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REVIEW ARTICLE

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Impact of timing on soft tissue augmentation during implant treatment: A systematic review and meta-analysis

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Abstract

Background: To achieve a predictable esthetic and functional outcome, soft tissue augmentation has become popular in implant treatment.

Objectives: The aim of this systematic review and meta-analysis was to assess the influence of different timing for soft tissue augmentation during implant treatment on soft tissue conditions and its stability.

Material and methods: Electronic and manual searches for articles written in English up to September 2017 were performed by two independent reviewers. Human clinical studies with the purpose of evaluating outcomes (at least 3-month follow-up) of autogenous soft tissue graft for augmentation during implant treatment, either simultaneous or after implant placement (staged), were included. Cumulative changes of keratinized tissue width (KTW), soft tissue thickness (STT), and mid-buccal mucosal recession (MR) data were analyzed with a random-effects model to compare the postoperative outcomes.

Results: Twenty-nine human studies (eight randomized clinical trials, six cohort studies, and 15 case series) that met the inclusion criteria were included. For the overall data, the weighted mean STT gain (1 year after surgery) was 1.03 mm (95% CI: 0.78–1.29 mm), among which the simultaneous group was 1.12 mm (95% CI: 0.75–1.49 mm) and staged group (3–6 months after implant placement) was 0.95 mm (95% CI: 0.58–1.31 mm). There was no statistically significant difference in KTW and MR between 3 months and more than 3 months after surgery.

Conclusions: This review revealed that the stability of soft tissue, in terms of KTW and mid-buccal MR, can be obtained 3 months after surgery. There is no difference between simultaneous and staged soft tissue augmentation during implant treatment, and both procedures significantly enhance KTW and STT.

KEYWORDS

dental implants, keratinized tissue, mucosal recession, soft tissue augmentation, soft tissue thickness, systematic review and meta-analysis

1 | INTRODUCTION

Dental implants are now widely used for missing teeth replacement. Today, most implantologists have shifted their focus from obtaining osseointegration to achieving a pleasing esthetic appearance. Hence, soft tissue augmentations around dental implants have slowly become an area of interest (Fu, Su, & Wang, 2012; Lin, Chan, & Wang, 2013; Thoma, Benić, Zwahlen, Hämmerle, & Jung, 2009; Thoma, Muhlemann, & Jung, 2014). When examining the soft tissue around the implant, keratinized tissue (KT) width (KTW) and soft

tissue thickness (STT) are the two most critical factors in esthetics, function, and long-term implant stability. In other words, a lack of KT around implants has been associated with higher plaque accumulation, inflammation, more mucosa recession, and a less esthetic appearance (Lin et al., 2013; Warrer, Buser, Lang, & Karring, 1995). Furthermore, STT has been regarded as a key protective feature in preventing metal color exposure and minimizing mucosal recession (MR) (Jung et al., 2008; Lops et al., 2016). Hence, it is often suggested to augment thin tissue biotype, especially in the highly esthetic areas (Rotundo, Pagliaro, Bendinelli, Esposito, & Buti, 2015; Thoma et al., 2009).

With respect to soft tissue augmentation surgery, different preferred materials and timings have been reported in various studies and reviews (Bassetti, Stähli, Bassetti, & Sculean, 2016; Esposito, Maghaireh, Grusovin, Ziounas, & Worthington, 2012; Fu et al., 2012; Lin et al., 2013; Rotundo et al., 2015; Thoma, Buranawat, Hammerle, Held, & Jung, 2014; Thoma et al., 2009; Thoma, Muhlemann et al., 2014 Wu et al., 2015). Over the years, autogenous soft tissue graft has been regarded as a gold standard for peri-implant soft tissue augmentation, although some have claimed that a new xenogenic collagen matrix might achieve comparable outcomes (Cairo et al., 2017; Zeltner, Jung, Hammerle, Husler, & Thoma, 2017). Aside from material of the graft, soft tissue augmentation surgeries can also be performed at different time points during implant treatment. In one review, the various time points were used that included prior to implant placement, during the phase of tissue integration, or after final restoration. However, 4–6 weeks before abutment connection was regarded as an optimal time point for this procedure. On the contrary, soft tissue augmentation after final restoration could be less predictable because of highly required skills (Thoma, Buranawat, et al., 2014; Thoma, Muhlemann et al., 2014). Currently, there is still no consensus in literature with regard to the effectiveness of timing upon soft tissue augmentation outcome. Furthermore, no study has compared a short- (<3 month) vs. long-term (≥3 months) STT gain after soft tissue augmentation.

Therefore, the purpose of this systematic review and meta-analysis was to examine the effect of timing on soft tissue augmentation outcome (e.g., KTW, STT, and MR) during implant treatment and to assess the soft tissue conditions as well as its stability overtime.

