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ORIGINAL ARTICLE

Effect of alveolar ridge preservation on peri-implant mucositis and peri-implantitis prevalence: A multicenter, cross-sectional study

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Abstract

Objectives: Alveolar ridge preservation (ARP) is a procedure with the aim to reduce bone resorption that occurs after tooth extraction, facilitating the following implant placement. The aim of this cross-sectional study was to evaluate the prevalence of mucositis and peri-implantitis around implants inserted in sites treated with ARP and to investigate possible risk factors.

Materials and methods: Patients who received at least one dental implant inserted in a grafted socket were considered eligible for this study. Patients were recalled for a follow-up visit; medical history, clinical and demographic data were collected. Univariate logistic regression analyses have been performed for both implant-level and patient-level variables. Indeed, moderation analysis was used to investigate the indirect relationship between age and marginal bone level.

Results: Fifty-one patients who received 61 implants were enrolled in this cross-sectional study. Thirty-three implants were classified as "healthy" (54.1%), 23 implants showed signs of peri-implant mucositis (37.7%), and 5 implants were diagnosed with peri-implantitis (8.2%). Data analyzed at the patient level showed that 49% of the patients were healthy, 45.1% of the patients had mucositis and 5.9% of the patients were affected by peri-implantitis. Mandibular sites and type III grafted sockets showed a significant association with peri-implantitis; in addition, a history of periodontitis and an increase in age showed higher risks of developing mucositis or peri-implantitis.

Conclusions: Implants inserted in grafted sockets showed favorable rates of healthy implants in the long term.

Clinical relevance: The ridge preservation procedures do not seem to increase the risk of developing mucositis or peri-implantitis.

Buonocunto Nino and Cinquini Chiara contributed equally to the study.

KEYWORDS
alveolar ridge preservation, dental implant, mucositis, peri-implantitis

What is known

Alveolar ridge preservation (ARP) is a well-established procedure, which enables the optimal positioning of dental implants in a prosthetically driven position.However, there is limited research available on the long-term outcomes of implants placed in sites treated with ARP.

What this study adds

This current study provides novel insights into the health status of implants placed in sites treated with ARP after a long follow-up period. The results of this study suggested that the health rates of these implants are favorable. Moreover, our findings highlighted a significant correlation between local and systemic factors and the occurrence of mucositis or peri-implantitis.

1 | INTRODUCTION

The extraction of a tooth triggers dimensional alterations of the residual alveolar ridge which lead to its progressive atrophy.[1–3] The volume shrinkage of the alveolar bone ridge, observed after tooth extraction, may affects the chance to replace the missing tooth with a dental implant[3] and it might require additional bone grafting procedures to achieve a prosthetically driven implant placement.[4] According to the most recent literature,[5] the burden of alveolar bone resorption depends on multiple factors, including the periodontal phenotypic characteristics of the site and its location.

Several alveolar ridge preservation (ARP) techniques are described in the literature to preserve the alveolar bone after tooth extraction and, among the different procedures, the "socket grafting" is the most used.[6–8] After a tooth extraction performed in the least traumatic way, the alveolar socket is grafted with a bone substitute with or without a membrane.[9] Many authors classified the alveolar sockets according to the characteristics of both hard and soft tissues[10–13] and to patient-related factors.[14]

The aim of the bone graft is to acts like a scaffold to promote bone formation and to maintain the ridge volume stable during the healing period.[6,15]

Therefore, ARP procedures can be considered a treatment to minimize dimensional bone changes, which physiologically occurs after tooth extraction,[3,8] and to facilitate the following implant insertion.[16]

Implant-supported prostheses have become widely used and have radically changed the methods in rehabilitating fully/partially edentulous patients[17] with favorable survival rates according to long-term evaluations.[18] On the other hand, despite the encouraging survival rates, technical and biological complications can occur around dental implants[19] affecting their survival and success.[20,21]

One of the main features of implant restorations should be longevity, and it is well known that dental implant failures are mainly caused by peri-implant pathologies.[22] Peri-implant mucositis is an inflammatory condition of the peri-implant soft tissue with no signs of peri-implant bone loss,[23] whilst peri-implantitis is a pathological condition characterized by clinical signs of inflammation and radiographic marginal bone loss.[24]

Patients affected by peri-implant mucositis may develop peri-implantitis, therefore it is imperative to maintain adequate plaque control[25] to stop the progression of this condition, since the treatment of peri-implantitis is complex and challenging with absence of a complete consensus on which is the best course of action.[26]

Currently, it is not clear whether the ARP could have an influence on the pathophysiology and on the prevalence of peri-implant pathologies for implants placed in grafted extraction sockets.[27]

Furthermore, according to the consensus report from the XV European Workshop in Periodontology,[28] researchers should focus their investigations on the possible correlation between local and systemic factors which could have an impact on hard and soft tissue healing (e.g., systemic conditions, medications, smoking habits, history of periodontitis, and parafunctional habits), and the clinical outcomes of ARP procedures. Subsequently, the outcomes of ARP are strictly related to the implant-prosthetic rehabilitation success.

Even though several publications had already suggested that implants should be evaluated with cumulative success rates over a period of at least 10 years,[29] more recent studies regarding ARP effects on implant-related outcomes reported only short-term results.

