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RESEARCH

Outcome indicators of non-surgical therapy of peri-implantitis: a prospective case series analysis

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Abstract

Objectives This study aims to identify patient and implant indicators influencing the non-surgical therapeutic outcomes of peri-implantitis at 6 months of follow-up.

Methods This case series involved patients with at least one implant diagnosed with peri-implantitis according to the 2017 World Workshop criteria. Non-surgical therapy consisted of mechanical debridement of the peri-implant pockets combined with metronidazole 500 mg 3 times a day for 7 days. At baseline and at 6 months, clinical and radiographic variables were collected to calculate treatment success (probing pocket depth reduction to 5 mm without bleeding on probing or < 5 mm irrespective of bleeding on probing at all implant sites, and lack of bone loss progression). The primary outcome was treatment success (%) at 6 months. The influence of the patient and implant/prosthetic variables upon disease resolution was assessed through simple and multiple logistic regression analyses at patient and implant level, using generalized estimation equations models.

Results A total of 74 patients and 107 implants were analyzed at 6 months. Disease resolution was established in 25.7% of the patients and 24.1% of the implants. Patients with stage IV and grade C periodontitis, inadequate oral hygiene at baseline, and wide diameter (≥ 4.5 mm) presented significantly greater treatment failure, whereas smokers and former smokers demonstrated a tendency toward failure. At 6 months, there was a significant decrease in probing pocket depth and bleeding on probing of 1.08 ± 1.06 mm and 14%, respectively. Radiographically, a significant gain in marginal bone level of 0.43 ± 0.56 mm was observed.

Conclusion Disease resolution after non-surgical treatment of peri-implantitis is negatively influenced by the loss of support of the adjacent periodontium, poor baseline oral hygiene, and wide diameter implants (≥ 4.5 mm).

Clinical relevance This study helps to discriminate the clinical situations in which non-surgical treatment is less likely to achieve treatment success at short term.

Keywords Peri-implantitis · Non-surgical · Adjunctive therapy · Antibiotics

Introduction

Peri-implantitis is a plaque-associated disease condition characterized by inflammation of the peri-implant mucosa and subsequent progressive bone loss [1]. Although the frequency of peri-implantitis varies among different populations, study designs, and case definitions, recent epidemiological data suggest that peri-implantitis occurs in approximately 2 out of 10 implants [2–4].

Histologically, peri-implantitis is described as an inflammatory process of microbial origin that commonly presents with a large inflammatory infiltrate and extensive bone destruction [5–8]. These histological observations

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are in line with the non-linear, accelerated, and progressive pattern of bone loss clinically evidenced in peri-implantitis lesion [9, 10], thus suggesting an "aggressive" nature of the disease. In this context, the primary aim of peri-implantitis treatment must be to secure resolution of the peri-implant soft tissue inflammation (i.e., absence of bleeding on probing and/or suppuration), with maintenance/stability of the supporting bone [11], and adequate patient satisfaction [12].

Although several clinical approaches have been proposed for the non-surgical and surgical management of peri-implantitis, the predictability and effectiveness of these interventions remain the subject of debate [13, 14]. Of note is the fact that the complete resolution of peri-implantitis after surgical treatment reportedly occurs in less than half of the implants at 5 years [11] or even at 10 years [15] with supportive peri-implant therapy. In light of this, a recent randomized clinical trial comparing surgical versus non-surgical treatment of peri-implantitis has concluded that both therapies afford similar clinical outcomes — although marginal bone levels were better improved with the surgical approach for sites presenting greater initial bone loss [16]. It also should be noted that surgical treatment may increase morbidity, treatment time, and cost for the patient.

Over the years, non-surgical treatment has been regarded as an essential step to improve soft tissue conditions and to monitor patient compliance with oral hygiene before a surgical approach is decided — although it has been claimed to have limited efficacy in the treatment of peri-implantitis [17]. Nonetheless, several research groups have recently evaluated different non-surgical strategies that seem to offer outcomes quite similar to those reported for surgical treatments [18–22]. In seeking to arrest the aggressive nature of peri-implantitis, a non-surgical protocol that includes mechanical debridement with soft tissue curettage and the self-administration of systemic antibiotics has been used by three different Spanish research groups, showing promising clinical, radiographic, and microbiological findings, with a success rate ranging from 40.9 to 56.3% [18–20, 23]. However, it is of paramount importance to identify indicators that may predict the success of the non-surgical treatment of peri-implantitis in order to identify those patients that can benefit from the treatment and those that would need additional therapy.

To date, no studies have been conducted to assess patient-, site-, and implant-related factors that may influence the short-term outcome of the mechanical non-surgical management of peri-implantitis with adjunctive systemic metronidazole. The purpose of the present investigation therefore was to identify those indicators that may impact upon the outcome of non-surgical therapy of peri-implantitis at 6 months.

Materials and methods

Study design

This prospective case series study was reported according to the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines [24] and was conducted in accordance with the Declaration of Helsinki (1975, as revised in 2013). The research protocol was registered in ClinicalTrials.gov (NCT 05539755) and approved by the Research Ethics Committee of *Universitat Internacional de Catalunya* (UIC) (Barcelona, Spain) (Ref.: PER-ECL-2020–06). All study participants provided informed consent prior to inclusion in the study.

Patient selection

Patients referred to the Department of Periodontology (CUO) at *Universitat Internacional de Catalunya* (UIC) (Barcelona, Spain) for the treatment of periodontal and/or peri-implant diseases and who meet the inclusion criteria were consecutively recruited from January 2021 to June 2022. The study included subjects (1) ≥ 18 years old and (2) with the presence of at least one implant in function for more than 1 year, diagnosed with peri-implantitis following the case definition of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions [1]: probing pocket depth ≥ 6 mm with bleeding on probing and/suppuration, and ≥ 3 mm of progressive bone loss after initial bone remodeling. Conversely, subjects were excluded on the basis of the following criteria: (1) previous non-surgical treatment at least 12 months before; (2) previous surgical treatment; (3) allergy or intolerance to metronidazole; (4) clinical implant mobility; (5) pregnancy or lactating women; (6) the use of systemic antibiotics during the previous three months; (7) the use of systemic antibiotics for endocarditis prophylaxis.