2 | MATERIAL AND METHODS

This systematic review and meta-analysis were written and conducted following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement (Moher, Liberati, Tetzlaff, Altman, & Group P, 2009) (Appendix S1).

2.1 | Focused question

Based on Population, Intervention, Comparison, and Outcome (PICO) criteria (Stone, 2002), the question for the present literature search was addressed as follows:

P: patients received dental implant placement in partial edentulous sites,

I: autogenous soft tissue graft (either free gingiva graft [FGG] or connective tissue graft [CTG]) was performed to improve the peri-implant soft tissue conditions,

C: perform soft tissue grafting at different time points during implant treatment, either simultaneously or after implant surgery (staged), and

O: improve the keratinized tissue width (KTW), STT and minimize mid-buccal MR.

Therefore, the focused question for this review is "Does the timing of soft tissue grafting during implant therapy have an impact on the outcomes of peri-implant soft tissue conditions?"

2.2 | Selection criteria

Eligible studies were included if they met the following criteria: (i) any human studies (prospective or retrospective, randomized or not, cohort or case series trials); (ii) dental implants should be located in single or partial edentulous areas; (iii) soft tissue augmentation/correction should be performed during or after implant placement; (iv) at least 3-month follow-up period after soft tissue augmentation; (v) autogenous soft tissue graft used for soft tissue augmentation/correction; (vi) data of KTW and/or STT and/or MR available; and (vii) full text in English.

2.3 | Search strategy

Electronic searches were performed in three databases—MEDLINE, EMBASE, and Cochrane Central—for articles written in English up to September 30, 2017. The search terms comprised the combination of key words were as follows:((immediate implant [Title/Abstract]) OR (immediate implant placement [Title/Abstract]) OR (early implant [Title/Abstract])) AND ((soft tissue graft [Title/Abstract]) OR (subepithelial connective tissue graft [Title/Abstract]) OR (connective tissue [Title/Abstract]) OR (FGG [Title/Abstract]) OR (gingival autograft [Title/Abstract]) OR (soft tissue augmentation [Title/Abstract]) OR (soft tissue transplantation [Title/Abstract]) OR (soft tissue defect [Title/Abstract]) OR (soft tissue correction [Title/Abstract])) AND ((re-entry [Title/Abstract]) OR (re-entry [Title/Abstract]) OR (second stage[Title/Abstract]) OR (second stage[Title/Abstract]) OR (stage two surgery[Title/Abstract])) AND ((attached gingiva[Title/Abstract]) OR (buccal STT [Title/Abstract]) OR (keratinized mucosa [Title/Abstract]) OR (soft tissue margin[Title/Abstract]) OR (attached mucosa [Title/Abstract]) OR (esthetic [Title/Abstract])).

In addition, a manual search of relevant articles was performed in the following journals: *Journal of Clinical Periodontology*, *Journal of Periodontology*, *International Journal of Oral & Maxillofacial Implants*, *Journal of Oral and Maxillofacial Surgery*, *Clinical Oral Implants Research*, *Journal of Oral Rehabilitation*, *Clinical Implant Dentistry and Related Research*, *International Journal of Periodontics* and *International of Periodontics and Restorative Dentistry*, *Implant*

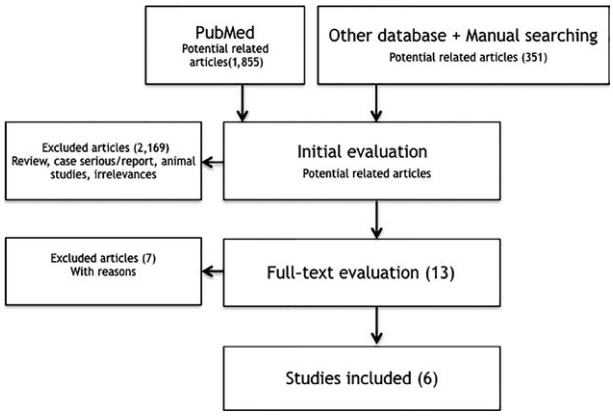

FIGURE 1 The articles selection process

Dentistry, *International Journal of Prosthodontics*, *International Journal of Oral and Maxillofacial Surgery*, *Journal of Oral Implantology*, and *European Journal of Oral Implantology*.

The screening process was conducted by two independent reviewers (CL and ZC) (Figure 1). According to selection criteria, titles and abstracts of search results were screened, and then potential articles were evaluated in full text. In the presence of duplicate publications, only the study with the most inclusive data was selected. The level of agreement between the reviewers regarding study inclusion was evaluated by κ value. If there was a disagreement, a decision would determine by further discussion and consultation by another reviewer (HLW).

