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ORIGINAL ARTICLE

Factors influencing the prevalence of peri-implantitis in implants inserted in augmented maxillary sinuses: A multicenter cross-sectional study

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Abstract

Background: Peri-implantitis is widely recognized as a major cause of late implant failure, both in pristine and regenerated bone. The present study aims to evaluate the prevalence of peri-implantitis in implants inserted in augmented maxillary sinuses and to analyze possible risk factors.

Methods: A cross-sectional study was conducted in four centers including patients who underwent lateral or transcrestal sinus augmentation and received dental implants. Clinical and anamnestic data were collected using a standardized form. Univariate and multivariate logistic regression analyses have been performed for both implant-level and patient-level variables. Subsequently, a multilevel logistic mixed-effect model was built to analyze variables correlated with the occurrence of peri-implantitis.

Results: A total of 156 patients (61 males and 95 females; mean age: 60.9 ± 11.6 years) with 315 implants inserted into augmented maxillary sinuses with a follow-up ranging from 1 to 18 years were evaluated. Seven implants in seven patients were previously lost for peri-implantitis (2.2% and 4.5% at implant- and patient-level, respectively); 250 implants showed no signs of peri-implant diseases (79.4%), 34 implants presented mucositis (10.8%), and 24 implants exhibited peri-implantitis (7.6%). Corresponding data evaluated at patient-level were 125 (80.1%), 17 (10.9%), and 14 (9.0%), respectively. At the multilevel analysis, history of periodontitis, sinus elevation with lateral approach, and one-stage sinus floor elevation significantly correlated with the occurrence of peri-implantitis ($P < 0.001$).

Conclusions: History of periodontitis confirmed its well-known role as a risk factor for peri-implant pathologies. In addition, both lateral window technique and one-stage sinus floor elevation seemed to represent significant risk factors for peri-implantitis.

KEYWORDS
bone graft(s), implantology, maxillary sinus augmentation, osseointegration, peri-implantitis

1 | INTRODUCTION

The placement of implants in the edentulous posterior maxilla can be challenging due to the insufficient residual bone height which results from the combination of post-extractive alveolar remodeling and maxillary sinus pneumatization.[1,2] When favorable inter-maxillary relationships are maintained, sinus floor elevation may represent a safe and reliable option to increase available bone height to allow implant placement.[3,4] This surgical technique is based on the detachment and elevation of the Schneiderian membrane from the sinus floor and walls, creating a space to be filled with bone substitutes or blood clot to allow new bone formation. Sinus floor elevation with either lateral and transcrestal approach have been widely studied since their introduction,[5,6] showing excellent long-term clinical predictability[7,8] and limited occurrence of intra- and postoperative complications.[9,10] In presurgical planning, several factors have to be evaluated in the choice between lateral and transcrestal approach: among them, bucco-palatal sinus width should be considered as one of the critical parameters.[11] Five-year implant survival rate reported in recent meta-analyses for implants inserted in augmented sinuses was reported to be about 98% for lateral approach[12,13] and 94% for transcrestal techniques.[14]

Peri-implant pathologies represent the leading cause of late dental implant failure.[15] According to the current definition, peri-implantitis is a plaque-associated pathological condition occurring in tissues around dental implants, characterized by inflammation in the peri-implant mucosa and subsequent progressive loss of supporting bone.[16] There is strong evidence that the multifactorial etiology of this disease is related to history of periodontitis and low compliance to home oral care and regular preventive maintenance, even if peri-implant and periodontal microbiomes seem to represent microbiologically distinct ecosystems.[17,18] Other possible risk factors such as smoking, diabetes, occlusal overload, absence of keratinized mucosa, presence of excess cement, and biocorrosion have been extensively studied but their role is still to be determined.[18,19]

Insufficient information is present in literature to ascertain if there are differences in the pathophysiology and prevalence of peri-implantitis at implants placed in pristine bone or in augmented sites. A recent meta-analysis was unable to draw conclusions on this topic, as only low-quality studies with high heterogeneity concerning patient sampling and case definitions of biological complications could be included.[20]

Therefore, the aim of the present multicenter cross-sectional study was to evaluate the prevalence of peri-implantitis in implants inserted in augmented maxillary sinuses and to analyze the influence of possible risk factors.

