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Peri-implantitis and maxillary sinus membrane thickening: A retrospective cohort study

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Abstract

Objective: The objective of this study is to investigate the association of peri-implantitis (PI) and sinus membrane thickening and to assess the resolution of membrane thickening following intervention (implant removal or peri-implantitis treatment) aimed at arresting PI.

Materials and Methods: Forty-five patients with 61 implants in the posterior maxillary region were retrospectively included in the study. Twenty-four patients were diagnosed with peri-implantitis (PI) and 21 had peri-implant health (PH). Cone-beam computed tomography (CBCT) scans were evaluated to assess maxillary sinus characteristics, including membrane thickening, sinus occupancy and ostium patency. The CBCT scans taken 6 months after intervention aimed at arresting disease (implant removal or treatment of PI) in the PI group were also appraised and compared to baseline scans.

Results: At baseline, all parameters evaluating membrane thickness disorders yielded significant differences between groups ($p < .001$). Patients with posterior maxillary implants diagnosed with PI were 7× more likely to present membrane thickening compatible with pathology when compared to patients with healthy implants (OR = 7.14; $p = .005$). Furthermore, the likelihood was 6x greater in implants diagnosed with PI to exhibit moderate membrane thickening (OR = 6.75, $p = .001$). The patients receiving interventions aimed at arresting PI experienced significant enhancement in all radiographic parameters related to the sinus cavity at the 6-month follow-up ($p < .001$), though these variations were similarly independent of whether treatment consisted of PI treatment or implant removal.

Conclusions: Maxillary sinus membrane thickening and the permeability/obstruction of the ostium are frequently associated with the presence of PI in posterior implants. Interventions targeting disease resolution effectively reduce membrane thickness to levels compatible with maxillary sinus health.

KEYWORDS
dental implants, diagnostic imaging, maxillary sinusitis, membrane thickening, peri-implantitis

1 | INTRODUCTION

Implants placed with the maxillary sinus floor elevation procedure have shown high survival rates (Uckan et al., 2011). However, different implant-related complications can occur both early and late after the procedure (Pignataro et al., 2008). In fact, maxillary sinusitis attributable to dental implants has been documented in 0%–20% of all patients (Kim et al., 2013). Furthermore, most of the literature on dental implant-associated maxillary sinusitis attributes it to immediate complications that occur during implant placement simultaneous to sinus lift.

In relation to these complications, sinus mucosal perforation is the most frequent intraoperative complication. Such perforation may result in displacement of the bone graft material, plugging of the ostium, migration of the implant into the sinus, and/or thickening of the sinus mucosa (Galindo et al., 2005; Hunter 4th et al., 2009; Timmenga et al., 2003). Surgical trauma in sinus floor elevation may adversely affect mucociliary clearance and the patency of the maxillary ostium (Timmenga et al., 2003). This can lead to immediate complications and may cause acute maxillary sinusitis.

The diagnosis of maxillary sinusitis is based on clinical, radiological and nasal endoscopic findings (Bell et al., 2011). Regarding the radiological findings, a sinus membrane or Schneider's membrane measuring greater than 2 mm in thickness indicates inflammation of the maxillary sinus (Maillet et al., 2011). In line with this, recent studies (Heilingoetter et al., 2018; Lim et al., 2017; Rey-Martínez et al., 2022) have underscored the pathological thickening of the maxillary sinus membrane as a key area of exploration within the field. A comprehensive understanding of its origins, whether influenced by systemic or local factors, is essential for devising effective diagnosis and treatment strategies. In the realm of systemic factors, numerous studies have conducted thorough investigations into bacterial, viral, and fungal infections (Osur, 2002; Raz et al., 2015; van Cauwenberge & Ingels, 1996), alongside allergic responses to particular airborne allergens (Bertrand et al., 1997; Dykewicz & Hamilos, 2010), the existence of nasal polyps, anatomical factors like septum deviation (Jorissen et al., 1997; Taghiloo & Halimi, 2019), immune system disorders, and environmental components such as tobacco and pollution (Hopkins et al., 2018; Lieu & Feinstein, 2000). Concerning local factors, different studies have reported sinus membrane thickening of dental origin associated with periodontal disease and periapical lesions (Lu et al., 2012; Phothikhun et al., 2012). Alike, peri-implantitis represents a biofilm-mediated chronic inflammatory condition (Schwarz et al., 2018). Therefore, it is hypothesized that peri-implantitis microorganisms can spread to the sinus mucosal membrane via the cancellous bone, blood vessels and lymphatic vessels similar to the pathway that follow periapical infections to the sinus mucosa. However, scientific evidence on the influence of peri-implantitis on Schneider's membrane thickening is scarce. In light of the extensive background outlined, the following hypothesis was formulated. The presence of implants associated with the maxillary sinus region, affected by peri-implantitis, might elevate the likelihood of identifying pathological sinus membrane thickening.

Likewise, current evidence regarding the potential decrease in maxillary sinus inflammation, leading to Schneider's membrane thinning subsequent to resolving peri-implantitis through treatment or implant removal, remains scarce and primarily confined to a case series (Park et al., 2019). The present retrospective cohort study was thus carried out to investigate the association between peri-implantitis and sinus membrane thickening in implants placed in the posterior maxillary region and the effect of disease resolution on membrane thinning.

2 | MATERIALS AND METHODS

A retrospective cohort study was carried out. The study complied with the principles of the Declaration of Helsinki and was approved by the Ethics Committee of the Universitat Internacional de Catalunya (Barcelona, Spain) (Reference: PER-ECL-2023-02). Each patient was informed about the details of the study and signed an informed consent form before data extraction was performed. The study was registered and approved by www.clinicaltrials. gov (NCT05924711). The study is reported in accordance with the STROBE statement.

2.1 | Study sample

Partially/fully edentulous patients who previously had implants placed in the posterior region of the maxilla for oral rehabilitation were eligible. Patient selection was based on historical clinical records, which eliminated the need to recall individuals for additional radiographic examinations. An a priori sample size was calculated based on a study published elsewhere (Ren et al., 2015) that reported the presence of mucosal thickness exceeding 2 mm in 88% of patients with severe periodontal bone loss and in 30% of patients with moderate bone loss. Consequently, it was determined that a difference of 58% following intervention would yield significance. Given an alpha error rate of .05 and a statistical power of 90%, a sample size of 24 patients diagnosed with peri-implantitis was deemed necessary.