Data collection

Patient and clinical assessment

The following patient characteristics were recorded at baseline: age (years), gender (male/female), diabetes mellitus (DM) (yes/no), smoking (non-smoker, former smoker, or current smoker) [25], previous history of periodontitis (yes/no), periodontitis stage (I–IV) and grade (A–C) [26], and compliance with supportive peri-implant maintenance therapy (PIMT) before enrollment in the study (≥ 2 PIMT/year; < 2 PIMT/year; 0 PIMT/year) [27].

The following implant-related data were recorded at baseline: implant site (anterior, premolars, molars), implant arch (maxilla, mandible), implant diameter (< 4 mm, ≥ 4 mm and < 4.5 mm, ≥ 4.5 mm), implant design (two-piece, one-piece), implant surface (smooth, minimally rough, moderately rough, rough) [28], type of prosthesis (single, fixed partial, cantilever, fixed full arch, overdenture), prosthesis retention (screwed/cemented), prosthesis removal (yes/no), prosthesis modification (yes/no), and previous bone augmentation (yes/no). All clinical examinations were performed using a UNC-15 periodontal probe by a calibrated examiner (MCS) before treatment (baseline) and at 6 months post-treatment at 6 sites per implant (mesial, medial, distal on buccal/lingual side), with recording of the following parameters:

- Probing pocket depth (PPD), calculated as the distance (mm) from the gingival peri-implant margin to the bottom of the peri-implant pocket.
- Bleeding on probing (BoP) and suppuration on probing (SUP), scored dichotomously (yes/no).
- Recession (REC), measured as the distance (mm) from the free marginal mucosa to the most apical portion of the crown.
- Keratinized mucosa width (KMW), measured as the distance (mm) from the mucosal margin to the mucogingival junction.
- Plaque index (PI), calculated by assigning a binary score to each surface (1 = plaque present, 0 = plaque absent).

The examiner (MCS) was calibrated for the clinical parameter BoP by collecting clinical measurements twice in five consecutive patients included in the study, spaced 30 min apart (kappa score = 0.82).

Radiographic assessment

Periapical radiographs were taken by means of long-cone parallel technique with the aid of standardized silicone stents to evaluate the peri-implant marginal bone level at baseline and after 6 months. The radiographs were analyzed using imaging software (ImageJ 1.47 V Wayne Rasband, National Institutes of Health). The known length of the implant was used in each radiograph for calibration of the measurements, and the implant shoulder was used as a fixed reference point. The intra-bony defect width (IDW) was measured as the distance (mm) between the distal and mesial interproximal bone crest and the implant surface, while the intra-bony defect angle (IDA) (°) resulted from a vertical line along the outer implant surface and a line extending along the peri-implant bone defect. To assess linear changes at inter-proximal alveolar crestal bone height, the distance from the implant shoulder to the most coronal bone to implant contact (marginal bone level (MBL)) was determined at both the mesial and distal aspect of each implant, and was expressed as the mean of both measurements in millimeters. Implant thread distance and implant pitch width were also radiographically measured in millimeters. A single independent examiner (RP) was calibrated in the radiographic analysis by measuring 10 sets of baseline radiographs of included patients 2 days apart with all the aforementioned distances and angles (intra-class correlation coefficient (ICC) = 0.87).

Intervention: non-surgical peri-implant treatment

All patients underwent comprehensive evaluation and received oral hygiene instructions on the modified Bass technique and the use of interproximal brushes. Subsequently, the patients were consecutively treated by trained third-year residents of the postgraduate program in Periodontology, supervised by an experienced periodontist (JV). The procedure was standardized as follows: the implant prosthesis was checked for cleansability with an interproximal brush and retrieved when possible. Then, the prosthesis was modified as described elsewhere [29]. After local anesthesia (4% articaine and adrenaline 1:100,000), the implant surfaces were cleaned with ultrasonic devices (Newtron P5; Satelec Acteon, Olliergues, France) with the steel alloy H3 dental ultrasonic scaler tip (H3; Satelec Acteon). Curettage of the bone defect was performed with Gracey curettes Younger-Good (SyG 7/89 Everedge; Hu-Friedy, Chicago, IL, USA), while glycine air powder was applied submucosal (Air-Flow powder subgingival PERIO; EMS, Nyon, France) with an air-flow Piezon device (Air-Flow master Piezon; EMS).

Oral hygiene instructions were given, and metronidazole 500 mg every 8 h for 7 days was prescribed. Patients were scheduled at 3 months for supragingival plaque control and supragingival debridement, if needed. After the 6-month study period, patients were enrolled in 3- or 6-month PIMT intervals considering the prognostic factors included in the implant disease risk assessment (IDRA) [30].

Outcome variables

The primary outcome variable was the percentage of disease resolution at 6 months. Disease resolution (also referred to as success) was defined as PPD reduction to 5 mm without BoP or < 5 mm irrespective of BoP at all implant sites, together with a lack of peri-implant bone loss progression [23]. As secondary outcomes, the following variables were considered: changes in PPD, BoP, SUP, REC, KMW, PI, IDW, IDA, and MBL from baseline to 6 months of follow-up.

Sample size power calculation

A post hoc sample size power calculation was performed. To detect success rates of 10% and 35% as significantly different in a sample of 108 independent implants with a confidence of 95%, a power of 86.7% was reached. Due to the multilevel design of the data (several implants per patient), the power was corrected and, assuming a moderate intra-subject correlation ($\rho = 0.5$), the power was found to be 78.6% under the same conditions.

Data analysis

A descriptive analysis was carried out, with the reporting of absolute and relative frequencies for categorical variables and the mean and standard deviation (SD) for continuous variables.