2 | MATERIALS AND METHODS

2.1 | Study design

The present study was a multicenter cross-sectional investigation conducted in strict accordance with the recommendations of the Declaration of Helsinki, as revised in Fortaleza (2013), for investigations with human subjects.[21] This article was written in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.[22] The study protocol was approved by the relevant Ethical Committee (Comitato Etico di Ateneo, University of Trieste, nr. 71-06-2016).

2.2 | Patient sample

All patients previously treated with dental implants and presenting for oral hygiene recalls in four private clinics in Italy (CS, Gorizia, Italy; TL, Cassano allo Ionio, Italy; RS, Genova, Italy; SS, Milano, Italy) from March 2018 to July 2019 were evaluated for possible inclusion in the present study. Eligible patients were thoroughly informed of the study protocol and signed an informed consent form in which all procedures were detailed. Patients authorized the use of their data for research purposes.

2.3 | Inclusion and exclusion criteria

All patients (aged >18 years) treated with ≥1 dental implants inserted in augmented sinuses, in function for at least 1 year, were eligible for inclusion. Patients with insufficient crestal width (≤6 mm) at the time of implant placement and/or undergoing horizontal augmentation procedures were excluded from the present study. Patients with uncontrolled diabetes (HbA1c >7.5) or under present or past treatment with any medication that may have an effect on bone turnover and mucosal healing (e.g. steroids, antiresorptives, chemotherapy drugs) were excluded. Pregnant or breastfeeding women were also excluded. Patients with incomplete or unavailable medical and periodontal charts (including radiographs) were excluded. Patients with postoperative complications (i.e., infection, flap dehiscence) were excluded.

2.4 | Clinical evaluation

Clinical evaluation and medical records examination were performed by trained and experienced examiners (CS, TL, RS, SS), who participated to a calibration meeting before the start of the study, to standardize the assessment of study variables and data acquisition. Data were recorded in a specific case report form.

The following patient-level information was collected: age, sex, 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). Patients who, before implant therapy, presented at least three sites with periodontal probing depth ≥5 mm and had received non-surgical and surgical periodontal therapy and/or dental extractions for periodontal reasons were categorized as patients with history of periodontitis. Because of the lack of specific guidelines, parafunctions assessment was based on the presence of significant wear of teeth or restorations, considering indicators such as exposed dentin, well-defined wear facets, hypertrophic masticatory muscles, and fractures of teeth or restorations.[23]

The following implant-level information was collected: residual crestal height on sinus floor before augmentation (mm), sinus floor elevation technique (lateral/transcrestal), grafting material, timing of implant insertion, implant surface (minimally rough/moderately rough),[24] implant/abutment connection, crown material, type of prosthetic retention (cemented/screw retained), and time in function.

The following clinical peri-implant parameters were assessed by using a UNC-15 periodontal probe: probing depth (PD) at six sites per implant (deepest value was recorded); bleeding on probing (BOP) at six sites per implant (presence/absence); and suppuration (presence/absence).

2.5 | Radiographic examination

Periapical radiographs were taken using the long-cone paralleling technique with Rinn-type film holder when implants showed PD ≥ 4 mm and/or BOP with or without suppuration. Radiographs showing any sign of deformation, darkness, or other problems were immediately repeated. Baseline radiographs (taken after 1 year of prosthetic loading) were collected from medical charts for comparison.

