The Significance of Surgically Modifying Soft Tissue Phenotype Around Fixed Dental Prostheses: An American Academy of Periodontology Best Evidence Review

Guo-Hao Lin, DDS, MS,* Donald A. Curtis, DMD,† Yvonne Kapila, DDS, PhD,* Diego Velasquez, DDS, MSD,‡ Joseph Y.K. Kan, DDS, MS,§ Peggy Tahir,‖ Gustavo Avila-Ortiz, DDS, MS, PhD,¶ Richard T. Kao, DDS, PhD.*#

* Department of Orofacial Sciences, School of Dentistry, University of California San Francisco, CA, USA

† Department of Preventive and Restorative Dental Sciences, School of Dentistry, University of California San Francisco, CA, USA

‡ Graduate Periodontics, Department of Periodontics & Oral Medicine, School of Dentistry, University of Michigan, Ann Arbor, MI, USA

§ Department of Restorative Dentistry, School of Dentistry, Loma Linda University, Loma Linda, CA, USA

‖ University of California San Francisco Library, CA, USA

¶ Department of Periodontics, College of Dentistry, University of Iowa, Iowa City, IA, USA

\# Private Practice, Cupertino, CA, USA

Corresponding author:

Guo-Hao Lin, DDS, MS
Assistant Clinical Professor
Department of Orofacial Sciences

University of California, San Francisco
707 Parnassus Ave
San Francisco, CA 94143
E-mail address: guo-hao.lin@ucsf.edu

Word count: 4,258

Tables and figures: 4 tables and 2 figures; 2 supplementary tables and 1 supplementary figure

Running title: Significance of soft tissue phenotype

Summary: Surgical modification of peri-implant soft tissue phenotype may decrease the amount of future recession around implant-supported prostheses.

Conflict of interest:
The authors have no conflicts of interest to declare in relation to the conduction of this systematic review.

Abstract

Aims: This systematic review endeavored to investigate the effect of soft tissue phenotype modification therapy (PhMT-s) at sites with a tooth or an implant supported fixed dental prosthesis.

Material and Methods: A comprehensive literature search was conducted by two independent examiners to identify relevant studies reporting differences in clinical, esthetic or radiographic outcomes of interest between sites underwent PhMT-s and sites that remained untreated. Risk of bias assessment was calculated for all included studies. Meta-analyses involving endpoints of interest were performed when feasible.

Results: No controlled studies pertaining to tooth sites were identified. A total of six articles reporting on the outcomes of buccal soft tissue phenotype modification around implants were selected, of which, five were included in the meta-analyses. Quantitative analyses showed a weighted mean difference (WMD) of 0.98 mm (95% CI = 0.25 to 1.72 mm, p = 0.009) for change of tissue thickness; a WMD of -4.87% (95% CI = -34.27 to 24.53%, p = 0.75) for bleeding on probing (BOP); a WMD of 0.36 mm (95% CI = 0.12 to 0.59 mm, p = 0.003) for mucosal recession (MR); a WMD of 0.13 mm (95% CI =

-0.11 to 0.36 mm, p= 0.30 for probing depth (PD); a WMD of 1.08 (95% CI = -0.39 to 2.55, p = 0.15) for pink esthetic score (PES), and a WMD of 0.40 mm (95% CI = -0.34 to 1.14 mm, p = 0.28) for marginal bone loss (MBL).

C**onclusions:** Surgical modification of peri-implant soft tissue phenotype via PhMT-s may decrease the amount of MR. Future clinical trials are needed to warrant the clinical benefits of modifying soft tissue phenotype around tooth-supported restorations.

Key Words: dental implants, dental implantation, esthetics, gingival recession, peri-implantitis, systematic review

Introduction

Phenotype can be defined as the "appearance of an organ based on a multifactorial combination of genetic traits and environmental factors."[1] The term "periodontal phenotype", which encompasses both the gingival phenotype (three-dimensional gingival volume) and the thickness of the buccal bone plate (dentoalveolar bone morphotype), was recently adopted by the specialty of Periodontics[1] to replace the largely misused term "biotype".[2] Historically, two main gingival phenotypes, thick-flat and thin-scalloped, have been widely employed to describe soft tissue appearance around teeth. Sites presenting a "thick-flat" phenotype are typically associated with squared tooth crown forms and wider contact areas between the teeth.[2] Additionally, the contact point is more apically positioned, often resulting in shorter interdental papillae. On the contrary, sites exhibiting a "thin-scalloped" phenotype normally present with tapered crown forms and shorter contact areas between the teeth. Since the contact point is usually located more coronally, the interdental papilla is often more volume.[2]

Unlike the dentate situation, the phenotypical categorization should be used with caution regarding implant sites due to wide variations resulting from site development procedures, implant placement, relative ridge positioning and restorative design.[3] While the relationship of the papilla to the restoration is changed,[4] much of the marginal inflammation and bone loss around peri-implant tissues may be related to the tissue phenotype.

The results of 2014 American Academy of Periodontology Regeneration Workshop provide us with a variety of strategies for phenotypic modification of thin to thick phenotype.[5] Decades of clinical experiences indicate that this is "best practice" strategy for preventing gingival recession and future loss of attachment.[5] Several methods have been proposed to categorize soft tissue phenotype around teeth and dental implants. Among all of them, visual assessment arguably the most popular method, due to its simplicity and non-invasiveness.[6] This method defines a thin periodontal phenotype if the outline of the probe can be visualized through the marginal soft tissue and a thick phenotype if the outline of the probe cannot be seen. This classification for determining thin versus thick phenotype has been widely used[6-8] and is reported to be a reliable alternative to other measurement. Due to its subjective nature, it is difficult to have an objective standard for comparison among studies. Alternatively, other proposed methods include direct clinical,[9] radiographic[10] or ultrasonic measurements[11] which provide objective measures for research comparisons. With the probe transparency method, a recent study[7] has shown that the tissue thickness was consistently qualified as thin if the thickness was 0.6 mm or less, and thick if this value was ≥1.2 mm. For thickness between 0.7 mm and 1.2 mm, the frequency distributions showed a descending trend in thin phenotype and an ascending trend in thick phenotype.[7]

A thin periodontal phenotype may predispose the initiation and/or progression of recession defects.[12, 13] Olsson and Lindhe analyzed the characteristics of maxillary central incisors in a cohort of 113 subjects and showed that long-narrow teeth presented more buccal marginal tissue recession than those with a

short-wide tooth form.[14] In addition, a native thick tissue phenotype has been associated with more favorable clinical outcomes following corrective periodontal procedures, such as root coverage[15] and periodontal regeneration.[16] Similarly, evidence supports that thin buccal peri-implant soft tissues are associated with an increased risk of future mucosal recession.[17, 18] However, the decision of surgically modifying a thin to a thick phenotype using soft tissue grafting procedures (soft tissue phenotype modification therapy, PhMT-s) with the ultimate goal of achieving satisfactory long-term outcomes remains a controversial topic.[19] The aim of this systematic review was to investigate the effect of modifying a thin to a thick buccal soft tissue phenotype via PhMT-s around tooth- and implant-supported fixed prostheses in function of relevant clinical, esthetic and radiographic endpoints.

Materials and Methods

This systematic review adhered to the PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analyses) statement guidelines.[20]

Focused question

What is the effect of surgically modifying a thin to a thick buccal soft tissue phenotype via PhMT-s around tooth- and implant-supported fixed prostheses in function of relevant endpoints, e.g., change in clinical, radiographic, and esthetic parameters.