At patient level, simple binary logistic regression models were estimated using generalized estimating equations (GEEs) in order to explain the probability of disease resolution (yes/no) after non-surgical treatment, based on the profile of the patient. Unadjusted estimates of odds ratio (OR) and 95% confidence interval (95% CI) were obtained from Wald's Chi^2 statistic. In addition, a multiple model was further estimated to adjust the results for all the independent variables where $p < 0.10$ in the simple regression analysis. At implant level, logistic regression models using GEE were calculated in order to control for within-subject correlation. The set of independent variables was extended to all those related to the implant, prosthesis, and site. Similarly, binary and multiple regression analyses with GEE were applied to analyze the variables that were related to BoP reduction after therapy. In order to explore the factors that influenced PPD reduction and MBL gain, simple linear regression models were applied under the GEE approach. Estimations of beta-coefficient (β) with 95% CI were obtained and later adjusted through a multiple model.

The SPSS version 15.0 statistical package (SPSS Inc., Chicago, IL, USA) was used throughout. The significance level used in the analyses was 5% ($\alpha = 0.05$).

Results

Study population

Of the 90 patients that were screened for eligibility, 14 were excluded on the basis of the inclusion/exclusion criteria. Among the 76 patients with 109 implants enrolled into therapy, one failed to attend the 6-month follow-up visit (unable to contact), while only one implant was lost during the 6-month period. Thus, overall, a total 74 patients with 107 implants completed the study and were analyzed. The overall implant survival rate during the 6-month period was (99.1%).

Sample description

The main patient and implant/prosthetic characteristics are reported in Tables 1 and 2, respectively. The mean age of the participants was 60.9 ± 11.9 years (range 35–82), and 40 were males (54.1%) and 34 were females (45.9%). The mean number of implants per patient was 1.5 ± 0.8. Around one-third of the patients were smokers (31.1%). Almost all of the patients presented with a history of periodontitis (97.2%), while approximately half of them were diagnosed as corresponding to stage III (47.3%) and grade B (56.8%).

The vast majority of the implants were two-piece (86%), and half of them were moderately rough (52.3%). The most frequent implant brands treated were 3i Biomet and Astra

Table 1 Description of the included patients ($n = 74$)

Patient-related variables	Data
Age (years), mean ± SD	60.9 ± 11.9
Gender, *n* (%)	
Male	40 (54.1%)
Female	34 (45.9%)
n implants, mean ± SD	1.5 ± 0.8
Smoking habit, *n* (%)	
Non-smoker	37 (50.0%)
Smoker	23 (31.1%)
Former smoker	14 (18.9%)
n cigarettes/day, mean ± SD	11.4 ± 9.1
Years smoking, mean ± SD	28.9 ± 14.5
Diabetes mellitus, *n* (%)	
Yes	5 (6.8%)
No	69 (93.2%)
History of periodontitis, *n* (%)	
Yes	72 (97.2%)
No	2 (2.8%)
Periodontitis stage, *n* (%)	
I	0 (0%)
II	18 (24.3%)
III	35 (47.3%)
IV	21 (28.4%)
Periodontitis grade, *n* (%)	
A	7 (9.5%)
B	42 (56.8%)
C	25 (33.8%)
Compliance PIMT/year, *n* (%)	
0 PIMT/year	31 (41.9%)
1 PMIT/year	32 (43.2%)
2 PIMT/year	9 (12.2%)
3 PIMT/year	2 (2.7%)

Table 2 Description of the included implants ($n = 107$)

Variables	Data
Implant site, *n* (%)	
Anterior	13 (12.1%)
Premolar	34 (31.8%)
Molar	60 (56.1%)
Implant arch, *n* (%)	
Maxilla	49 (45.8%)
Mandible	58 (54.2%)
Implant diameter, *n* (%)	
< 4 mm	10.5
≥ 4 mm and < 4.5 mm	59
≥ 4.5 mm	30.5
Implant design, *n* (%)	
Two-piece	92 (86%)
One-piece	15 (14%)
Implant surface, *n* (%)	
Smooth	0 (0%)
Minimally rough	38 (36.5%)
Moderately rough	56 (52.3%)
Rough	13 (12.2%)
Type of prosthesis, *n* (%)	
Single	26 (24.3%)
Partial	67 (62.6%)
Cantilever	4 (3.7%)
Full removable	2 (1.9%)
Full fixed	8 (7.5%)
Prosthesis retention, *n* (%)	
Screwed	86 (80.4%)
Cemented	19 (17.8%)
Bar	2 (1.8%)
Prosthesis removal, *n* (%)	
Yes	92 (86%)
No	15 (14%)
Prosthesis modification, *n* (%)	
Yes	67 (72.8%)
No	25 (27.2%)
Previous bone augmentation, *n* (%)	
Yes	26 (24.3%)
No	82 (76.7%)

SD standard deviation, *n* number, *PIMT* peri-implant maintenance therapy

(Online Resource 1). Almost two-thirds of the implants were restored with fixed partial prostheses (62.6%), and most of them carried screwed-retained restorations (80.4%). In 86% of the implants, the prostheses could be removed and, of these, 72.8% were properly modified.

After the final re-evaluation at 6 months, 3 implants were removed, 12 implants received soft tissue augmentation by means of an apically positioned flap plus epithelialized free gingival grafting, 6 implants underwent surgical bone reconstructive therapy, 4 implants needed surgical resective therapy, and the remaining 82 implants continued with PIMT.

Outcome indicators of success at patient level

The 6-month overall success rate at patient level was 25.7% (95% CI 15.7–35.6%). The simple binary logistic regression analysis indicated that those patients with a poorer periodontal status and smokers presented a significantly lower probability of treatment success ($p = 0.009$ and $p = 0.047$, respectively), while regular PIMT compliers had a higher probability of disease resolution ($p = 0.021$) (Table 3).

