progression was already suggested previously, albeit based on small numbers and limited follow-up of 18 months.[16] They stated that bone loss exceeding 0.44 mm at 6 months post-loading induced ongoing crestal bone loss, implying an increased risk for implant failure.[16] The current study confirms these findings on a much larger time perspective and with more patients included.

Bone loss threshold	Odds	95% CI lower	95% CI upper	Sig.
3 months > 0.5 mm	3.86	2.24	6.65	<0.001
3 months > 1.0 mm	5.82	2.49	13.57	<0.001
1 year > 0.5 mm	5.43	2.98	9.89	<0.001
1 year > 1.0 mm	9.07	4.26	19.35	<0.001
2 years > 0.5 mm	9.68	4.97	18.86	<0.001
2 years > 1.0 mm	12.78	5.61	29.12	<0.001

TABLE 2 Odds for peri-implantitis in implants which exceeded certain thresholds in regard to early bone loss after 3 months, at the first and second year in function

	Non-smoker (135)				Smoker (30)			
	No perio (46)		Perio (89)		No perio (9)		Perio (21)	
	n	%	*n*	%	*n*	%	*n*	%
Peri-implantitis	11/46	23.9	19/89	21.3	2/9	22.2	13/21	61.9
Implant loss	3/46	6.5	17/89	19.1	1/9	11.1	9/21	42.9

Note: The green, orange and red color represents respectively implants at low, moderate, and high risk for peri-implantitis and implant loss.

TABLE 3 Occurrence of peri-implantitis and implant loss after 10 years for implants with bone levels >0.5 mm at 3 months post-operative (165 of 1352 implants with 3 months data)

	Non-smoker (1031)				Smoker (156)			
	No perio (379)		Perio (652)		No perio (21)		Perio (135)	
	n	%	*n*	%	*n*	%	*n*	%
Peri-implantitis	11/379	2.9	78/652	12.0	0/21	0.0	30/135	22.2
Implant loss	6/379	1.6	20/652	3.1	0/21	0.0	10/135	7.4

Note: The green, orange and red color represents respectively implants at low, moderate, and high risk for peri-implantitis and implant loss.

TABLE 4 Occurrence of peri-implantitis and implant loss after 10 years for implants with bone levels ≤0.5 mm at 3 months post-operative (1187 of 1352 implants with 3 months data)

TABLE 5 Probability of peri-implantitis and comparison with the group of implants in patients with smoking habits, a history of periodontitis, and early bone loss exceeding 0.5 mm (worst scenario)

Subgroup	Probability of peri-implantitis (95% CI)	*p* Value
Non-smoker, no history of periodontitis, ≤0.5 mm early bone loss	0.08% (0.01–0.83%)	**0.013**
Non-smoker, no history of periodontitis, >0.5 mm early bone loss	0.51% (0.05–4.88%)	0.175
Smoker, no history of periodontitis, ≤0.5 mm early bone loss	0.35% (0–36.09%)	0.591
Smoker, no history of periodontitis, >0.5 mm early bone loss	0.83% (0–76.19%)	0.86
Non-smoker, history of periodontitis, ≤0.5 mm early bone loss	0.13% (0.01–1.3%)	**0.024**
Non-smoker, history of periodontitis, >0.5 mm early bone loss	2.07% (0.23–16.31%)	0.54
Smoker, history of periodontitis, ≤0.5 mm early bone loss	0.48% (0.02–9.11%)	0.113
Smoker, history of periodontitis, >0.5 mm early bone loss	52.06% (2.64–97.75%)	Reference group

The bold values are the only values who where statistical significant.

Early implant exposure forms a potential tread for maintaining a stable peri-implant environment in the long term. In the literature, its origin has been related to a combination of mechanical and biological factors: First, the degree of surgical trauma to the bone and periosteum during surgery.[12,26] Second, the establishment of the biologic width, in relation to the soft-tissue thickness.[9,10,12,14,25,26] Vervaeke

