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Influence of keratinized mucosa on the surgical therapeutical outcomes of peri-implantitis

Andrea Ravidà[1] | Islam Saleh[1] | Rafael Siqueira[1] | Carlos Garaicoa-Pazmiño[2] | Muhammad H. A. Saleh[1,3] | Alberto Monje[4] | Hom-Lay Wang[1]

[1]Department of Periodontics and Oral Medicine, University of Michigan School of Dentistry, Ann Arbor, MI, USA

[2]Department of Periodontology, School of Dentistry, Oregon Health & Science University, Portland, OR, USA

[3]Department of Periodontics, University of Louisville School of Dentistry, Louisville, KY, USA

[4]Department Periodontology, Universitat Internacional de Catalunya, Barcelona, Spain

Correspondence
Hom-Lay Wang, Department of Periodontics and Oral Medicine, University of Michigan School of Dentistry, 1011 North University Avenue, Ann Arbor, MI, USA.
Email: homlay@umich.edu

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Abstract

Aim: To assess the impact of keratinized mucosa (KM) width around dental implants on surgical therapeutic outcomes when treating peri-implantitis.

Material and Methods: Surgically treated peri-implantitis implants were divided into two groups (KM width < 2 mm and ≥2 mm). Retrospective data were obtained after implant placement (T0) and the day of peri-implantitis surgical treatment (T1). Patients were later recruited (≥1 year after T1) for clinical and radiographic examination (T2). Outcomes were analysed using generalized estimating equation (GEE) models.

Results: A total of 40 patients (68 implants) (average follow-up: 52.4 ± 30.5 months) were included in this study. From T0 to T1, no differences were found between KM groups in terms of peri-implant probing depths (PPD) and bleeding on probing (BOP). However, sites with <2 mm KM exhibited significantly higher suppuration (SUP) and lower marginal bone level (MBL) ($p > .01$). Between T1 and T2, no major differences were noted on PPD reduction, BOP and MBL changes between the two groups. GEE modelling demonstrated that MBL severity prior to surgical therapy was a better predictor for implant survival than KM width.

Conclusion: Surgical outcome in treating peri-implantitis was influenced by the severity of bone loss present at the time of treatment and not by the presence of KM at the time of treatment.

KEYWORDS

dental implants, disease management, keratinized mucosa, peri-implantitis

1 | INTRODUCTION

It is beyond dispute that dental implants have long-term (≥10 year) survival rates over 90% (Howe, Keys, & Richards, 2019; Pjetursson, Thoma, Jung, Zwahlen, & Zembic, 2012). However, dental implants are subject to biological complications known as peri-implant diseases (Renvert, Persson, Pirih, & Camargo, 2018). While tissue inflammation is a hallmark of both peri-implant mucositis and peri-implantitis, only the latter form presents with progressive loss of supporting bone (Lindhe et al., 2008). The reported prevalence of peri-implant mucositis ranged from 19% to 65% (weighted mean of 42.9%), while for peri-implantitis prevalence ranged from 1% to 47% (weighted mean of 22%) (Derks & Tomasi, 2015). Peri-implantitis prevalence was positively correlated with function time and negatively correlated with threshold for bone loss (Derks & Tomasi, 2015).

Several conditions have been identified as putative risk factors or risk indicators for peri-implantitis including diabetes, smoking, history of periodontitis, poor plaque control, lack of regular maintenance therapy, inadequate width of keratinized mucosa (KM), implant malpositioning, among others (Hammerle & Tarnow, 2018; Schwarz, Derks, Monje, & Wang, 2018). One factor that is routinely

investigated is the significance of KM on peri-implant health (Chung, Oh, Shotwell, Misch, & Wang, 2006; Kim et al., 2009; Lin, Chan, & Wang, 2013). A lack of KM has been associated with higher levels of prostaglandin E2 (Zigdon & Machtei, 2008), which might explain the positive effect of KM on the development and resolution of experimental mucositis in humans (Schwarz et al., 2018b). Hence, its presence seems essential for maintenance of long-term peri-implant health (Listgarten, Lang, Schroeder, & Schroeder, 1991). While few studies reported that presence of KM was associated with peri-implantitis (Roos-Jansaker, Lindahl, Renvert, & Renvert, 2006), there is building evidence to support a positive correlation between the presence of peri-implantitis and sites with <2 mm KM (Bouri, Bissada, Al-Zahrani, Faddoul, & Nouneh, 2008), where others suggest that the evidence to support this finding is limited (Bengazi, Wennstrom, & Lekholm, 1996; Crespi, Cappare, & Gherlone, 2010; Frisch, Ziebolz, Vach, & Ratka-Kruger, 2015; Wennstrom, Bengazi, & Lekholm, 1994; Wennstrom & Derks, 2012). Recent data support the understanding that an adequate width of KM is crucial in patients exhibiting poor compliance with peri-implant maintenance (Monje & Blasi, 2019), but plays a lesser role in fully compliant patients (Lim, Wiedemeier, Hammerle, & Thoma, 2019).