Marginal bone levels were assessed using measuring software* by a single calibrated examiner (AR) on a 30-inch led-backlit color diagnostic display. Because of the lack of standardization of baseline radiographs, known implant dimensions were used as reference to set the scale for measurements. Each measurement was repeated three times at three different time points as described by Gomez-Roman and Launer.[25] Examiner calibration was performed by assessing ten radiographs, with a different author (CS) who served as reference examiner. Intra-examiner and inter-examiner intraclass correlation coefficients were 0.928 (95% CI, 0.907-0.956) and 0.886 (95% CI, 0.849 to 0.914), respectively.[26]

Marginal bone level was calculated on each radiograph as the linear measurement of the distance between the most coronal point of the implant platform and the most coronal bone-to-implant contact, corrected referring to the known length and diameter of each implant. Measurements were taken on both mesial and distal aspects of each implant. Marginal bone loss was defined as the difference between baseline and follow-up bone levels.

2.6 | Case definition

Criteria proposed by the Workgroup 4 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions[16] were used for the diagnosis of peri-implantitis: presence of bleeding and/or suppuration on gentle probing; increased probing depth compared with baseline examination; and presence of radiographic marginal bone loss ≥0.5 mm when compared with baseline radiograph.

2.7 | Statistical analysis

All the analyses have been performed with the software Stata 16.0.† Descriptive statistics have been reported as frequencies, means, and standard deviations. Univariate and multivariate logistic regression analysis have been performed to select both implant-level and patient-level factors associated with presence/absence of peri-implantitis. In addition, considering the hierarchical structure of data with some patients receiving ≥1 implant, a multilevel logistic mixed-effect model (*melogit* function in Stata software) was built adding variables significant at the aforementioned analysis. Evidence of significant clustering of data included in the cohort was tested analyzing residual independence by means of intraclass correlation coefficient (*estat icc* in Stata software). In addition, multilevel modeling was performed by adding level 1 and 2 variables to the null model and testing model performance by means of

* ImageJ 1.48a, National Institutes of Health, Bethesda, MD

† StataCorp, College Station, TX

likelihood-ratio test, Akiake information criterion (AIC), and Bayesian information criterion (BIC).

3 | RESULTS

3.1 | Clinical outcomes

A total of 243 patients with implants inserted into augmented maxillary sinuses were recalled and screened for inclusion in the four clinical centers. Eighty-seven patients were excluded: 68 had incomplete or unavailable medical and/or periodontal charts and/or baseline radiographs, four presented uncontrolled diabetes, 13 were under therapy with medications that may have an effect on bone turnover, and two patients refused to participate in this study. A total of 156 patients (61 males and 95 females; age range, 22 to 86 years; mean, 60.9 ± 11.6 years) with 315 implants inserted into augmented maxillary sinuses with a follow-up varying from 1 to 18 years were included in the present study. Mean follow-up period from sinus augmentation surgery and from prosthesis delivery were 67.65 ± 36.68 and 55.65 ± 34.79 months, respectively.

TABLE 1 Implant-level variables

Implant-level variables	n = 315 n	%
Surgical approach		
Lateral/Transcrestal	205/110	65.08/34.92
Grafting material		
Auto/Homo/Xeno/Syn	3/26/62/224	0.95/8.25/19.68/71.11
Implant Surface		
Min/Mod Rough	116/199	36.83/63.17
Implant-abutment connection		
Ext/Int/Con	98/153/64	31.11/48.57/20.32
Prosthetic retention		
Screwed/Cemented	117/198	37.14/68.62
Timing of implant placement		
Immediate/Delayed	236/79	74.92/25.08
Residual bone height		
≤3 mm / >3 mm	84/231	26.67/73.33
Implant Failure		
Yes/No	7/308	2.22/97.78
Status at last follow-up		
Healthy/Muc/Per	250/34/24	79.37/10.79/7.62

Auto, autologous; Con, conical connection; Ext, external hex; Homo, homologous; Int, internal hex; Min, minimally rough; Mod, moderately rough; Muc, mucositis; Per, peri-implantitis; Syn, synthetic; Xeno, xenograft.