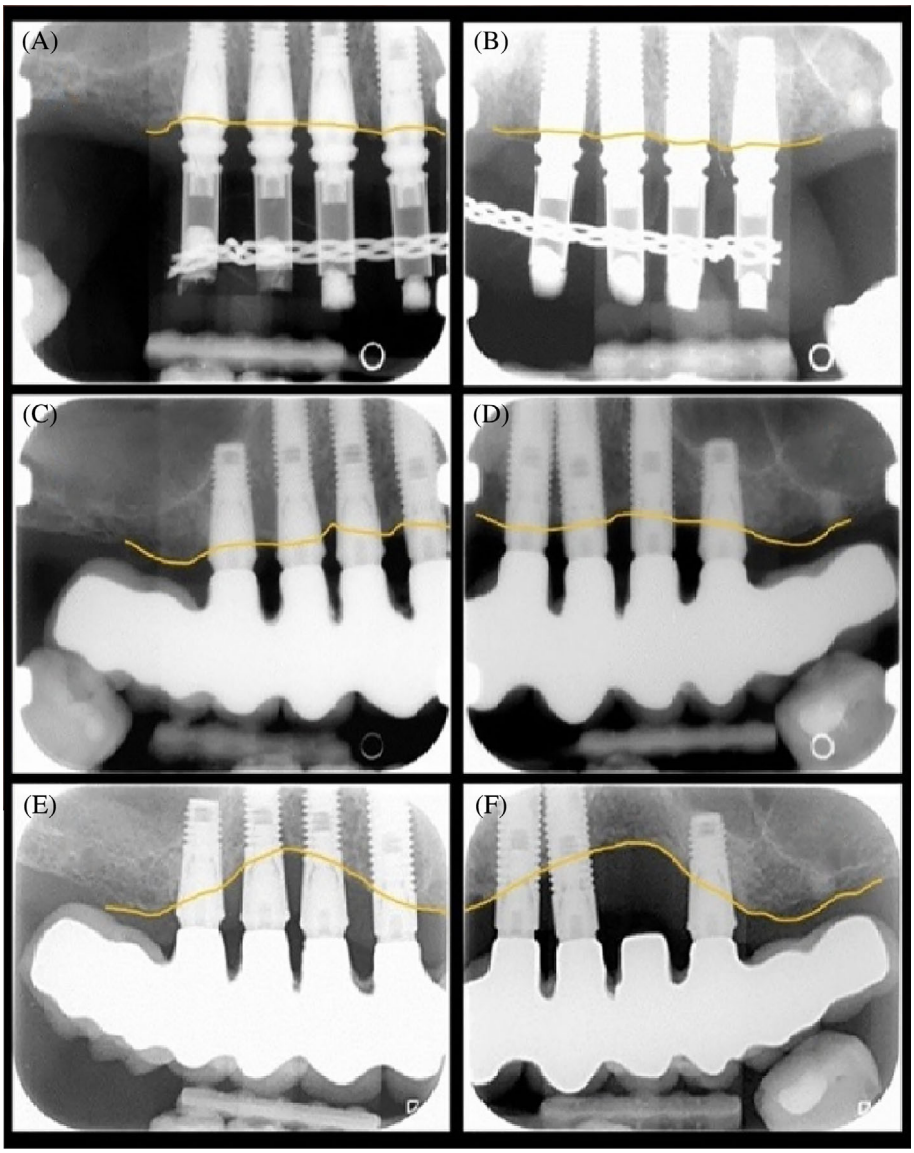

FIGURE 6 Example of a patient with early bone loss which further developed into peri-implantitis. (A and B) The initial situation after immediate loading; (C and D) The bone levels after 1.5 years, with obviously early bone loss exceeding 0.5 and 1 mm thresholds; (E and F) The 10 years results after surgical treatment op peri-implantitis and removal of 1 implant

and colleagues identified the abutment height, reflecting the initial soft tissue thickness, as a predictor for early bone loss (after 1 year), with more bone loss around low abutments because of the re-establishment of these dimensions around the implant.[29] Subsequently, implant placement depth may influence early bone loss.[9,12] Implant features such as width, surface topography, neck design, microgap existence, and a one- or two-piece design can also play a role.[12,25,26] More recently, the occurrence of titanium degradation (corrosion) leading to the release of titanium particles (which may have cytotoxic and genotoxic potential) has also been proposed.[9,26,30,39] Other possible contributing factors are less-than-ideal initial fit between the implant and the bone, loading conditions, insufficient bone morphology, a poor overall patient health and harmful patient habits.[12,25] A number of studies reported stable bone levels once the initial remodeling was established,[40-42] while other studies reported ongoing bone loss in time from 1 year after implant placement.[17,29,40-42] The present study is in accordance with the latter, showing more bone loss with higher odds for peri-implant pathology when early bone loss exceeds certain thresholds. The mechanism behind this ongoing bone loss is certainly inflammation, but its trigger may vary and includes bad quality of the soft-tissue barrier, bone morphology and especially plaque-accumulation/bacteria.[25] Early bone loss results in unwanted exposure of the moderately rough implant surface to soft tissues and the microbiome of the oral cavity. Surface roughness exerts a dominant impact on biofilm formation, because this facilitates bacteria adhesion, maturation and colonization.[43] Biofilm adherence to the moderately rough implant surface may enhance an inflammatory response which in turn may lead to further bone loss, development of peri-implantitis and ultimately implant loss, especially in patients with other known risk factors.[17,44-47] The greater the early implant surface exposure, the more surface to be colonized by bacteria. This may explain the fact that when in the present study a higher threshold of bone loss was exceeded, a higher odds for peri-implantitis and lower implant survival was seen.