The following inclusion criteria were applied: patients aged between 18 and 80 years, with at least one implant in the posterior maxilla that had been in function for more than 5 years, and the availability of a cone-beam computed tomography (CBCT) scan performed for implant assessment or for other reasons. Furthermore, those patients with a diagnosis of peri-implantitis (PI) were required to have a second CBCT scan performed 6 ± 2 months after intervention was carried out. The exclusion criteria were: patients displaying evidence of disease in the opposing sinus as identified through CBCT evaluation, pregnancy or lactation, uncontrolled systemic medical conditions, patients with zygomatic or pterygoid implants, and patients taking medications known to modify bone metabolism or presenting degenerative bone disease (hyperparathyroidism, osteoporosis), as well as those patients who had taken antibiotics, nonsteroidal antiinflammatory drugs or corticosteroids for more than 2 weeks in the 3 months prior to both examinations.

2.2 | Case definition of peri-implantitis

Peri-implantitis (PI) was defined according to the 2017 World Workshop of Periodontal and Peri-implant Diseases (Berglundh et al., 2018). The case definition applied was therefore as follows:

- Presence of bleeding and/or suppuration on gentle probing.
- Probing depth ≥ 6 mm.
- Bone level ≥ 3 mm apical to the most coronal portion of the implant or at the rough-smooth interface in tissue-level implants.

If the examiner deemed access unsuitable, the prosthesis was retrieved for accurate diagnosis.

2.3 | Radiographic assessment

Cone-beam computed tomography scans were performed by an experienced radiologist (V.C.). Images of the included patients were obtained with the CBCT-ICAT Model 17–19 (Imaging Sciences International LLC, Hatfield, PA, USA). The settings were 16 × 13 mm in width and depth, 120 kVp, 20.27 mAs, scan time 14.7 s, resolution at 0.25 voxels and field of view varying according to the region scanned (axially from the superior wall of the frontal sinuses to the maxillary dental arch and coronally from the anterior wall of the maxillary sinus to the posterior wall of the sphenoid sinus). Radiographic evaluation included analysis of implants, peri-implant defects and maxillary sinuses/sinus membranes.

2.4 | Radiographic evaluation of the implants

A previously calibrated examiner (R.P.) analyzed each of the implants included in the study using coDiagnostiX software (Implant planning Software, Dental Wings GmbH, Chemnitz, Germany). The following parameters were assessed:

- Radiographic peri-implant bone loss: assessed at four sites per implant (mesial, distal, buccal and palatal) in mm and defined as the distance from the implant platform to the first bone-to-implant contact (Figure 1).

These radiographic measurements were repeated again in the PI group after PI was treated. The time interval between intervention and re-evaluation was ~6 months.

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2.5 | Maxillary sinus assessment

In cases of Schneiderian membrane inflammation around teeth and implants, especially in scenarios of irritation or chronic infection, a thorough assessment extending beyond linear measurements, such as a 2 mm thickness, is essential. A previously calibrated examiner (M.G.) analyzed each maxillary sinus using Dolphin 3D Images software following the methodology outlined in the work of Kim et al., 2018, which stressed the importance of evaluating surface area and volume changes of the Schneiderian membrane to accurately diagnose and manage inflammatory conditions associated with dental implants and periapical lesions. Thus, an increased thickness of the membrane was considered when the sinus membrane or Schneider's membrane was thicker than 2 mm (García-Denche et al., 2013). The following parameters were assessed (Figure 2):

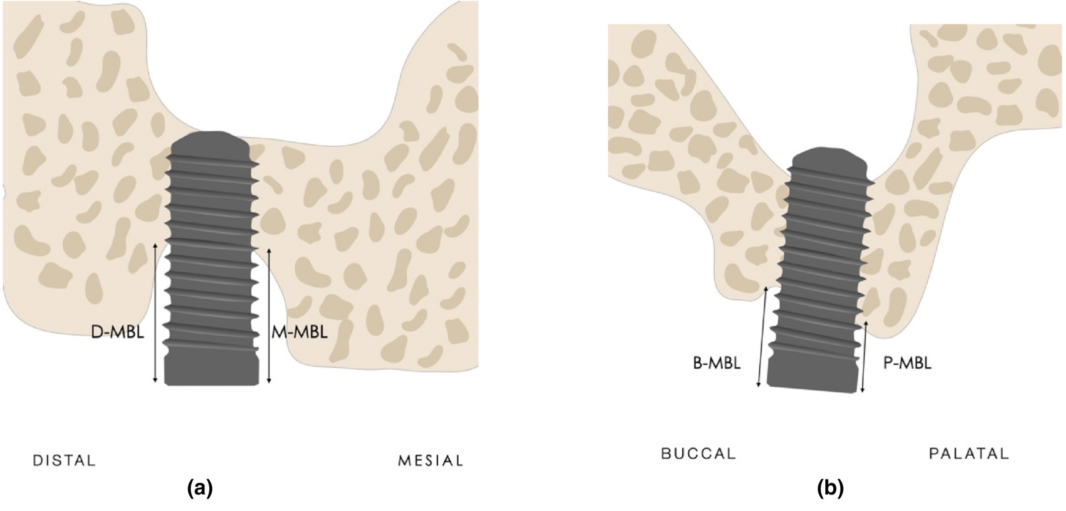

FIGURE 1 Radiographic peri-implant bone loss: assessed at four sites per implant (a) mesial (M-MBL) and distal (D-MBL) and (b) buccal (B-MBL) and palatal (P-MBL), and defined as the distance from the implant platform to the first bone-to-implant contact.