The aim of the present cross-sectional study was to evaluate the prevalence of peri-implant pathologies for implants inserted in grafted sockets and to analyze the influence of possible risk factors associated with peri-implantitis.

2 | MATERIALS AND METHODS

The present multicenter, cross-sectional, clinical, and radiographic investigation was conducted in accordance with the Good Clinical Practice Guidelines (GCPs), and the paper is reported in accordance with the STROBE statement (https://www.strobe-statement.org/).

The study was approved by the Local Ethical Committee "Comitato Etico Area Vasta Nord-Ovest" (approval form 57 489/2019) and

followed the recommendations of the Declaration of Helsinki for investigations of human subjects as amended in October 2013.[30]

All patients treated with at least one implant in a grafted alveolar socket at the University Hospital of Pisa (Italy) or at the School of Dental Medicine, Tel-Aviv (Israel) were considered potentially eligible in this study.

2.1 | Eligibility criteria

The following inclusion criteria had to be fulfilled to enroll the patients:

- Patients (aged >18 years) treated with at least one dental implant inserted in a grafted alveolar socket;
- Ability to understand and sign a consent form.

The following exclusion criteria were:

- Patients under treatment with any medications that could affect bone turnover or mucosal healing;
- Patients who were pregnant or breast-feeding;
- Patients who suffered from a systemic pathology that wasn't under control;
- Implants with less than 2 years of function;
- Implants inserted in spontaneously healed sites;
- Incomplete patient medical data records.

After a screening of the patients' medical records retained in the two experimental centers, all the potentially eligible patients were recalled for a follow-up visit and a clinical examination in a period ranging from January 2021 to April 2022.

During the follow-up visit, every patient received detailed information about the study protocol in written and oral form and signed a consent form to express their willingness to participate in the study. After a calibration meeting, two different examiners (N.B, E.M) performed the clinical and radiographic evaluation and, subsequently, collected the medical records. The calibration probing session was performed by the two examiners on a subject not recruited in the study, until the agreement rate was at least 85%.

The examiners were different clinicians from those who treated the patients and did not have access to the patients' medical records before the clinical evaluation.

The following information was collected: age, gender, systemic diseases, medications, smoking habits (yes/no), history of periodontitis (yes/no), presence of parafunctional habits (yes/no), compliance with oral hygiene recalls (number of maintenance appointments per year).

History of periodontitis was defined by the following criteria: the presence of at least three sites with periodontal probing depth ≥5 mm and previous non-surgical and surgical periodontal therapy and/or dental extractions for periodontal reasons.[31]Parafunctional habits were defined by using the following criteria: the presence of significant wear of teeth or restorations, exposed dentin, well-defined wear facets, hypertrophic masticatory muscles, and fractures of teeth or restorations.[32]

All the ridge preservation procedure information was collected from the patients' medical record: date of tooth extraction, tooth type, reason for tooth extraction (decay, endodontic failure, fracture, periodontitis, orthodontic reasons, prosthetic reasons), type of tooth extraction (simple or complex, requiring osteotomy and flap raising), type of extraction socket on the basis of post-extractive hard and soft tissue characteristics (adequate or type I, compromised or type II, and deficient or type III),[33] type of healing (primary or secondary), biomaterial used (type, amount), collagen membrane used, antibiotics treatment and dosage, pre or post-operative adverse events.

All the patients included in the study had been treated by two expert operators (AB and NTG), with more than 20 years of clinical experience in bone regeneration and implant surgery.

According to the medical records, the tooth extraction procedure was performed with great care to reduce the trauma on the buccal bone plate and to keep the integrity of a four-wall bone morphology and accurate debridement of the extraction socket.

For the ARP procedure, two different grafting materials were used: pre hydrated collagenated cortico-cancellous porcine bone (Osteobiol®, MP3®, Tecnoss, Giaveno, Italy), anorganic bovine bone (Bio-Oss®, Geistlich Pharma, Wolhusen, Switzerland). Fresh alveolar sockets were filled with graft materials up to the buccal and palatal alveolar bone walls and a collagen membrane (Osteobiol®, Evolution®, Tecnoss, Giaveno, Italy) was used to completely cover the socket, the membrane was left intentionally exposed to the oral cavity and stabilized with the use of synthetic 4.0 absorbable sutures made of glycolide and lactide copolymers.

Moreover, all the implant-prosthetic information was collected: timing of implant insertion, implant position, implant features (tissue or bone level), implant diameter and length, implant surface (B+ mono-molecular layer of multi phosphonates, MIS Implants technologies, Bar-Lev, Israel; Ossean surface, sand-blasted and Dual Etched, Intralock, Salerno [SA], Italy; Osteotite, sand-blasted and Dual-Etched, Biomet 3i, Palm Beach Garden [FL], USA), abutment connection (external/internal/conical), insertion torque values, implant stability (stable, spinning, not stable), residual peri-implant bone defect—when present-, need for additional bone or soft tissue augmentation at the time of implant insertion, complications during or after surgery, type of prosthetic restoration (cemented/screw retained), and time of function.