After adjusting for confounders, periodontitis stage was seen to be the most relevant parameter predicting disease resolution, as stage IV periodontitis patients had an 89% lower probability of treatment success ($p = 0.031$). Similarly, smokers and former smokers presented a lower likelihood of peri-implantitis resolution (OR = 0.34, 95% CI 0.07–1.67, $p = 0.184$ and OR = 0.17, 95% CI 0.03–1.10, $p = 0.063$, respectively) — although statistical significance was not reached (Table 3).

Outcome indicators of success at implant level

The 6-month overall success rate at implant level was 24.1% (95% CI 16.0–32.1%). In the bivariate analysis, the patient-related variables influencing treatment success at implant level were similar to those identified at patient level. Thus, implants exhibited a significant higher probability of incomplete disease resolution if the patients were smokers or diagnosed with stage III and IV periodontitis, while a higher likelihood of treatment success was observed among PIMT compliers. In addition, implants restored with cantilevers showed significantly greater disease resolution, whereas those that presented plaque at baseline and a higher number of sites with BoP at baseline showed lower treatment success. Moreover, a statistical tendency toward treatment success was observed for one-piece (OR = 3.27, $p = 0.063$) and regular diameter implants (OR = 2.77, $p = 0.075$) (Table 4).

The multivariate analysis confirmed a significantly lower probability of non-surgical treatment success in those implants treated in grade C periodontitis patients (OR = 0.08, $p = 0.044$), wide diameter implants (OR = 0.04, $p = 0.001$), and higher plaque levels at baseline (OR = 0.06, $p = 0.002$) (Table 4).

Clinical and radiographic outcomes

All the clinical and radiographic parameters are summarized in Table 5. From baseline to 6 months, the mean PI at the implant sites significantly decreased from 87 to 59.8% ($p < 0.001$), BoP also significantly decreased from

Table 3 Association between predictors and non-surgical therapy success at patient level: results of binary and multiple logistic regression model with generalized estimating equations (GEEs)

Variable	Simple binary regression analysis		Multiple regression analysis	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Gender				
Male	1			
Female	1.44 (0.50–4.09)	0.499		
Age	0.98 (0.94–1.02)	0.360		
Smoking habit		0.110		0.110
No	1		1	
Yes	0.25 (0.06–0.98)	**0.047***	0.34 (0.07–1.67)	0.184
Former smoker	0.27 (0.05–1.41)	0.121	0.17 (0.03–1.10)	0.063
Number of cigarettes/day	0.91 (0.75–1.11)	0.337		
Years smoking	0.99 (0.93–1.06)	0.851		
Diabetes mellitus				
No	–			
Yes	–	0.319 (Fis)		
History of periodontitis				
No	–			
Yes	–	0.069 (Fis)		
Periodontitis stage		**0.015***		0.060
II	1		1	
III	0.24 (0.07–0.85)	**0.027***	0.25 (0.06–1.05)	0.057
IV	0.10 (0.02–0.57)	**0.009***	0.11 (0.03–1.10)	**0.031***
Periodontitis grade		0.212		
A	1			
B	0.96 (0.16–5.95)	0.968		
C	0.29 (0.04–2.30)	0.239		
Compliance PIMT		0.435		0.435
0 times a year	1		1	
Once a year	1.46 (0.41–5.23)	0.563	1.60 (0.39–6.60)	0.517
2–3 times a year	6.00 (1.30–27.6)	**0.021***	3.13 (0.55–17.7)	0.198

Reference event = success

OR odds ratio, *CI* confidence interval, *PIMT* peri-implant maintenance therapy, *Fis* Fisher exact test if OR non-estimable

*$p < 0.05$

100 to 86% ($p < 0.001$), and SUP was reduced from 28.7 to 17.15% ($p < 0.001$). A significant mean PPD reduction of 1.08 ± 1.06 mm was observed ($p < 0.001$), and a significant mean soft tissue marginal recession of 0.45 ± 0.58 was also noted ($p < 0.001$). Similarly, the shrinkage of KM width from baseline to 6 months amounted to 0.16 ± 0.47 mm ($p < 0.001$).

Radiographically, there was a significant gain in MBL of 0.43 ± 0.56 mm ($p < 0.001$). The bone defect width decreased significantly by 0.16 ± 0.42 mm ($p < 0.001$), while the peri-implant defect angle significantly became $3.98 \pm 0.42°$ wider ($p < 0.001$). The clinical and radiographic improvements are shown in Figs. 1 and 2.

Outcome indicators of PPD reduction

The multiple linear regression analysis showed implants treated in PIMT compliers to be associated with significantly greater PPD reduction at 6 months ($\beta = -0.86$, $p < 0.001$), and an initially deeper PPD was significantly related to increased PPD reduction ($\beta = -0.53$, $p < 0.001$) (Online Resource 2).

Outcome indicators of BoP reduction

At 6 months, a total of 77 implants (71.9%) improved the number of sites with BoP. After adjusting for possible

Table 4 Association between predictors and non-surgical therapy success at implant level: results of binary simple and multiple logistic regression model with generalized estimating equations (GEEs)