2.4 | Risk of bias assessment

The quality assessment of included randomized controlled trials (RCTs) was conducted using the Cochrane collaboration's tool for assessing risk of bias. All selected RCTs were assessed by the RCT checklist, including random sequence generation, allocation concealment, blinding of outcome assessment, incomplete outcome data, selected reporting, and other bias (Higgins et al., 2011). If all criteria were met, degrees of bias were categorized as low risk. Those missing criteria were considered as moderate risk, and those missing more than two criteria were ranked as high risk. At the same time, the included cohort study was assessed by Newcastle–Ottawa scale, and each article was rated from 0 to 8 stars for each parameter in the scale (Department of Epidemiology and Community Medicine, 2013).

2.5 | Data extraction and statistical analyses

The data from the eligible articles were extracted by two reviewers (CL and ZC) independently. Any inter-reviewer disagreement was resolved by discussion and consultation with another reviewer (HLW). Corresponding authors of studies were contacted in cases of unclear or missing data.

All statistical analyses were conducted using one statistical software program (Stata software, v14.0; StataCorp, College Station, TX, USA). For the overall studies, the cumulative mean changes of KTW and STT were calculated by the random-effects model to avoid potential bias induced by methodological differences. Regarding the change in KTW, we conducted analyses based upon baseline KTW (<2 mm or ≥2 mm). The change in STT was calculated in simultaneous and staged group, respectively. Data of KTW and MR were analyzed with a random-effects model to compare the postoperative 3-month outcome with that of more than 3 months. Heterogeneity was estimated by the Q statistic (significant at $p < .10$) and quantified with the I^2 test. The value of $I^2 > 75\%$ suggests high heterogeneity (Higgins & Thompson, 2002).

The possibility of publication bias was assessed with Egger funnel plots for continuous data elements (Figure S1). A significant publication bias was considered if $p < .05$. However, results of these tests were not separately reported as this method is considered unreliable when studies included in the meta-analysis are <10.

3 | RESULTS

3.1 | Study selection

The screening process is shown in Figure 1. Using electronic and manual searching in PubMed and other database, 1,855 and 351 potential related articles were selected respectively. After initial evaluation, 2,169 studies that were assessed as reviews, and animal studies or irrelevant articles were excluded. Thirty-nine articles had been through full-text evaluation, and 10 of them were excluded with reasons (Table 1). At last, there were 20 studies included for further assessment in this systemic review. In addition, the k value for inter-reviewer agreement was 0.97 between the two reviewers.

3.2 | Description of studies

Main features of the included studies were summarized with details in Table 2(a–e). To emphasize timing of soft tissue graft augmentation during implant treatment, all included articles were sorted into five groups: (i) simultaneous soft tissue graft + immediate implant (SI group) (Table 2a); (ii) simultaneous soft tissue graft + nonimmediate implant (SN group) (Table 2b); (iii) staged soft tissue graft + immediate implant (StI group) (Table 2c); (iv) staged soft tissue graft + nonimmediate implant (StN group) (Table 2d); (v) staged soft tissue graft after final prosthesis loading (StP group) (Table 2e). Among all groups with staged soft tissue graft, soft tissue augmentation could be performed 1.5–6 months after implant placement, and the time points of intervention could also be found either prior, during stage 2 surgery, or after implant restoration.

In SI group, eight articles (Bianchi & Sanfilippo, 2004; Chung, Rungcharassaeng, Kan, Roe, & Lozada, 2011; Covani et al., 2007; Kan, Rungcharassaeng, Morimoto, & Lozada, 2009; Lee et al., 2012; Migliorati, Amorfini, Signori, Biavati, & Benedicenti, 2015; Tsuda et al., 2011; Zuiderveld, Meijer, Hartog, Vissink, & Raghoebar, 2018) were included. In general, CTG was mostly harvested from palate; however, other locations such as tuberosity or edentulous ridge

TABLE 1 Excluded articles with reasons

Author (year)	Excluded articles with reasons
Kablan and Laster (2014)	Soft tissue they used is "free fat tissue" from buccal fat pad. No data of soft tissue conditions.
Deeb, Kain, Wilson, and Laskin (2016)	Insufficient sample size. No data of soft tissue conditions.
Stimmelmayr, Allen, Reichert, and Iglhaut (2010) and Stimmelmayr, Stangl, Edelhoff, and Beuer (2011)	No data of soft tissue conditions
Grunder (2011)	
Rungcharassaeng et al. (2012)	
da Rosa, Rosa, Fadanelli, and Sotto-Maior (2014)	
Kolerman et al. (2016)	
Hanser and Khoury (2016)	
Bienz et al. (2017)	
Redemagni, Cremonesi, Garlini, and Maiorana (2009)	Incomplete data of soft tissue conditions
Schneider, Grunder, Ender, Hämmerle, and Jung (2011)	
Tunkel, de Stavola, and Khoury (2013)	
Sanz-Martín, Sailer, Hämmerle, and Thoma (2016)	Soft tissue placement in pontic sites without implants.
Herford, Cooper, Maiorana, and Cicciù (2011)	No free soft tissue graft was performed. (They used connective tissue flap instead.)
El Chaar et al. (2017)	No free soft tissue graft was performed. (They used modified palatal pedicle connective tissue flap instead.)
Park and Wang (2012)	No free soft tissue graft was performed. (The article focused on modified roll technique.)
Raghoebar, Slater, Hartog, Meijer, and Vissink (2009)	Soft tissue augmentation before implant placement or simultaneous during ridge preservation procedure.
Karaca, Er, Gülşahı, and Köseoğlu (2015)	