The following clinical peri-implant parameters were assessed during the recall visit using a 15 mm standardized periodontal probe (UNC): probing depth (PD) at six sites per implant (6 values were recorded), bleeding on probing (BOP) at six sites per implant (presence/absence evaluated 15 s after probing), suppuration (presence/absence) and visual signs of inflammation of the soft tissues at the probing site (red or pink, swollen vs. not swollen, soft vs firm tissue consistency). The Periodontal Screening and Recording (PSR) score was also registered for each patient. The pressure of probing was gentle until the detection of a light resistance at the pocket's base.[34]

Digital intraoral periapical radiographs were taken (70 kVp, 7 mA) using a parallel cone technique with a digital sensor (Schick Technologies, Long Island City, NY) and a radiographic positioner (Rinn device).

Baseline radiographs (taken immediately after prosthetic loading) were collected from patients' medical records for comparison. Peri-implant marginal bone level (MBL) was evaluated on intraoral radiographs at the mesial (mMBL) and distal (dMBL) sites.

This parameter was set as the distance from the reference point (fixture–abutment interface) to the most apical contact between fixture and bone.

Calibration was performed using the known thread-pitch distance of the implants (pitch of 1.0 mm). Previously known value, such as fixture length, were used for calibration when the threads were not clearly visible on the radiographs. Measurements were taken to the nearest millimeter using digital imaging software DBSwin (Air Techniques Inc, Melville, NY) measurement tool.

2.2 | Primary and secondary outcomes

The primary outcome of this study was to evaluate the prevalence of peri-implantitis of the implants inserted in alveolar sockets grafted with biomaterials.

Criteria proposed by the 4th Workgroup of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions were used for the diagnosis of peri-implant mucositis and peri-implantitis.[24]

Peri-implant mucositis was defined as the presence of any bleeding/suppuration on probing, that is combined with visual inflammatory changes of the tissues at the site of probing, an increase in probing depths compared to baseline and absence of bone loss beyond crestal bone level changes resulting from the initial remodeling.

Peri-implantitis was defined as the presence of bleeding and/or suppuration on gentle probing with probing depths ≥6 mm and crestal bone levels ≥3 mm apical to the most coronal portion of the intraosseous part of the implant.

The secondary outcome was to investigate any association between the following parameters and peri-implant status, as they follow:

At the patient level:

- Age
- History of periodontitis, (yes/no);
- Parafunctional habits (yes/no);
- Number of oral hygiene recalls per year.

At the implant level:

- Mean Marginal Bone Level Change (MBLC): it was defined as the mean difference between baseline and follow-up bone levels;
- Periodontal Screening Record (PSR)[35]: Using the special PSR probe, six sites were checked on each tooth (implants were excluded). The PSR code was determined by the worst finding in the whole mouth. Code 0 was used for a probing depth (PD) below 3.5 mm with no BOP and no supragingival plaque/calculus detected. Code 1 was used with the same PD, but in the presence of BOP. If plaque/calculus was also detected, then a Code 2 was assigned. Code 3 was used in case of 3.5 mm < PD <5.5 mm, and code 4 in case of PD >5.5 mm, independently from the BOP or plaque/calculus detection;
- Tooth position (incisor, canine, premolar, molar);
- Reason for tooth extraction (decay, fracture, endodontic failure, periodontitis, orthodontic reason or prosthetic reason);
- Type of Extraction socket (I, II, or III);
- Insertion torque values (≤35 N or > 35 N);
- Implant position: Maxilla/Mandible, Anterior (central incisors, lateral incisors, cuspids)/Posterior (premolars, molars);
- Systemic diseases and medications taken.

2.3 | Statistical analysis

The sample size was calculated based on a 10% prevalence of peri-implantitis,[31] 7.5% precision, and 95% confidence intervals. The minimum required total sample size is 61 implants.

Descriptive statistics were produced using patients ($n = 51$) and implants ($n = 61$) as the unit of analysis. The bar graph was used to depict the prevalence of disease conditions in both subjects and implants. For continuous variables, the median, first (q1) and third quartile (q3) or mean (SD = standard deviation) were presented, according to their distribution. Shapiro–Wilk was used to test normality distribution for continuous variables. The absolute frequency (n) and column percentage (%) were reported for categorical variables.

The association between the implant level status and patients and implant characteristics was assessed by the univariate logistic regression model estimated the Odds ratios (ORs). Where necessary, Haldane correction was used to calculate the ORs. The 95% confidence interval was reported for the ORs, the association was assessed using the Chi-square test or Fisher exact test (frequency ≤5), and the *p*-value was reported. For MBLC, qualitative differences among the diseased (i.e., mucositis, peri-implantitis) and healthy implant groups were assessed using the Kruskal–Wallis test (at the implant level). If the Kruskal–Wallis test revealed significant differences among the groups, Dunn's post hoc multiple comparisons test was used, and *p*-values were adjusted using the "holm"-method. A multilevel multivariate regression model was used to assess the moderating effect of periodontitis history in the association between Age and MBLC. Because some patients have more than one implant, evidence of significant clustering of data was tested by comparing the null and final models using the likelihood-ratio test. Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC) were used to assess the model's performance.

All statistical tests were 2-sided with a significance level set at $p \leq 0.05$. All analyses were performed with the open-source statistical R environment (version 3.4.3, the R Foundation for Statistical Computing, Vienna, Austria).

