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Review
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Influence of implant mucosal thickness on early bone loss: a systematic review with meta-analysis

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Author Contributions
Conceptualization: Antonio Barone, Riccardo Di Gianfilippo; Formal analysis: Riccardo

ABSTRACT

Purpose: Marginal bone loss (MBL) is an important clinical issue in implant therapy. One feature that has been cited as a contributing factor to this bone loss is peri-implant mucosal thickness. Therefore, in this report, we conducted a systematic review of the literature comparing bone remodeling around implants placed in areas with thick (≥2-mm) vs. thin (<2-mm) mucosa.
Methods: A PICO question was defined. Manual and electronic searches were performed of the MEDLINE/PubMed and Cochrane Oral Health Group databases. The inclusion criteria were prospective studies that documented soft tissue thickness with direct intraoperative measurements and that included at least 1 year of follow-up. When possible, a meta-analysis was performed for both the overall and subgroup analyses.
Results: Thirteen papers fulfilled the inclusion criteria. A meta-analysis of 7 randomized clinical trials was conducted. Significantly less bone loss was found around implants with thick mucosa than around those with thin mucosa (difference, −0.53 mm; P<0.0001). Subgroups were analyzed regarding the apico-coronal positioning, the use of platform-matched vs. platform-switched (PS) connections, and the use of cement-retained vs. screw-retained prostheses. In these analyses, thick mucosa was found to be associated with significantly less MBL than thin mucosa (P<0.0001). Among non-matching (PS) connections and screw-retained prostheses, bone levels were not affected by mucosal thickness.
Conclusions: Soft tissue thickness was found to be correlated with MBL except in cases of PS connections used on implants with thin tissues and screw-retained prostheses. Mucosal thickness did not affect implant survival or the occurrence of biological or aesthetic complications.

Trial Registration: International Prospective Register of Systematic Reviews (PROSPERO): CRD42018084598

Keywords: Alveolar bone loss; Dental implant-abutment design; Dental implants; Meta-analysis; Systematic review; Wound healing

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Conflict of Interest
No potential conflict of interest relevant to this article was reported.

INTRODUCTION

Contemporary dentistry is characterized by the large-scale use of implants and implant-supported restorations, which demonstrate predictable long-term results [1]. However, an undesirable process of bone resorption, termed marginal bone loss (MBL), occurs after implant uncovering [2]. The etiology of this early remodeling is unknown, and a number of possible causes have been considered. Among the most extensively investigated potential factors are the size of the implant-abutment microgap positioned below or even with the crest [3-5], the subcrestal placement of a smooth collar [6,7], infection [8,9], excess subgingival cement [10], and contamination of the abutment surface [11].

Interestingly, regardless of the cause of MBL, peri-implant tissues seem to react similarly, with bone loss and the re-establishment of a protective collar of connective tissue [12]. In this re-establishment of the biological width, the phenotype of the soft tissue is considered to be a key factor in the maintenance of bone stability over time [13] and is often measured as the thickness (in millimeters) of the mucosa covering the bone or implant. Gargiulo et al. [14] reported a mean biological width, comprising both epithelial and connective tissue attachment, of 2.04 mm. Animal studies comparing the biological width around implants and teeth reported higher measurements around implants [15], with a width of connective tissue of 1.66 mm around implants and 1.12 mm around teeth and with a similar length of epithelial attachment for both implants and teeth. In this light, the supposed protective function of supracrestal soft tissues in maintaining an undisturbed seal around the implant is crucial [16-18].

Evidence has emerged that if the occlusal soft tissue is less than 2 mm thick before implant surgery, crestal bone loss occurs regardless of the use of platform-switched (PS) connections [19] or supracrestal placement [20]. Several systematic reviews with meta-analyses that have focused on implant-abutment connections have documented a smaller amount of MBL for PS than for non-PS implants, although these reviews lacked subgroup analyses regarding soft tissue thickness [21,22]. On the contrary, some randomized clinical trials (RCTs) have concluded that PS plays a minor role compared with tissue thickness in determining the final level of the bone [23-25].

Therefore, in this systematic review, we aimed to investigate whether early marginal bone resorption is conditioned by the crestal soft tissue thickness at the time of implant placement. As a secondary outcome, we aimed to investigate how prosthetic variables can affect MBL in cases of thin or thick mucosa.

MATERIALS AND METHODS

The present systematic review was registered in the International Prospective Register of Systematic Reviews (PROSPERO) with the following identification number: CRD42018084598.

PICO question

For patients provided with 1 or more implant-supported restorations, is the MBL greater around implants placed in sites with less than 2 mm of tissue thickness than around those placed in sites with more than 2 mm?

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Search strategy

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) principles were followed for the retrieval and analysis of data [26]. Electronic searches of the MEDLINE/PubMed and Cochrane Oral Health Group databases were performed to find studies related to aesthetic and clinical outcomes after implant placement in sites with different mucosal thicknesses.

The screening processes were conducted between November 2017 and February 2018. Relevant articles published up to December 1, 2017 were searched using the following key terms and Boolean operators (AND, OR, NOT): ((dental implants) OR (dental implantation) OR (dental prosthesis implant supported) OR (oral implants) OR (endosseous implants) OR (implant restoration) OR (osseointegrated implants)) AND ((clinical outcomes) OR (implant failure) OR (implant survival) OR (implant success) OR (early bone loss) OR (marginal bone loss) OR (bone level changes) OR (marginal bone level) OR (marginal bone resorption) OR (marginal bone remodeling) OR (marginal bone preservation) OR (crestal bone level) OR (crestal bone loss) OR (crestal bone resorption) OR (crestal bone remodeling) OR (crestal bone preservation)) AND ((tissue thickness) OR (tissue biotype) OR (tissue phenotype)).