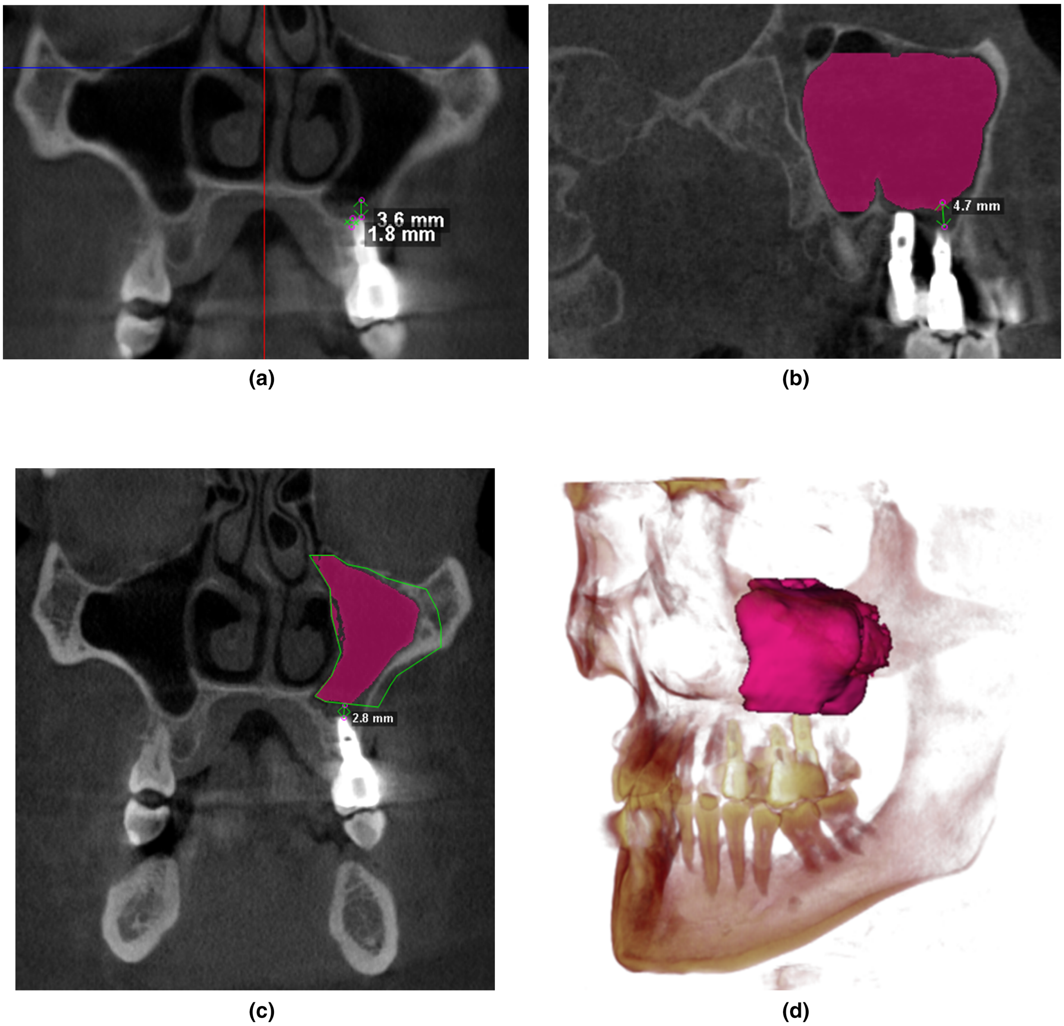

FIGURE 2 Radiographic evaluation of the maxillary sinus; (a) proximity of the implant to the maxillary sinus; (b) sinus membrane thickening (sagittal); (c) sinus membrane thickening (coronally); and (d) volume of the maxillary sinus occupied by the sinus membrane.

- Distance from the apex of the implant to the maxillary sinus floor: distance (mm) from the apical portion of the maxillary sinus cortical floor to the apex of the implant following the longitudinal axis of the implant.
- Sinus membrane thickening (sagittal): distance (mm) from the cortical bone of the sinus floor to the upper margin of the sinus mucosa at the point of greatest thickening.
- Sinus membrane thickening (coronal): distance (mm) from the cortical bone of the sinus floor to the upper margin of the sinus mucosa at the point of greatest thickening.
- Maxillary sinus membrane volume: the total volume of the sinus membrane (in mm^3 and %) in relation to the total volume of the maxillary sinus.

These radiographic measurements were repeated again in the PI group after PI was treated. The time interval between intervention and re-evaluation was ~6 months.

In addition, the following information was obtained for each scan in the assessment of the:

- Degree of membrane thickening: 0 (clear sinus), 1 (mild membrane thickening or 2–5 mm) and 2 (moderate membrane thickening or 5–10 mm) (Rapani et al., 2016).
- Sinus ostium patency: 0 (patent ostium) or 1 (obstructed ostium).
- Implant-to-sinus ratio: 0 (distance between the implant apex and sinus with the presence of cancellous bone and cortical bone between implant and sinus), 1 (the implant contacts the sinus cortical bone) and 2 (the implant is partially inserted into the sinus).

2.6 | Standardization and calibration of radiographic measurements

To prevent measurement errors across different CBCT recordings at each time point, emphasis was placed on implementing the 3D voxel-based superimposition protocol before conducting measurements throughout the study. The software orientation calibration tool was used along pitch (*x*), yaw (*y*), and roll (*z*). Each patient had 2

CBCT data sets (T0 and T1) that were superimposed in accordance with the voxel-based superimposition protocol described by Haas Junior et al. (2019) and Hernández-Alfaro et al. (2021). Data were primarily saved in DICOM (Digital Imaging and Communications in Medicine) format using a 3D software (version 11.0; Dolphin Imaging, Chatsworth, CA). Orientation of both the base volume (original DICOM) and second volume (duplicate DICOM) was undertaken to achieve the same original positions of the CBCTs. Then, superimposition of the preoperative CBCTs (T0) and T1 was performed using the cranial base, as it remains stable. The software allowed a proper manual adjustment following the superimposition 3-step protocol: (1) landmark-based superimposition (side-by-side super- imposition), (2) voxel-based superimposition (overlay superimposition by volume subregions), and (3) head orientation export (export to second volume). This indicated that both images (T0 and T1) were aligned in the same coordinate position following voxel-based superimposition. Then, landmarks were placed at the same anatomical places at both pre- and post op scans, meanwhile the CBCTs were superimposed. Both linear and volumetric measurements were conducted after the superimposition at step 3 (sagittal slice), where the software enables the measurement of both CBCT scans, simultaneously to mitigate biases in editing. This enhanced the comprehensibility of the methodology and ensured transparency in the measurement process.

To ensure truly accurate and reproducible measurements and to avoid landmark errors produced by magnification and distortion, both examiners (M.G. and R.P.) were previously calibrated and tagged all virtual models independently on two separate occasions (2 weeks apart), thus avoiding inter and intra-observer differences, respectively. Inter- and Intra-class correlation coefficient analyses (ICC) were used to calculate examiner differences and reliability. Calibration and ICC analyses followed (Lagravère et al., 2010; Zhu et al., 2018) previous studies, and the measurements (landmarks) (3D measurements at a 3D software) were taken in the three axes (*x*, *y*, *z*). The ICC obtained by the authors for the measurement variability was <0.01 mm.

- The intra-examiner ICC obtained for measured displacements was ICC = 0.97–0.99 for all the examiners and 0.97 for the inter-examiner ICC, respectively.
- Thus, the ICC results obtained were in line with those previously accepted by the literature. Although CBCT landmarks were statistically reliable, the authors remained aware in identifying potential errors in identification or measurement for each landmark.

2.7 | Statistical analysis

Descriptive statistical analyses were made for both quantitative (mean and standard deviation [SD]) and qualitative variables (absolute and relative frequencies). The chi-squared test, Fisher's exact test and two-sample *t*-test were, respectively, used to explore the homogeneity of the groups (PI/PH) at the patient level.