TABLE 1 Summary descriptive statistics for baseline patient-level characteristics expressed as median [q1 = first quartil, q3 = third quartil] and absolute frequency (*n*) and column percentage (%).

Patients level variables	Overall *n* = 51	Healthy *n* = 25	Mucositis *n* = 23	*p*-Value Mucositis vs. Healthy	Peri-implantitis *n* = 3	*p*-Value Peri-implantitis vs. Healthy	OR (Healthy vs. Mucositis)	OR (Healthy vs. Perimplantitis) [95%CI]
Age, years, median [q1; q3]	56.00 [51.00;62.00]	54.00 [50.00;58.00]	56.00 [52.5;66.50]	0.169#	77.00 [67.00;81.50]	0.026#	1.04 [0.98;1.11]	1.20 [1.02;1.42]
Gender, *n* (%)				0.596§		0.234§		
Female	38 (74.50)	18 (72.00)	19 (82.60)		1 (33.30)		Ref.	Ref.
Male	13 (25.50)	7 (28.00)	4 (17.40)		2 (66.70)		0.56 [0.12;2.22]	4.57 [0.32;1.59]
Tobacco use, *n* (%)				0.487§		1.000§		
No	41 (80.40)	21 (84.00)	17 (73.90)		3 (100.00)		Ref.	Ref.
Yes	10 (19.60)	4 (16.00)	6 (26.10)		0 (0.00)		1.81 [0.43;8.45]	0.68 [0.03; 15.65]
History of periodontitis, *n* (%)				0.155+		0.188§		
No	32 (62.70)	19 (76.00)	12 (52.20)		1 (33.30)		Ref.	Ref.
Yes	19 (37.30)	6 (24.00)	11 (47.80)		2 (66.70)		2.81 [0.83;10.40]	5.55 [0.39;19.50]
Parafunctional habits, *n* (%)				0.402+		0.543§		
No	28 (54.90)	16 (64.00)	11 (47.80)		1 (33.30)		Ref.	Ref.
Yes	23 (45.10)	9 (36.00)	12 (52.20)		2 (66.70)		1.90 [0.60;6.32]	3.22 [0.23;11.10]
Oral hygiene recalls per year, *n* (%)				0.502+		0.258§		
<2	18 (35.30)	11 (44.00)	7 (30.40)		0 (0.00)		Ref.	Ref.
≥2	33 (64.70)	14 (56.00)	16 (69.60)		3 (100.00)		1.76 [0.53;6.13]	5.55[0.26;118.72]
Pathologies and medication taken, *n* (%)				0.424+		0.804+		
Multiple pathologies	10 (34.50)	4 (33.30)	4 (28.60)		2 (66.70)		Ref.	Ref.
Endocrine disorders	9 (31.00)	4 (33.30)	4 (28.60)		1 (33.30)		1.00[0.14;7.10]	0.50 [0.03;7.99]
Psychological or psychiatric disorders	2 (6.90)	2 (16.70)	0 (0.00)		0 (0.00)		0.20[0.00;5.45]	0.20 [0.00;5.45]
Other diseases	4 (13.80)	1 (8.33)	3 (21.40)		0 (0.00)		3.00[0.21;42.62]	0.60 [0.02; 20.98]
Cardiovascular diseases	4 (13.80)	1 (8.33)	3 (21.40)		0 (0.00)		3.00[0.21;42.62]	0.60 [0.02; 20.98]

Note: *p*-Value derived from Mann–Whitney *U* test for continuous variable and Chi-squared test or or Friedman exact test for categorical one. Indeed, the OR (Healthy vs. Peri-implantitis) was reported as a risk measure. § = Fisher exact test, + = Chi-Squared test, # = Mann U Whitney test.

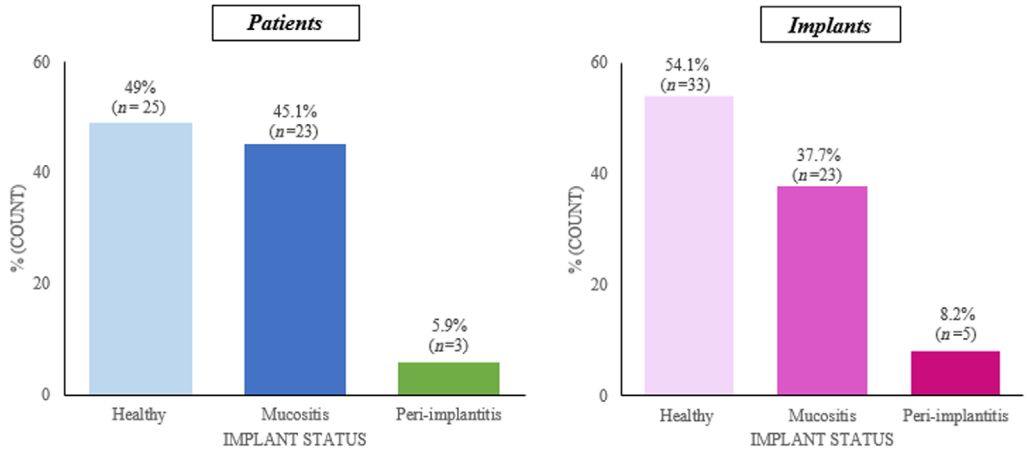

FIGURE 1 Prevalence of Healthy, Mucositis and Peri-implantitis at patients and implant levels expressed as absolute frequency (*n*) and column percentage (%).