Although disagreement exists in the literature, the majority of studies agreed that the absence or lack (<2 mm) of KM was more likely to be associated with increased plaque accumulation, tissue inflammation, recession, attachment loss and reduced quality of self-performed oral hygiene measures (Gobbato, Avila-Ortiz, Sohrabi, Wang, & Karimbux, 2013; Lin et al., 2013; Ueno et al., 2016). These findings suggest that the presence of KM should be important not only for maintaining peri-implant health, but also during surgical therapy of peri-implantitis and long-term maintenance.

The influence of KM on the prevalence of peri-implant diseases can be argued according to population studies. However, it remains unknown whether the presence of KM plays a significant role in the treatment of peri-implant diseases. Hence, the aim of this study was to explore the impact of KM on the outcomes of peri-implantitis treatment before and after surgical therapy.

Clinical Relevance

Scientific rationale for the study: The significance of keratinized mucosa (KM) on peri-implant diseases has been extensively investigated. Nevertheless, the impact of KM on therapeutic outcomes remains unknown.

Principal findings: Keratinized mucosa might play a more crucial role in the progression of peri-implant diseases rather than in the response to surgical therapy.

Practical implication: While progression of peri-implantitis is associated with a lack of KM, therapeutic outcomes are mainly influenced by severity of bone loss.

2 | MATERIAL AND METHODS

This retrospective study was conducted in accordance with the Declaration of Helsinki on human studies, approved by the University of Michigan School of Dentistry Institutional Review Board (IRB) for Human Studies (HUM00148346), and registered in Clinicaltrials.gov (ID: NCT03772652). Physical and digital records collected from patients treated for peri-implantitis from 2008 to 2018 at the University of Michigan School of Dentistry were screened and evaluated by three examiners (IS, AR, RS). Patients with functional treated implants were invited to participate in the study and recruited after signing a written informed consent form for data collection from January 2019 to June 2019. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines were followed during the preparation of the manuscript.

2.1 | Eligibility criteria

To be included in this study, patients had to fall under the following predetermined eligibility criteria: (a) presence of at least one dental implant previously diagnosed with peri-implantitis using the American Academy of Periodontology (AAP)/European Federation of Periodontology (EPF) 2017 World Workshop on the Classification of Periodontal and Peri-implant Diseases and Conditions guidelines (Berglundh, Armitage, et al., 2018), (b) complete clinical and radiographic pre-surgical documentation, (c) documented follow-up of ≥1 year following surgical therapy for peri-implantitis with either resective or regeneration therapy (Table S1), (d) ≥1 maintenance session per year within the University of Michigan School of Dentistry after surgical treatment of peri-implantitis and (e) presence of opposing occlusion. Patients were excluded if: (a) clinical and radiographic records were incomplete or not available, (b) follow-up <1 year after surgical therapy and (c) peri-implantitis treatment and maintenance therapy was rendered outside the University of Michigan School of Dentistry.

2.2 | Data collection and classification

As part of the data collection process, all relevant patient information including gender, age at the time of the treatment of peri-implantitis, self-reported cigarette consumption (≥1 cigarette/day), diabetes and history of periodontal disease as defined by the World Workshop (Tonetti, Greenwell, & Kornman, 2018) were collected. Patients were assessed at T0, T1 and T2, where T0 represented implant placement or prosthetic placement, T1 represented peri-implantitis treatment and T2 represented follow-up after treatment where patients were recalled. Patients files were examined at T0 to collect clinical parameters such as KM width and radiographs. KM width was defined as the distance measured between the free mucosal margin to the mucogingival junction at the mid-buccal site,

utilizing the North Carolina probe (Hu-Friedy, Chicago, IL, USA). The selected cases were then separated into two groups based on the amount of KM: KM < 2 mm and KM ≥ 2 mm. The following information was collected from patient files at T1: KM width, radiographs, peri-implant probing depths (PPD) (recorded in millimetres using a North Carolina probe), bleeding on probing (BOP) and suppuration (SUP) (dichotomous (1/0) scale using a North Carolina probe) and peri-implant marginal bone level (MBL). Peri-implant MBL was considered as the distance between the most coronal part of the implant expected to be in bone-to-implant contact (for tissue-level implants: the interface between the polished collar and rough surface, and for bone level implants with rough surface: the platform level) to the most coronal point of the implant body in contact with bone. For each radiograph, the MBL was measured by two authors (CGP, RS) at the mesial and distal aspects of the affected implants using commercially available software (ImageJ, U. S. National Institutes of Health, Bethesda, MD, USA). MBL was also categorized in percentage (<25%; 25%–50%; or >50%) of the implant at the interproximal sites that had no bone-implant-contact considering the length of the implant. Implant design was taken in consideration for this analysis, and therefore, implants with a polished collar were analysed as complete length being from the smooth-rough interface in apical direction. Repeated measurements of 15 implants were conducted to quantify mean intra- and inter-agreement measurement errors: 0.36 ± 0.4 and 0.57 ± 0.6, respectively. Changes in the width of KM from T0 to T1 were observed. Implants that were initially in the KM ≥ 2 mm group at T0 might have switched to the KM < 2 mm group by this point (T1) or vice versa; depending on the rendered KM lose or gain.