Population: Adult individuals presenting intraoral sites with fixed tooth- or implant-supported prostheses

Intervention: Surgical augmentation procedures (PhMT-s) to modify the buccal soft tissue phenotype after restoration

Comparison: No surgical augmentation procedures to modify the buccal soft tissue phenotype

Outcomes: Changes in clinical, radiographic or esthetic parameters with at least a 6-month follow-up

Article eligibility criteria

The included articles had to fulfill all the following criteria:

1) Randomized controlled trials (RCTs), non-randomized controlled trials, cohort studies, case-control studies, or case series
2) A minimum of 10 treatment sites per group
3) Report at least one of the aforementioned outcomes of interest
4) Published in English

Information sources and Literature search strategy

An electronic search of Ovid MEDLINE, EMBASE, Web of Science and Cochrane Central was conducted on October 23rd 2018 to identify relevant studies.

The search terms used for Ovid MEDLINE, where mh represented the Medical Subject Headings (MeSH), were: ("Gingival recession"[mh] OR "gingival recession"[all] OR "peri-implantitis"[mh] OR "periimplantitis"[all] OR "peri-implantitis"[all] OR "dental implants"[mh] OR "dental implants"[all] OR "esthetics, dental"[mh] OR "esthetics"[all] OR "papilla"[all] OR "complication"[all] OR "complications"[all]) AND ("dental"[all] or "dentistry"[all]) AND ("phenotype"[all] OR "biotype"[all])

The search terms used for EMBASE, where exp represented the explosion in the search strategy, were: ('gingiva disease'/exp OR 'gingiva disease' OR 'periimplantitis'/exp OR periimplantitis OR 'tooth implantation'/exp OR 'tooth implantation' OR 'dental procedure'/exp OR 'dental procedure' OR 'esthetics'/exp OR esthetics OR 'papilla'/exp OR papilla OR 'complication'/exp OR complication OR 'complications'/exp OR complications) AND ('dental'/exp OR dental OR 'dentistry'/exp OR dentistry) AND ('biotype'/exp OR biotype OR 'phenotype'/exp OR phenotype)

The search terms used for Web of Science were: (peri-implantitis or periimplantitis or "dental implants" or "gingival recession" or papilla or complication or complications or esthetics) AND (dental or dentistry) AND (biotype or phenotype)

The search terms used for Cochrane Central were a combination of different keywords, including peri-implantitis, biotype, phenotype, dental implants, etc.

A hand search was also carried out in dental and implant-related journals from January 2018 to October 2018, including *Journal of Periodontology, Journal of Clinical Periodontology, Clinical Implant Dentistry and Related Research, International Journal of Oral and Maxillofacial Implants, Clinical Oral Implants Research, Journal of Dental Research, Journal of Prosthetic Dentistry, International Journal of Prosthodontics, Journal of Oral Implantology, and International Journal of Periodontics and Restorative Dentistry*. Additionally, a hand search of the references in the included papers and review articles was conducted for relevant publications. For the search of grey literatures, Google Scholar was used to identify any articles not included in the aforementioned databases.

Literature selection

The initial screening of titles and abstracts was performed independently by two reviewers (GL and DC). Potential articles were examined in full-text after the initial screening and their eligibility for this review was confirmed after discussion. Agreement between the reviewers regarding study inclusion was calculated using kappa statistics.

Data extraction

Data pertaining the pre-established outcomes of interest were extracted from the included studies by two independent reviewers (GL and DC) for subsequent qualitative and quantitative analyses. Data

collected from each study included authors' names, year of publication, study design, sample size, demographic information of the participants (age, gender and smoking status), tooth/implant location, type of surgical approach, and follow-up period. Outcomes that were considered for the analyses included soft tissue dimensional changes, bleeding on probing (BOP), plaque index (PI), papillary fill index,[21] keratinized tissue width (KTW), mid-buccal recession (MR), probing depth (PD), pink esthetic score (PES),[22] and marginal bone level (MBL). Corresponding authors of reviewed citations were contacted if further clarification regarding study methods and/or a more detailed data were needed.

Risk of bias assessment

The Randomized Clinical Trial Checklist of the Cochrane Center[23] criteria were applied to evaluate the following methodological aspects of included RCTs: random sequence generation, allocation concealment method, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data addressed, selective reporting and other bias (Table 1). The degree of bias was categorized as: low, high, or uncertain risk.[23] Meanwhile, the included non-RCTs were assessed using the Newcastle–Ottawa Scale (Table 2).[24] Each non-RCT study was evaluated and rated from a maximum of nine stars to a minimum of no stars. Two reviewers (GL and DC) assessed all the included articles independently.

Data synthesis

The primary outcome was the difference in the recorded parameters when comparing the sites with and without soft tissue grafting procedures to modify the tissue phenotype. For each parameter, the pooled weighted mean difference (WMD) between the grafted and non-grafted sites was estimated with

computer software.[**] The contribution of each article was weighed based on sample size. Forest plots were produced to graphically represent outcome differences between the grafted and non-grafted groups using the number of sites as the unit of analysis. In addition, funnel plots (see supplementary Figures 1A to 1F in online *Journal of Periodontology*) were generated to assess the presence of publication bias. A p value = 0.05 was used as the level of significance. Heterogeneity was assessed with a chi-square test and I^2 test, which ranges between 0% and 100% with lower values indicating less heterogeneity. Random-effects meta-analyses of the selected studies were applied if the I^2 test showed a value of more than 50%; fixed-effects meta-analyses were applied if the I^2 test presented a value less than 50%.

Results

The screening process is shown in Figure 1. Electronic and hand searches yielded 1,831 entries. After screening titles and abstracts, 32 articles were selected for full-text evaluation. Twenty-six articles were further excluded from the qualitative and quantitative analyses;[9, 25-49] the reasons for exclusion are listed in Table 3. After full-text review, no literature regarding tooth-supported prostheses was identified. Therefore, this specific aim could not be assessed due to lack of evidence. For implant-supported prostheses, six articles[50-55] were included for qualitative/quantitative analyses. The kappa value for inter-reviewer agreement was 0.91 for identified titles and abstracts and 0.92 for full-text articles, indicating an "almost perfect" agreement between the two reviewers.[56] The main features and conclusions of the included studies were summarized in Table 4. The features and outcomes of the studies that included a secondary outcome analysis of tissue phenotype are displayed in supplementary Table 1 (around implants)[3, 37-40, 43, 57-75] and supplementary Table 2 (around teeth)[48, 76] in online *Journal of Periodontology* where the influence of phenotype on clinical outcomes is identified.

[**] Review Manager (RevMan). Version 5.0. Copenhagen; The Nordic Cochrane Centre, The Cochrane Collaboration, 2008

Features of the included studies (implant-supported restorations)

Study design and participant features

Four RCTs,[52-55] 1 cohort study,[51] and 1 case-control study[50] were included. The age of the participants ranged from nineteen[55] to eighty-seven[54] years of age. Three studies[53-55] excluded smokers from participating their studies. All included studies had one study arm using subepithelial connective tissue graft (SCTG) for PhMT-s to thicken the buccal soft tissue phenotype and another study arm without using SCTG to serve as a control.

Assessment method of tissue volumetric change

In terms of the methods to measure the phenotype change, one article[50] used stereolithographic files to assess the volumetric change digitally. Two studies[54, 55] determined the phenotype based on the transparency of a periodontal probe. Another two studies[52, 53] used endodontic reamers to assess the volumetric change. One article[51] did not specify the method of assessing phenotype.

Anatomic location of study sites

In four of the six included studies,[50, 52, 54, 55] all fixtures were placed in either the anterior or premolar regions of the maxillary arch. One study reported placement of the implant fixtures only in the premolar or molar sites of the maxillary or mandibular arch. [53] One study did not specify the implant location.[51]

Bone grafts and membranes

In addition to SCTG procedure, xenogeneic bone grafting materials and collagen membranes were used in 1 study[51] in which buccal augmentation via guided bone regeneration (GBR) was applied. The other studies did not perform GBR procedures in the study sites.