Variable	Simple binary regression analysis		Multiple regression analysis	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Gender				
Male	1			
Female	1.10 (0.42–2.87)	0.841		
Age	0.98 (0.95–1.02)	0.342		
Smoking habit		0.110		0.153
No	1		1	
Yes	0.33 (0.11–0.99)	**0.049***	1.70 (0.31–9.22)	0.539
Former smoker	0.22 (0.04–1.16)	0.074	0.16 (0.02–1.60)	0.118
Number of cigarettes/day	0.91 (0.76–1.09)	0.283		
Years smoking	1.02 (0.96–1.07)	0.596		
Diabetes mellitus				
No	–			
Yes	–	–		
History of periodontitis				
No	–			
Yes	–	–		
Periodontitis stage		**0.040***		0.336
II	1		1	
III	0.24 (0.07–0.85)	**0.027***	0.22 (0.02–2.03)	0.183
IV	0.21 (0.06–0.78)	**0.020***	0.14 (0.01–2.13)	0.157
Periodontitis grade		**0.036***		**0.008***
A	1		1	
B	1.68 (0.27–10.4)	0.578	0.71 (0.07–7.55)	0.778
C	0.34 (0.05–2.61)	0.301	0.08 (0.01–0.94)	**0.044***
Compliance PIMT		**0.033***		0.519
0 times a year	1		1	
Once a year	0.91 (0.31–2.68)	0.870	1.57 (0.31–7.95)	0.584
2–3 times a year	5.60 (0.31–2.68)	0.016	5.40 (0.30–97.5)	0.254
Implant site		0.789		
Anterior	1			
Premolar	0.86 (0.19–4.00)	0.852		
Molar	1.21 (0.29–5.11)	0.793		
Implant arch	0.98 (0.95–1.02)	0.342		
Maxilla	1			
Mandible	1.45 (0.55–3.83)	0.452		
Implant diameter		0.110		
≥ 4.5 mm	1			
≥ 4 mm and < 4.5 mm	2.77 (0.90–8.49)	0.075		
< 4 mm	–	–		
Implant thread distance	0.62 (0.07–5.52)	0.666		
Implant pitch width	0.09 (0.01–5.68)	0.250		
Implant design				
Two-piece	1			
One-piece	3.27 (0.94–11.4)	0.063		
Implant surface		0.133		0.181
Minimally rough	1		1	
Moderately rough	3.46 (0.89–13.5)	0.073	4.41 (0.91–21.3)	0.065
Rough	5.33 (0.85–33.6)	0.074	1.96 (0.43–8.78)	0.386
Implant-prosthesis type		**< 0.001****		

Table 4 (continued)

Variable	Simple binary regression analysis		Multiple regression analysis	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Single restoration	1			
Fixed partial restoration	0.72 (0.24–2.17)	0.556		
Cantilever	2.71 (1.13–6.54)	**0.026***		
Removable overdenture	–	**–**		
Fixed full arch	0.34 (0.04–2.99)	0.330		
Prosthesis retention		**0.036***		
Screwed	1			
Cemented	1.62 (0.56–4.73)	0.378		
Removable	–	–		
Prosthesis removal				
No	1			
Yes	3.10 (0.34–28.2)	0.316		
Prosthesis modification		0.212		
No	1			
Yes	0.53 (0.17–1.63)	0.267		
Previous bone regeneration				
No	1			
Yes	1.00 (0.37–2.73)	1.000		
PI at baseline	0.18 (0.05–0.62)	**0.007***	0.06 (0.01–0.35)	**0.002***
PPD at baseline	0.65 (0.38–1.12)	0.122		
No of BoP sites at baseline	0.65 (0.38–1.12)	**0.023***	0.61 (0.36–1.04)	0.070
SUP at baseline	0.65 (0.38–1.12)			
No	1			
Yes	0.51 (0.18–1.48)	0.217		
KM at baseline	0.82 (0.61–1.10)	0.184		
REC at baseline	1.10 (0.53–2.27)	0.808		
MBL at baseline	0.85 (0.61–1.19)	0.348		
IDW at baseline	1.00 (0.61–1.65)	0.996		
IDA at baseline	0.99 (0.95–1.03)	0.555		

Reference event = success

OR odds ratio, *CI* confidence interval, *n* number, *PIMT* peri-implant maintenance therapy, *PPD* probing pocket depth, *PI* plaque index, *BoP* bleeding on probing, *KM* keratinized mucosa, *REC* marginal mucosal recession, *MBL* marginal bone loss, *IDW* intra-bony defect width, *IDA* intra-bony defect angle

*$p < 0.05$, **$p < 0.001$

confounders, only grade C periodontitis patients presented an 81% lesser probability of BoP reduction at 6 months (OR = 0.19, $p = 0.004$). A tendency toward lesser reduction of BoP was also found at those sites characterized by initially greater marginal soft tissue recession (OR = 0.15, $p = 0.095$) (Online Resource 3).

Outcome indicators of MBL gain

Briefly, it was shown that implants treated in stage IV periodontitis patients (β = 0.31, $p = 0.033$), in former smokers (β = 0.25, $p = 0.045$), in full-arch dentures (β = 0.28, $p = 0.044$), and greater initial marginal soft tissue recession (β = 0.12, $p = 0.049$) presented significantly lower marginal bone gains (Online Resource 3). It was further observed that one-piece implants and prosthesis removal significantly obtained 0.27 and 0.26 mm more marginal bone gain, respectively. However, the multiple regression analysis failed to show any independent variable to be significantly related to MBL (Online Resource 4).

Discussion

Main findings

Improvement of the clinical and radiographic parameters was observed after non-surgical mechanical debridement of

Table 5 Clinical and radiographic measurements at baseline and 6 months (expressed as mean ± SD and % (95% CI))

Variable	Baseline	6 months	Changes (6 months–baseline)	*p* value
Clinical variables				
PPD, mean ± SD	5.64 ± 1.28	4.59 ± 0.99	− 1.08 ± 1.06	< 0.001
PI, %	87.0 (80.3, 92.8)	59.8 (50.3, 68.6)	− 27.2% (20.4, 37.2)	< 0.001
BoP, %	100 (96.57, 100)	86 (78.15, 91.31)	− 14% (8.7, 21.9)	< 0.001
BoP per site, % (0–1-2–3-4–5-6)	0–1.9–5.6–10.2–10.2–11.1–61.1	14–17.8–17.8–14.0–15-2.8–18.7	–	< 0.001
SUP, %	28.7 (21.0, 37.9)	17.1 (11.1, 25.5)	− 11.6% (7.38, 20.0)	< 0.001
KM width, mean ± SD	2.51 ± 1.51	2.35 ± 1.47	− 0.16 ± 0.47	0.004
REC, mean ± SD	0.27 ± 0.61	0.76 ± 0.88	0.45 ± 0.58	< 0.001
Radiographic variables				
MBL, mean ± SD	4.56 ± 1.46	4.14 ± 1.57	− 0.43 ± 0.56	< 0.001
IDW, mean ± SD	2.17 ± 0.82	2.01 ± 0.85	− 0.16 ± 0.42	< 0.001
IDA, mean ± SD	45.42 ± 13.44	49.40 ± 15.29	3.98 ± 8.38	< 0.001