If the treated implant was found to be in function based on the information on file in the patient chart during the last appointment in our clinic, the patient was contacted and invited to participate in this study (T2 appointment). In case of implant failure, the date of the implant removal was recorded, and the implant was included in the analysis, but the patient was not contacted (no T2 appointment). During patient recalls, all the aforementioned clinical and radiographic parameters were remeasured. In addition, plaque index (Silness & Loe, 1964) was recorded by one expert examiner (CGP). Additional information regarding type of surgical intervention (resective surgery or guided bone regeneration), previous non-surgical therapy, number of maintenance visits, systemic antibiotic prescription, and the characteristics of the implants and prosthesis were also gathered.

2.3 | Treatment success

An extensive search of all available peri-implantitis treatment success criteria was performed. The most employed success criteria after treatment of peri-implantitis were defined as PPD < 5 mm, absence of BOP/SUP, and no progressive radiographic marginal bone loss (Criteria 1) (Berglundh, Wennstrom, & Lindhe, 2018; Cha, Lee, & Kim, 2019; Charalampakis, Rabe, Leonhardt, & Dahlen, 2011; Heitz-Mayfield & Mombelli, 2014; Heitz-Mayfield et al., 2018; Isler, Soysal, Ceyhanli, Bakirarar, & Unsal, 2018; de Tapia et al., 2019). Criteria 1 were used to define success after both resective and regenerative treatment at T2. An additional composite modified criteria (Criteria 2) were used at T2 to define success around implant sites treated with regenerative therapy (PPD < 5 mm, modified sulcus bleeding index [SBI] in <25% of sites, and defect bone fill of >25% or >1 mm) (Mombelli, Oosten, Schurch, & Land, 1987; Renvert, Roos-Jansaker, & Persson, 2018; Roos-Jansaker, Persson, Lindahl, & Renvert, 2014).

2.4 | Statistical analysis

Binary logistic regression was conducted to evaluate post-surgical outcomes based on pre-surgical KM width using generalized estimating equations (GEE) adjusted to account for differences in follow-up period, number of maintenance visits and type of procedure performed between T0, T1 and T2. The changes in BOP and SUP rates from T1 to T2 among the two KM groups were analysed with a model labelled as "interaction group KM-time." For changes in mean PPD (at six sites) and mean MBL (mesial and distal), general linear models were used under the GEE approach. The GEE methodology was used to control the intra-subject correlation due to the multiplicity of implants. The level of significance utilized in the analyses was 5% ($\alpha = 0.05$). A logistic regression model reached a power of 82.6% to detect an odds ratio (OR) = 4 and deemed significant in a hypothetical sample of 68 totally independent implants assuming a confidence level of 95%. Due to the multi-level design of the data (several implants per patient), the power was corrected assuming a moderate intra-subject correlation ($\rho = 0.5$) resulting in a power of 72%.

3 | RESULTS

One hundred forty-three patients received treatment of peri-implantitis at University of Michigan school of Dentistry; however, 103 were excluded for the following reason: 23 patients had the implants placed outside the school and information at T0 were not available, 2 patients passed away, 6 patients moved and were not able to come to the appointment at T2, 14 patients could not be contacted, 33 patients had incomplete information at T0 or T1, 14 did not want to be part of the research study, 5 patients were treated before implants were restored, and for 6 patients the implants were extracted < 1 year after surgical treatment of peri-implantitis. A total of 40 patients including 22 women (55%) and 18 men (45%) with a mean age of 64.5 ± 9.0 years (range: 43–87 years) were recruited for this study. At T0, a total of 68 implants (KM < 2 mm = 26; KM ≥ 2 = 42) were included in the study (Table S2). Thirteen implants with KM ≥ 2 mm at T0 (implant placement) lost KM width due to the peri-implant disease process and were then moved to the KM < 2 mm group at T1 (peri-implantitis surgical treatment). Hence, 39 implants with < 2 mm KM and 29 with ≥2 mm KM were