Additional screening was conducted of the websites of most notable scientific journals in the fields of implantology, periodontology, oral surgery, and oral medicine.

Two reviewers (RDG and NAV) independently evaluated the titles and abstracts in the first phase of screening and the full-text articles in the second phase. At the end of each phase, 2 separate reviewers (AB and HLW) and a statistician (PT) were consulted in cases of disagreement.

Inclusion criteria

The inclusion criteria included 1) randomized and non-randomized comparative trials reporting on the MBL around implants placed in edentulous ridges of measured mucosal thickness, 2) a follow-up duration of at least 12 months, 3) implant placement in healed sites, and 4) the evaluation of at least 10 implants.

No limitations were applied on the type of healing (submerged or exposed), the timing of prosthetic loading, the use of splinted or non-splinted restorations, the abutment materials used, the date of publication, or the language.

Exclusion criteria

Pre-clinical studies, animal studies, cross-sectional studies, retrospective studies, repeated reports from the same study or author, studies evaluating immediate implants, and studies evaluating implants with machined or smooth surfaces were excluded. Furthermore, studies were excluded if the mucosal thickness was not evaluated from the occlusal portion of the crest via direct transmucosal measurements.

Data extraction and collection

After the screening processes, articles were downloaded as full-text versions, data were extracted independently by 2 authors (RDG and NAV), and any disagreement was resolved via consultation with 2 additional reviewers (AB and HLW) and a statistician (PT). Each included study was analyzed to obtain data regarding the number of patients and implants at the beginning and the end of the study, the study setting, the drop-out rate, the types of implants

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and connections used, the type of restorations used, any antibiotics administered, mucosal thickness, the use of either flap or flapless surgery, the apico-coronal positioning, the use of grafting, the type of healing, the timing of loading, the use of cement-retained or screw-retained restorations, the sextant of placement, the number and rate of implants lost, the success and survival rates, the number and rate of biological and mechanical complications, and the MBL at ≥1 year follow-up. If data were missing, the corresponding authors were contacted to request additional information. Domains from the Cochrane Collaboration tool scale [27] and the Newcastle Ottawa scale were used to review the quality of RCTs and other prospective studies, respectively.

MBL was defined as the linear distance in millimeters, as measured on periapical radiographs, from the most coronal endosseous surface of the implant to the most coronal point of bone-implant contact.

Secondary variables included implant failure, which was recorded as the implant not being present at the time of evaluation, and biological complications, which included any adverse event associated with pus, neurological dysfunction, pain, or significant swelling. Peri-implant mucositis was defined as the presence of profuse bleeding and/or suppuration associated with clinical signs of inflammation with 2 mm of MBL or less. Peri-implantitis was defined as a progressive increase in probing depth with clinical signs of inflammation and MBL non-compatible with initial bone remodeling. Prosthetic failure was recorded in cases of fracture or detachment of the suprastructure or loosening of any prosthetic component.

Statistical analysis

The single implant was used as the statistical unit for implant failure and MBL, while the patient was used as the statistical unit for biological and prosthetic complications. Different continuous outcomes were analyzed separately. For each RCT, the intervention effects were estimated, and the associated sampling variance was calculated. The intervention effects were measured using standardized mean differences (SMDs). All comparisons were coded so that the experimental intervention was compared with the primary comparator (mucosal thickness) for unfavorable outcomes. Continuous outcomes were coded so that an SMD <0 indicated a beneficial effect of the thick mucosa. The Cochran Q and I^2 statistics were determined, and *P* values were calculated with a level of significance of 0.05. All statistical analyses and graphical presentations were conducted using Comprehensive Meta-Analysis (Biostat, Englewood, NJ, USA) to calculate 95% confidence intervals (CIs) using the sample size (n) and the standard error, with a level of statistical significance set at α=0.05. To establish the robustness of the present results, a sensitivity analysis was performed by recalculating the SMDs after deleting the studies one at a time.

RESULTS

Search

The selection process from the MEDLINE/PubMed database, the Cochrane Oral Health Group database, and additional sources subjected to manual search yielded 336 articles, as reported in the PRISMA flowchart (Figure 1). A total of 47 studies were included after abstract screening, and 13 reports satisfied the inclusion and exclusion criteria after full-text screening [11,13,19,20,28-36]. Two clinical trials published by the same group [20,33] reported data

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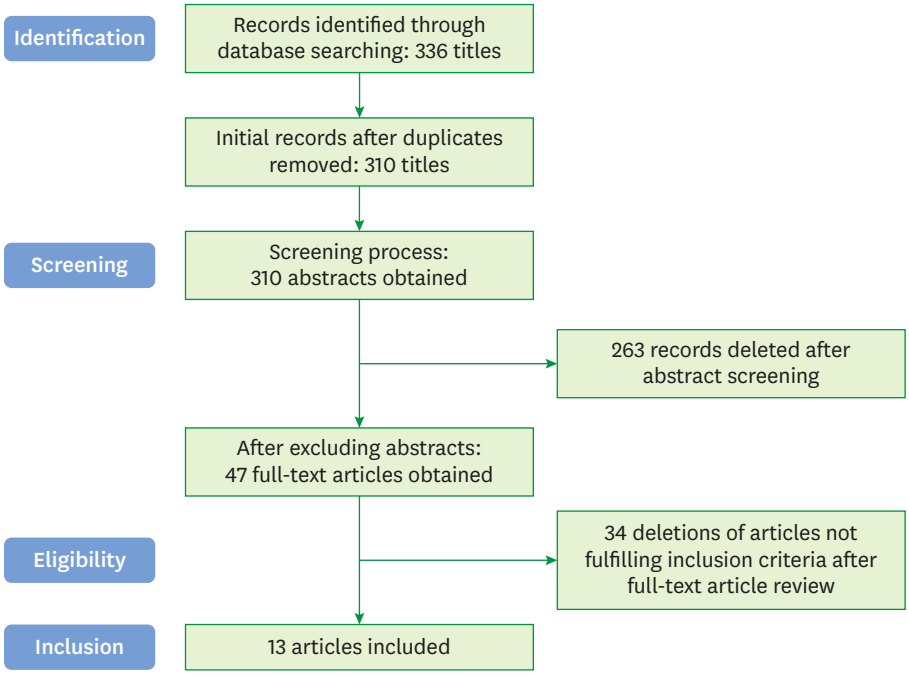