were also considered in one article (Bianchi & Sanfilippo, 2004). In all articles except one, envelope flap without vertical releasing lines was performed and involved guided bone regeneration (GBR) (Lee et al., 2012). Even though full mouth tooth sites were able to be chosen (Bianchi & Sanfilippo, 2004), the majority of implant sites were located at upper dentition, including esthetic priority areas (maxillary premolar to premolar). On the other hand, only two studies (D'Elia et al., 2017; Wiesner, Esposito, Worthington, & Schlee, 2010) were associated with nonimmediate implant and soft tissue graft at the same time in SNI group. Unlike tunnel technique for minimal-invasive considerations, one study placed soft tissue graft with concomitant GBR procedure, and access flap was performed (D'Elia et al., 2017). In StI and StN groups, soft tissue augmentation can be performed from 1.5 to 6 months after implant placement or at the uncovered stage, and there was only one article included from the StI group (Cosyn, Bruyn, & Cleymaet, 2013). With respect to multiple implant sites, apically positioned flap (APF) combined with FGG was applied in two articles, and vestibuloplasty was also performed in extensive mandibular areas (Schmitt et al., 2013, 2016). In StP group, soft tissue augmentation was one of the treatment options after implant-supported prosthesis loading, and four articles (Lorenzo, Garcıa, Orsini, Martin, & Sanz, 2012; Roccuzzo, Gaudioso, Bunino, & Dalmasso, 2014; Sanz, Lorenzo, Aranda, Martin, & Orsini, 2009; Zucchelli et al., 2013) were included. Only single implant situations could be dealt with soft tissue augmentation in all studies in this group, and three (Lorenzo et al., 2012; Sanz et al., 2009; Zucchelli et al., 2013) of them used APF with CTG. Yet, Roccuzzo et al. harvested de-epithelized CTG from tuberosity as the graft material. Particularly, split-thickness envelope flap was used to repair peri-implant MR (Roccuzzo et al., 2014).

3.3 | Differences in measurement methods

As for measurement methods, different systems were used for soft tissue assessment (STT; Table 3). In the view of STT, most articles performed measurement with endodontic file with stopper, which would be fixed and transformed to numbers by periodontal probe or caliper (D'Elia et al., 2017; Wiesner et al., 2010; Zucchelli et al., 2013). There was one exception where the study used an ultrasonic device (De Bruyckere, Eghbali, Younes, De Bruyn, & Cosyn, 2015). In addition, the soft tissue change was measured by means of superimposed digital models, and the data obtained from linear deviation only represented the contour change rather than pure soft tissue gain (Zeltner et al., 2017). To measure KTW, one study determined the location of MGJ using the staining method (Zucchelli et al., 2013) and the others performed the measurement using a periodontal probe directly (Covani et al., 2007; D'Elia et al., 2017; Lee et al., 2012; Lorenzo et al., 2012; Migliorati et al., 2015; Sanz et al., 2009; Schmitt et al., 2013, 2016; Zucchelli et al., 2013). The measurement methods varied in MR assessment: three articles used casts with a customized stent (Chung et al., 2011; Cosyn et al., 2013; Tsuda et al., 2011); three studies utilized photographic images of surgical sites or casts (Lee et al., 2012; Migliorati et al., 2015; Zuiderveld et al., 2018); two papers just measured with periodontal probes or calipers straight away (Lorenzo et al., 2012; Roccuzzo et al., 2014); and two studies followed the reference line of collateral or adjacent tooth to conduct the measurement (Bianchi & Sanfilippo, 2004; Zucchelli et al., 2013).