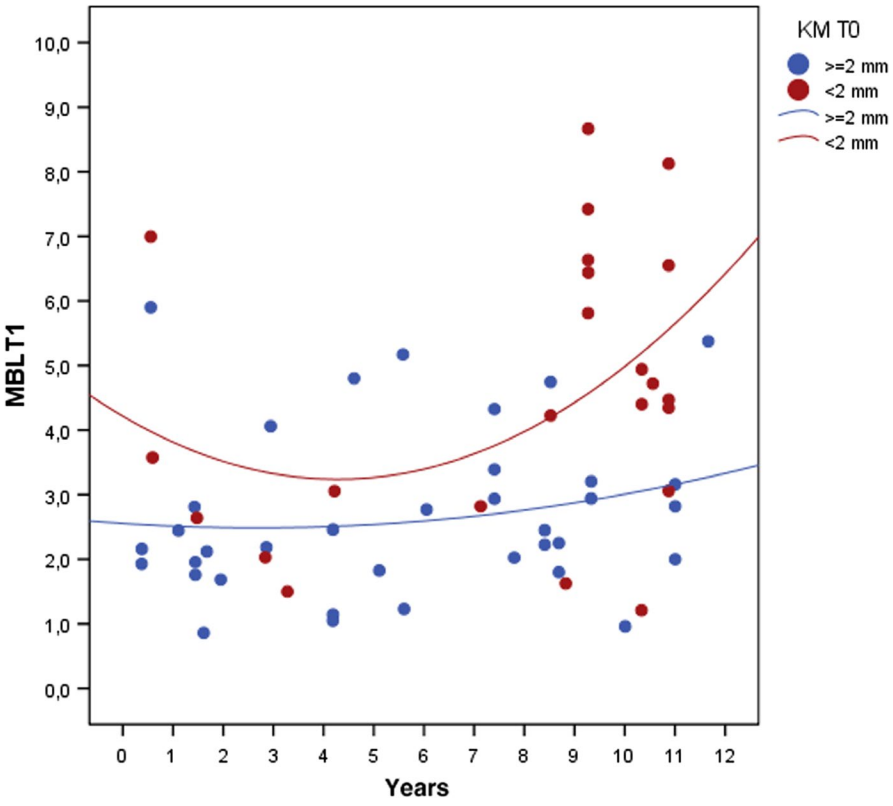

FIGURE 1 Implant marginal bone level (MBL) distribution between T0 and T1 according to time (years) and keratinized mucosa (KM) width

diagnosed with and treated for peri-implantitis (T1) receiving either resective or regenerative therapy with a mean follow-up of 52.4 ± 30.5 months (Figure S1). In total, 10% percent of the patients were smokers, 10% presented with hyperglycaemia, and 62.5% had a history of periodontitis at the time of the surgical phase for the management of peri-implantitis. Demographic data and relevant pre- surgical treatment of peri-implantitis (T1) information were included in Table 1.

3.1 | Changes from implant placement to the day of surgery (T0–T1)

The duration of time between implant placement and surgical treatment of peri-implantitis was longer for dental implants with <2 mm KM relative to those with ≥2 mm KM (T0–T1) (p = .087). Furthermore, patients with peri-implant sites presenting with <2 mm KM exhibited a similar frequency of periodontal maintenance sessions (p = .607). The association between KM, clinical, and radiographic parameters at T1 are shown in Figure 1 and Table 2. At T1 no statistically significant difference was found between the two groups of KM width in terms of PPD and BOP (p > .05). However, sites with <2 mm KM had a fivefold increase (OR = 5.02) in SUP compared to sites with ≥2 mm KM (p = .025). Simple linear regression using GEE to control differences in time and maintenance showed that sites with < 2mm KM exhibited significantly lower MBL at T1 than sites with ≥2 mm KM (p < .01). Sites with <2 mm KM had a fivefold higher risk for having MBL > 25% (p = .012) and 11-fold higher risk for MBL > 50% (p = .011) compared to sites with ≥2 mm KM.

3.2 | Changes after treatment of peri-implantitis (T1–T2)

Clinical and radiographical parameters prior surgical treatment for peri-implantitis are shown in Table 3. Twelve out of 68 implants were removed after surgical treatment giving an overall survival rate of 82.4%. When considering KM width, 11 out of 39 implants (28.2%) were removed in the <2 mm KM group, while only 1 out of 29 implants (3.4%) were lost in the ≥2 mm KM group. Treated implant sites with <2 mm KM displayed a shorter follow-up after treatment (p = .075) when compared to ≥2 mm KM sites.

After adjusting the model for the number of maintenance visits and MBL at T1, it was found that sites with <2 mm KM had sixfold increased risk for failure relative to sites with ≥2 mm KM (p = .13). It should be noted that multivariate analysis yielded that the position of the MBL could predict implant survival rate prior to treatment being rendered (p = .05) (Table 4). Seven of the 11 implant failures in the <2 mm KM group presented with MBL > 50% at T1. The risk of future implant failure increased by 65% for each additional millimetre of MBL measured at T1.