Inferential analysis involved estimation using generalized estimating equations (GEE) of multilevel logistic regression models. Calculations were performed to assess associations between any variable used in the diagnosis of sinusitis (e.g., membrane thickness, percentage sinus occupancy) with respect to each of the groups (PI/PH), acting as an independent factor in the model. The 95% confidence interval (95%CI) for the coefficients was obtained from the Wald Chi2 statistic.

Additionally, an ordinal regression model with generalized estimating equations (GEE) was employed, wherein the dependent variable comprised the ordinal variable representing the degree of membrane thickening, and the independent variable consisted of the group (PI/PH). Estimates of OR and 95% CI were derived, and the model's validity was assessed through the parallel lines test.

Lastly, a Brunner Langer non-parametric model for correlated data was used to assess the impact of the intervention to resolve PI upon the different parameters and variables characteristic of sinusitis. The statistical packages SPSS version 15.0 (SPSS Inc., Chicago, IL, USA), STATISTICS version 7.1 (StatSoft, Inc., USA) and R 2.14.0 were used for data analysis.

3 | RESULTS

3.1 | Demographics

Of the 54 consecutive patients (72 implants) initially screened, 45 (61 implants) were found to be eligible for the study. The main reasons for exclusion were illegible radiographic images, failures in the DICOM files or artifacts that prevented correct visualization of the implants or the maxillary sinus.

The two groups were balanced in terms of age (average age was 64.4 years in PH group vs. 66.9 in PI group), sex (28.6% of men in PH group vs. 33.3% in PI group) and ethnicity (all study participants were Caucasian), according to the independent *t*-test and the w2 test. Twenty-four patients (53.3%) were diagnosed with peri-implantitis (PI group) and 21 (45.7%) presented peri-implant health (PH group). The final sample comprised 31 females (68.9%) and 14 males (31.1%), with a mean age of 65.7 ± 8.4 years. Each patient contributed with one or two implants associated with the sinus region, for a total of 61 implants (37 in the PI group and 24 in the PH group). All patients in the PI group had a history of periodontal disease, versus only 76.2% of the PH group. In turn, 83.3% of the subjects in the PI group had stage III–IV periodontitis, versus 62.6% of the PH group (16 out of 21). The demographic characteristics of the two study groups are summarized in Table 1.

A total of 24 (39.3%) of the 61 implants included in the study were diagnosed as healthy, while 37 (60.7%) were diagnosed PI. Their position in the arch was mainly in the region of the first molars (45.9%), followed by the second premolars (26.2%). The mean bone loss of the implants studied was 3.78 ± 2.03 mm. The differences between groups were statistically significant ($p < .001$); the PI group showed a mean bone loss of 5.05 ± 1.60 versus 1.84 ± 0.54 mm in the PH group.

TABLE 1 Demographic data of the included patients and implants, distributed according to study group (PH group or PI group).

General characteristics of the study population, *N* = 45	Overall	PH group (*N* = 21)	PI Group (*N* = 24)
Gender, *N* (%)			
Male	14 (31.1)	6 (28.6)	8 (33.3)
Female	31 (68.9)	15 (71.4)	16 (66.7)
Age (years), mean (SD)	66.7 (8.4)	64.4 (8.9)	66.9 (7.9)
History of periodontal disease, N (%)			
Absence	5 (11.1)	5 (23.8)	0 (0.0)
Presence	40 (88.9)	16 (76.2)	24 (100.0)
Periodontitis Stage, *N* (%)			
Stage 2	10 (25.0)	6 (37.5)	4 (16.7)
Stage 3	13 (32.5)	5 (31.3)	8 (33.3)
Stage 4	17 (42.5)	5 (31.3)	12 (50.0)
Periodontitis Grade, *N* (%)			
Grade A	10 (25.0)	3 (18.8)	7 (29.2)
Grade B	14 (35.0)	7 (43.8)	7 (29.2)
Grade C	16 (40.0)	6 (37.5)	10 (41.7)
Number of implants, *N* (%)			
1 implant related to sinus	29 (64.4)	18 (85.7)	11 (45.8)
2 implants related to sinus	16 (35.6)	3 (14.3)	13 (54.2)
General characteristics of the implants, *N* = 61	**Overall**	**PH Group (*N* = 24)**	**PI Group (*N* = 37)**
Implant position, *N* (%)			
Premolar	23 (37.7)	7 (29.2)	16 (43.2)
Molar	38 (62.3)	17 (70.8)	21 (56.8)
Marginal Bone loss (mm) mean (SD)			
MBL at T0	3.7 (2.0)	1.8 (0.5)	5.0 (1.6)
MBL at T1	3.4 (1.6)	–	3.4 (1.6)
Differences MBL T1 – T0	−1.0 (1.4)	–	−1.0 (1.4)

Note: Periodontitis stage and grade according to Papapanou et al. (2018).

Abbreviations: MBL, marginal bone loss; PH Group, group with peri-implant health; PI Group, group with peri-implantitis; SD, standard deviation.

With regard to peri-implant defect morphology, the most frequently identified defects were type II (51.4%) and IIIc defects (18.9%) (Monje et al., 2019). In relation to peri-implant defect severity, 59.5% of the implants in the PI group were classified as advanced (>6 mm or >50% of the implant length), 24.3% as moderate (4–5 mm or ≥25%–50% of the implant length) and 16.2% as slight (3–4 mm or <25% of the implant length). The treatment was provided according to the configuration of the defect (resective, reconstructive or combined) in 75.7% of the implants, while 24.3% of the implants had to be removed due to advanced severity.

3.2 | Association between peri-implantitis and maxillary sinus membrane thickness

Sinus membrane thickness differed significantly between the groups at both sagittal ($p = .001$) and coronal levels ($p = .001$). In this regard, the mean sagittal and coronal membrane thickness values were 4.93 ± 6.95 and 4.58 ± 6.36 mm, respectively, in the PH group, and increased to 13.84 ± 9.00 and 11.04 ± 7.28 mm in the PI group. On evaluating sinus membrane thickening three-dimensionally and thus in terms of percentage sinus occupancy instead of linear measurements, the results obtained proved similar, with sinus occupancy in the PI group (44.7 ± 31.8%) being significantly greater than in the PH group (12.9 ± 14.1%) ($p = .001$) (Figure 3). In this sense, other potential factors such as age, implant molar position, and sinus-to-implant distance were analyzed in relation to the percentage of sinus occupancy. Only age demonstrated a correlation with the occupied volume ($p = .047$). With each additional year of age, the percentage of occupied sinus increased by 1.09%. Nonetheless, upon adjusting the analysis for potential confounding variables, the percentage of sinus occupancy remained significant in the PI group ($p < .001$), while the influence of age weakened ($p = .065$). Table 2 depicts the data on the association between PI and maxillary sinus membrane thickness.