Immediate implant placement and provisionalization (IIPP)

In addition to SCTG procedure, IIPP protocol was used in two studies.[54, 55] One study[54] used xenogeneic graft material to fill the gap between the implant and buccal plate, while another study[55] used a combination of autogenous and xenogeneic graft to fill the gap.

Results of meta-analyses (implant-supported restorations)

The meta-analysis conducted in the current study only included cohort studies and RCTs with data comparing the clinical parameters between groups with and without SCTG. One case-control study[50] was excluded from the meta-analyses since the study performed soft tissue grafting procedures only in sites with a volume deficit on the buccal aspect of the implants, and therefore posed a risk of bias in baseline conditions between the grafted and non-grafted groups. The information of this case-control study is still shown in Table 4 for further reference.

Two RCTs[52, 53] evaluated change in tissue thickness. The results presented a WMD of 0.98 mm (95% CI = 0.25 to 1.72 mm, p = 0.009, Figure 2A), favoring the SCTG group. The comparison presented a high heterogeneity between the pooled studies (I^2 = 80%).

Two articles[51, 52] evaluated BOP reduction. The results indicated a WMD of -4.87% (95% CI = -34.27 to 24.53%, p = 0.75). No statistical significance was found (Figure 2B) between groups. The comparison presented a high heterogeneity between the pooled studies (I^2 = 77%).

Three articles[51, 54, 55] evaluated MR. The results indicated a WMD of 0.36mm (95% CI = 0.12 to 0.59 mm, p = 0.003). A statistically significant difference was detected (Figure 2C), favoring the SCTG group. There was a low (I^2 = 31%) heterogeneity among compared studies.

Regarding PD reduction, three articles[51, 52, 55] were analyzed. The results indicated a WMD of 0.13 mm (95% CI = -0.11 to 0.36 mm, p = 0.30). No statistical significance was found (Figure 2D) between groups. The comparison presented a low heterogeneity among the pooled studies (I^2 = 0%).

In terms of PES, three studies[52, 53, 55] were analyzed. The results indicated a WMD of 1.08 (95% CI = -0.39 to 2.55, p = 0.15). No statistical significance was found (Figure 2E) between groups. The comparison presented a high heterogeneity among the pooled studies (I^2 = 90%).

Four RCTs[52-55] were pooled to evaluate MBL. The results presented a WMD of 0.40 mm (95% CI = -0.34 to 1.14 mm, p = 0.28). No statistical significance was found (Figure 2F). The comparison presented a high heterogeneity (I^2 = 77%) among the studies.

Due to the lack of sufficient data, a meta-analysis could not be completed on PI, KTW and papillary index. One cohort study[51] reported the outcome of PI and did not detect a statistically significant difference between the grafted and non-grafted groups (p = 0.118). Only one study[52] reported the change of KTW after grafting and did not find a significant difference. One RCT[54] reported the outcome of papillary index and did not find a statistically significant difference between the grafted and non-grafted groups (p = 0.47 for mesial papilla and p= 0.35 for distal papilla, respectively). The findings for PI and papillary fill index were also reported in a case-control study,[50] where no difference in these parameters was identified between groups with and without SCTG.

Risk of bias assessment

The risk of bias evaluation for RCTs were summarized in Table 1. Of the 4 included RCTs, one study[55] was ranked low for risk of bias in every category. Two studies[52, 54] were considered to have a category

with an uncertain risk of bias. One study[53] was identified with an uncertain risk of bias in one area and a high risk of bias in a second category.

The risk of bias assessment for non-RCTs were summarized in Table 2. The two studies[50, 51] were scored 6 stars out of 9 stars according to the Newcastle–Ottawa Scale,[24] and therefore were determined to have a considerable risk of bias.

Discussion

The significance of KTW around teeth with restorations[77, 78] or dental implants[79] has been evaluated while the importance of soft tissue phenotype has not been widely analyzed. Therefore, the current review aimed to identify the potential benefit of modifying thin phenotype to thick phenotype through PhMT-s. From this review process, only two articles[48, 76] (see supplementary Table 2 in online *Journal of Periodontology*) were identified that contained secondary data analyses related to tooth-borne restorations. One in-vitro study[76] concluded that a thick gingival phenotype could prevent tissue color change caused by the materials. Another study[48] concluded that crowns with a thick gingival phenotype resulted in significantly less recession than those with a thin phenotype when using metal-ceramic crowns. Due to the scarcity of clinical trials, future studies are warranted to evaluate the clinical benefits of surgically augmenting a thin gingival phenotype to a thick phenotype around a tooth-borne restoration.

Several studies[11, 80, 81] have reported a positive correlation between the gingival phenotype and the buccal plate thickness. Therefore, when encountering a site with a thin gingival phenotype, clinicians should be aware of a possible thin underlying buccal plate for future implant placement. Interestingly, one study[3] reported that there was no significant correlation between the gingival phenotype before tooth extraction and the peri-implant tissue phenotype after implant placement. This lack of correlation

may result from several factors, including tissue remodeling processes, implant type, implant orientation/position, and possible grafting procedures.[3, 82] Clinicians are advised to consider soft tissue grafting procedures when an undesirable implant outcome is foreseen.[83]

PhMT-s has been widely used to successfully modify a thin tissue phenotype to a thick tissue phenotype around dental implants.[55, 84] Our study confirmed the efficacy of PhMT-s and found that approximately a 1 mm gain of tissue thickness can be expected from this approach based on the meta-analysis. Therefore, a gain of 1 mm tissue thickness should be considered an endpoint for PhMT-s utilizing SCTG aiming to thicken tissue phenotype. In a recent study,[52] it was reported that sites with SCTG gained 34.3% tissue thickness after two years of follow-up, whereas sites without SCTG lost 9.9% tissue thickness. In addition, when performing IIPP procedure, the use of SCTG procedure has been shown to result in a more favorable peri-implant tissue thickness than the one without SCTG procedure.[85] Therefore, performing soft tissue grafting procedures to change tissue phenotype seems to be an enduring and predictable approach.

Increasing the soft tissue thickness provides the advantages of decreasing the soft tissue discoloration and show-through when a patient has a thin tissue phenotype and the implant or abutment is visible through the tissue. The thickened tissue also provides the restorative dentist more tissue volume by which to develop more idealized crown contours, which has both esthetic and biologic advantages.[86-89] When the soft tissue phenotype is thin, ridge lapping is often necessary which limits access for cleaning and is not stable esthetically.[90] By thickening the patient's soft tissue phenotype, it is easier to avoid the ridge-lap of crown restorations and develop a crown emergence profile that is more esthetic and biologically stable to facilitate patient's oral hygiene and tissue health.

In terms of peri-implant parameters, our results did not detect a difference in BOP between the sites with and without PhMT-s, which is in agreement with previous studies.[54, 83] This indicates that BOP around implants depends on the health of the peri-implant tissue instead of the tissue phenotype. If the tissue presents healthy, BOP should not be a common finding on examination.[91] However, soft tissue grafting procedures have been widely performed as one of the treatment modalities to manage peri-implantitis.[72] With the modification of prosthetic designs, soft tissue grafting procedures have also been introduced to manage mal-positioned implant fixtures.[92] In addition, evidence supports that PhMT-s can increase KTW and further improve patient comfort and compliance during oral hygiene.[93] Therefore, the need for these procedures should be based on the health status of the peri-implant tissue and is determined on a case-by-case basis.