3 | RESULTS

Sixty-nine patients with at least one implant inserted in a ridge-preserved site were initially screened to be included in the study.

Eighteen of them were excluded for the following reasons: 12 were untraceable, 5 refused to participate in the study, and one patient, after being enrolled in the study, did not have a full data record completely available. Finally, a total of 51 patients (38 females, 13 males), ranging from 37 to 86 years (median 56 years), who received 61 implants (follow-up range 2.5–15.0 years), were included in this study. Forty patients were included at the University Hospital of Pisa (Italy), whilst 11 patients were recruited at the School of Dental Medicine, Tel-Aviv, (Israel).

The demographic patients' data are reported in Table 1.

Thirty-three implants out of 61 enrolled were classified as healthy (54.1%), 23 implants showed signs of mucositis (37.7%), and 5 implants showed signs of peri-implantitis (8.2%). The analysis at the patient level showed that 25 (49.0%) patients out of 51 were healthy, 23 (45.1%) patients were diagnosed with mucositis and 3 (5.9%) patients were diagnosed with peri-implantitis (Figure 1).

The mean follow-up period from prosthesis delivery was 8.7 ± 3.5 years and the mean healing time between ARP and prosthetic loading was 9.54 ± 3.62 months.

Of the 51 included patients, 12 (35.3%) attended to less than two oral hygiene recalls per year, whilst 33 (64.7%) attended two or more recalls per year.

Table 2 reports the summary descriptive statistics for implant-level variables. The most common reason for tooth extraction was decay (46.7%), followed by fracture (26.7%), periodontal disease (15.0%) and endodontic failure (11.7%). The proportion of simple/complex tooth extractions was 4 to 1. The fresh extraction socket type was 24.6%, 68.9%, and 6.6% for type I, type II and type III, respectively.

The materials used for the ARP were pre hydrated collagenated cortico-cancellous porcine bone (47 sites, 77.0%) and anorganic bovine bone (14 sites, 23.0%).

No implant was lost for periimplantitis before the beginning of the present study.

Implant position (mandible/maxilla) showed a significant association between peri-implantitis and mandible (OR = 10.88; CI [1.37; 86.39]; $p = 0.05$), this means a significantly higher prevalence of peri-implantitis in mandibular sites. Implant position (anterior vs posterior) did not show a significant association with the presence of peri-implantitis ($p = 0.076$). No statistically significant difference in terms of peri-implantitis rates was observed for the different implant surfaces ($p = 0.339$) and for the different biomaterials used for the ARP ($p = 0.337$).

Other significant associations with the primary outcome were found with extraction socket type III (OR = 31.67; CI [0.97;103.89]; $p = 0.043$) and soft tissue recession (OR = 34.90, [2.88;127.10]; $p = 0.005$). The implant-level variables and their association with peri-implantitis are reported in Table 2.

No statistically significant difference was found between healthy and mucositis groups for MBLC values (Table 3).

Figure 2 shows the relationship between age and MBLC, highlighting that this relationship is different depending on the history of periodontitis. In fact, it turned out that the interaction between age and history of periodontitis was statistically significant ($\beta = -0.096$ (95% CI −0.15; −0.03); p-value = 0.003), showing that in patients with a history of periodontal disease the more the age increases, the more the bone loss would be (Table 4). Regarding the oral hygiene recalls per year, no association was found with this parameter and the development of peri-implantitis ($p = 0.258$).

The multilevel multivariate regression model showed no significant difference of data clustering (likelihood-ratio test $p = 0.438$) (Table 4).

TABLE 2 Summary descriptive statistics for Implant-level variables expressed as median [q1 = first quartil, q3 = third quartil] and absolute frequency (*n*) and column percentage (%).