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram of the study selection process.

from the same pool of patients. Therefore, data were evaluated from only 1 of these studies [20] in order to avoid counting the same population twice.

An assessment of quality and bias was conducted using the Cochrane Collaboration tool for RCTs included in the quantitative review (Table 1), while the Newcastle Ottawa Scale was used for the remaining included prospective studies (Table 2). A comprehensive overview of the implant-supported rehabilitation strategies for partially edentulous patients with different amounts of mucosal thickness covering the surgical site is reported in Table 3. The included studies were divided into 2 categories based on the presence or absence of a comparison by tissue thickness:

Table 1. Assessment of quality and risk of bias for the studies included in the quantitative analysis

Study reference	Risk of bias						Risk of bias (other sources)			
	Random sequence generation	Allocation concealment	Blinding of patients and surgeons	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Group imbalance	Sample size	Conflict of interest	Radiographic outcome
Linkevicius et al. [28]	N/A	N/A	N/A	High	Low	N/A	Low	Low	N/A	Low
Canullo et al. [29]	N/A	N/A	High	Low	High	N/A	High	High	Low	Low
Jeong et al. [31]	N/A	N/A	N/A	Low	Low	N/A	High	Low	High	Low
Linkevicius et al. [20]	High	High	N/A	N/A	High	N/A	Low	Low	High	Low
Linkevicius et al. [34]	N/A	N/A	N/A	High	High	N/A	Low	Low	High	Low
van Eekeren et al. [35]	High	Low	Low	Low	High	N/A	Low	Low	Low	Low
Bhat et al. [36]	N/A	N/A	N/A	N/A	Low	Low	Low	High	Low	Low

Each domain was ranked based on options of high, low, or N/A risk of bias.
N/A: not assessable.

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Table 2. Assessment of quality and risk of bias for prospective studies not included in the quantitative analysis

Study reference	Selection				Comparability	Exposure		
	Case definition	Representativeness of the cases	Selection of controls	Definition of controls	Comparability of cases and controls	Ascertainment of exposure	Same method of ascertainment	Non-response rate
Linkevicius et al. [19]	*	*	*		**	*		
Bruschi et al. [30]	*	*			**	*		
Canullo et al. [11]	*	*	*		**	*		
Linkevicius et al. [32]	*	*	*		**	*	*	
Puisys and Linkevicius [13]	*	*	*	*	**	*	*	*

Each domain has a potential value of either 1 or 0 stars except comparability, which has a maximum of 2 stars.

Group A included studies that reported a comparison of clinical and radiographical outcomes of implants surrounded by thick mucosa (≥2 mm) vs. thin mucosa (<2 mm). Studies in group A were included in the qualitative and quantitative analysis and were subjected to meta-analysis [20,28,29,31,34-36].

Group B included studies that investigated implant outcomes and provided the mucosal thickness, but lacked comparison of groups with different mucosal thicknesses [11,13,19,30,32]. Trials in group B were included in the qualitative analysis only.

Population epidemiology

The qualitative analysis included studies from both groups A and B, for a total of 13 publications from 12 patient cohorts [11,13,19,20,28-36]. A total of 1,167 implants were placed in 930 patients and were followed for biological and technical complications for at least 1 year. Most of the studies reported results over 1 year of follow-up from prosthesis connection, while 2 studies reported 3-year results [29,30], and only 1 study followed patients for 5 years [11]. The survival rate at 1 year of follow-up was 99.47% due to 3 early implant failures. However, no information was provided regarding the mucosal thickness associated with the failed implants. No prosthetic failure was registered, and the prosthesis survival rate was 100% at the 1-year mark. Considering the subgroup in which implants were positioned in sites with thick mucosa, 3 failures were registered out of 297 implants (a survival rate of 98.99%). No biological complications were reported in any of the considered studies. None of the included reports described cases of peri-implantitis or peri-implant mucositis. The MBL reported for the implants surrounded by thin mucosa ranged from 0.1 mm to 1.73 mm within 1 year of follow-up, whereas for implants surrounded by thick mucosa, the MBL ranged from 0.17 mm to 0.61 mm. Changes in soft tissue thickness during different phases of implant rehabilitation were reported in 2 studies. Those changes were characterized by a reduction in thickness from the time of fixture placement to the time of prosthesis cementation followed by a gain in thickness noted at subsequent follow-up exams [11,36]. Additional details regarding the included studies are reported in Table 3.