TABLE 2 Patient-level variables

Patient-level variables	n = 156 n	%
Sex		
Male/Female	61/95	39.1/60.9
Smoking		
No/Yes	127/29	81.41/18.59
Compensated diabetes		
No/Yes	153/3	98.07/1.93
History of periodontitis		
No/Yes	123/33	78.84/21.16
Parafunctions		
No/Yes	150/6	96.15/3.85
Oral hygiene compliance		
<2 / ≥2 recalls per year	46/110	29.49/70.51
Age	60.86 ± 11.56	

Age is reported in years as mean ± SD.

Seven implants in seven included patients were lost for peri-implantitis before the beginning of the present study (2.2% and 4.5% at implant- and patient-level, respectively). At implant-level examination, 250 implants showed no signs of peri-implant diseases (79.4%), 34 implants presented mucositis (10.8%), and 24 implants exhibited peri-implantitis (7.6%). Corresponding data evaluated at patient-level were 125 (80.1%), 17 (10.9%), and 14 (9.0%), respectively. Implants diagnosed with peri-implantitis had a mean function time of 81.3 ± 27.1 months.

Descriptive statistics of implant- and patient-related characteristics are presented in Tables 1 and 2, respectively.

3.2 | Risk indicators for peri-implantitis

3.2.1 | Implant-level factors

Multivariate logistic regression showed that one-stage sinus elevation (odds ratio [OR] = 11.271; 95% CI, 2.39 to 53.18; $P = 0.002$), lateral window technique (OR = 10.207; 95% CI, 2.28 to 45.70; $P = 0.002$) and moderately rough implant surface (OR = 0.207; 95% CI, 0.57 to 0.75; $P = 0.016$) showed a significant association with peri-implantitis. ORs for each investigated implant-related risk factor are summarized in Table 3.

3.2.2 | Patient-level factors

Multivariate logistic regression showed that history of periodontitis (OR = 13.458; 95% CI, 2.99 to 60.46; $P = 0.001$) resulted significantly associated with peri-implantitis. ORs

TABLE 3 Univariate and multivariate logistic regression analyses at implant-level

Implant-level variables (n = 315)	Univariate analysis			Multivariate analysis		
Peri-implantitis	**OR**	**95% CI**	***P* value**	**OR**	**95% CI**	***P* value**
Surgical approach						
Transcrestal	1			1		
Lateral	6.750	1.56 to 29.27	0.011*	10.207	2.28 to 45.70	0.002*
Implant placement						
Delayed	1			1		
Immediate	4.091	0.94 to 17.81	0.060	11.271	2.39 to 53.18	0.002*
Residual bone						
≤3 mm	1			1		
>3 mm	0.794	0.32 to 1.99	0.624	0.717	0.25 to 2.50	0.532
Prosthetic retention						
Screwed	1			1		
Cemented	7.485	1.73 to 32.45	0.007*	1.141	0.13 to 9.82	0.908
Implant connection						
External hex	1			1		
Internal hex	0.944	0.32 to 2.74	0.916	1.749	0.53 to 5.77	0.359
Conical	2.647	0.89 to 7.86	0.080	2.425	0.83 to 21.40	0.202
Implant surface						
Minimally rough	1			1		
Moderately rough	0.662	0.28 to 1.53	0.336	0.207	0.57 to 0.75	0.016*

CI, confidence interval; OR, odds ratio.
*Statistically significant.

for each investigated patient-related risk factor are summarized in Table 4.

3.2.3 | Multilevel analysis

Multivariate multilevel logistic mixed-effects models (null model and final model) for diagnosis of peri-implantitis were applied. All the predictors were tested when building the model, whilst the final model comprised only predictors demonstrating a statistically significant influence on the study outcome. The analysis demonstrated that history of periodontitis (fixed-effects coefficient = 5.37; 95% CI, 3.22 to 7.51; P <0.001), one-stage sinus elevation (fixed-effects coefficient = 5.41; 95% CI, 2.95 to 7.88; P <0.001) and lateral window technique (fixed-effects coefficient = 4.41; 95% CI, 1.97 to 6.86; P <0.001) were significantly associated with peri-implantitis. Complete data of multilevel analysis are listed in Table 5.