Implant level variables	Overall *n* = 61	Healthy *n* = 33	Mucositis *n* = 23	*p*-Value Mucositis vs. Healthy	Peri-implantitis *n* = 5	*p*-Value peri-implantitis vs. Healthy	OR [95%CI] Healthy vs. Mucositis	OR [95%CI] Healthy vs Peri-implantitis
PSR, *n* (%)								
3,4	30 (49.20)	13 (39.40)	14 (60.90)	0.190[+]	3 (60.00)	0.632[§]	Ref. 0.43 [0.14;1.27]	Ref. 0.45 [0.05;3.36]
0,1,2	31 (50.80)	20 (60.60)	9 (39.10)		2 (40.00)			
Soft tissue recession, *n* (%)								
No	55 (90.20)	32 (97.0)	21 (91.30)	0.562[§]	2 (40.00)	0.005[§]	Ref. 2.82 [0.22;92.40]	Ref. 34.9 [2.88;127.10]
Yes	6 (9.84)	1 (3.03)	2 (8.70)		3 (60.00)			
Tooth type								
CI (Cuspid, Incisor)	7 (11.50)	2 (6.10)	3 (13.00)	0.392[§]	2 (40.00)	0.076[§]	Ref. 0.45 [0.05;3.18]	Ref. 0.11 [0.01;1.34]
MP (Molar, Premolar)	54 (88.50)	31 (93.90)	20 (87.00)		3 (60.00)			
Reason for tooth Extraction, *n* (%)								
Caries	28 (46.70)	17 (53.10)	9 (39.10)	0.364[+]	2 (40.00)	0.078[+]	Ref. 4.34 [0.73;39.20]	Ref. 1.40 [0.05; 38.45]
Endodontic lesion	7 (11.70)	2 (6.25)	5 (21.70)		0 (0.00)		1.46 [0.39;5.41]	0.37 [0.02;8.49]
Fracture	16 (26.70)	9 (28.10)	7 (30.40)		0 (0.00)		0.97 [0.10;6.44]	6.38 [0.79; 51.78]
Periodontal	9 (15.00)	4 (12.50)	2 (8.70)		3 (60.00)			
Tooth Extraction, *n* (%)								
Complex	16 (26.20)	11 (33.30)	4 (17.40)	0.308[§]	1 (20.00)	0.308[§]	Ref. 2.30 [0.65;9.75]	Ref. 1.81 [0.22;53.70]
Simple	45 (73.80)	22 (66.70)	19 (82.60)		4 (80.00)			
Type of extraction socket, *n* (%)								
I	15 (24.60)	9 (27.30)	6 (26.10)	1.000[+]	0 (0.00)	0.043[+]	Ref. 1.04 [0.30;3.73]	Ref. 2.83 [0.13; 60.21]
II	42 (68.90)	23 (69.70)	16 (69.60)		3 (60.00)		1.46 [0.03;64.6]	31.67 [0.97;103.89]
III	4 (6.60)	1 (3.03)	1 (4.35)		2 (40.00)			
Implant position, *n* (%)								
Maxilla	36 (59.00)	17 (51.50)	4 (17.40)	0.035[§]	0 (0.00)	0.050[§]	Ref. 4.26 [1.25;17.8]	Ref. 10.88 [1.37; 86.39]
Mandible	25 (41.00)	16 (48.50)	19 (82.60)		5 (100.00)			
Implant position, *n* (%)								
Anterior	7 (11.50)	2 (6.10)	3 (13.00)	0.392[§]	2 (40.00)	0.076[§]	Ref. 0.45 [0.05;3.18]	Ref. 0.11 [0.01;1.34]
Posterior	54 (88.50)	31 (93.90)	20 (87.00)		3 (60.00)			
Insertion Torque (Ncm) *n* (%)								
≤35	29 (47.50)	15 (45.50)	11 (47.80)	1.000[+]	3 (60.00)	0.653[§]	Ref. 0.91 [0.31;2.70]	Ref. 0.58 [0.06;4.26]
>35	32 (52.50)	18 (54.50)	12 (52.20)		2 (40.00)			

(Continues)

TABLE 2 (Continued)

Implant level variables	Overall *n* = 61	Healthy *n* = 33	Mucositis *n* = 23	*p*-Value Mucositis vs. Healthy	Peri-implantitis *n* = 5	*p*-Value peri-implantitis vs. Healthy	OR [95%CI] Healthy vs. Mucositis	OR [95%CI] Healthy vs Peri-implantitis
Bone augmentation, *n* (%)								
No	52 (85.20)	28 (84.80)	19 (82.60)	1.000§	5 (100.00)	1.000§	Ref. 1.18 [0.25;5.23]	Ref. 0.47 [0.02;9.80]
Yes	9 (14.80)	5 (15.20)	4 (17.40)		0 (0.00)			
Soft tissue augmentation, *n* (%)								
No	56 (91.80)	31 (93.90)	20 (87.00)	0.392§	5 (100.00)	1.000§	Ref. 2.24 [0.31;20.7]	Ref. 1.15 [0.05; 27.23]
Yes	5 (8.20)	2 (6.10)	3 (13.00)		0 (0.00)			
Bone and soft tissue augmentation, *n* (%)								
No	57 (93.40)	31 (93.9)	21 (91.30)	1.000§	5 (100.00)	1.000§	Ref. 1.47 [0.14;15.0]	Ref. 1.15 [0.05; 27.23]
Yes	4 (6.56)	2 (6.10)	2 (8.70)		0 (0.00)			
Months from implant insertion at the last follow up, median [q1; q3]	103.00 [84.80;138.00]	98.00 [84.00;126.00]	132.00 [90.00;151.00]	0.053#	84.00 [83.00;103.00]	0.387#	Ref. 1.02 [1.00;1.03]	Ref. 0.98 [0.94;1.02]
Implant surface, *n* (%)								
B+, mono-molecular layer of multi phosphonates		4 (12.10)	2 (9.09)	0.123+	2 (40.00)	0.339§	Ref. 0.73 [0.11;6.92]	Ref. 0.23 [0.02;2.72]
Ossean surface, sand-blasted and Dual Etched		19 (57.60)	7 (31.80)		2 (40.00)			
Osteotite, sand-blasted and Dual-Etched		10 (30.30)	13 (59.10)		1 (20.00)		2.45 [0.37;23.00]	0.23 [0.01;3.62]
Biomaterial, *n* (%)								
Anorganic Bovine Bone		11 (33.30)	8 (34.80)	0.910+	3 (60.00)	0.337§	Ref. 0.94 [0.30;2.99]	Ref. 0.35 [0.04;2.62]
Cortico-Cancellous Porcine Bone		22 (66.70)	15 (65.20)		2 (40.00)			

Note: *p*-Value derived from Mann U Whitney test for continuous variable and Chi-squared test or Friedman exact test for categorical one. Indeed, the OR (Healthy vs. Peri-implantitis) was reported as a risk measure. § = Fisher exact test, + = Chi-Squared test, # = Mann U Whitney test.