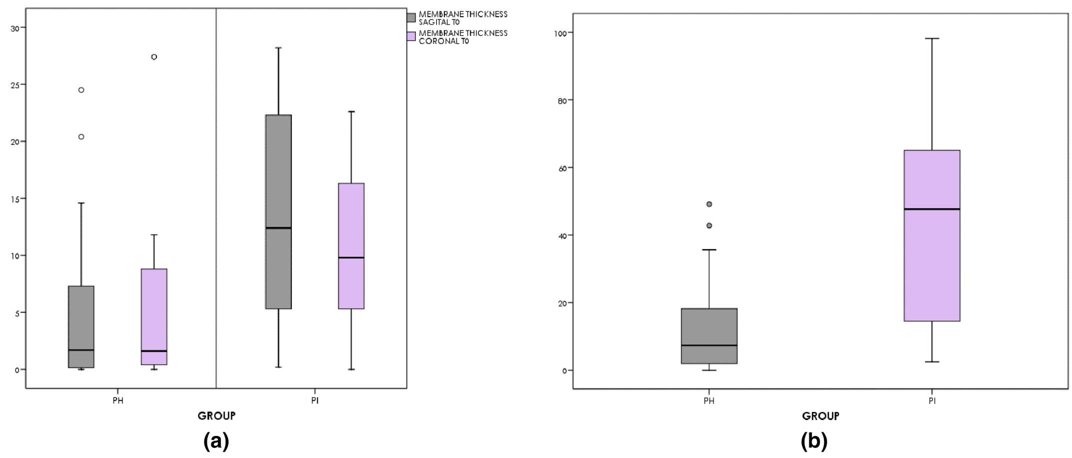

FIGURE 3 Boxplots representing the differences between both groups (PH group and PI group) at baseline in terms of (a) sagittal and coronal sinus membrane thickening and (b) sinus occupancy percentage.

The degree of membrane thickening and patency of the ostium were also evaluated. In this regard, patients with implants exhibiting PI had a 6-fold higher likelihood of exhibiting moderate membrane thickening (OR = 6.75; $p = .001$) than patients with healthy implants. In the assessment of the maxillary sinus, patency of the ostium was classified as a patent or an obstructed ostium. In this case, no statistically significant differences were observed between the groups ($p = 0.232$). Sinus obstruction was encountered in 27% of the implants in the PI group, versus in 21.3% of the implants in the PH group.

The proximity of the implant to the floor of the maxillary sinus was also considered. Implants were classified as being positioned away from, close to, or partially inserted inside the sinus. In this context, the GEE analysis revealed that the distance of the implant to the floor of the sinus had no impact on the degree of membrane thickening ($p = .169$). Nevertheless, it was noted that implants in close proximity to and especially those partially inserted into the sinus were twice as likely (OR = 2.12) to exhibit PI compared to those situated farther away. While statistical significance was not attained ($p = .130$), a discernible trend was observed.

Considering all available criteria used for the diagnosis of pathological maxillary membrane thickening, it was seen that 81.1% of the implants with PI were associated with pathological membrane thickening, while only 37.5% of the implants that were healthy were associated with such thickening. In this sense, the GEE analysis showed that patients with implants in the maxillary region presenting PIs were 7x more likely to have an increased thickness of the sinus membrane compared with PH (OR = 7.14; $p = .005$).

3.3 | Association between peri-implantitis treatment and reduction of membrane thickness

The reduction of membrane thickness after the intervention provided was statistically significant at both sagittal ($p < .001$) and coronal levels ($p < .001$). In this sense, 81.1% of the implants with PI demonstrated membrane thickening in the initial CBCT scans, and this figure dropped to 29.7% as determined 6 months after intervention. In other words, 70.3% of the implants treated for PIs did not show membrane thickening consistent with maxillary sinus disease after intervention (Figure 4). Interestingly, these values resembled those observed at baseline in the PH group, which showed membrane thickening associated with 37.5% of the implants. On differentiating between the two interventions, PI treatment was noted to reduce membrane thickness from 88.9% to 33.3%, while the reduction was from 78.6% to 28.6% in the case of implant removal. The decrease in membrane thickness was significant with both interventions ($p < .001$). Furthermore, it was of equal magnitude at both coronal ($p = .940$) and sagittal levels ($p = .971$). Such reduction in membrane thickness could also be evidenced three-dimensionally based on percentage sinus occupancy. Accordingly, the mean reduction of total sinus occupancy in the PI group decreased from 44.7% to 8.0%, showing a statistically significant mean reduction of 36.6% ($p < .001$); again, there were no differences between the therapeutic approaches ($p = .658$) (Figure 4).

Sinus obstruction was identified in 27% of the patients in the PI group. After intervention delivery, total patency was achieved in all patients (100%). Therefore, the achievement of patency was statistically confirmed ($p = .002$) and could be achieved to a similar extent with both therapeutic options (surgery or implant removal) ($p = .656$).

Lastly, membrane thickening present at baseline was also significantly reduced. At baseline, 91.8% of the implants with peri-implantitis had mild or moderate membrane thickening—being moderate in half of the cases—while only 8.1% had no thickening. After intervention delivery, the percentage of implants with membrane thickening was reduced to 27%, being moderate in only 5.4% of the cases. In relation to the intervention provided, only 33.3% of the maxillary sinuses of patients subjected to implant removal showed membrane thickening, versus 25% of those subjected to PI treatment.

TABLE 2 Description of maxillary sinus parameters at baseline (T0) and 6 months (T1), expressed in mm and %.