The significance of data clustering in the cohort was analyzed by comparing the null model to the logistic regression, hence performing a likelihood-ratio test (P = 0.027) and analyzing intraclass correlation coefficient (ICC) with implants clustered in patients (ICC, 0.26; 95% CI, 0.15 to 0.42). In addition, final model performance was analyzed by means of AIC and BIC, resulting in a higher quality data fitting when compared with the null model (Table 5).

4 | DISCUSSION

To the best of our knowledge, the present cross-sectional study is the first to focus on the prevalence of peri-implantitis and the analysis of possible risk factors for implants placed in combination with maxillary sinus augmentation procedures. In the present study, criteria for diagnosis of peri-implantitis proposed by Workgroup 4 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions were adopted.[16] The prevalence of patients presenting peri-implant pathologies was 19.9% (in detail, 10.9% mucositis and 9% peri-implantitis) with a follow-up ranging from 1 to 18 years after prosthetic loading (mean follow-up, 4.6 years). Our findings are slightly higher in comparison with a recent prospective study analyzing implants placed in two-stage maxillary sinus augmentation, reporting 6.6% patient-level prevalence of peri-implantitis.[27] This discrepancy could be likely due to different sample features between the two studies (e.g., 100% two-stage sinus elevation versus 75% one-stage). However, a comparison between the outcomes of the present investigation and the

TABLE 4 Univariate and multivariate logistic regression analyses at patient-level

Patient-level variables (n = 156)	Univariate analysis			Multivariate analysis		
Peri-implantitis	**OR**	**95% CI**	***P* value**	**OR**	**95% CI**	***P* value**
Sex						
Female	1			1		
Male	1.010	0.31 to 3.21	0.989	0.739	0.17 to 3.23	0.689
Smoking						
No	1			1		
Yes	4.472	1.37 to 14.52	0.013*	3.335	0.81 to 13.76	0.096
Compensated diabetes						
No	1			1		
Yes	5.875	0.49 to 69.57	0.160	9.990	0.45 to 222.69	0.532
History of periodontitis						
No	1			1		
Yes	18.333	4.67 to 61.99	0.001*	13.458	2.99 to 60.46	0.001*
Parafunctions						
No	1			1		
Yes	6.318	1.04 to 38.41	0.045*	2.040	0.21 to 16.01	0.574
Oral hygiene compliance						
<2 recalls per year	1			1		
≥2 recalls per year	1.503	0.46 to 4.86	0.496	0.983	0.23 to 4.13	0.981
Age	1.029	0.97 to 1.08	0.296	1.011	0.94 to 1.08	0.770

CI, confidence interval; OR, odds ratio.
*Statistically significant.

TABLE 5 Multivariate multilevel logistic mixed-effects model

Multilevel logistic mixed-effects model	Null model		Final model		
Peri-implantitis	**Coefficient**	**Standard error**	**Coefficient**	**Standard error**	***P* value**
Fixed-effects					
Intercept	0.067	0.032	−12.53	2.29	
Surgical approach			4.41	1.24	< 0.001*
Timing of implant placement			5.41	1.26	< 0.001*
History of periodontitis			5.37	1.09	< 0.001*
Random-effects					
Patient variance	3.56	1.12	1.96	3.34	
Log likelihood	−84.13		−42.87		
Model performance					
AIC	172.26		93.75		
BIC	179.72		108.67		

Multivariate multilevel logistic mixed-effects model including both implant-level and patient-level features as independent variables and setting "diagnosis of peri-implantitis" as dependent variable. The model considers the hierarchical structure of data with some patients receiving >1 implant. AIC, Akaike information criterion; BIC, Bayesian information criterion.
*Statistically significant.

prevalence of peri-implantitis reported by other authors had a limited significance, due to the absence of consistent diagnostic criteria among studies. Koldsland, Scheie, and Aass reported substantial variations in the prevalence of peri-implantitis in the same group of patients (11.3% to 47.1%), when applying different case definitions.[28]