Results indicated a significantly less MR at sites with PhMT-s via SCTG than those without. Although the WMD was only 0.36 mm, two[51, 55] out of the three pooled studies reported a decrease in MR in the SCTG group. In contrast, the group without SCTG exhibited increased MR. This finding is consistent with other studies,[54, 61] and thus support the concept that modification of a thin to thick tissue phenotype by soft tissue augmentation could potentially reduce the amount of MR. With the use SCTG, creeping attachment may occur around natural teeth[94] or dental implants,[95] which could further reduce the amount of MR. Therefore, clinicians should consider developing a thick tissue phenotype through grafting procedures whenever possible if the site presents with a high risk of future recession.

Our review shows that there is no statistically significant difference in change of PD when comparing sites with SCTG to the ones without SCTG. Previously published studies[96, 97] have shown that the healing after SCTG procedure is mediated by a combination of epithelial down growth and connective tissue attachment. Therefore, the difference in change of PD between the sites with and without SCTG was expected to be minimal, and the utilization of SCTG procedure will not result in deeper PD.

There was no difference in papillary fill reported between groups having or not having soft tissue grafting procedures that were performed to thicken the phenotype.[50, 54] Although a recent study[26] reported that the phenotype may impact the heights and fill of interdental papilla by affecting papilla proportion and distances between the facial and palatal papilla, most studies[4, 98] showed that the papillary fill depends on the distance between the adjacent bone level and the contact point of the crowns. Currently there is insufficient evidence to support the rationale for modifying tissue phenotype to enhance papillary fill.

It remains controversial whether thickening the peri-implant phenotype could result in an improved PES.[53] Although some evidence[52, 53] suggested a potential benefit of improved esthetics, the meta-analysis did not detect a significant improvement in PES with SCTG procedure. Among the three studies[52, 53, 55] pooled in the meta-analysis, two studies[52, 53] reported a significant improvement in PES after thickening the tissue phenotype while a third study[55] reported no significant change in PES after surgically thickening the phenotype.

Based on the results of the meta-analysis, peri-implant sites, which are surgically modified to a thick soft tissue phenotype, do not exhibit a reduced amount of MBL compared to sites with a thin phenotype. This is consistent with several published reports.[53, 55] Whether a peri-implant site is with a thick or thin tissue phenotype, bone remodeling is an unavoidable process that occurs after tooth extraction;[99] therefore, other surgical modalities such as bone augmentation[52] should be considered if MBL is detected. Performing PhMT-s to thicken the peri-implant soft tissue phenotype may minimize but not prevent future bone loss.

Recent studies[53, 55] have also investigated the influence of PhMT-s to increase the amount of KTW utilizing soft tissue grafting procedures. A systematic review by Thoma et al.[83] concluded that PhMT may result in more favorable peri-implant tissue health such as a gain of KTW, an improvement of bleeding indices, and a higher marginal bone levels. Based on this review, higher bone level was noted in sites with apically positioned flap (APF) plus autogenous grafts versus all control treatments, including APF or vestibuloplasty procedure alone, APF with the use of collagen matrix, no treatment with or without residual keratinized tissue. Therefore, increasing soft tissue thickness and the amount of KTW via PhMT-s may be beneficial for providing more favorable peri-implant tissue health. In addition, despite a lack of strong evidence, PhMT-s should be considered to achieve a wide band of KTW around tooth-borne restorations with a subgingival margin to facilitate gingival health.[77, 78] Whenever a gain of KTW is needed, APF plus autogenous grafts is considered as the gold standard among all available treatment modalities.[83]

All the studies pertaining to peri-implant mucosa thickening included in this systematic review involved a PhMT-s using an autologous SCTG after delivering the final implant-supported restoration. Interestingly, a recently published RCT[100] investigated the effect on MBL of peri-implant soft tissue phenotype modification via CTG at the time of implant placement in a submerged approach (test), as compared to conventional implant placement (control). At implant uncovering, test sites presented less MBL compared to controls. However, this finding was only significant in sites with thin peri-implant soft tissue ($\leq$ 2.5 mm) at baseline, but not in sites that presented thick tissue (>2.5 mm). This study also concluded that interim soft tissue modification before crown delivery did not significantly increase KTW. Therefore, if the peri-implant soft tissue thickness is $\leq$ 2.5 mm at baseline, it may be beneficial to perform PhMT-s to thicken the tissue simultaneously with implant placement with the purpose of minimizing MBL.

The limitations of this systematic review include 1) only five papers with comparable data were identified and pooled in the meta-analyses; 2) relatively short follow-up period of the included articles was noted; 3) considerable risk of bias was identified in non-RCTs; 4) four out of six reported meta-analyses had a high heterogeneity; 5) large variations in the study designs, implant placement protocols, outcome assessment methods, and reported parameters. Therefore, clinicians should interpret the results of this study cautiously after considering all the aforementioned limitations.

Conclusions

On the basis of the evidence included in this systematic review, it was observed that surgical modification of peri-implant soft tissue phenotype (PhMT-s) may decrease the amount of MR (WMD = 0.36 mm based on the meta-analysis) around implants. However, it remains inconclusive whether thickening the peri-implant soft tissue positively influences PD, BOP and esthetic parameters, such as papillary fill and PES. In addition, clinical trials are needed to explore the effect of soft tissue phenotype modification around tooth-supported fixed dental prostheses.

Acknowledgements

The authors have no conflicts of interest to declare in relation to the conduction of this systematic review.

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Table 1: Risk assessment of publication bias for the included RCTs

Study	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data addressed	Selective reporting	Other bias
Migliorati et al. (2015)[52]	Low	Uncertain	Low	Low	Low	Low	Low
Wiesner et al. (2010)[53]	Low	Uncertain	Low	High	Low	Low	Low
Yoshino et al. (2014)[54]	Low	Low	Low	Uncertain	Low	Low	Low
Zuiderveld et al. (2018)[55]	Low	Low	Low	Low	Low	Low	Low

Table 2. Newcastle-Ottawa Quality Assessment Scale of included non-RCTs

	Selection	Comparability	Outcome
Bienz et al. (2017)[50]	★★★	★	★★
Fenner et al. (2016)[51]	★★	★	★★★

Table 3: Summary of the excluded articles

Reason for exclusion	Author (year)
No data on comparing groups with and without soft tissue grafting procedures	Aguirre-Zorzano et al. 2013[25] Ahmed et al. 2018[26] Akcali et al. 2017[27] An et al. 2009[28] Bhat et al. 2015[31] Cosyn et al. 2011[34] Cosyn et al. 2013[33] Kan et al. 2003[38] Kan et al. 2011[37] Kim et al. 2016[39] Nisapakultorn et al. 2010[40] Paniz et al. 2016[41] Patil et al. 2013[42] Ross et al. 2014[43] Spinato et al. 2012[46] Studer et al. 2000[47] Tao et al. 2014[48] Yilmaz et al. 2012[49]
No control group	Anderson et al. 2014[29] Batista et al. 2001[30] De Bruyckere et al. 2015[35] Hutton et al. 2018[9] Schneider et al. 2011[44] Speroni et al. 2010[45]
Inadequate data to be pooled in meta-analyses	Bianchi and Sanfilippo 2004[32] Jyothi et al. 2013[36]

Table 4: Summary of the articles analyzing the soft tissue outcomes between sites with and without soft tissue grafting procedures