In terms of PPD reduction, no statistically significant difference was found after adjusting for differences in follow-up time and number of maintenance visits between the two KM width groups regardless of regenerative (p = .1) or resective therapy (p = .5) (Figure 2a). At

TABLE 1 Overall demographic data prior to the surgical treatment for peri-implantitis (T1)

	KM				
	≥2 mm	<2 mm	OR	95% CI	*p*-value
n (Implants) T1	29	39			
Mean KM T1 (mm)	3.03 ± 1.59	0.38 ± 0.49			
Time between T1 andT2 (months)	60.9 ± 31.3	46.0 ± 28.5	0.98	0.97–1.00	.075
Implant site (T1)					.224
Incisor	4 (13.8)	8 (20.5)	1		
Canine	1 (3.4)	4 (10.3)	2.00	0.35–11.3	.433
Premolar	13 (44.8)	7 (17.9)	0.27	0.06–1.21	.087
Molar	11 (37.9)	20 (51.3)	0.91	0.21–3.97	.899
Area (T1)					
Anterior	5 (17.2)	12 (30.8)	1		
Posterior	24 (82.8)	27 (69.2)	0.47	0.11–2.00	.469
Maxillary	15 (51.7)	11 (28.2)	1		
Mandibular	14 (48.3)	28 (71.8)	2.73	0.91–8.15	.073
Number of maintenance visits					.036*
1/per year	16 (55.2)	9 (23.1)	1		
2/per year	8 (27.6)	18 (46.2)	4.00	1.13–14.2	.032*
≥3/per year	5 (17.2)	12 (30.8)	4.27	1.12–16.3	.034*
Bone Graft (T1)					
No	14 (51.9)	31 (79.5)	1		
Yes	13 (48.1)	8 (20.5)	0.28	0.09–0.86	.027*
Implant design (T1)					
Bone level	26 (89.7)	34 (87.2)	1		
Soft tissue level	3 (10.3)	5 (12.8)	1.28	0.28–5.72	.752
Implant-abutment connection (T1)					.360
Internal	19 (65.5)	21 (53.8)	1		
External	9 (31.0)	16 (41.0)	1.61	0.46–5.66	.459
Ball Attachment	1 (3.4)	2 (5.1)	1.81	0.79–4.14	.160
Type of prosthesis retention (T1)					.001**
Cement	22 (75.9)	25 (64.1)	1		
Screw	6 (20.7)	10 (25.6)	1.47	0.47–4.60	.511
Locator/bar attachment	1 (3.4)	4 (10.3)	3.52	1.58–7.83	.002**
Splinted (T1)					
No	17 (58.6)	13 (33.3)	1		
Yes	12 (41.4)	26 (66.7)	2.83	0.87–9.25	.084
Opposing dentition (T1)					
Natural	23 (79.3)	29 (74.4)	1		
Others	6 (20.7)	10 (25.6)	1.32	0.32–5.50	.701
Previous non-surgical therapy					
No	16 (55.2)	16 (41.0)	1		
Yes	13 (44.8)	23 (59.0)	1.77	0.59–5.34	.312

(Continues)

TABLE 1 (Continued)

	KM				
	≥2 mm	<2 mm	OR	95% CI	*p*-value
Surgical approach (T1)					
Regenerative	20 (69.0)	19 (48.7)	1		
Resective	9 (31.0)	20 (51.3)	2.34	0.74–7.41	.148
Type of bone graft T1(*n* = 39)	*n* = 20	*n* = 19			
Allograft	17 (85.0)	18 (94.7)	1		
Xenograft	3 (15.0)	1 (5.3)	0.32	0.05–1.88	.205
Antibiotics (T1)					.883
No	9 (31.0)	10 (25.6)	1		
Amoxicillin	13 (44.8)	19 (48.7)	1.32	0.37–4.73	.675
Azithromycin	2 (6.9)	5 (12.8)	2.25	0.12–43.8	.593
Clindamycin	5 (17.2)	5 (12.8)	0.90	0.21–3.78	.886

Abbreviation: KM, keratinized mucosa.
*$p < .05$; **$p < .01$.

TABLE 2 Clinical and radiographical parameters occurring from T0 to T1 utilizing the width KM at T0 as the predictor

	≥2 mm	<2 mm	OR	95% CI	*p*-value
n (Implants)	42	26			
Suppuration					
No	17 (40.5)	4 (15.4)	1		
Yes	25 (59.5)	22 (84.6)	5.02	1.22–20.6	.025*
BOP					
No	0 (0.0)	0 (0.0)			
Yes	42 (100)	26(100)	—	—	1.000
% MBL					.014*
<25%	30 (73.3)	5 (19.2)	1		
25%–50%	9 (21.5)	13 (50.0)	5.43	1.45–20.4	.012*
>50%	3 (7.2)	8 (30.8)	10.9	1.75–67.9	.011*
Mean MBL (mm)	2.66 ± 1.24	4.38 ± 2.13	1.62	1.15–2.28	.005**
Mean PPD (mm)	5.67 ± 1.59	5.75 ± 1.34	0.88	0.62–1.24	.451

Abbreviations: BOP, bleeding on probing; MBL, marginal bone level; PPD, peri-implant probing depths.
*$p < .05$; **$p < .01$.