MBL in thick and thin mucosa

The quantitative analysis of the 7 studies in group A [20,28,29,31,34-36] included a total of 801 implants from 571 patients. Meta-analysis regarding the MBL associated with implants placed in areas with thick or thin tissues found significantly greater bone preservation for implants placed in sites with thick mucosa (Figure 2A), with a difference of −0.530 mm (95% CI, −0.691, −0.369 mm; P<0.0001). Although these data suggest a smaller amount of MBL around implants covered with thick mucosa, no conclusions were drawn regarding either aesthetic/biological complications or survival outcomes due to the very low failure rates registered in the short term. Subgroup analyses in which soft tissue thickness was analyzed

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Table 3. Population pool and outcomes of studies reporting on MBL around implants placed in sites with measured tissue thickness

Study reference	Patients	Groups	Study information									Outcomes				
			Subjects	Implants	Protocols	Restoration retention	Implant neck position (under/equi/above the crest)	Loaded within 1 yr	Follow-up duration (yr)	Drop-out, patients (implants)	Thin vs. thick (mm)	Implant failure	Prosthesis failure	Complications	Soft tissue changes (mm)	MBL (mm)
Linkevicius et al. [28] (group A)	80	2	40	40	Flap transmucosal, PS	Screw-retained	Equi	Yes	1	0 (0)	Thin, 1.53	0	0	N/A	N/A	1.18 (1.2)
		1	40	40	Flap transmucosal, PS	Screw-retained	Equi	Yes	1	0 (0)	Thick, 2.98	0	0	N/A	N/A	0.22 (0.00)
Sig.											<0.001					<0.001
Linkevicius et al. [19] (group B)	30	1	30	30	Flap transmucosal	Cement-/screw-retained	Equi	Yes	1	0 (0)	Thin, 1.76	0	0	N/A	N/A	1.41±0.42
		2	30	30	Flap transmucosal, PS	Cement-/screw-retained	Equi	Yes	1	0 (0)	Thin, 1.63	0	0	N/A	N/A	1.43±0.23
Sig.																0.976
Canullo et al. [29] (group A)	26	1	18	40	Flap transmucosal, PS	Cement-retained	Under	Yes	3	2 (N/A)	Thin, ≤2.00	0	0	N/A	N/A	0.27
		2	10	28	Flap transmucosal, PS	Cement-retained	Under	Yes	3	0 (0)	Thick, >2.00	0	0	N/A	N/A	0.17
Sig.																0.414
Bruschi et al. [30] (group B)	120	N/A	120	135	Partial-thickness flap, PS	Cement-retained	Equi	Yes	3	0 (0)	Thick, 3.00	3	N/A	N/A	N/A	−1.09±0.38
Canullo et al. [11] (group B)	35	Test	15	15	Flap covered, plasma of argon, PS	Cement-retained	Under	Yes	5	0 (0)	Thin, ≤1.00	0	0	N/A	−0.48±0.40	0.11±0.14
		Control	15	15	Flap covered, cleaning by steaming, PS	Cement-retained	Under	Yes	5	0 (0)	Thin, ≤1.00	0	0	N/A	−0.39±0.31	0.38±0.43
Sig.															-	0.026
Jeong et al. [31] (group A)	241	Thin	241	318	Flapless transmucosal, PS	Screw-retained	N/A	Yes	1	0 (0)	Thin, <3.00	0	0	N/A	N/A	0.3±0.2
		Thick		114	Flapless transmucosal, PS	Screw-retained	N/A	Yes	1	0 (0)	Thick, ≥3.00	0	0	N/A	N/A	0.3±0.6
Sig.																-
Linkevicius et al. [20] (group A)	23	A	23	23	Flap transmucosal, not indicated	Cement-retained	Above	Yes	1	3 (0)	Thin, 1.95	0	0	0	N/A	1.45±0.55
		B		23	Flap transmucosal, not indicated	Cement-retained	Equi	Yes	1		Thick, 3.32	0	0	0	N/A	0.17±0.19
Sig.																-
Linkevicius et al. [32] (group B)	4	Thin	4	12	Flap transmucosal, PS, PM	Cement-retained	Equi	Yes	1	0 (0)	Thin, 1.79	0	0	0	N/A	1.60±1.81

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Table 3. (Continued) Population pool and outcomes of studies reporting on MBL around implants placed in sites with measured tissue thickness

Study reference	Patients	Groups	Study information									Outcomes				
			Subjects	Implants	Protocols	Restoration retention	Implant neck position (under/equi/above the crest)	Loaded within 1 yr	Follow-up duration (yr)	Drop-out, patients (implants)	Thin vs. thick (mm)	Implant failure	Prosthesis failure	Complications	Soft tissue changes (mm)	MBL (mm)
Linkevicius et al. [33] (group A)	34	Test	26	12	Flap transmucosal, not indicated	Cement-retained	Above	Yes	1	7 (7)	Thin, ≤2.0	0	0	0	N/A	1.35±0.33
				12	Flap transmucosal, not indicated	Cement-retained	Above	Yes	1		Medium, 2.1–3.0	0	0	0	N/A	0.32±0.44
				8	Flap transmucosal, not indicated	Cement-retained	Above	Yes	1		Thick, ≥3.1	0	0	0	N/A	0.12±0.16
	34	Control	26	12	Flap transmucosal, not indicated	Cement-retained	Equi	Yes	1	7 (7)	Thin, ≤2.0	0	0	0	N/A	1.83±0.52
				12	Flap transmucosal, not indicated	Cement-retained	Equi	Yes	1		Medium, 2.1–3.0	0	0	0	N/A	1.62±0.63
				8	Flap transmucosal, not indicated	Cement-retained	Equi	Yes	1		Thick, ≥3.1	0	0	0	N/A	1.55±0.47
Sig.		Test Control														0.503
Linkevicius et al. [34] (group A)	113	A	34	34	Flap transmucosal, PM	Cement-retained	Above	Yes	1	N/A	Thin, 1.51	2 early	0	0	N/A	1.73±0.07
		C	34	34	Flap transmucosal, PM	Cement-retained	Above	Yes	1	N/A	Thick, 2.98				N/A	0.46±0.07
Sig.																0.000
Puisys and Linkevicius [13] (group B)	102	T1	33	33	Flap transmucosal, PS	Screw-retained	Equi	Yes	1	N/A	Thin, ≤2.00	0	0	0	N/A	1.18±0.07
		C	32	32	Flap transmucosal, PS	Screw-retained	Equi	Yes	1	N/A	Thick, >2.00	0	0	0	N/A	0.21±0.06
Sig.																0.000
van Eekeren et al. [35] (group A)	33	MC	33	17	Flap transmucosal, PM	Screw-retained	Equi	Yes	1	1 (2)	Thin, ≤2.00	1 early	N/A	N/A	N/A	0.6±0.5
				20	Flap transmucosal, PM	Screw-retained	Equi	Yes	1		Thick, >2.00		N/A	N/A	N/A	0.2±0.4
	33	LC	33	15	Flap transmucosal, PM	Screw-retained	Above	Yes	1	1 (2)	Thin, ≤2.00	0	N/A	N/A	N/A	0.1±0.5
				22	Flap transmucosal, PM	Screw-retained	Above	Yes	1		Thick, >2.00		N/A	N/A	N/A	0.2±0.4
Sig.		MC LC														0.003 0.518
Bhat et al. [36] (group A)	22	Thin biotype	20	17	Flap covered, not indicated	Cement-retained	Equi	Yes	1	2 (0)	Thin, 1.09	N/A	N/A	N/A	0.50±0.24	1.70±0.36
		Thick biotype		16	Flap covered, not indicated	Cement-retained	Equi	Yes	1		Thick, 2.20	N/A	N/A	N/A	1.22±0.24	0.61±0.36
Sig.																-