3.4 | Risk of bias

Among all related articles, there were eight RCTs, one controlled clinical trial, four cohort studies, and seven case series. The risk of

TABLE 2 Included articles divided into different groups with general information and clinical outcomes in keratinized tissue width (KTW), soft tissue thickness (STT), and mid-buccal mucosal recession (MR) (mm). (a) Simultaneous soft tissue graft + immediate implant (SI group); (b) simultaneous soft tissue graft + nonimmediate implant (SN group); (c) staged soft tissue graft + immediate implant (StI group); (d) staged soft tissue graft + nonimmediate implant (StN group); (e) staged soft tissue graft after final prosthesis loading + nonimmediate implant (StP group)

(a) SI group

Simultaneous soft tissue graft + immediate implant

Authors (Order)	Study type	SCTG donor site	Number (test/control)	Technique	Recipient Location
Bianchi and Sanfilippo (2004)	RCT	P, T, E	116/20	Envelope	Full mouth
Covani et al. (2007)	CRS	P	10	No flap	Upper Pr-Pr
Kan et al. (2009)	CRS	P	20	Bilaminar envelope	Upper C-C
Chung et al. (2011)	CRS	P	10	Envelope	C–C+Pr
Tsuda et al. (2011)	CRS	P	10/28	Envelope	Upper Pr-Pr
Lee et al. (2012)	CRS	P	11	Flapped	Upper L-L
Migliorati et al. (2015)	RCT	P	24/23	No flap	Upper Pr-Pr
Zuiderveld et al. (2018)	RCT	T	29/29	Envelope	Upper Pr-Pr

(b) SN group

Simultaneous soft tissue graft + nonimmediate implant

Authors	Study type	SCTG donor site	Number (test/control)	Technique	Location
Wiesner et al. (2010)	CCT	P	10/10	Open flap	Posterior mandible
D'Elia et al. (2017)	RCT	P	16/16	Access flap	Upper Pr-Pr

(c) StI group

Staged soft tissue graft + Immediate implant

Authors	Study type	Donor site	Numbers (test/control)	Technique	Location
Cosyn et al. (2013)	CRS	P	22→21→20	Envelope (pouch)	Upper Pr-Pr

(d) StN group

Staged soft tissue graft + nonimmediate implant

Authors	Study type	Donor site	Numbers (test/control)	Technique	Location
Schmitt et al. (2013)	CRS	P (FGG)	7/7	APF+ vest	Mandible (Multiple)
De Bruyckere et al. (2015)	CRS	P	37	Envelope	Upper Pr-Pr
Schmitt et al. (2016)	CRS	P (FGG)	21	APF+ vest	Mandible (Multiple)
Zeltner et al. (2017)	RCT	P	10	Pouch	Upper Pr-Pr

(e) StP group

Staged soft tissue graft (after final prosthesis loading) + nonimmediate implant

Authors	Study type	Donor site	Numbers (test/control)	Technique	Location
Sanz et al. (2009)	RCT	Palate	12	APF	Full mouth
Lorenzo et al. (2012)	RCT	Palate	12	APF	Mandible
Zucchelli et al. (2013)	CRS	Palate	10	APF	Maxilla
Roccuzzo et al. (2014)	Case reports	De-epithelialized tuberosity	6	Envelope (split-thickness)	Maxilla (Single)

APF, apically positioned flap; RCT, randomized clinical trial; CCT, controlled clinical trial; CRS, case report/series; SCTG, subepithelial connective tissue graft; FGG, free gingival graft; P, palate; T, tuberosity; E, edentulous; Pr, premolar; C, canine; L, lateral; NR, not reported; SD, significant difference; F/U, follow-up.

KTW (Mean [SD])			STT (Mean [SD])			MR (Mean [SD])	
Baseline	3 month	>3 month	Baseline	3 month	>3 month	3 month	>3 month
NR	2 (No SD)	NR	NR	NR	NR	1 (No SD)	1 (No SD)
1.3 (0.6)	NR	4.1 (0.5)	NR	NR	NR	NR	NR
NR	NR	NR	NR	NR	NR	NR	0.13 (0.61)
NR	NR	NR	NR	NR	NR	3.89 (1.1)	3.72 (1.03)
NR	NR	NR	NR	NR	NR	2.3 (1)	2.25 (1.21)
1.1 (0.4)	3.7 (0.7)	3.6 (0.5)	NR	NR	NR	2.1 (0.7)	1.7 (0.7)
3.3 (1.2)	3.1 (1.2)	3 (1.2)	1.1 (0.6)	2.3 (0.8)	1.8 (0.8)	0.42 (0.5)	0.73 (0.51)
NR	NR	NR	NR	NR	NR	0.1 (0.9)	0 (0.3)

KTW (Mean [SD])			STT (Mean [SD])			MR (Mean [SD])	
Baseline	3 month	1–2 year	Baseline	3–6 month	1 year	3 month	>3 month
NR	NR	NR	2 (0.47)	NR	3.2 (0.42)	NR	NR
4.06 (0.8)	5.4 (1.05)	5.16 (1.22)	2.7 (1.4)	3.56 (1.23)	3.7 (1.0)	0	0.23 (0.34)

KTW (Mean [SD])			STT (Mean [SD])			MR (Mean [SD])	
Baseline	3 month	1–2 year	Baseline	3–6 month	1 year	3 month	>3 month
NR	NR	NR	NR	NR	NR	0.3 (0.8)	0.2 (0.4)