Maxillary sinus parameters	Overall (N = 61)	PH group (N = 24)	PI Group (N = 37)	p Value
Sinus membrane thickening (sagittal) in mm (Mean + SD)				
Membrane thickness (T0)	10.3 ± 9.2	4.9 ± 6.9	13.8 ± 9.0	<.001***
Membrane thickness (T1)	3.0 ± 3.5	–	3.0 ± 3.5	
Membrane thickness (Dif. T0 – T1)	−10.7 ± 8.53	–	−10.7 ± 8.53	<.001***
Sinus membrane thickening (coronal) in mm (Mean + SD)				
Membrane thickness (T0)	8.5 ± 7.5	4.5 ± 6.3	11.0 ± 7.2	<.001***
Membrane thickness (T1)	3.0 ± 3.8	–	3.0 ± 3.8	
Membrane thickness (Dif. T0 – T1)	−8.0 ± 6.8	–	−8.0 ± 6.8	<.001***
Maxillary sinus occupancy (%) (Mean + SD)				
Sinus occupancy (T0)	32.1 ± 30.4	12.0 ± 14.0	44.7 ± 31.8	<.001***
Sinus occupancy (T1)	8.0 ± 11.3	–	8.0 ± 11.3	
Sinus occupancy (Dif. T0 – T1)	−36.6 ± 29.9	–	−36.6 ± 29.9	<.001***
Sinus ostium patency (N/%)				
Sinus ostium patency (T0)				
Patent ostium	48 (71.7)	21 (87.5)	27 (73.0)	.232
Obstructed ostium	13 (21.3)	3 (12.5)	10 (27.0)	
Sinus ostium patency (T1)				
Patent ostium	37 (100)	–	37 (100)	.002**
Obstructed ostium	0.0 (0.0)	–	0.0 (0.0)	
Degree of membrane thickening (N/%)				
Degree of membrane thickening (T0)				
No	13 (21.3)	10 (41.7)	3 (8.1)	
Mild	24 (39.3)	10 (41.7)	14 (37.8)	.112
Moderate	24 (39.3)	4 (16.7)	20 (54.1)	.006**
Degree of membrane thickening (T1)				
No	27 (73.0)	–	27 (73.0)	
Mild	8 (21.6)	–	8 (21.6)	<.001***
Moderate	2 (5.4)	–	2 (5.4)	<.001***

Abbreviations: PH Group, group with peri-implant health; PI Group, group with peri-implantitis; SD, standard deviation.
*$p < .05$; **$p < .01$; ***$p < .001$.

4 | DISCUSSION

4.1 | Principal findings

The present retrospective CBCT study highlights the possible association between PI in implants close to the maxillary sinus and pathological thickening (>2 mm) of the sinus membrane. In fact, the prevalence of maxillary sinus membrane thickening in our study was 37.5% among the patients exhibiting PH compared to 81.1% in those with PI. According to our findings, the mean sinus membrane thickness was significantly greater in the PI group ($p < .001$), being 11 mm, whereas in the PH group was 4.5 mm. Indeed, patients with posterior maxillary implants diagnosed with PI were 7× more likely to present pathological membrane thickening. Similarly, other radiographic variables analyzed in this study related to sinus disease (sinus occupancy, degree of membrane thickening, and ostium patency) differed significantly between patients with PH and those with PI. These observations could be of importance in anticipating possible maxillary sinus complications due to PI, particularly when the implants are placed close to the floor of the sinus. It is also underlined the relevance of disease resolution by means of PI treatment or implant removal to enhance maxillary sinus function and ostium permeability (Figure 5).

4.2 | Agreements and disagreements with respect to previous studies

Reports to date seem to support the existence of an association between different local factors, including specific pathologies like periodontitis (Keller et al., 2013; Ren et al., 2015) and periapical infections (Nunes et al., 2016), as well as iatrogenic factors (Rey-Martínez et al., 2022), and the occurrence of maxillary sinus diseases. Similarly, implant therapy such as implant placement through the sinus floor

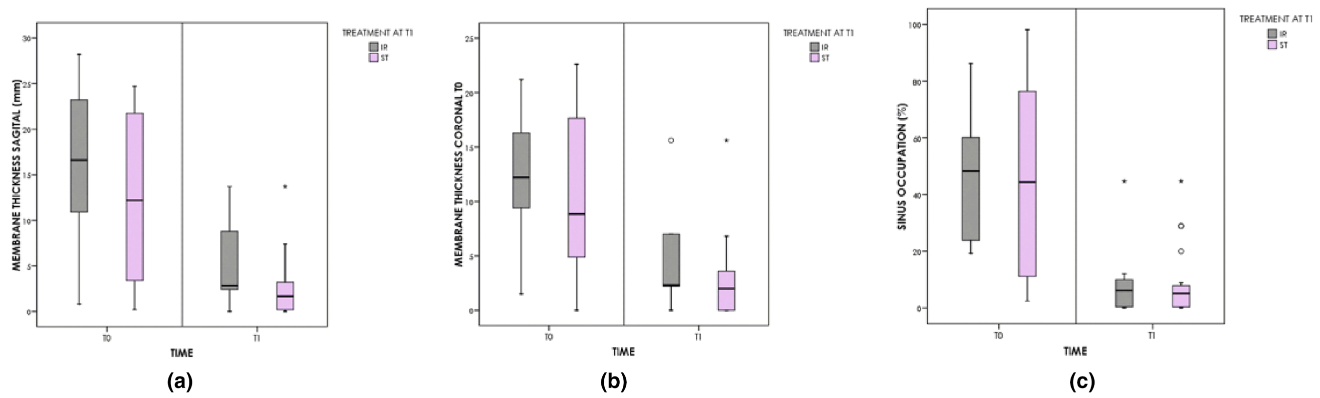

FIGURE 4 Boxplots representing the effect, at 6 months, of the treatment performed in the PI group (surgical therapy of peri-implantitis or implant removal) on (a) sagittal membrane thickening; (b) coronal membrane thickening; and (c) percentage of sinus occupancy.

(Chirilă et al., 2016; Park et al., 2023), sinus lift techniques (Chiapasco et al., 2013) or oroantral communication caused by tooth extraction (Sabatino et al., 2023) has also been associated with dimensional changes of the sinus membrane. However, to date, the link between PI and these pathologies has been established solely in a single case series, which was constrained by a limited sample size (Park et al., 2019).

A tendency toward increased sinus membrane thickness has been seen in patients with periodontitis—a fact attributable to the proinflammatory cytokines involved in this scenario (Monje et al., 2016). Additionally, periodontitis, as an inflammatory condition, may spread through the lymphatic vessels and blood (Lane & O'Neal, 1984). Specifically, different routes of spread have been suggested. It has been postulated that the bony floor of the maxillary sinus is not continuous but is perforated by several vessels, allowing close approximation of the maxillary sinus mucosa and periodontal ligament in the endosteal bone space adjacent to the maxillary molars (Hauman et al., 2002). Moreover, the roots of the maxillary premolar and molar teeth are normally separated from the floor of the sinus by dense cortical bone of variable thickness—though in some individuals this separation is only represented by of the mucoperiosteum. The latter circumstance is thought to favor the spread of inflammation to Schneider's membrane (Pagin et al., 2013).

In addition, it is considered that the height of the posterior maxilla is reduced immediately after tooth extractions, the implants being more likely to approach the floor of the maxillary sinus, come into contact with it, or even partially penetrate into the sinus. In this regard, a recent retrospective cohort study has suggested that patients with <6.7 mm of bone from the furcation to the sinus prior to tooth extraction are at an increased risk of having insufficient bone to support a dental implant without additional grafts in the maxillary first molar position (Clarot et al., 2022). Therefore, the closer the implant is to the maxillary sinus, the greater the need for bone grafting, thus increasing the likelihood of damage to the sinus membrane that would contribute to sinus membrane thickening.