Authors (year)	Design	Individuals		Implants				MBL (mm) (negative value=bone loss)		Tissue thickness (mm)		PI (%)/ BOP (%)		Papillary index		MR (mm) (negative value=recession)		KTW (mm)		PES		PD (mm)		Main conclusions
		N	Age (gender)	TN of T	CN of C	Follow-up months	Location	T	C	T	C	T	C	T	C	T	C	T	C	T	C	T	C	
Bienz et al. (2017) [50]	Case-control	18	27-76.6 11f 7m	8 GBR+SCTG	10 GBR	Average 60.5 53-152	all max ant or premolars	NA	NA	-0.50 (0.20)	-0.41 (0.41)	PI 10 (15); BOP 38 (26)	PI 14 (17); BOP 38 (29)	1.38 (1.04)	1.55 (0.70)	-0.47 (0.32)	-0.35 (0.30)	NA	NA	NA	NA	3.67 (0.79)	3.65 (1.38)	Implant sites with and without soft tissue grafting showed only minimal changes and stability of peri-implant parameters over 5 years.
Fenner et al. (2016) [51]	Cohort	28	27-82 13f 15m	14 SCTG	22	Average 86.4 63.6-111.6	?	NA	NA	NA	NA	PI 15 (32); BOP 56 (32)	PI 28 (28); BOP 46 (24)	NA	NA	0.03 (0.66)	-0.06 (0.47)	NA	NA	NA	NA	4.09 (0.96)	3.97 (1.07)	No statistically significant difference in the clinical parameters was observed between the sites with or without soft tissue grafting procedures.
Migliorati et al. (2015) [52]	RCT	48	22-70 25f 23m	24 SCTG	23	24	all max ant or premolars	-0.06 (0.09)	-0.17 (0.06)	0.40 (0.97)	-0.20 (0.70)	BOP 20 (30)	BOP 40 (40)	NA	NA	NA	NA	-0.4 (1.66)	-0.7 (1.57)	7.46 (0.83)	6.39 (0.99)	3.4 (0.5)	3.2 (0.5)	None of the clinical parameters showed statistically significant difference between groups except for PES. Sites that received SCTG

This is the th manuscript accepted for publication and has undergone full peer review but has not been through the pyediting, typesetting, pagination and proofreading process, which may lead to differenc between this version and the Version of Record. Please cite this article as doi: 10.1002/JPER.19-0310.

																								presented with more favorable PES than sites without SCTG.
Wiesner et al. (2010) [53]	RCT	10	25-60 7f 3m	10 SCTG	10	12	all premolars or molars	-1.14 (0.29)	-1.06 (0.41)	1.20 (0.63)	-0.15 (0.34)	NA	NA	NA	NA	NA	NA	NA	NA	11.32 (1.63)	8.45 (1.46)	NA	NA	Based on the outcomes of this split-mouth RCT, sites that received SCTG presented more favorable PES outcome when compared to sites without SCTG.
Yoshino et al. (2014) [54]	RCT	20	27-87 13f 7m	10 IIPP+SCTG	10 IIPP	12	all max ant or premolars	-0.01 (0.27)	-0.14 (0.53)	NA	NA	NA	NA	2.10 (1.02)	2.15 (0.75)	-0.25 (0.35)	-0.70 (0.48)	NA	NA	NA	NA	NA	NA	Subjects who underwent IIPP+SCTG experienced less facial gingival level change than those who did not receive a SCTG.
Zuiderveld et al. (2018) [55]	RCT	60	19.5-82.2 32f 28m	29 IIPP+SCTG	29 IIPP	12	all max ant or premolars	-0.03 (0.41)	-0.05 (0.40)	NA	NA	NA	NA	NA	NA	0.1 (0.8)	-0.5 (1.1)	NA	NA	6.4 (1.5)	6.8 (1.5)	2.55 (0.95)	2.68 (1.12)	IIPP+SCTG leads to less recession of the peri-implant soft tissue. No significant differences regarding other outcome variables were observed.

RCT: Randomized controlled trial; N: Number; T: Test group (with soft tissue grafting procedures); C: Control group (without soft tissue grafting procedures); f: females; m: males; max: Maxillary; mand: Mandibular; ant: Anterior teeth; MBL: Marginal bone loss; PI: Plaque index; BOP: Bleeding on probing; MR: Mucosal recession; KTW: Keratinized tissue width; PES: Pink esthetic score; PD: Probing depth; IIPP: Immediate implant placement and provisionalization; GBR: Guided bone regeneration; SCTG: Subepithelial connective tissue graft; NA: Not available; Data in parentheses represent standard deviation.

Supplementary Table 1: Summary of the articles analyzing the peri-implant soft tissue outcomes between thin and thick tissue phenotypes

Authors (year)	Design	Individuals		Implants				Tissue phenotype		MBL (mm) (negative value=bone loss)		PI (%)/ BOP (%)		Papillary fill (mm) (negative value=recession)		MR (mm) (negative value=recession)		Main conclusions
		N	Age (gender)	T N of T	C N of C	Follow-up months	Location	SCTG	Measurement method	Thick	Thin	Thick	Thin	Thick	Thin	Thick	Thin	
Bressan et al. (2011) [57]	CS	20	?	Abutment Gold: ? Titanium: ? Zirconium: ?	No	7	all max ant	No	Direct at second stage Thick: >2mm Thin: ≤2mm	NA	NA	NA	NA	NA	NA	NA	NA	The peri-implant soft tissue phenotype did not appear to be a crucial factor in the soft tissue color.
Cabello et al. (2013) [58]	CS	14	34-71 7f 7m	IIPP 14	No	12	all max ant	No	Direct, 5mm below FGM	NA	NA	NA	NA	Mesial: -0.38 (0.60) Distal: -0.80 (0.96)		-0.45 (0.25)		No correlation between gingival phenotype and marginal soft tissue levels was found.
Canullo & Rasperini (2007) [59]	CS	9	33-69 7f 2m	IIPP+platform switching 10	No	22	all max ant/ premolars	No	Probe transparency	0.78 (0.36)		BOP: 0	BOP: 0	Mesial: +0.4 (0.52) Distal: +0.1 (0.32)		+0.2 (0.42)		Peri-implant soft tissue phenotype did not seem to influence the final esthetics, clinical, or radiographic outcomes after IIP treatment.
Chen et al. (2007) [60]	RCT	30	45.2 (10.1) 20f 10m	T1: IIPP+BG 10 T2: IIP+BG+Memb 10	IIP 10	6	all max ant/ premolars	Yes, in 30 sites	?	T1: 0.4 (0.8); T2: -0.6 (1.8) C: -0.7 (1.4)		PI: 6.9% (16.7) after 3 years		NA	NA	-1 to -3 in 10 sites		Mucosal recession was significantly associated with buccally positioned implants but not tissue phenotype after IIP treatment.
Chen et al. (2009) [61]	CS	85	17.6-72.2 53f 32m	IIP+flapless+SCTG 49	IIP+flapless 36	12	all max ant	Yes, in 36 sites	Determined by the height of the keratinized mucosa	NA	NA	NA	NA	Mesial: -5.3 % (6.3) Distal: -6.1 % (6.8)	Mesial: -7.0 % (7.1) Distal: -8.5 % (7.9)	-4.3 % (6.6)	-4.9 % (7.0)	Recession was seen in a higher proportion of thin phenotype sites compared to thick phenotype sites.

Cordaro et al. (2009)[62]	RCT	30	18-70 ?	IIP (transmucoal) 16	IIP (submerged) 14	12	max or mandant/premolars	No	?	T: 0.26 (0.34); C: 0.46 (0.40)	No significant differences between T and C	NA	NA	≥2: 1 site	≥2: 3 sites	Implants placed in patients with a thin tissue phenotype showed more recession than implants placed in cases of a thick phenotype.