KTW (Mean [SD])			STT (Mean [SD])			MR (Mean [SD])	
Baseline	3 month	6 month –1 year	Baseline	1–3 month	6 month –1 year	3 month	>3 month
0.88 (0.65)	9.81 (2.45)	3.7 (No SD)	NR	NR	NR	NR	NR
NR	NR	NR	1.51 (0.46)	2.6 (0.54)	2.5 (0.56)	NR	NR
0.7 (0.69)	9.39 (2.66)	8.46 (2.68)	NR	NR	NR	NR	NR
NR	NR	NR	NR	NR	0.54 (0.71)	NR	NR

KTW (Mean [SD])			STT (Mean [SD])			MR (Mean [SD])	
Baseline	3 month	6 month –1 year	Baseline	3–6 month	1 month	3 month	>3 month
0.42 (0.51)	2.67 (1.44)	2.75 (1.5)	NR	NR	NR	NR	NR
1.75	NR	2	NR	NR	NR	1.17 (1.3)	1.17 (1.27)
0.2 (0.42)	3.1 (0.87)	2.6 (0.96)	0.92 (0.27)	NR	2.5 (0.39)	NR	0.1 (0.44)
NR	NR	NR	NR	NR	NR	NR	0.3 (0.3)

bias in eight included RCTs were assessed and summarized (Table S1), two studies (Bianchi & Sanfilippo, 2004; Sanz et al., 2009) (25%) of unclear risk of bias for allocation concealment, one study (Bianchi & Sanfilippo, 2004) (12.5%) of high risk, and two studies (Sanz et al., 2009; Zuiderveld et al., 2018) (25%) of unclear risk of bias for participants and personnel, and one study (D'Elia et al., 2017) (12.5%) with selective reporting due to no baseline data. Also, most of the included articles (7 of 14, 87.5%) revealed an unclear risk of bias for blinding of the outcome assessment (Bianchi & Sanfilippo, 2004; Cairo et al., 2017; D'Elia et al., 2017; Lorenzo et al., 2012; Sanz et al., 2009; Zeltner et al., 2017; Zuiderveld et al., 2018). Only one controlled clinical trial had seven stars and showed the "medium–high" level of evidence (Wiesner et al., 2010) (Table S2). For the seven case series (Chung et al., 2011; Cosyn et al., 2013; Covani et al., 2007; De Bruyckere et al., 2015; Lee et al., 2012; Roccuzzo et al., 2014; Tsuda et al., 2011) and four cohort studies (Kan et al., 2009; Schmitt et al., 2013, 2016; Zucchelli et al., 2013), the majority (7 of 11, 63.6%) were prospective in design with consecutively enrolled subjects. Six (6 of 11, 54.5%) articles were assessed as low–moderate risk. Among the five high-risked articles, all of them were due to the lack of data for KTW, STT. Hence, the evaluation of primary outcomes of soft tissue condition is mainly based on the articles with low–moderate risk.

3.5 | Results for KTW

With respect to KTW at peri-implant area, four RCTs (Cairo et al., 2017; D'Elia et al., 2017; Migliorati et al., 2015; Sanz et al., 2009), one cohort (Zucchelli et al., 2013), and two case series (Covani et al., 2007; Lee et al., 2012; Sanz et al., 2009) were included. Based on the baseline data of KTW, these studies could be divided into two groups: ≥2 mm (Cairo et al., 2017; D'Elia et al., 2017; Migliorati et al., 2015) and <2 mm (Covani et al., 2007; Lee et al., 2012; Sanz et al., 2009; Zucchelli et al., 2013). From baseline to more than 1 year, the weighted mean of KTW change was 0.55 mm (95% CI: −0.34 to 1.45 mm) in ≥2 mm group, and 2.56 mm (95% CI: 2.30–2.82 mm) in <2 mm group with 1.69 mm (95% CI: 0.87–2.52 mm) as the overall mean value (Figure 2a). Adding timing as one of the considerations, all relevant articles were distributed into four groups based on baseline and different time points of soft tissue augmentation. KTW revealed more change in the group with KTW <2 mm but similar values in simultaneous and staged groups (2.61 mm [95% CI: 2.32–2.97 mm]; 2.38 mm [95% CI: 1.85–2.970 mm]) (Figure 2b). There were five publications (Lee et al., 2012; Migliorati et al., 2015; Sanz et al., 2009; Schmitt et al., 2016; Zucchelli et al., 2013) with complete data, and their values of KTW were compared at 3 months and >3-month healing. The results revealed that the KTW gain at 3 months was more than that at >3 months (weighted mean difference [WMD]: 0.21, 95% CI: 0.13–0.55) with a low degree of heterogeneity (I^2 = 0.0%; p = .81); however, no statistically significant difference was found (Figure 3).