All data were collected after an observational period of 12 months from prosthetic loading. The level of significance refers to comparisons between thin and thick mucosa.
N/A: not provided, PS: platform-switched connections, PM: platform-matched connections, MBL: marginal bone loss, Equi: equicrestal, Sig.: significance.

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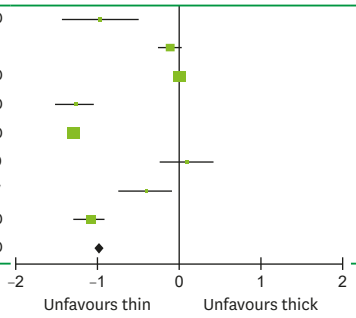
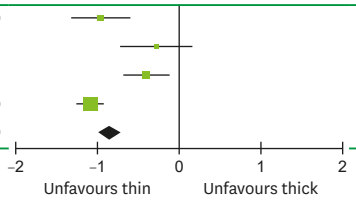
Study name	Outcome	Statistics for each study							Sensitivity analysis (omitted study)		
		Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-value	*P*-value	Lower limit	Difference in means	Upper limit
Linkevicius et al. [28]	MBL	−0.960	0.190	0.036	−1.332	−0.588	−5.060	0.000	−1.021	−0.992	−0.964
Canullo et al. [29]	MBL	−0.100	0.060	0.004	−0.217	0.017	−1.669	0.095	−1.077	−1.048	−1.018
Jeong et al. [31]	MBL	0.000	0.038	0.001	−0.075	0.075	0.000	1.000	−1.188	−1.157	−1.126
Linkevicius et al. [20]	MBL	−1.280	0.121	0.015	−1.518	−1.042	−10.549	0.000	−1.016	−0.988	−0.959
Linkevicius et al. [34]	MBL	−1.270	0.017	0.000	−1.303	−1.237	−74.805	0.000	−0.644	−0.482	−0.321
van Eekeren et al. [35]	MBL	0.100	0.148	0.022	−0.191	0.391	0.675	0.500	−1.031	−1.003	−0.974
van Eekeren et al. [35]	MBL	0.400	0.148	0.022	−0.690	−0.110	−2.704	0.007	−1.026	−0.998	−0.969
Bhat et al. [36]	MBL	−1.090	0.089	0.008	−1.264	−0.916	−12.299	0.000	−1.018	−0.989	−0.960
		−0.992	0.015	0.000	−1.020	−0.963	−68.280	0.000			



Model	No. of studies	Effect size and 95% CI					Test of null (2-Tail)		Heterogeneity			
		Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-value	*P*-value	Q-value	df (Q)	*P*-value	I^2
Fixed	8	−0.530	0.082	0.007	−0.691	−0.369	−6.447	0.000	243.960	7	0.000	97.131
Random	8	−2.350	0.587	0.345	−3.502	−1.199	−4.000	0.000				

B

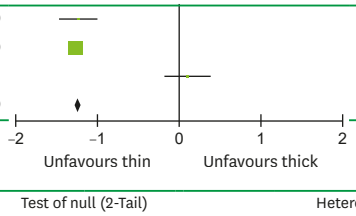
Study name	Outcome	Statistics for each study							Sensitivity analysis (omitted study)		
		Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-value	*P*-value	Lower limit	Difference in means	Upper limit
Linkevicius et al. [28]	MBL	−0.960	0.190	0.036	−1.332	−0.588	−5.060	0.000	−0.987	−0.845	−0.704
Linkevicius et al. [33]	MBL	−0.280	0.229	0.052	−0.728	0.168	−1.224	0.221	−0.992	−0.860	−0.728
van Eekeren et al. [35]	MBL	−0.400	0.148	0.022	−0.690	−0.110	−2.704	0.007	−1.129	−0.980	−0.832
Bhat et al. [36]	MBL	−1.090	0.089	0.008	−1.264	−0.916	−12.299	0.000	−0.747	−0.543	−0.340
		−0.860	0.067	0.005	−0.992	−0.728	−12.750	0.000			