T1, BOP was present at 100% of peri-implant sites in both groups. At T2, BOP was measured at 90% of sites in both groups after regenerative therapy, and at 88.9% (KM < 2 mm) and 87.5% (KM ≥ 2 mm) after resective therapy ($p > .05$). SUP was reduced from 80% to 40% at sites with <2 mm KM and from 60% to 45% at sites with ≥2 mm when treated with regenerative therapy ($p > .05$). SUP decreased from 72.2% to 5.6% in the <2 mm KM group and from 57% to 42.9% at sites with ≥2 mm KM after resective therapy ($p < .01$). MBL changes in both KM groups showed no differences ($p > .05$) between resective or regenerative treatment approaches (Figure 2b).

During T2, PI scores were 1.37 ± 0.88 at the sites with <2 mm KM and 1.36 ± 0.81 at sites with ≥2 mm KM ($p > .05$). GI score was significantly ($p = .013$) lower at sites with <2 mm KM (1.56 ± 0.64) when compared to the ≥2 mm KM group (1.92 ± 0.57). Maintenance frequency exhibited a significant effect on GI score (beta = −0.33, $p = .001$); for each additional annual maintenance visit, the GI score was reduced by 0.20 points.

3.3 | Success rate after treatment of peri-implantitis

Table 5 shows the number and percentage of implants that responded to surgical therapy. Based on the selected criteria, the overall treatment success was accomplished in 10.3% and 7.7% of cases among sites with ≥2 mm and <2 mm KM, respectively. Success rates were 9.1% and 23.5% when regeneration therapy was performed at

TABLE 3 Clinical and radiographical parameters prior to surgical treatment of peri-implantitis (T1)

	KM				
	≥2 mm	<2 mm	OR	95% CI	*p*-value
n (Implants)	29	39			
Suppuration					
No	13 (44.8)	8 (20.5)	1		
Yes	16 (55.2)	31 (79.5)	3.15	0.99–10.0	.052
BOP					
No	0 (0.0)	0 (0.0)			
Yes	29 (100)	39 (100)	—	—	1.000
% MBL					.004**
<25%	22 (75.9)	13 (33.3)	1		
25%–50%	5 (17.2)	17 (43.6)	6.22	1.79–21.7	.004**
>50%	2 (6.9)	9 (23.1)	8.25	1.45–47.0	.018*
Mean MBL (mm)	2.47 ± 1.25	3.98 ± 1.95	1.87	1.23–2.85	.003**
Mean PPD (mm)	5.79 ± 1.57	5.63 ± 1.44	0.93	0.69 –1.26	.628

Abbreviations: BOP, bleeding on probing; MBL, marginal bone level; PPD, peri-implant probing depths.

*$p < .05$; **$p < .01$; ***$p < .001$.

TABLE 4 Clinical and radiographical parameters between T1 and T2 adjusted by number of maintenance visits and MBL utilizing KM at T1 as predictor

	Implant failure				
	No	Yes	OR	95% CI	*p*-value
n (implant)	56	12			
KM					
≥2 mm	28 (96.6)	1 (3.4)	1		
<2 mm	28 (71.8)	11 (28.2)	5.55	0.59–52.3	.13
Number of maintenance visits			0.96	0.45–2.05	.91
MBL			1.65	0.99–2.72	.05

sites with ≥2 mm and <2 mm KM, respectively. Overall, no significant influence of the KM width on the criteria was found between the groups ($p > .05$).

4 | DISCUSSION

4.1 | Principal findings

The significance of KM width on frequency of peri-implant diseases is a heavily debated subject in the literature. Current evidence underlines the importance of frequent periodontal and peri-implant maintenance, suggesting that in highly compliant patients, KM plays a null role in the prevention of biological complications (Lim et al., 2019). Conversely, in poorly compliant patients, the presence of ≥2 mm of KM has been demonstrated to be beneficial for long-term outcomes (Monje & Blasi, 2019; Romanos, Grizas, & Nentwig, 2015). Generally, the influence of peri-implant KM on peri-implantitis therapeutic outcomes is poorly understood.

Findings from this retrospective analysis suggest that peri-implant sites with minimal KM display more severe forms of peri-implantitis. Nevertheless, our results failed to exhibit an association between the width of the initial band of KM and the therapeutic outcome of peri-implantitis. Our findings revealed that lower MBL around implants prior to surgical treatment contributes towards therapeutical success and implant survival to a greater extent than KM width. However, the presence of ≥2 mm of KM around implant sites diagnosed with peri-implantitis led to higher survival rates compared to sites lacking KM. Regardless of the presence or absence of KM, severe forms of peri-implantitis are more prone to showing unsatisfactory outcomes after surgical therapy. Following treatment, BOP was yet measured at 90% of sites in both groups after either therapies. Noticeable variations between the incidence of BOP and clinically manifested peri-implantitis was previously reported (Mombelli, Muller, & Cionca, 2012). More recently, another group reported that following surgical peri-implantitis therapy, no BOP was demonstrated in only 14% of implants treated, and almost only 2% at patient level