3.6 | Results for STT

To focus on the effects of timing on soft tissue augmentation in STT, seven articles were extracted with four (D'Elia et al., 2017; Migliorati et al., 2015; Rungcharassaeng, Kan, Yoshino, Morimoto, & Zimmerman, 2012; Wiesner et al., 2010) in simultaneous and three (Cairo et al., 2017; De Bruyckere et al., 2015; Schmitt et al., 2016) in staged treatment groups. To specify the time points, soft tissue augmentation could be performed 3–6 months after implant placement (De Bruyckere et al., 2015; Schmitt et al., 2016) or even at stage 2 surgery (Cairo et al., 2017). The weighted mean STT gain (1 year after surgery) was 1.03 mm (95% CI: 0.78–1.29 mm), among which the simultaneous group was 1.12 mm (95% CI: 0.75–1.49 mm) and staged group was 0.95 mm (95% CI: 0.58–1.31 mm) (Figure 4).

3.7 | Results for MR

With regard to mid-buccal MR change after soft tissue graft, six articles were qualified (Chung et al., 2011; Cosyn et al., 2013; Lee et al., 2012; Lorenzo et al., 2012; Migliorati et al., 2015; Tsuda et al., 2011). Results showed no statistically significant difference in MR between 3 months after soft tissue augmentation and 1-year follow-up (−0.13; 95% CI: −0.34 to 0.09; I^2 = 0.0%; p = .961) (Figure 5).

4 | DISCUSSION

Undoubtedly, more emphasis has been placed on soft tissue surrounding peri-implant areas for improving esthetic outcomes and minimizing future biological complications (Esposito et al., 2012; Fu et al., 2012; Lin et al., 2013; Rotundo et al., 2015; Thoma et al., 2009; Wu et al., 2015). Previous implant soft tissue studies have mostly aimed to examine biological width (BW), papilla height, KT, and tissue biotype (Thoma et al., 2009; Thoma, Buranawat, et al., 2014; Thoma, Muhlemann et al., 2014). However, our review was focused on the KTW and STT to illustrate their influence on the peri-implant soft tissue stability and its relationship to the mid-buccal MR. Furthermore, we have also assessed the impact of soft tissue grafting timing during implant therapy.

4.1 | Width of keratinized tissue gain

Conflicting data existed if KT is needed for prevention of peri-implantitis as well as maintenance of implant long-term stability. However, majority of the studies are in favor of having a band of KT to not only improve esthetic appearance but also to facilitate oral hygiene performance for better implant long-term stability (Bouri, Bissada, Al-Zahrani, Faddoul, & Nouneh, 2008; Chung, Oh, Shotwell, Misch, & Wang, 2006; Kim et al., 2009; Lin et al., 2013; Thoma, Buranawat, et al., 2014; Thoma, Muhlemann et al., 2014). Among all related articles, APF plus vestibuloplasty and autogenous grafts, such as FGG or subepithelial connective tissue graft (SCTG), was regarded as the most effective technique to obtain KT (Bassetti et al.,

TABLE 3 Differences of measurement methods in included articles

Authors	Measurement (STT)	Measurement (KTW)	Measurement (MR)
Bianchi et al. (2004)	NR	NR	Refer to emergence line
Covani et al. (2007)	NR	Periodontal probe directly	NR
Kan et al. (2009)	NR	NR	NR
Chung et al. (2011)	NR	NR	Casts+ customized stent+ probe
Tsuda et al. (2011)	NR	NR	Casts+ customized stent
Lee et al. (2012)	NR	Periodontal probe directly	Digital photographic images
Migliorati et al. (2015)	Stent+ endodontic reamer with stopper	Periodontal probe directly	Casts were photographed with millimeter grid
Zuiderveld et al. (2018)	NR	NR	Photographs+ periodontal probe
Wiesner et al. (2010)	Endodontic micro-opener+ silicone stop (1 mm below crest) + endodontic longimeter	NR	NR
D'Elia et al. (2017)	Calibrated endodontic file (2 mm below crest) + Periodontal probe	Periodontal probe directly	Periodontal probe directly
Cosyn et al. (2013)	NR	NR	Customized stent+ probe
Schmitt et al. (2013)	NR	Periodontal probe directly	NR
De Bruyckere et al. (2015)	Ultrasonic device (EPOCH, Olympus, Aartselaar, Belgium)	NR	NR
Schmitt et al. (2016)	NR	Periodontal probe directly	NR
Zeltner et al. (2017)	Digital models to obtain linear change (Not included in meta-analysis)	NR	NR
Sanz et al. (2009)	NR	North Carolina University probe	NR
Lorenzo et al. (2012)	NR	North Carolina University probe	North Carolina University probe directly
Zucchelli et al. (2013)	Anesthesia needle+ silicone stop (1.5 mm below crest)+ caliper	Lugol staining + probe	Comparing to contralateral tooth
Roccuzzo et al. (2014)	NR	NR	Castroviejo Caliper Short (Salvin Dental Specialties, Inc., USA)

KTW, keratinized tissue width; MR, mucosal recession; STT, soft tissue thickness.