Model	No. of studies	Effect size and 95% CI					Test of null (2-Tail)		Heterogeneity			
		Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-value	*P*-value	Q-value	df (Q)	*P*-value	I^2
Fixed	4	−0.860	0.067	0.005	−0.992	−0.728	−12.750	0.000	23.109	3	0.000	87.018
Random	4	−0.702	0.213	0.045	−1.119	−0.285	−3.300	0.001				

C

Study name	Outcome	Statistics for each study							Sensitivity analysis (omitted study)		
		Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-value	*P*-value	Lower limit	Difference in means	Upper limit
Linkevicius et al. [33]	MBL	−1.230	0.126	0.016	−1.477	−0.983	−9.743	0.000	−1.285	−1.252	−1.219
Linkevicius et al. [34]	MBL	−1.270	0.017	0.000	−1.303	−1.237	−74.805	0.000	−0.859	−0.671	−0.483
van Eekeren et al. [35]	MBL	0.100	0.148	0.022	−0.191	0.391	0.675	0.500	−1.302	−1.269	−1.236
		−1.252	0.017	0.000	−1.285	−1.219	−74.879	0.000			



Model	No. of studies	Effect size and 95% CI					Test of null (2-Tail)		Heterogeneity			
		Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-value	*P*-value	Q-value	df (Q)	*P*-value	I^2
Fixed	3	−1.252	0.017	0.000	−1.285	−1.219	−74.879	0.000	84.333	2	0.000	97.628
Random	3	−0.811	0.366	0.134	−1.528	−0.093	−2.215	0.027				

Figure 2. (A) Forest plot of peri-implant marginal bone levels between thin and thick mucosa groups: analysis for the full set of studies. (B) Forest plot of peri-implant marginal bone levels between thin and thick mucosa groups: analysis for the subgroup with equicrestal placement of the implant shoulder. (C) Forest plot of peri-implant marginal bone levels between thin and thick mucosa groups: analysis for the subgroup with supracrestal placement of the implant shoulder. CI, confidence interval.

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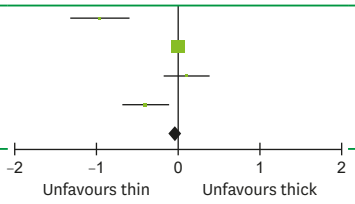
D

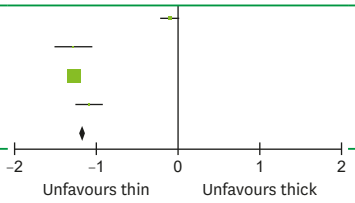
Study name	Outcome	Statistics for each study							Sensitivity analysis (omitted study)		
		Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-value	*P*-value	Lower limit	Difference in means	Upper limit
Linkevicius et al. [28]	MBL	−0.960	0.190	0.036	−1.332	−0.588	−5.060	0.000	−0.089	−0.018	0.053
Jeong et al. [31]	MBL	0.000	0.038	0.001	−0.075	0.075	0.000	1.000	−0.519	−0.340	−0.160
van Eekeren et al. [35]	MBL	0.100	0.148	0.022	−0.191	0.391	0.675	0.500	−0.132	−0.060	0.012
van Eekeren et al. [35]	MBL	−0.400	0.148	0.022	−0.690	−0.110	−2.704	0.007	−0.101	−0.030	0.042
		−0.051	0.035	0.001	−0.120	0.019	−1.432	0.152			



Model	No. of studies	Effect size and 95% CI					Test of null (2-Tail)		Heterogeneity			
		Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-value	*P*-value	Q-value	df (Q)	*P*-value	I^2
Fixed	4	−0.051	0.035	0.001	−0.120	0.019	−1.432	0.152	31.313	3	0.000	90.419
Random	4	−0.290	0.195	0.038	−0.672	0.092	−1.489	0.136				

E

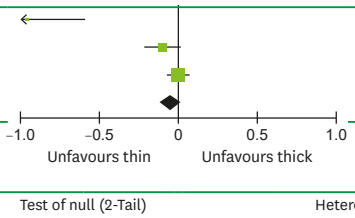
Study name	Outcome	Statistics for each study							Sensitivity analysis (omitted study)		
		Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-value	*P*-value	Lower limit	Difference in means	Upper limit
Canullo et al. [29]	MBL	−0.100	0.060	0.004	−0.217	0.017	−1.669	0.095	−1.296	−1.264	1.232
Linkevicius et al. [20]	MBL	−1.280	0.121	0.015	−1.518	−1.042	−10.549	0.000	−1.211	−1.180	−1.149
Linkevicius et al. [34]	MBL	−1.270	0.017	0.000	−1.303	−1.237	−74.805	0.000	−0.625	−0.535	−0.445
Bhat et al. [36]	MBL	−1.090	0.089	0.008	−1.264	−0.916	−12.299	0.000	−1.216	−1.185	−1.153
		−1.182	0.016	0.000	−1.213	−1.150	−74.205	0.000			



Model	No. of studies	Effect size and 95% CI					Test of null (2-Tail)		Heterogeneity			
		Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-value	*P*-value	Q-value	df (Q)	*P*-value	I^2
Fixed	4	−1.815	0.184	0.034	−2.176	−1.454	−9.847	0.000	159.390	3	0.000	98.118
Random	4	−5.513	1.539	2.370	−8.530	−2.496	−3.582	0.000				