Thus, and given the similarities between periodontitis and PI from an etiological point of view (Salvi et al., 2017), it can be assumed that PI could have a similar effect as periodontitis on sinus membrane thickening. Nevertheless, such effect could be even greater due to the fact that PI lesions usually presents a larger inflammatory lesion (Schwarz et al., 2018), a non-linear accelerated pattern of bone loss (Derks et al., 2016) and greater tissue loss, compared to the periodontal lesions.

According to our analysis, the mean thickness of the sinus membrane ranged between 0.2 and 28.2 mm and was significantly greater in the PI group ($p < .001$). On the other hand, previous research has reported different mucosal thicknesses, with mean values ranging from 1.17 to 2.69 mm (Khorramdel et al., 2017), 2.45 ± 2.58 mm (Sghaireen, 2020) to 19.44 ± 9.22 mm (Park et al., 2023). This disparity of membrane thicknesses may be attributed to the average age of the study populations involved (Aimetti et al., 2008; Lin et al., 2016). In this regard, it could be postulated that older individuals (in our study the mean patient age was 65.7 years) are exposed to more chronic inflammatory diseases (i.e., atherosclerosis or periodontitis) and therefore may have a thicker sinus membrane than younger patients. Nevertheless, upon accounting for various confounding factors, age did not exhibit statistical significance in our study, whether considering membrane thickening in the sagittal and coronal directions or the percentage of sinus occupancy. It is also important to note that the system used in this study to assess the thickness of the sinus membrane may overestimate the membrane size by 2.5 times when compared to histological analysis (Monje et al., 2016).

The prevalence of maxillary sinus membrane thickening in our study was 63.9%. This was 37.5% in patients with PH and 81.1% in those with PI. These results are in line with the findings of other authors, in which membrane thickening was reported to be 33% (Yildirim et al., 2017), 38% (Ritter et al., 2011) and up to 64% as assessed radiographically by means of CBCT scans (Schneider et al., 2013). Similarly, when compared with studies focusing on periodontitis, Ren et al. (2015) reported a prevalence of membrane thickening of 14.5%, 29.5% and 87.9% in patients with mild, moderate and severe alveolar bone loss, respectively. This seems to indicate that as the periodontal/peri-implant conditions deteriorate, thickening of the sinus membrane increases. Previous studies are in agreement with these results (Phothikhun et al., 2012; Vallo et al., 2010), establishing the contribution of periodontal disease to membrane thickening. In line with Phothikhun et al., who demonstrated a three-fold

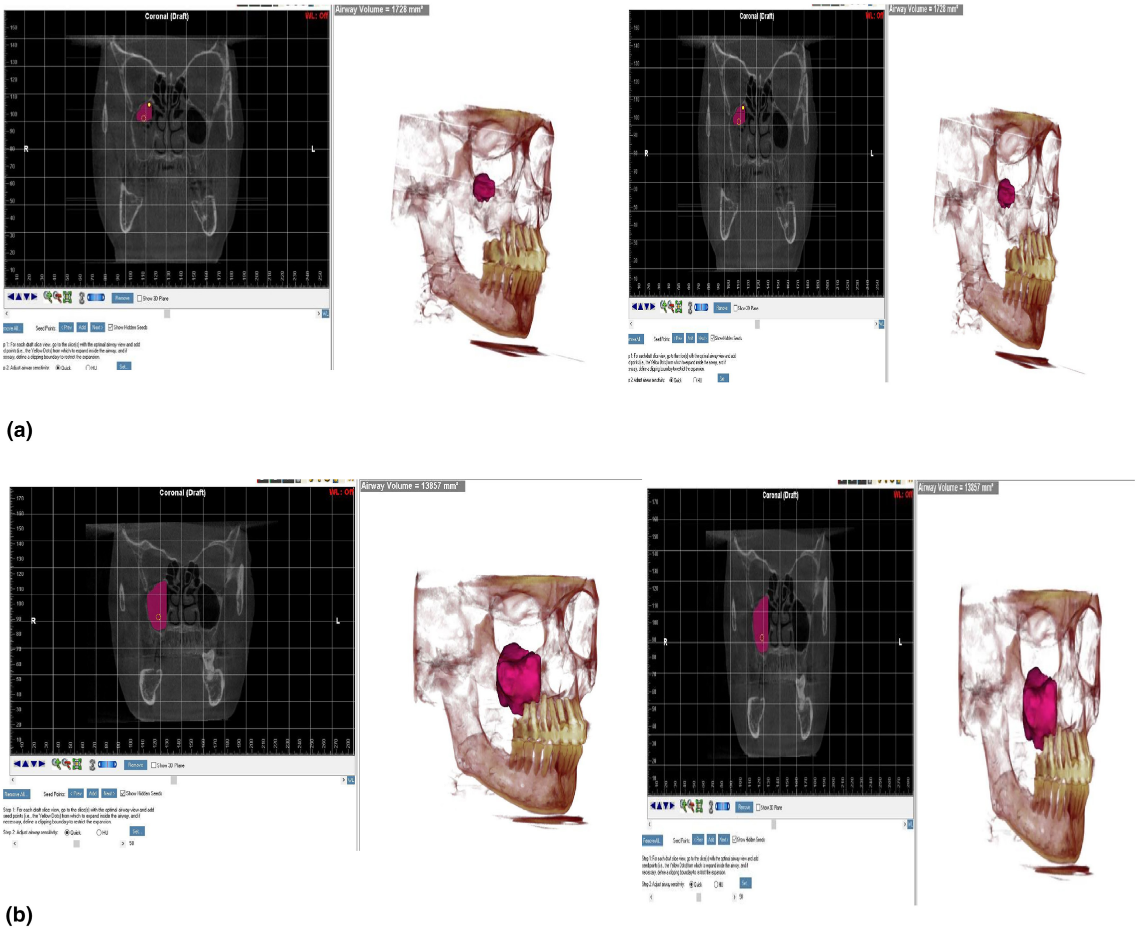

FIGURE 5 Representative case of pathologic membrane thickening with subsequent maxillary sinus occupation in a patient with peri-implantitis. Volumetric pre- and post-operative superposition in the same registration before and after peri-implantitis treatment, illustrating the improvement in maxillary sinus volume gain following the treatment. In purple, the volume of sinus space not occupied by the sinus membrane (a) in baseline and (b) 6 months after surgical treatment of peri-implantitis.

increase in the likelihood of membrane thickening with severe periodontitis (OR = 3.02), we found that patients diagnosed with PI were 7× more likely (OR = 7.14) to have pathological membrane thickening than patients with PH.