Supplementary Table 1: continued

Authors (year)	Design	Individuals		Implants				Tissue phenotype		MBL (mm) (negative value=bone loss)		PI (%)/ BOP (%)		Papillary fill		MR (mm) (negative value=recession)		Main conclusions
		N	Age (gender)	T N of T	C N of C	Follow-up months	Location	SCTG	Measurement method	Thick	Thin	Thick	Thin	Thick	Thin	Thick	Thin	
Cosyn et al. (2013)[63]	CS	104	22-80 61f 43m	T1: IIPP 28, T2: Implant +GBR 32	Standard placement 44	17-42	all max ant/ premolars	No	Probe transparency	1.34 (1.17)		BOP: 33% (20)		Incomplete papillary fill was more often in thin tissue phenotype.		NA	NA	A thin tissue phenotype (OR= 3.7) increased the risk for incomplete distal papillary fill.
De Marchi et al. (2012)[68]	CS	46	14-45 9f 37m	Standard placement 20	Tooth retouring with composite resin 26	Average 3.5-3.9 years	all max ant	No	?	NA	NA	No significant differences between T and C		NA	NA	With recession in T: 4 sites C: 2 sites	With recession in T: 10 sites C: 5 sites	The absence of gingival recession was associated with thick phenotype around implants. This association was only observed for T group but not C group.
Evans and Chen (2008)[64]	CS	42	47.9 (12.8) 25f 17m	IIP 42	No	18.9 (11)	max or mand ant/premolars	No	Probe transparency	Mesial: -1.7 (0.74) Distal: -1.7 (0.77)		NA	NA	Mesial: -0.5mm (0.52) Distal: -0.5mm (1.00)		-0.7 (0.57)	-1 (0.9)	Recession was observed at both thin and thick phenotype sites. However, recession at thin phenotype sites tended to be of a greater magnitude.
Ferrari et al. (2015)[3]	RCT	47	22-72 26f 21m	Abutment T1, Gold-hue titanium: 18 T2, Titanium: 15 T3, Zirconium: 14	No	24	?	No	Probe transparency	T1: -0.48 T2: -0.42 T3: -0.57		NA	NA	NA	NA	Recession seen at 13.4% of implant sites		No correlation between gingival phenotypes and marginal soft tissue levels was found. The peri-implant phenotype correspond

																ed with the periodontal phenotype only in 60.82% of implant sites.
Furhauser et al. (2017)[65]	CS	77	48.8 (16.1) 46f 31m	IIPP 77	No	60	all max ant/ premolars	No	Thick/flat vs. thin/scalloped	Optimum:76% Compromised:24% Poor:0%	NA	NA	Mesial: Optimum:77% Compromised:22% Poor:1% Distal: Optimum:83% Compromised:16% Poor:1%		-0.3 (1.0)	No association of gingival phenotype to pink esthetic scores could be established at any time point when performing IIP.

Supplementary Table 1: continued

Authors (year)	Design	Individuals		Implants				Tissue phenotype		MBL (mm) (negative value=bone loss)		PI (%)/ BOP (%)		Papillary fill		MR (mm) (negative value=recession)		Main conclusions
		N	Age (gender)	TN of T	CN of C	Follow-up months	Location	SCTG	Measurement method	Thick	Thin	Thick	Thin	Thick	Thin	Thick	Thin	
Guarnieri et al. (2016)[66]	CS	39	? 18f 21m	Standard placement 39	No	60	all max ant/ premolars	No	Probe transparency	NA	NA	8/39 with BOP, 10/39 with plaque		No significance between papilla score and tissue phenotype		4/18 sites with recession	15/21 sites with recession	No association between the peri-implant phenotype and the papilla score was found. The phenotype was significantly associated with facial marginal mucosal level.
Kan et al. (2003)[38]	CS	45	20-82 25f 20m	Standard placement 45	No	Average 32.5, 12-78	all max ant	No	Probe transparency	NA	NA	NA	NA	NA	NA	Improved peri-implant mucosal dimensions noted in the presence of the thick phenotype		For implants placed with a staged approach, improved peri-implant mucosal dimensions were noted in the presence of a thick peri-implant phenotype.
Kan et al. (2011)[37]	CS	35	18-65 ?	IIPP 35	No	96	all max ant	Yes, in 3 sites	Probe transparency	-0.68 (0.19)	-0.59 (0.22)	PI 0: 29 patients PI 1: 6 patients		Mesial: -0.27 mm (0.30) Distal: -0.21 mm (0.32)	Mesial: -0.18 mm (0.36) Distal: -0.21 mm (0.46)	-0.56 (0.46)	-1.50 (0.88)	The effect of soft tissue phenotype on peri-implant tissue stability seems to be limited to facial gingival recession and does not affect interproximal papilla or proximal marginal bone levels.
Van Kesteren et al.	RCT	28	28-76 ?	IIP 24	Standard placement	6	max or mand ant/premolars	No	?	NA	NA	NA	NA	T: -0.26mm (1.01) C: 0.21mm (0.69)		Mesial: -1.73 (0.71) Distal:		Tissue phenotype failed to show any

(2010)[73]					26											-1.48 (0.80)		significant relationship with the soft tissue changes identified.
Kim et al. (2016)[39]	CS	30	?	Abutment T1, Gold-hue titanium: 10 T2, Titanium: 10 T3, Zirconium: 10	No	NA	all max ant	No	Direct Thick: ≥2mm Thin: <2mm	NA	NA	NA	NA	NA	NA	NA	NA	There was no significant correlation between tissue phenotype and color change, but thick phenotype, demonstrated a smaller color difference. Zirconia abutment showed the least color difference compared to other materials.

Supplementary Table 1: continued

Authors (year)	Design	Individuals		Implants				Tissue phenotype		MBL (mm) (negative value=bone loss)		PI (%)/ BOP (%)		Papillary fill		MR (mm) (negative value=recession)		Main conclusions
		N	Age (gender)	TN of T	CN of C	Follow-up months	Location	SCTG	Measurement method	Thick	Thin	Thick	Thin	Thick	Thin	Thick	Thin	
Lops et al. (2017) [67]	CS	15	48 9f 6m	Abutment T1, Gold: 8 T2, Titanium: 7	No	NA	max or mandant/premolars	No	Direct Thick: >2mm Thin: ≤2mm	NA	NA	NA	NA	NA	NA	NA	NA	For peri-implant soft tissue of ≤2 mm, gold or zirconia abutments are recommended in anterior areas.
Nisapa-kultorn et al. (2010) [40]	CS	40	45.2 (13.9) 18f 22m	Standard placement 40	No	NA	all max ant	No	Probe transparency	NA	NA	With plaque: 27 No plaque: 13		<half fill: 8 ≥half fill: 66		<1mm: 14 ≥1mm: 26		A thin phenotype was the most significant factor in determining the facial marginal mucosal level (OR= 18.8). In contrast, the distance from the contact point to the bone crest was the only factor significantly associated with less papilla fill. The association between a thin phenotype and less papilla fill did not reach statistical significance (OR=4).
Petsos et al. (2017) [69]	CS	60	50.85 (16.1) 33f 27m	Standard placement 82	No	NA	all max ant	No	Probe transparency	NA	NA	NA	NA	NA	NA	NA	NA	Phenotype has not been demonstrated to be an objective parameter for the subjective perception of esthetics. However, thin phenotype was associated with a less pronounced distal papilla and with defects of the

																		alveolar ridge.
Romeo et al. (2008)[70]	CS	48	18-63 26f 22m	IIP 48	No	12	max or mand ant/premolars	No	Probe transparency	NA	NA	NA	NA	84% present	42.8% present	NA	NA	A thick tissue phenotype was statistically associated with papilla presence.
Ross et al. (2014)[43]	CS	47	18-81 28f 19m	IIPP 47	No	60	all max ant	No	Direct Thick: ≥2mm Thin: <1.5mm	NA	NA	NA	NA	NA	NA	-0.30		Implant diameter, soft tissue phenotype, and surgical technique can influence the amount of gingival recession occurring over 5 years. Recession was seen more in sites with thin phenotype and a wider diameter implant.