F

Study name	Outcome	Statistics for each study							Sensitivity analysis (omitted study)		
		Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-value	*P*-value	Lower limit	Difference in means	Upper limit
Linkevicius et al. [28]	MBL	−0.960	0.190	0.036	−1.332	−0.588	−5.060	0.000	−0.093	−0.029	0.034
Canullo et al. [29]	MBL	−0.100	0.060	0.004	−0.217	0.017	−1.669	0.095	−0.112	−0.038	0.036
Jeong et al. [31]	MBL	0.000	0.038	0.001	−0.075	0.075	0.000	1.000	−0.290	−0.178	−0.066
		−0.055	0.032	0.001	−0.118	0.007	−1.739	0.082			



Model	No. of studies	Effect size and 95% CI					Test of null (2-Tail)		Heterogeneity			
		Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-value	*P*-value	Q-value	df (Q)	*P*-value	I^2
Fixed	3	−0.055	0.032	0.001	−0.118	0.007	−1.739	0.082	25.360	2	0.000	92.114
Random	3	−0.266	0.146	0.021	−0.552	0.020	−1.823	0.068				

Figure 2. (Continued) (D) Forest plot of peri-implant marginal bone levels between thin and thick mucosa groups: analysis for the subgroup with screw-retained prostheses. (E) Forest plot of peri-implant marginal bone levels between thin and thick mucosa groups: analysis for the subgroup with cement-retained prostheses. (F) Forest plot of peri-implant marginal bone levels between thin and thick mucosa groups: analysis for the subgroup with platform-switched connections.
CI, confidence interval.

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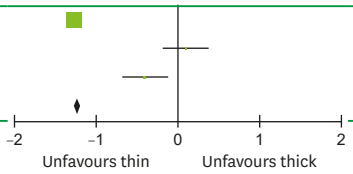
G

Study name	Outcome	Statistics for each study							Sensitivity analysis (omitted study)		
		Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-value	*P*-value	Lower limit	Difference in means	Upper limit
Linkevicius et al. [34]	MBL	−1.270	0.017	0.000	−1.303	−1.237	−74.805	0.000	−0.356	−0.150	0.055
van Eekeren et al. [35]	MBL	0.100	0.148	0.022	−0.191	0.391	0.675	0.500	−1.292	−1.259	−1.226
van Eekeren et al. [35]	MBL	−0.400	0.148	0.022	−0.690	−0.110	−2.704	0.007	−1.285	−1.252	−1.219
		−1.241	0.017	0.000	−1.274	−1.208	−74.071	0.000			



Model	No. of studies	Effect size and 95% CI					Test of null (2-Tail)		Heterogeneity			
		Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-value	*P*-value	Q-value	df (Q)	*P*-value	I^2
Fixed	3	−1.241	0.017	0.000	−1.274	−1.208	−74.071	0.000	117.060	2	0.000	98.291
Random	3	−0.532	0.468	0.219	−1.449	0.386	−1.135	0.256				

Figure 2. (Continued) (G) Forest plot of peri-implant marginal bone levels between thin and thick mucosa groups: analysis for the subgroup with platform-matched connections.
CI, confidence interval.

in the context of apico-coronal placement, the use of screwed vs. cemented prostheses, and the use of PS vs. platform-matched (PM) connections were performed and are displayed in Figures 2B-G.

Apico-coronal implant placement

Data originating from 5 studies [28,33-36] were subjected to meta-analysis based on apico-coronal implant placement. When implants placed at the crestal level were categorized based on mucosal thickness, a significantly greater amount of bone preservation was reported in thick than in thin tissues, with a difference of −0.860 mm (95% CI, −0.992, −0.728 mm; *P*<0.0001) (Figure 2B). Similarly, a significantly greater amount of bone preservation was observed in thick than in thin tissues for supracrestally-placed implants, with a difference of −1.252 mm (95% CI, −1.285, −1.219 mm; *P*<0.0001) (Figure 2C). Only a study by Canullo et al. [29] investigated the effect of tissue thickness on subcrestal implants; this study reported a statistically insignificant difference of 0.10 mm between the thick and thin groups (0.27 mm vs. 0.17 mm for the thin vs. thick mucosa, respectively; *P*=0.414).

Screwed and cemented prostheses

Studies eligible for meta-analysis were divided into 2 subgroups depending on the type of prosthetic retention (screw- or cement-retained restorations). In the screwed prostheses, the difference in MBL between implants surrounded by thin or thick tissues was statistically insignificant (difference, −0.051 mm; 95% CI, −0.120, 0.019 mm; *P*=0.152) (Figure 2D), whereas in cemented prostheses, a statistically significantly greater amount of bone loss was observed in the thin group than in the thick group (difference, −1.815 mm; 95% CI, −2.176, −1.454 mm; *P*<0.0001) (Figure 2E).

Platform matching and platform switching connections

Regarding data on the PM and PS subgroups, a significantly greater degree of bone preservation of the thick mucosa group relative to the thin group was not observed for PS connections (difference, −0.055 mm; 95% CI, −0.118, −0.007 mm; *P*=0.082) (Figure 2F). However, among the PM connections, greater bone stability was found to be associated with thick tissues (difference, −1.241 mm; 95% CI, −1.274, −1.208 mm; *P*<0.0001) (Figure 2G).

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Sensitivity analysis

Sensitivity analyses were performed for all subgroups to evaluate whether any individual study effect influenced the pooled effect size. The outcome of the current meta-analysis can be considered to be stable with the exception of the study by Linkevicius et al. [34], the absence of which seemed to affect the results of the meta-analysis by reducing the difference between the 2 compared groups.

DISCUSSION

The present meta-analysis indicated that a mucosal thickness of at least 2 mm on the day of implant placement is a prognostic predictor of reduced bone loss in the first year after prosthesis delivery. When evaluating other outcomes such as survival rate and biological and aesthetic complications, no differences were found between thin and thick tissues due to the limited occurrence of these events over the short follow-up period.