PPD probing pocket depth, *PI* plaque index, *BoP* bleeding on probing, *KM* keratinized mucosa, *REC* marginal mucosal recession, *MBL* marginal bone loss, *IDW* intra-bony defect width, *IDA* intra-bony defect angle

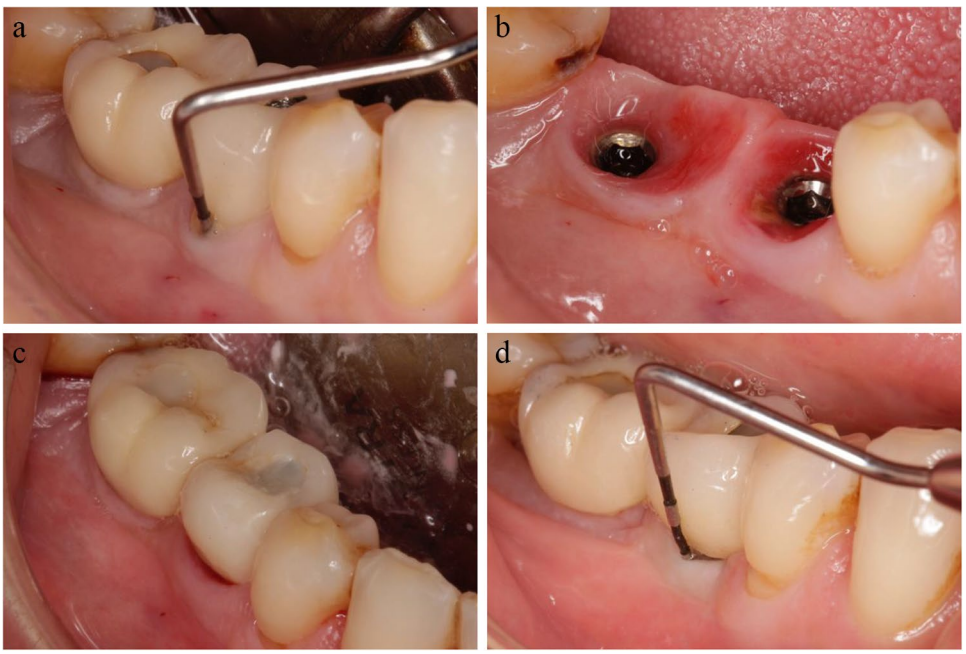

Fig. 1 Description and clinical outcomes of the non-surgical treatment protocol in an implant placed in position 4.5: **a** 8-mm peri-implant PPD at the buccal aspect; **b** peri-implant soft tissue conditions after restoration removal; **c** immediately after mechanical debridement; **d** clinical outcomes at 6 months of follow-up with 3 mm of PPD and no BoP

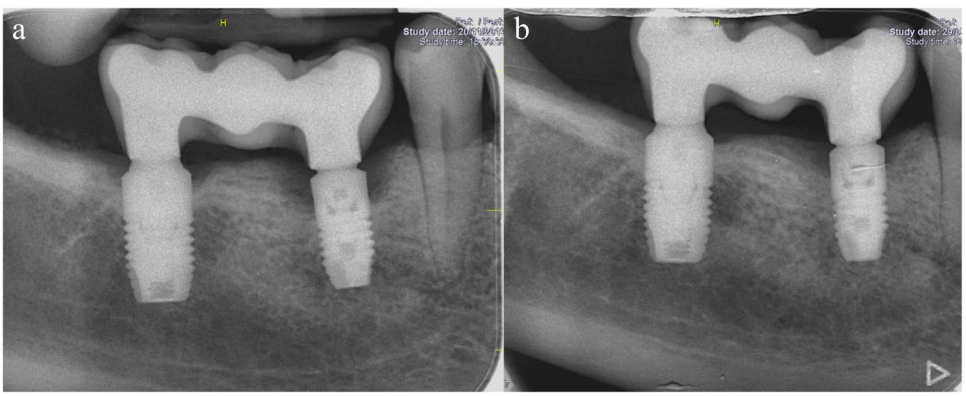

Fig. 2 **a** Radiographic evaluation of implants in positions 4.5 and 4.7 at baseline; **b** and at 6 months after non-surgical-treatment, where radiographic bone fill can be observed. Note as well that the contours of this fixed multiple unit restoration were modified to allow proper interproximal self-performed oral hygiene

peri-implantitis with the adjunctive use of systemic metronidazole. Disease resolution was achieved in 25.7% of the patients and in 24.1% of the implants. Patients with stage IV and grade C periodontitis, inadequate oral hygiene at baseline, and wide diameter implants presented a significantly higher probability of not achieving disease resolution, whereas smokers and former smokers demonstrated a certain tendency toward lesser disease resolution.

Agreements and disagreements with previous studies

Our clinical and radiographic findings are in line with those of most of the previous studies evaluating the efficacy of the non-surgical mechanical treatment of peri-implantitis with adjunctive self-administration of systemic antibiotics [18–20, 23]. In a prospective private study [20], PPD and BoP were reduced 1.65 mm and 57.6%, respectively. In addition, the MBL gain was 1.31 mm, the peri-implant defect width was reduced by 0.65 mm, and the defect angle increased 11.81°. Similarly, in a retrospective study conducted in the university setting in which the combination of amoxicillin 500 mg plus metronidazole 500 mg was prescribed [19], PPD and BoP decreased 1.92 mm and 18%, respectively, whereas the MBL gain amounted to 0.9 mm. However, in a retrospective case series study performed in private practice [18], PPD was reduced 4.66 mm and MBL increased 2.6 mm, while the peri-implant defect angle increased 34.3%. The more favorable clinical and radiographic outcomes reported by the latter study [18] could not only be explained by the inclusion of more severe forms of peri-implantitis with intra-bony defects of > 2 mm (initial PPD and marginal bone loss amounted to 8.72 ± 2.13 mm and 4.52 ± 2.14 mm, respectively), but also by patient enrollment in the context of 4 to 6 months of PIMT during the study period [18].