Supplementary Table 1: continued

Authors (year)	Design	Individuals		Implants				Tissue phenotype		MBL (mm) (negative value=bone loss)		PI (%)/ BOP (%)		Papillary fill		MR (mm) (negative value=recession)		Main conclusions
		N	Age (gender)	T N of T	C N of C	Follow-up months	Location	SCTG	Measurement method	Thick	Thin	Thick	Thin	Thick	Thin	Thick	Thin	
Siqueira et al. (2013)[71]	CS	18	19-72 8f 10m	Standard placement 82	No	60	max ant/ premolars	No	Direct Thick: ≥2.5mm Thin: <2.5mm	NA	NA	NA	NA	40% present	22.22% present	NA	NA	The presence of the interdental papilla was not influenced by phenotype but by the vertical distance between contact to the alveolar crest.
Stiller et al. (2015)[72]	Cohort	28	59.4 21f 7m	Standard placement 54	No	Average 63.24 (44.4)	max or mandant	Yes (free gingival graft)	Probe transparency	NA	NA	BOP: 23 sites before graft; 8 sites after graft		NA	NA	NA	NA	Soft tissue grafting to thicken tissue phenotype could potentially decrease pocket depth and BOP for implants with peri-implantitis.
Wallner et al. (2018)[75]	CS	41	18-76 28f 13m	Tissue level 20	Bone level 22	Average 58.8 for tissue level; 22.8 for bone level	all max ant	No	Probe transparency	Tissue level: -0.21 (0.43) Bone level: -0.03 (038)	Tissue level: -0.05 (0.47) Bone level: 0.09 (0.32)	NA	NA	NA	NA	NA	NA	Peri-implant bone loss did not show an association with implant design or peri-implant tissue phenotype.
Zhao et al. (2016)[74]	CS	45	18-56 20f 25m	Standard placement 45	No	Average 74.1, 61-96	all max ant	No	Probe transparency	1.10 (0.92)		PI: 0.62 (0.56) BI: 0.65 (0.58)		NA	NA	4 sites with recession	9 sites with recession	Mid-facial recession could cause unfavorable aesthetic outcomes and the incidence of recession at thin biotype sites tends to be higher than at thick biotype

																sites.

RCT: Randomized controlled trial; CS: Case series; N: Number; T: Test group; C: Control group; f: females; m: males; max: Maxillary; mand: Mandibular; ant: Anterior teeth; MBL: Marginal bone loss; PI: Plaque index; BOP: Bleeding on probing; MR: Mucosal recession; PD: Probing depth; IIP: Immediate implant placement; IIPP: Immediate implant placement and provisionalization; BG: Bone grafting procedure; Memb: Barrier membrane; GBR: Guided bone regeneration; SCTG: Subepithelial connective tissue graft; NA: Not available; Data in parentheses represent standard deviation.

Supplementary Table 2: Summary of the articles analyzing the gingival tissue outcomes between thin and thick tissue phenotypes

Authors (year)	Design	Individuals		Teeth				Tissue phenotype		MBL (mm)		PI (%)/ BOP (%)		Papillary fill		MR (mm) (negative value=recession)		Main conclusions
		N	Age (gender)	T N of T	C N of C	Follow-up months	Location	SCTG	Measurement method	Thick	Thin	Thick	Thin	Thick	Thin	Thick	Thin	
Jung et al. (2007)[76]	In vitro	10	NA	Crown/Abutment T1, Titanium; T2, Titanium with veneered ceramic; T3, Zirconium; T4, Zirconium with veneered ceramic	No	NA	NA	NA	In vitro 1.5mm 2mm 3mm	NA	NA	NA	NA	NA	NA	NA	NA	If a 3mm mucosal thickness is present, no change in color caused by the materials could be distinguished on any specimen. In patients with thinner mucosa, zirconia showed the least color change.
Tao et al. (2014)[48]	Cohort	100	20-70 57f 43m	Metal-ceramic crown; thick phenotype: 50	Metal-ceramic crown; thin phenotype: 50	Average 63 (1.8)	all maxillary anterior	No	Probe transparency	NA	NA	NA	NA	NA	NA	-0.31 (0.21)	-1.09 (0.22)	For metal-ceramic crowns, thick gingival phenotype presented significantly less recession than crowns with thin phenotype.

N: Number; T: Test group; C: Control group; f: females; m: males; max: Maxillary; ant: Anterior teeth; MBL: Marginal bone loss; PI: Plaque index; BOP: Bleeding on probing; MR: Mucosal recession; SCTG: Subepithelial connective tissue graft; NA: Not available; Data in parentheses represent standard deviation.

Figure Legends

Figure 1. Flow chart illustrating the publication selection process

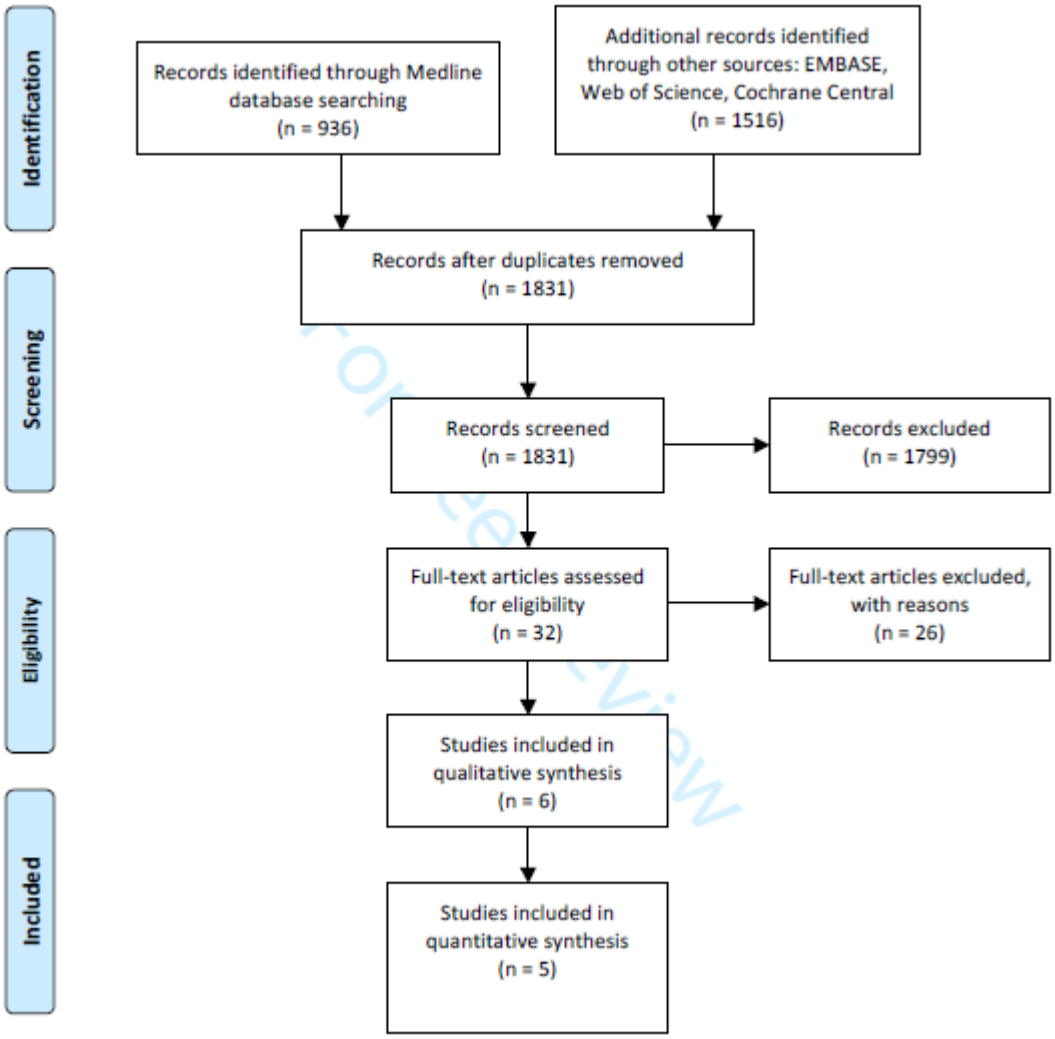


Figure 2A. The result of meta-analysis for the change of peri-implant tissue thickness presented a WMD of 0.98 mm (95% CI = 0.25 to 1.72 mm, p = 0.009), favoring the SCTG group. The comparison presented a high heterogeneity (I^2 = 80%).