The hypothesis that implants with thin mucosa exhibit greater bone loss than implants with thick mucosa was originally raised in classical dog studies [12,37]. Abrahamsson et al. [37] proposed that at sites where the mucosa was thin, angular bone defects created a biological barrier similar to that found in thick mucosa. Berglundh and Lindhe [12], in a dog split-mouth study, found higher marginal bone resorption at sites with experimentally thinned soft tissue. Nonetheless, surgical trauma at thin sites could be a reason for this increased MBL [38]. While experimental thin mucosa was achieved at test sites by removing tissue after elevating a partial-thickness flap during the same procedure as implant placement, control implants were placed after conventional full-thickness flap elevation. Further animal and human studies have stressed the correlation of tissue thickness with peri-implant bone loss. Animal studies have reported the occurrence of progressive bone remodeling to establish a distance of 3.2 mm between the crest and the soft tissue margin [39], while reduced bone loss has been documented at sites augmented with soft tissue grafts [40]. Vervaeke et al. [41], in a human study, documented lower bone resorption around implants that were connected with higher abutments due to thick mucosa.

The findings of previous systematic reviews on this topic are contradictory. Significantly higher bone resorption for thin tissues was reported by Suárez-López Del Amo et al. [42]. However, this meta-analysis was based on data from 2 studies of the same patients [20,33] and therefore counted the same population twice. Akcalı et al. [43] reported that the difference in MBL between implants with thin and thick mucosa was statistically insignificant; however, only 2 studies in that report were subjected to meta-analysis, and all of the included references described a smaller degree of bone loss in the thick than in the thin soft tissue groups. The same study reported a relatively high degree of heterogeneity, since some authors recorded soft tissue thickness intraoperatively with a probe after buccal flap elevation [13,19,28,34], while others used indirect methods such as cone-beam computed tomography [44]. Regarding the number of RCTs evaluated, the present study included 7 RCTs in the meta-analysis as opposed to 2 [43]. The much larger sample size may have played a role in this study's demonstration of significantly greater bone preservation in the thick mucosa group.

In addition to mucosal thickness, many factors have been found to be associated with MBL. The apico-coronal position of the implant-abutment microgap has been considered one of

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the main variables associated with bone resorption, mainly due to bacterial microleakage, inflammatory infiltrate [4], and abutment micromovement [3]. The present systematic review indicated that thin soft tissues exhibited more bone remodeling than thick soft tissues regardless of crestal or supracrestal implant placement. These data contradict the assumption that supracrestal implant positioning can preserve marginal bone [3,45,46]. In accordance with our findings, Ercoli et al. [47] concluded that crestal bone levels measured from the implant platform do not differ regardless of whether implants are placed subcrestally, equicrestally, or supracrestally.

RCTs and meta-analyses have reported significant less MBL around PS than around PM connections [21,22,48]. However, results from RCTs that simultaneously evaluated the effects of tissue thickness and the use of PS have produced different results. Linkevicius et al. [32] and Vandeweghe and De Bruyn [24] showed no significant difference in peri-implant bone stability for PS connections vs. PM connections in patients with thin mucosa. Canullo et al. [29] obtained opposite results, in which bone preservation was noted for PS connections, while initial soft tissue thickness had an insignificant effect on bone loss around PS implants. The results of the present review are supported by the findings of Canullo et al. [29]. Indeed, the significant bone preservation of the thick mucosa was not confirmed in the analysis of the subgroup with PS connections.

The biological effects of screw retention vs. cement retention in implant restorations have been extensively discussed in the past [49]. Despite a lack of significant difference in survival rates [50], renewed concern has been raised regarding the biological effect of residual subgingival cement. Commonly-used cements trigger a chronic inflammatory reaction sustained by plasma cells [51], leading to biological complications such as bone loss and peri-implant mucositis [52]. In the present analysis, favorable bone preservation was observed for cemented restorations in patients with thick tissues. Considering the challenges inherent to the detection and removal of subgingival cement, thick peri-implant mucosa could serve as a protective cushion to mitigate the irritating effect of subgingival cement on surrounding tissue. The thickness of the peri-implant mucosa did not seem to impact screw-retained restorations, which—due to the lack of subgingival irritants—are more often associated with healthier peri-implant tissues than are cemented restorations [53].

The obtained results are not immune to limitations and should be interpreted cautiously. While a full set of 7 RCTs was included in the meta-analysis investigating the effect of tissue thickness on MBL, the subgroup analysis included a smaller sample size, reducing the external validity and making the results difficult to generalize. The short follow-up period of 1 year after prosthesis delivery represents a second limitation of the review. The literature lacks trials with longer follow-up periods, and the effect of time on peri-implant biological width formation remains to be determined. Finally, although a tendency for bone level preservation was reported among the patients of the thick mucosa group, no differences were noted regarding the survival rate or aesthetic and biological complications in the short follow-up period.

Further RCTs examining the impact of tissue thickness on early bone remodeling are needed to strengthen the existing evidence and to clarify the role of confounding variables. New studies that simultaneously evaluate the effect of tissue thickness and the apico-coronal implant placement, type of connection, or type of prosthetic retention are encouraged. New studies may propose thresholds of tissue thickness different from 2 mm and evaluate patients over a follow-up period longer than 1 year.

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Within the limitations of a low sample size and short follow-up duration, this report demonstrated that implant placement in sites with thin vertical soft tissue is followed by a greater degree of bone remodeling than placement in sites covered by thick tissues. The beneficial effect of thick vertical mucosa seems to persist for implants with different apico-coronal positioning, while it appears to be lost for PS implants.

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