(Koldsland, Wohlfahrt, & Aass, 2018). Both findings in addition to the results of the current study agree with the conclusions of a recent systematic review; that the extent to which BOP can identify peri-implantitis seems to be limited (Hashim, Cionca, Combescure, & Mombelli, 2018). Noteworthy is also that only one group (KM ≥ 2mm) experienced bone gain (Figure 2b). This might be partially explained by the wide-ranging standard deviation we had, were few implants had modest amounts of bone gain, others had significant bone loss. In contrast, a systematic review reported that 10.4% of the included implants from six clinical trials showed complete bone fill, 85.5% showed partial defect fill and only 4% experienced bone loss (Sahrmann, Attin, & Schmidlin, 2011).

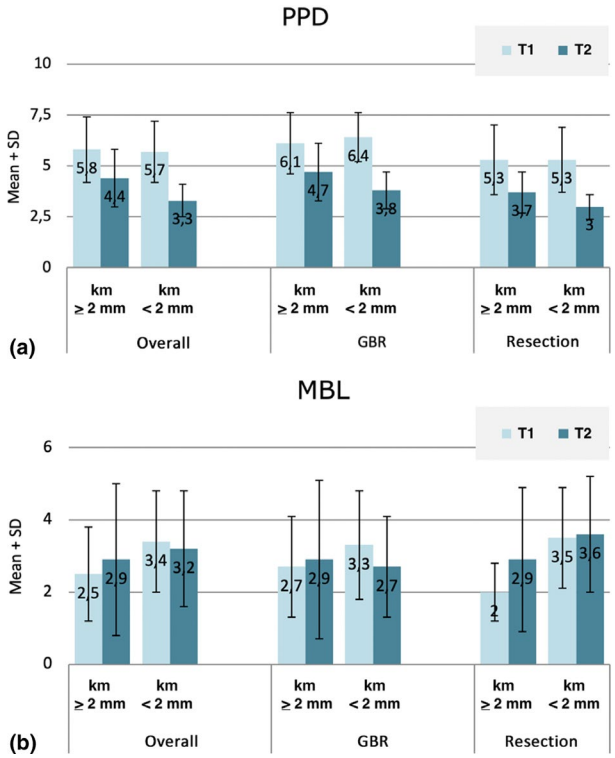

FIGURE 2 Changes in probing pocket depths (PPDs) (a) and implant marginal bone loss (MBL) (b) between T1 and T2 according keratinized mucosa (KM) width

4.2 | Agreements and disagreements with previous studies

Peri-implantitis is characterized by a non-linear and accelerating pattern of peri-implant marginal bone loss (Derks et al., 2016), where a lack of KM has been suggested to contribute towards the onset of peri-implantitis (Gobbato et al., 2013; Lin et al., 2013). In fact, a very recent prospective follow-up study demonstrated that KM width and time in function had a statistically significant effect on MBL (Perussolo, Souza, Matarazzo, Oliveira, & Araujo, 2018). This was supportive of previous findings (Zigdon & Machtei, 2008). Schwarz et al. (2018a) showed that sites with ≥2 mm KM displayed less efficient resolution of experimental peri-implant mucositis. Our findings underlined that the lack of KM contributes towards increased peri-implantitis severity.

This study is the first to investigate the impact of KM width on peri-implantitis therapeutic outcomes. Recent clinical trials concurred that non-surgical treatments are often insufficient in preventing further bone loss at peri-implantitis sites, and that only surgical approaches significantly diminish the progression of bone loss (Faggion, Listl, Fruhauf, Chang, & Tu, 2014; Karlsson et al., 2019). It is also safe to assume that surgical interventions are best reserved for moderate and advanced peri-implantitis cases (Aljateeli, Fu, & Wang, 2012; Esposito, Grusovin, & Worthington, 2012). As for the modality of surgery, a systematic review that investigated different surgical modalities for treatment of peri-implantitis was unable to support a specific type of treatment modality (Heitz-Mayfield & Mombelli, 2014). Our findings further elucidated that advanced bone loss present at the time of peri-implantitis treatment has a major impact on determining therapeutic outcomes. Hence, the therapeutic prognosis of advanced forms of peri-implantitis in the vast majority of cases is unfavourable or hopeless, regardless of the presence or lack of KM. In this sense, 7 of the 11 failures in the <2 mm KM group presented at T1 with MBL > 50%. Our study demonstrated there was no difference in PI, PPD reduction or MBL between both KM groups at T2. However, the effects of KM width on SUP need further clarification, since resective procedures decreased SUP from 72.2% to 5.6% in the <2 mm KM group, but only decreased SUP from 57% to 42.9% in the ≥2 mm KM group ($p < .01$). It is speculated that this marked reduction of SUP is merely due to the high implant failure rate seen in the <2 mm KM group, where nine implants with SUP failed, and thus were not included in the analysis. Based on our analysis, each