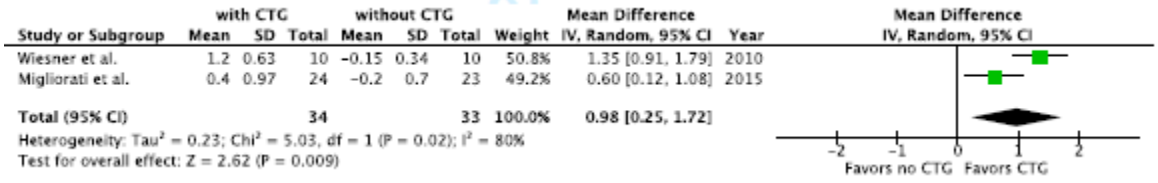


Figure 2B. The result of meta-analysis for BOP reduction at implant sites presented a WMD of -4.87% (95% CI = -34.27 to 24.53%, p = 0.75). No statistical significance was found. The comparison presented a high heterogeneity (I^2 = 77%).

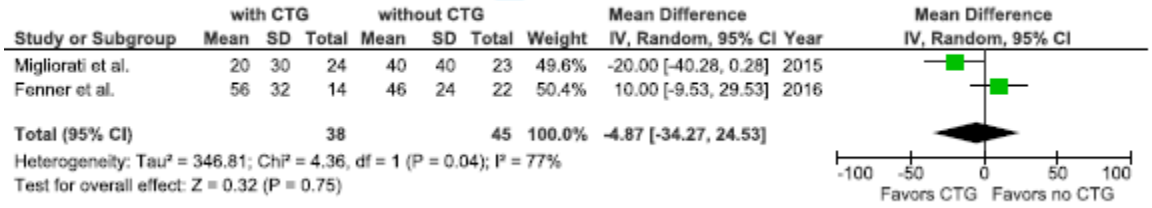


Figure 2C. The result of meta-analysis for MR at implant sites presented a WMD of 0.36 mm (95% CI = 0.12 to 0.59 mm, p = 0.003), favoring the SCTG group. The comparison presented a low heterogeneity (I^2 = 31%).

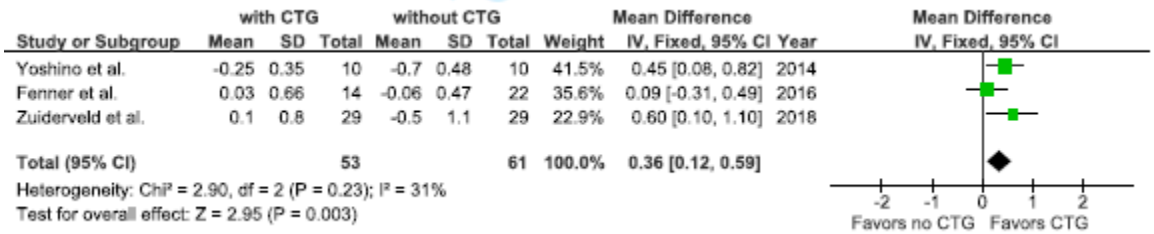


Figure 2D. The result of meta-analysis for PD reduction at implant sites presented a WMD of 0.13mm (95% CI = -0.11 to 0.36mm, p = 0.30). No statistical significance was found. The comparison presented a low heterogeneity (I^2 = 0%).

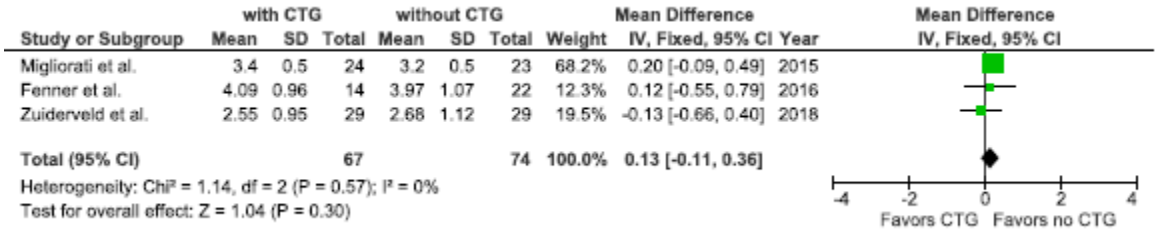


Figure 2E. The result of meta-analysis for PES at implant sites presented a WMD of 1.08 (95% CI = -0.39 to 2.55, p = 0.15). No statistical significance was found. The comparison presented a high heterogeneity (I^2 = 90%).

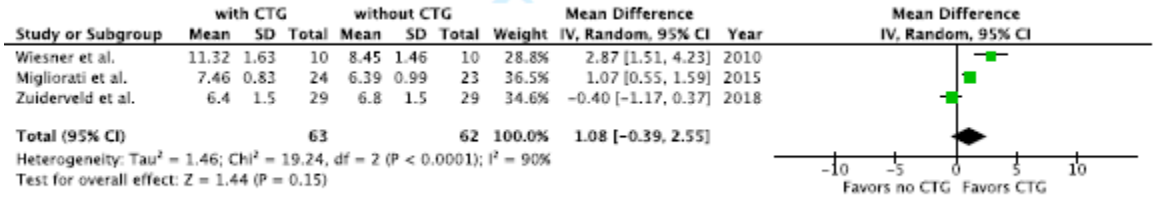
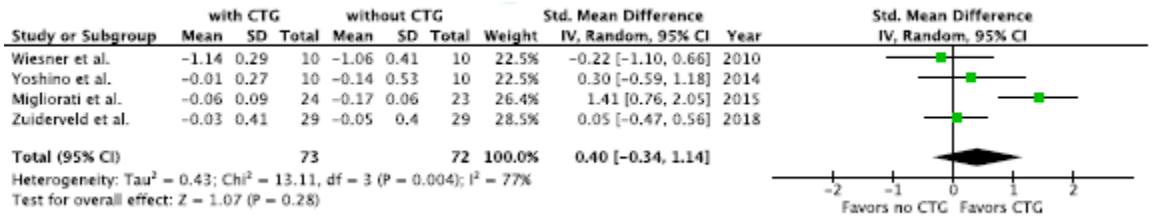


Figure 2F. The result of meta-analysis for MBL at implant sites presented a WMD of 0.40 mm (95% CI = -0.34 to 1.14 mm, p = 0.28). No statistical significance was found. The comparison presented a high heterogeneity (I^2 = 77%).



Supplementary Figure 1A. Funnel plot of the meta-analysis for the change of peri-implant tissue thickness.

Supplementary Figure 1B. Funnel plot of the meta-analysis for BOP reduction at implant sites.

Supplementary Figure 1C. Funnel plot of the meta-analysis for MR at implant sites.

Supplementary Figure 1D. Funnel plot of the meta-analysis for PD reduction at implant sites.

Supplementary Figure 1E. Funnel plot of the meta-analysis for PES at implant sites.

Supplementary Figure 1F. Funnel plot of the meta-analysis for MBL at implant sites.