The differential contribution of this study lies in the fact that sinus occupancy secondary to membrane thickening was not only assessed by means of linear measurements in the sagittal and coronal sections of the CBCT scans but also analyzed three-dimensionally in terms of the volume (mm^3) of free or occupied air capacity within the sinus space. The differences between them made it possible to determine the overall percentage of sinus occupancy. Thus, mean sinus occupancy in the present study was 12.8% in the PH group and 44.7% in the PI group—the difference being statistically significant ($p < .001$). Similarly, a volumetric study of the maxillary sinuses in patients with sinus disease found the three-dimensional occupancy of diseased sinuses to be 62.5%, while in healthy patients this percentage decreased to 22.8% (Pérez Sayáns et al., 2020). These results suggest that membrane thickening and thus sinus occupancy are directly related to the presence or absence of disease in the maxillary-sinus complex.

Likewise, the aforementioned three-dimensional analysis made it possible to show that PI treatment (28 of 37 implants) or implant removal (9 of 37 implants) significantly reduced percentage sinus occupancy from 44.7% to 8.0% at 6 months post-intervention ($p < .001$) (Figure 5). Similarly, the linear measurements also showed significant differences in the reduction of membrane thickening after PI treatment or implant removal, with an average reduction of 10.7 and 8.0 mm at sagittal and coronal levels, respectively ($p < .001$). These results are consistent with those of a recent retrospective study that analyzed the variation in Schneider's membrane thickness before and after endodontic procedures, evidencing a mean decrease in membrane thickness ranging from 3.9 to 5 mm 1 year after treatment (Van Den Munckhof et al., 2020). In line with this, Park et al. (2023) observed that sinus mucosal thickness gradually reduced from 19.44 ± 9.22 to 4.16 ± 4.91 mm with removal of compromised teeth and drainage during lateral sinus augmentation. On the other hand, in a split mouth study in patients with chronic periodontitis, a reduction in the maxillary sinus membrane thickness of up to 1.5 mm was observed after surgical periodontal therapy (Lathiya et al., 2018). Therefore, it seems evident that specific treatment of the primary disorder causing secondary maxillary sinus disease not only allows resolution of the primary disorder but also reduces the condition that causes the sinus disease to be maintained. Lastly, it should be noted that the PI treatment or implant removal resulted in significant changes in all of the parameters related to the diseased maxillary sinus (e.g., sinus membrane thickening, sinus occupancy, degree of membrane thickening and ostium patency). Furthermore, no significant differences were observed between the interventions provided.

4.3 | Limitations of the study and future recommendations

One possible limitation of the present study is that the system used to assess sinus membrane thickness may overestimate the size of the membrane by 2.5-fold compared with histological analysis. In this same context, mention should be made of the difficulty of obtaining certain radiographic measurements due to the severity of peri-implant bone loss, the presence of metallic devices generating artifacts in the radiographic images, or the presence of sinus membranes so thin that accurate measurement proves quite difficult.

On the flip side, as this was a retrospective, non-controlled and non-randomized radiographic study, various confounding factors need consideration. These include patient age, aspects related to implant placement (e.g. sinus floor elevation and simultaneous regeneration, membrane perforation), prior dental pathology, respiratory conditions (such as asthma), previous sinus pathology (e.g. acute/chronic rhinosinusitis, nasal polyps), and the potential impact of smoking, among other variables, on membrane thickening could not be explored. In turn, it is worth mentioning that the diagnosis of pathological membrane thickening was based on thickening of the membrane to beyond values considered as normal, but without the support of a more accurate evaluation by an ear, nose and throat specialist. In addition, another possible limitation of the present study is the modest sample size, although it was representative and significant for the type of study being performed. Indeed, several patients were excluded due to illegible CBCT images, failed DICOM files or artifacts that made their analysis impossible, which further reduced the final sample size.

In relation to future investigations, longitudinal studies with larger sample sizes would be necessary to assess the dynamics of the association between PI and maxillary sinus disease over time. In other words, research should be conducted to determine how the pathological thickening of the membrane evolves as the bone loss of implants affected by PI progresses. In this way, the exact time of onset of the sinus disorder, i.e., immediately after implant placement or once the implant starts to develop peri-implant disease, could also be ascertained. In addition, it would be interesting to carry out this longitudinal evaluation with an ear, nose and throat specialist, as doing so would allow a more accurate diagnosis of maxillary sinus disease.

4.4 | Clinical implications

A number of clinical implications can be drawn from this retrospective cohort study. The prevention of PI may not only have a local effect, preserving the implant in healthy conditions over time but also have a systemic effect by reducing the likeliness of developing sinus membrane thickening—a condition that precedes more serious conditions such as mucous retention cysts, sinus polyps, mucocele and acute or chronic maxillary sinusitis. The appearance of these disorders in turn could require treatment with systemic antibiotics and corticosteroids in the best of cases, or functional endoscopic surgery or the Caldwell-Luc surgical procedure in more advanced cases, i.e., those characterized by recurrent disease or in which the respiratory capacity of the patient is impaired.

Another significant finding is that the PI treatment or implant removal is associated with reducing thickening of the sinus membrane, reducing its size and the degree of thickening, increasing ostium patency through the reduction of sinus occupation, and therefore decreasing the probability of suffering maxillary sinus disease. In this way, the early detection of PI and the application of effective treatment according to the morphology and severity of the peri-implant defect can significantly reduce thickening of the membrane as a precursor to more advanced maxillary sinus disease, and thereby, enhancing ostium permeability and sinus health.

Lastly, the evidence available to date on this topic is scarce. Longitudinal and prospective controlled studies therefore should be made to determine the strength of the association between PI and pathologic membrane thickening as a precursor of maxillary sinus disease, as well as to clarify the direction of this association.

5 | CONCLUSIONS

Maxillary sinus membrane thickening and the permeability/obstruction of the ostium are frequently associated with the presence of PI in posterior implants. Interventions aimed at halting disease progression have proven effective in reducing membrane thickness to levels consistent with maxillary sinus health.

AUTHOR CONTRIBUTIONS

R.P. and M.G. contributed to data acquisition, analysis, and interpretation, and drafted the manuscript. B.T. contributed to data interpretation. J.N., F.H.-A. and A.M. contributed to the study conception and design, and critically reviewed the manuscript. All authors gave their final approval and agreed to be accountable for all aspects of the work.

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CONFLICT OF INTEREST STATEMENT

The authors declare that they have no potential conflicts of interest with respect to the authorship and/or publication of the article.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author, AM, upon reasonable request.

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