The adjunctive administration of systemic antibiotic after the non-surgical treatment of peri-implantitis may be justified by the large extension of the peri-implant lesion and by the surface topography of the implant, which in turn may jeopardize adequate debridement of the biofilm with a closed approach. In this context, several recently published randomized clinical trials have evaluated the adjunctive benefit of systemic antibiotic in the non-surgical management of peri-implantitis, with conflicting results so far [23, 31–33]. In one of these studies [31], which combined the administration of metronidazole plus amoxicillin, no significant differences were observed at 3 months of follow-up in terms of the analyzed clinical and microbiological parameters. Nevertheless, a slight clinical benefit of systemic antibiotic was observed in relation to deep peri-implant pockets (≥ 7 mm). Similarly, in a 3-month randomized controlled trial, the antibiotic treatment group (amoxicillin + metronidazole) showed no significant decrease in PPD and BoP versus the control group [33]. In contrast, Blanco et al. reported significant 1-year improvements in the clinical/radiographic parameters and microbiological counts after administrating systemic metronidazole, with a higher success rate in the antibiotic group (56.3%) versus the control group (25%) [23]. The disagreements between studies could be attributed to differences in the mechanical debridement approaches used, follow-up periods, antibiotic prescription, and the initial depth of the peri-implant pockets. In light of these data, the prescription of antibiotic as adjuvant therapy to mechanical debridement of peri-implantitis lesions should be individualized to each patient and clinical scenario.

Peri-implantitis resolution 6 months after non-surgical treatment occurred in 25.7% of the patients and in 24.1% of the implants. In other words, one out of four implants did not require any further treatment at 6 months, apart from PIMT. Although different criteria for treatment success have been implemented in the literature [19, 20, 23, 32, 33], resolution after the non-surgical management of peri-implantitis with systemic antibiotics generally tends to take place in approximately half of the implants. However, a recently published 3-month study has indicated that treatment success when prescribing systemic antibiotics occurred in 0.5% of the implants [33]. These unsatisfactory results could be ascribed to the lack of superstructure removal during submucosal debridement, the strict success criteria applied (PPD < 5 mm, no BoP and/or no SUP), and the limited follow-up period involved. The moderately low success rate reported in our study could be partly justified by the short-term follow-up assessment of the treatment with just a single submucosal instrumentation, low patient improvement in terms of oral hygiene habits (since the plaque index at implant sites remained as high as 59.8% at 6 months), and the large proportion of periodontally susceptible patients in the population sample.

Our study showed that the severity of periodontitis (stage IV and grade C), a higher initial plaque index at implant sites, and wider implants were the factors significantly associated with incomplete disease resolution at 6 months. Although it has been extensively reported that a poorer periodontal condition and higher plaque levels could be related to a higher risk of developing peri-implantitis [1, 34–37], little information is available on the impact of the periodontal condition and oral hygiene upon the outcomes of the non-surgical or surgical management of peri-implantitis [19, 38]. In fact, a retrospective long-term study conducted in a university-based setting found that patients receiving supportive periodontal care with severe periodontitis and suboptimal oral hygiene had a significant 5.7- and 2.9-fold decrease in peri-implantitis treatment (non-surgical, flap, or regenerative surgery) success rate, respectively [34]. Most of the patients included in our study received basic periodontal

therapy simultaneous to non-surgical treatment of peri-implantitis, while a few of them were already enrolled in supportive periodontal care. It may be hypothesized that the simultaneous performance of both treatments might not be as effective as if the patients were enrolled in a maintenance program, due to the different microbiological dysbiosis that may be present between patients with active periodontal disease compared to individuals under maintenance therapy. Hence, initial periodontal status and the timing of the non-surgical treatment of peri-implantitis may be viewed as clinically relevant factors in relation to treatment success. In addition, the rationale behind a lower success rate in wide diameter implants (≥ 4.5 mm) compared to standard diameter implants (≥ 4, < 4.5 mm) could be ascribed to the residual bacterial deposits attached to the titanium surface — as a larger implant surface colonized by biofilm might be expected in wider implants. Moreover, it is hypothesized that wider implants are more prone to invade the critical buccal bone thickness [39]. This may lead to excessive vertical bone loss at the buccal aspect of the implant, leading to colonization by pathogenic bacteria. Furthermore, posterior implants are often placed in molar sites, where access for the operator and for self-performed oral hygiene proves challenging.

It is worth mentioning that a statistical trend toward disease resolution was found in non-smokers. The negative impact of smoking upon the management of peri-implantitis is not surprising in the light of all the scientific evidence in the periodontal literature, indicating a lesser probability of PPD reduction and pocket closure after the non-surgical and surgical treatment of periodontitis [40–43]. Specifically, our study recorded treatment success in 37.8% of the non-smokers versus in 13% of the smokers. In a study evaluating the prognostic indicators referred to the surgical resective management of peri-implantitis [44], smoking was found to increase treatment failure 3.82-fold. Therefore, clinicians should advise smokers to quit smoking as part of their non-surgical peri-implantitis treatment strategy.