TABLE 3 Marginal bone level (MBL) measurement expressed as mean (SD = standard deviation).

Variables	Overall *n* = 61	Healthy (a) *n* = 33	Mucositis (b) *n* = 23	Peri-Implantitis (c) *n* = 5	*p*
MBLC	−0.85 (1.34)	−0.37 (0.49)	−0.75 (0.91) [(c)]	−4.51 (1.26) [(a)(b)]	<0.001
Δ-mMBL	−0.80 (1.45)	−0.28 (0.45)	−0.66 (0.80) [(a)]	−4.92 (1.74) [(a)(b)]	<0.001
Δ-dMBL	−0.91 (1.37)	−0.47 (0.64)	−0.84 (1.28) [(c)]	−4.10 (1.22) [(a)]	<0.001

Note: *p*-Value results from the nonparametric test for independent samples. For analyzing the specific sample pairs for stochastic dominance, Dunn's test was used. To show the pairwise differences, we assigned a letter to each group: Healthy = (a); Mucositis = (b); Peri-implantitis = (c). Δ = absolute differences between follow-up and baseline. mMBL = Mesial MBL, dMBL = Distal MBL. MBLC = mean between Δ-mMBL and Δ-dMBL.

FIGURE 2 Moderation analysis considers the history of Peri-implantitis as a moderator between the relationship of age to MBLC. $\beta = -0.096$ (95%CI −0.15; −0.03) (SE = 0.030); *p*-value = 0.003).

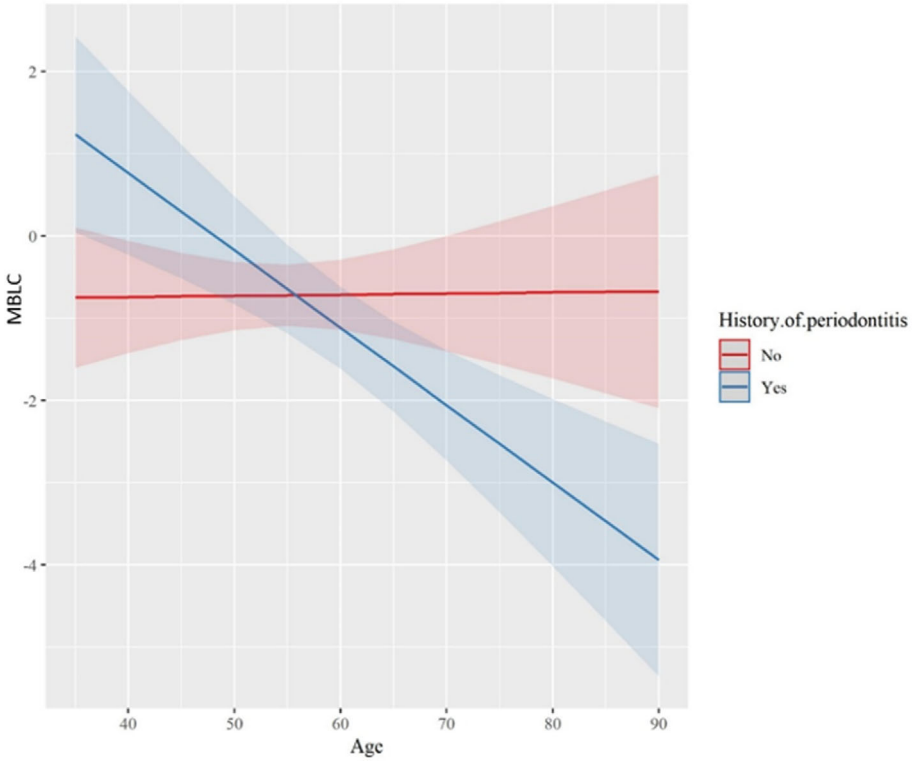

TABLE 4 Multivariate multilevel mixed-effects model.

Predictors	Estimates	95%CI	*p*	Estimates	95%CI	*p*
(Intercept)	−0.79	−1.15; −0.44	**<0.001**	−5.65	−10.57; −0.73	**0.025**
Age				0.09	0.01; 0.18	**0.036**
History of periodontitis				4.98	1.48; 8.47	**0.006**
Age × history of periodontitis				−0.09	−0.15; −0.03	**0.003**
Random effects						
Patients variance	1.22			0.89		
ICC	0.75			0.69		
AIC	199.66			202.95		
BIC	206.00			215.61		
Likelihood-ratio *p*-value = 0.438						

Note: The model considers the hierarchical structure of data with some patients receiving >1 implant. Statistically significant null and final models using the likelihood-ratio test.
Abbreviations: AIC, Akaike information criterion; BIC, Bayesian information criterion.