Most of the published studies on peri-implantitis have a cross-sectional design and report only on prevalence without longitudinal observations. In contrast, the present study reports on peri-implantitis incidence (i.e., the number of new cases in a given time period) and reports a peri-implantitis incidence of 11.8% and 18.7% after 10 years on implant and patient level, respectively. These figures are higher than those reported in a recent systematic review, estimating an incidence of less than 5% after 10 years.[25] This difference may be the result of the inclusion of a large number of periodontally compromised patients. It is obvious that regular professional maintenance care, especially in this patient group, is critical for the long-term outcome. However, a majority of the patients did not respond to the recall invitation of the periodontal clinic and returned to the general/prosthetic dentist for supportive care. Hence, it is unclear if patients were compliant, and if maintenance was conducted based on the individual patient's needs. It is well-known that the lack of proper oral hygiene or maintenance care increases peri-implant incidence,[24] as observed in the present study population.

Treatment of peri-implantitis is challenging and unpredictable leading to implant failure, recurrence of peri-implantitis and post-treatment complications.[48-52] Consequently, it is important to stress the need for prevention through a careful clinical monitoring, especially in patients who are at risk for biological complications. Identifying risk factors/indicators may help clinicians to categorize an individual patient for his/her susceptibility, and may also alter the maintenance protocol in order to prevent complications. For patients exhibiting early bone loss exceeding a certain threshold stricter monitoring may be advantageous to prevent further development of biological complications.[22,31] However, it is unknown whether preventive measures alone can arrest further peri-implant bone loss or avert late development of peri-implantitis.

Several risk factors/indicators have been suggested in the literature, albeit with different weight of evidence. A history of chronic periodontitis, poor oral hygiene, and absence of regular professional maintenance care increase the risk for peri-implantitis.[1,15,24-26,28,29,53-57] The detrimental time-dependent effect of smoking on peri-implant bone loss as well as the negative effect on implant survival, have been described.[22,29,44,58] On the contrary, the relation between smoking and occurrence of peri-implantitis remains a point of discussion.[1,24,28] A recent long-term study by Windael and colleagues reported that implants placed in patients with smoking habits experienced a 2.6 times higher risk for peri-implantitis compared with implants placed in non-smokers. Moreover, a synergistic effect between history of periodontitis and smoking on peri-implant bone loss has been described.[29] This synergistic effect is confirmed in this study, especially in cases showing early bone loss. Implants in patients with smoking habits and a history of periodontitis, are at the highest risk of developing peri-implantitis and experiencing implant loss if early bone loss exceeds the threshold of 0.5 mm at 1 year. The worst patient category, periodontitis susceptible smokers with early bone loss exceeding 0.5 mm after 1 year, show a probability of an implant to develop peri-implantitis to be 52.06%. Only two subgroups, namely non-smokers showing no early bone loss above 0.5 mm with or without a history of periodontitis, show statistical significant better performance than the other subgroups.

5 | CONCLUSION

The present study reports an implant survival rate of 94.7% and a mean bone loss of 0.81 mm after 10 years. Peri-implantitis incidence was 11.8% on implant level and 18.7% on patient level. Early bone loss was identified as a predictor for the development of peri-implantitis, especially in combination with well-known risk factors such as smoking, periodontal disease and absence of oral hygiene/maintenance care.

CONFLICT OF INTEREST

Dr. Bruno Collaert received a research grant from Dentsply Sirona (York, Pennsylvania). Prof. De Bruyn has a collaboration agreement with Dentsply Sirona (York, Pennsylvania). All other authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Simon Windael: Data analysis/drafting of article. Bruno Collaert: concept of study/data collection/surgery. Stefanie De Buyser: statistics/data analysis. Hugo De Bruyn: critical revision of article/design. Stijn Vervaeke: critical revision of article, design.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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