Despite the fact that only 15 one-piece implants (14% of the total) were included in the analysis, a statistical trend toward treatment success was also observed for one-piece implants, with a likelihood of disease resolution of 46.7% in comparison to 21.1% in the case of two-piece implants. In addition, one-piece implants also presented a significant 0.26 mm more of marginal bone gain versus two-piece implants. It has been claimed that one-piece implants may play a protective role against peri-implantitis and crestal bone loss [45], especially in non-compliant patients. In the light of our findings, it could be hypothesized that the transmucosal part of the one-piece implants may help to obtain a more stable peri-implant mucosal seal — thus preventing bacterial downgrowth, enhancing pocket closure, and favoring marginal hard tissue gain. Apart from the implant design, attention should also focus on the impact of surface roughness upon the success of non-surgical treatment, as most of the one-piece implants presented with a moderately rough or rough surface. Interestingly, our study has demonstrated a greater probability of success with moderately rough (OR = 4.41, 95% CI 0.91–21.3) and rough (OR = 1.96, 95% CI 0.43–8.78) compared to minimally rough implants. Similarly, the benefit of systemic antibiotic was also evidenced in favor of rough surfaces in a randomized clinical trial comparing the surgical treatment of peri-implantitis with or without systemic antibiotics [46]. Both findings could be explained by the smaller and less aggressive peri-implant bone defects commonly found around smooth implants, with less bacterial invasion, which in turn may benefit less from adjuvant antibiotic administration.

It was not surprising in the present study that an initially deeper PPD led to greater probing depth reduction at 6 months. Previous research in the periodontal and peri-implant field has explained this finding in terms of the greater soft tissue shrinkage and clinical attachment gain that may occur after the non-surgical debridement of deep periodontal/peri-implant pockets [13, 47, 48]. Moreover, it was observed that BoP reduction was less likely at those sites with greater marginal soft tissue recession at baseline — especially at the mid-buccal sites of the implants. At the same time, it was further shown that a wider band of KM was related to greater BoP reduction, although not to a statistically significant degree. Therefore, it could be speculated that the amount of tissue recession and KM width could play an important role in BoP resolution at 6 months of non-surgical treatment for peri-implantitis.

This study evidenced that almost all the implant-supported restorations could be removed before mechanical instrumentation, and of these, almost 73% were modified for better access to oral hygiene. In fact, prosthesis removal was seen to be associated to a threefold greater probability of disease resolution than non-removal in the simple regression analysis. From a clinical perspective, there is improved accessibility for performing submucosal mechanical instrumentation when restorations are removed — thus probably affording greater bacterial decontamination. Similarly, an improper prosthetic design, which impairs adequate self-performed oral hygiene, has been commonly associated with the occurrence of peri-implant disease [49–51]. It also should be highlighted that over-contoured restorations are often emerged from a deficient three-dimensional implant position — this also being a relevant factor in the effectiveness of the non-surgical treatment of peri-implantitis. With this in mind, prosthesis modification within the management of peri-implant disease should be regarded as an essential step for securing a better scenario for oral hygiene and for improving the peri-implant inflammatory parameters [29].

Clinical implications of the study

Although 12 months of follow-up has been recommended as the ideal moment to evaluate the success of non-surgical treatment [11], a crucial issue may arise 6 months after the completion of non-surgical management, related to the need for further treatment beyond PIMT. It is well known that the presence of residual PPD ≥ 5 mm, BoP, and marginal bone loss at re-evaluation may be a useful criterion for predicting further disease progression [46]. Indeed, the lack of success in obtaining this clinical endpoint may guide the performance of further additional therapy. In our study, the implants were prescribed with different therapeutic approaches after the 6 months re-evaluation, such as implant removal, soft tissue augmentation, bone reconstructive therapy, and resective therapy, and in most of the cases the implants went through PIMT. In this context, we believe that the present study provides relevant information for the clinician and the patient since it helps to discriminate those clinical situations where non-surgical management is less likely to secure treatment success over the short term — i.e., it may contribute to anticipate and identify those patients/implants that would probably need further corrective treatment.

Limitations and recommendations for future research

A number of issues should be addressed for proper interpretation of the results obtained. First, treatment, although supervised by an experienced periodontist, was performed in a university environment by five residents trained in this type of treatment. This fact could partially explain the variability of the clinical and radiographic findings when compared to studies made in private offices by a single operator. Second, the present study lacked a microbiological and/or immunochemical analysis. We believe that such analyses would have helped to better understand and characterize the results. The sample was slightly heterogeneous in terms of the implant and prosthesis features, with a lower number of cases in some categories, which may have interfered with the estimates of the regression analysis. It could be speculated that more restrictive inclusion/exclusion criteria regarding the implant or prosthetic characteristics could have improved parameterization of the models. Lastly, it is important to note that almost all the included patients had a history or periodontitis or active periodontitis — this factor being strongly associated to lesser treatment success.

The findings of this exploratory study may serve as a starting point to better understand the influence of patient, implant, and prosthetic features upon the effectiveness of non-surgical treatment for peri-implantitis. In other words, the study may assist the clinician in knowing beforehand in which clinical scenarios the non-surgical management of peri-implantitis becomes more predictable. To substantiate and to better comprehend our findings, further randomized clinical studies involving specific patient profiles are needed.

Conclusions

The present study evidenced that disease resolution after the non-surgical treatment of peri-implantitis is influenced by the loss of support of the periodontium, poor baseline oral hygiene, and wide diameter implant. Non-smokers and one-piece implants may tend to achieve greater treatment success. Therefore, it is important to bear all these patient- and implant/site-related factors in mind in order to anticipate the magnitude of disease resolution after the non-surgical treatment of peri-implantitis.

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Author contribution JV, MCS, CV, AM, and JN prepared the study protocol; JV, MCS, and RP collected the data; JV, MCS, and RP analyzed the data; JV and MCS supervised the writing; JV, MCS, RP, CV, GB, AM, and JN revised the drafted manuscript.

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Data availability The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethical approval The study protocol was approved by the Ethics Committee of *Universitat Internacional de Catalunya* (UIC) (Barcelona, Spain) (Ref.: PER-ECL-2020–06).

Conflict of interest The authors declare no competing interests.

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