4 | DISCUSSION

The main purpose of this study was to evaluate the long-term prevalence of mucositis and peri-implantitis (Berglundh and co-workers[24]) among dental implants inserted in grafted alveolar sockets. Findings from the present study, which included only implants inserted in grafted sockets, showed that the prevalence of mucositis and peri-implantitis at the implant level was 37.7% and 8.2%, respectively. Some other authors,[31] who evaluated the prevalence of peri-implantitis for implants inserted in augmented maxillary sinuses, observed similar results with a prevalence of peri-implantitis of 9%. The main difference between our study and Stacchi's study[31] is that their study was focused on implants inserted after maxillary sinus augmentation while our study was focused on implants placed in grafted alveolar sockets. Indeed in their study, the authors[31] enrolled implants inserted in augmented sinuses with a residual ridge height of at least 3 mm, therefore, the implant platform was placed in the pristine bone, and the rest of the implant in the augmented bone, whilst in our study, the implant platform was placed at the level of augmented bone. This fundamental consideration suggests that augmented bone could be as stable as pristine bone, or even more stable, thus giving more value to our peri-implantitis rate of 8.2%.

The current epidemiological data regarding mucositis and peri-implantitis are limited by different diagnostic definitions[36] and local factors such as implant surface characteristics.[37]

Nevertheless, several systematic reviews and meta-analytical data suggested a mean mucositis rate of 29.48% and a mean peri-implantitis rate of 9.25%.[37,38]

A secondary goal of our analysis was to investigate any association between several clinical factors and peri-implantitis. Among all parameters, we found three significant associations.The first is that dental implants placed in mandibular grafted sockets were more likely to develop peri-implantitis compared to implants placed in maxillary grafted sockets.

This difference was also found in another study which included implants placed in augmented socket sites.[6]

The second association found in this study involved extraction socket type: implants placed in grafted type III sockets showed a higher risk of developing peri-implantitis compared to implants placed in grafted sockets type I and II.

The third association involves age and MBLC values: it turned out that if a patient had a history of periodontitis, the bone loss increased with increasing age. These findings agreed with other authors' conclusions,[6,31] pointing out that two possible risk factors for mucositis and peri-implantitis were history of periodontitis and increase of age.

To the best of our knowledge, the results of our study enrich the previous findings and shift the focus on age as a potential factor when associated with the history of periodontitis. This highlights how patients' features may influence the success of our treatment more than the type of tooth extraction or implant characteristics.

Moreover, no statistically significant difference in terms of peri-implantitis rates was observed for the different implant surfaces and biomaterials used for the ARP. Therefore, we could affirm that the implant surfaces and biomaterials used in this study, are effective in the long-term period to achieve stable implant-prosthetic rehabilitations.

However, this cross-sectional study has some limitations that should be acknowledged.

Firstly, the heterogeneity of the extraction socket types (24.6% type I, 68.9% type II, and 6.6% type III) and the small prevalence of implants in the anterior zone as respect to posterior sites (7 implants vs. 54 implants), could represent a limit for the association between peri-implantitis and extraction socket type/implant position, therefore our results should be interpreted with caution.

Moreover, the clinical diagnosis of health and mucositis conditions could be considered a second shortcoming; indeed, the discrepancy in health and mucositis rates between our study and other studies in the literature may be due to a lack of standardization in the diagnostic protocols. In this study, a critical issue was to standardize the probing force of the two examiners (NB and EM), with a possible impact on the diagnosis of mucositis as compared to peri-implant health.[39]

Furthermore, the definition of peri-implant health includes, among other parameters, the absence of profuse bleeding on probing. However, minor local bleeding may be caused by a traumatic probing force and should not be pathognomonic of mucositis in absence of other signs of inflammation.[40] The difference between minor and profuse bleeding is extremely subjective and can easily influence the diagnosis of mucositis, in accordance with what is reported by some other authors.[23]

Another shortcoming was the small number of peri-implantitis cases (5 implants in 3 patients) which reflects the high variability in ORs Confidence Interval 95%(CI); on one hand this shows the predictability of the treatment, on the other hand these numbers may not be very representative. Furthermore, the clinical evaluations were performed at variable time intervals since the last oral hygiene sessions, which may be a weak point of our study.

5 | CONCLUSIONS

In conclusion, within the limitations of this study, implants inserted in grafted sockets showed favorable rates of healthy implants in the long term. The resulting data on prevalence of mucositis and peri-implantitis at implant level did not differ from data in the literature. The ridge preservation procedures do not seem to increase the rate of mucositis or peri-implantitis.

However, due to the small sample size of our study, larger prospective studies should be conducted to better understand the local and systemic factors affecting peri-implant health.

AUTHOR CONTRIBUTIONS

All authors have made substantial contributions to conception and design of the study.

Barone Antonio and Tagger-Green Nirit were involved in patients' treatments.

Buonocunto Nino and Mijiritsky Eitan have been involved in data collection and patients' examination.

Porreca Annamaria and Di Nicola Marta performed the statistical analysis.

Cinquini Chiara has been involved in data interpretation and drafting the manuscript.

Iezzi Giovanna has revised critically the manuscript.

All authors have given final approval of the version to be published.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Research data are not shared.

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