In the present investigation, implants diagnosed with peri-implantitis had a mean time in function of almost 7 years. This finding is in perfect accordance with previous studies suggesting that peri-implantitis presents a non-linear progression pattern and demonstrating a significant positive relationship between the

prevalence of peri-implantitis and implant function time.[29,30]

At patient-level, smoking, history of periodontitis, and presence of parafunctions resulted significantly associated with peri-implantitis in the univariate regression model. However, only the predictor "history of periodontitis" showed a significant correlation with peri-implantitis both in the univariate and the multivariate/multilevel logistic regressions (P <0.001). These findings are in accordance with numerous studies demonstrating the key role of the history of periodontitis as a risk factor for peri-implantitis, together with the still limited evidence supporting the negative effect of smoking and parafunctions on peri-implant health.[18,31–36]

Among all implant level variables, only "one-stage sinus elevation" and "lateral window technique" resulted strongly associated with peri-implantitis both in the univariate and the multivariate/multilevel logistic regressions (P <0.001). Early marginal bone loss has always been considered as a negative prognostic indicator for implant survival[37]; in particular, a recent study shows that if marginal bone loss exceeds 0.44 mm at 6 months post-loading, the risk of its progression seems to be significantly higher (33 times), with an increased risk of implant failure.[38] Previous studies demonstrated that marginal bone loss is higher around implants placed with a one-stage procedure in augmented sinuses than around implants placed in pristine maxillary bone.[39,40] Several surgical factors could determine impaired bone healing and marginal bone resorption after lateral sinus augmentation with simultaneous implant insertion. First, lateral sinus augmentation implies an extensive full thickness flap and a prolonged surgical time: these factors induce osteoclastic activity and may result in bone resorption.[41,42] Second, blood supply to alveolar bone crest in the posterior maxilla derives from the posterior superior alveolar artery, the greater and lesser palatine arteries, the ascending pharyngeal branch of the external carotid artery, and the ascending palatine branch of the facial artery.[43] The creation of a bony window on the lateral sinus wall may significantly compromise the vascularization of the underlying alveolar crest, possibly resulting in bone resorption. Third, undersized implant site preparation is necessary to achieve adequate primary stability in a limited vertical bone height when performing one-stage sinus augmentation. Excessive stress and compression of the cortical layer, especially in a bone with impaired vascularity, may lead to marginal bone resorption.[44,45] The combination of the three aforementioned factors could result in increased early marginal bone loss, possibly favoring the onset of peri-implant pathologies.

This multicenter cross-sectional investigation presents some limitations inherent to the type of study as well as to the characteristics of the included patients. The selected sample could be not representative of the entire population, limiting study generalizability. As data on each participant were recorded only once, it was not possible to infer the temporal association between possible risk factors and peri-implantitis. Moreover, timing of observation is not guaranteed to be representative. Due to the nature of the present study, it was not possible to collect and analyze detailed data regarding periodontal parameters (i.e., peri-implant phenotype at baseline; plaque and bleeding scores during the follow-up period). For the same reason, also prosthetic restoration characteristics potentially influencing peri-implant health (i.e., emergence angle, crown margins, cleansability) could not be standardized. Finally, possible heterogeneity in clinical practice among centers may be a major confounding factor in interpreting the results of the present study.

5 | CONCLUSION

Within the limitations of the present study, prevalence of peri-implantitis in implants inserted into augmented sinuses were 7.6% and 9.0% at implant and patient level, respectively. The most important risk indicators for peri-implantitis in this cohort of patients were history of periodontitis, one-stage sinus elevation and lateral window technique.

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AUTHOR CONTRIBUTIONS

All authors have made substantial contributions to conception and design of the study. Claudio Stacchi, Giuseppe Troiano, Antonio Rapani, Rosario Sentineri, Stefano Speroni, and Federico Berton have been involved in data collection and data analysis. Claudio Stacchi, Giuseppe Troiano, Antonio Rapani have been involved in data interpretation and drafting the manuscript. Teresa Lombardi and Roberto Di Lenarda revised it critically. All authors have given final approval of the version to be published.

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