	KM				
	≥2 mm	<2 mm	OR	95% CI	*p*-value
n (Implants)	29	39			
Criteria 1					
Success	3 (10.3)	3 (7.7)	1		.704
Failure	26 (89.7)	36 (92.3)	1.39	0.26–7.41	
n (Implants)	22	17			
Criteria 2 (Regeneration)					
Success	2 (9.1)	4 (23.5)	1		.299
Failure	20 (90.9)	13 (76.5)	0.33	0.04–2.65	

TABLE 5 Treatment success rate at final recall (T2)

additional millimetre of MBL increased the risk of implant failure by 65%. While such association has not been reported in previous clinical trials, it seems to be in agreement with the general consensus of the literature (Froum & Rosen, 2012; Schwarz, Sahm, Schwarz, & Becker, 2010; Sinjab, Garaicoa-Pazmino, & Wang, 2018).

All patients recruited for this study were compliant with peri-implant maintenance therapy having a minimum of one maintenance session per year after treatment of peri-implantitis. A recent study investigated the outcomes of surgically treated implants with peri-implantitis that were maintained regularly (Serino, Turri, & Lang, 2015). Results showed that 39% of the treated implants had concomitant BOP/SUP upon probing after 6 months. Interestingly, in our study GI scores were significantly lower at sites with <2 mm KM (1.56 ± 0.64) than sites with ≥2 mm KM (1.92 ± 0.57). It is noteworthy that our patients that fell within the <2 mm KM group exhibited a relatively increased frequency of supportive peri-implant maintenance visits from T1 to T2. This is in agreement with previous findings (Lim et al., 2019).

Treatment success was set according to the most commonly used criteria proposed by Heitz-Mayfield and Mombelli (Heitz-Mayfield & Mombelli, 2014) and a specific criteria intended for regenerative approaches (Mombelli et al., 1987; Renvert, Roos-Jansaker, et al., 2018; Roos-Jansaker et al., 2014). Our treatment success rates might seem to be significantly lower compared with other studies (Heitz-Mayfield et al., 2018; Renvert, Roos-Jansaker, et al., 2018), mainly due to a high rate of residual BOP at T2. BOP has been suggested to be a clinical sign of peri-implant mucositis and peri-implantitis. As inferred before, the magnitude to which BOP, as a single variant, indicates the presence of peri-implantitis remains unknown (Monje, Caballe-Serrano, et al., 2018a). Marked variations between the incidence of BOP and clinically manifested peri-implantitis exist (Mombelli et al., 2012). In fact, assessments comparing teeth and implants in the same patients have shown that in the absence of disease, BOP was more frequent at implant sites (Cionca, Hashim, Cancela, Giannopoulou, & Mombelli, 2016). These findings could result from disturbing blood vessels due to an increased depth of probe penetration into healthy peri-implant mucosa. Hence, careful interpretation of BOP values is necessary, since it might lead to a high false-positive rate when identifying the presence of peri-implant disease. Assessment of bleeding tendency using the modified sulcus bleeding index, or mucosal inflammation using the implant mucosal index, is likely more accurate in the detection of true peri-implant breakdown (French, Cochran, & Ofec, 2016; Mombelli et al., 1987; Monje, Insua, et al., 2018b).

4.3 | Limitations and recommendations for future studies

Our study is not free of limitations inherent to the retrospective design of the investigation. Although our study included only compliant patients, some could be considered erratic compliers (<2 visits/year). Erratic compliers have been reported to perform as poorly as non-compliant patients (Monje, Wang, & Nart, 2017). Furthermore, the length, diameter, brand and surface treatment of implants were not included in the multivariate analysis, since the number of implant variations used was too substantial to yield statistical significance for the patient sample studied. Due to the multi-level design of the statistical analysis, a power of 72% was reached.

It should be noticed that the implant literature has been scarce in terms of considering KM association with the outcome of surgical procedures of peri-implantitis. Efforts should therefore be undertaken to include such outcome measures in future clinical studies.

5 | CONCLUSION

Peri-implant bone loss as a result of peri-implantitis is further aggravated in scenarios lacking KM. Nevertheless, surgical outcome in treating peri-implantitis was influenced by the severity of bone loss present at the time of treatment and not by the presence of keratinized mucosa at the time of treatment. Hence, the assessment of peri-implant bone loss prior to surgical therapy is a more accurate predictor of therapeutic outcomes when treating peri-implantitis.

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CONFLICT OF INTEREST

The authors do not have any financial interests, either directly or indirectly, in the products or information listed in the paper.

ORCID

Andrea Ravidà https://orcid.org/0000-0002-3029-8130
Rafael Siqueira https://orcid.org/0000-0003-4081-0959
Carlos Garaicoa-Pazmiño https://orcid.org/0000-0001-8486-6810
Alberto Monje https://orcid.org/0000-0001-8292-1927
Hom-Lay Wang https://orcid.org/0000-0003-4238-1799

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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