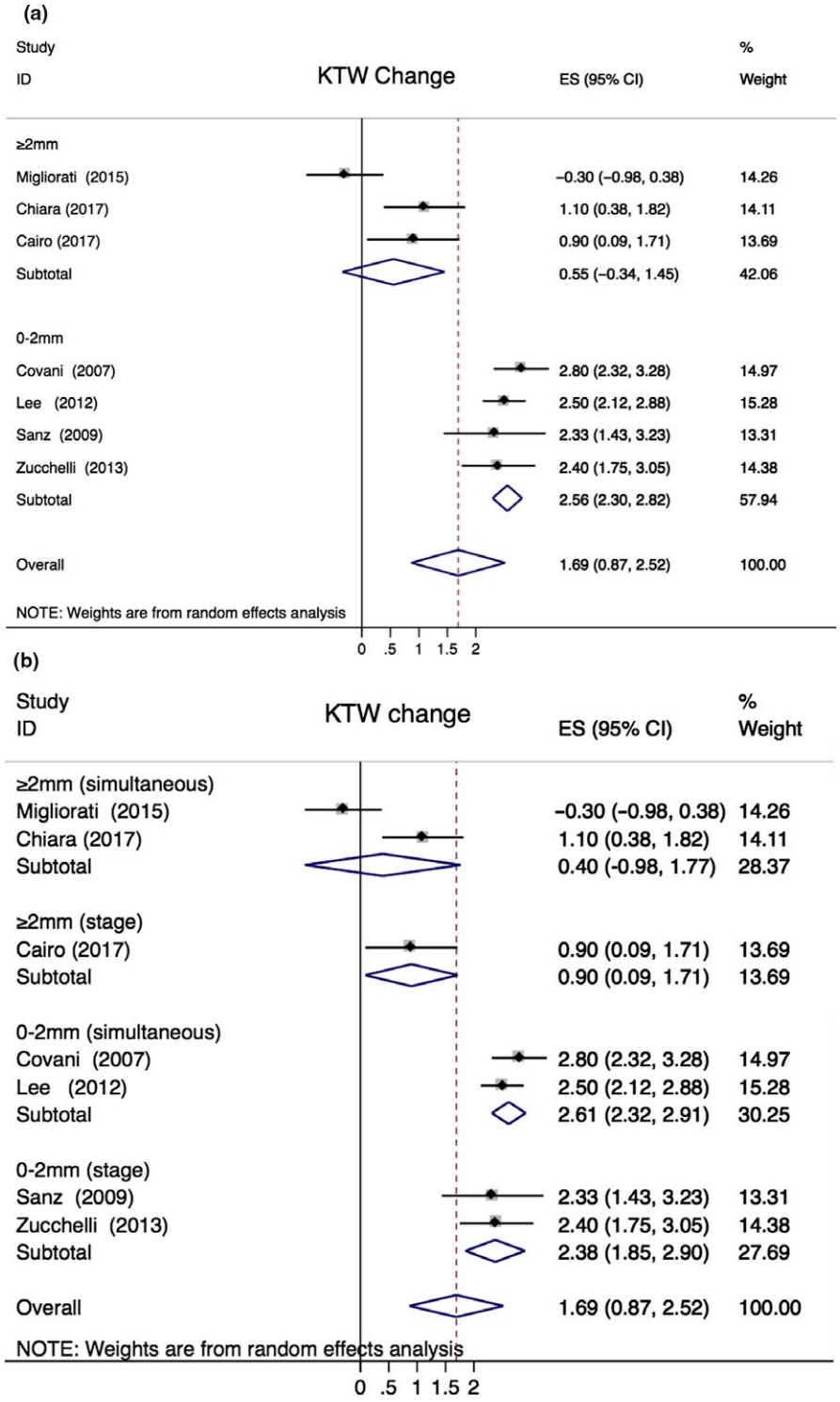

FIGURE 2 (a) Meta-analysis was conducted in assessing keratinized tissue width (KTW) change of different thickness (≥2 mm vs. <2 mm) at different time points. (b) Meta-analysis of KTW was performed to look into the influence of timing on soft tissue augmentation during implant therapy

2016; Thoma et al., 2009; Thoma, Buranawat, et al., 2014; Thoma, Muhlemann et al., 2014). One review showed that APF, APF with SCTG, and roll techniques performed at second-stage surgery were able to gain 4.63, 4.10, and 1.35 mm of KTW, respectively (Bassetti et al., 2016). In spite of less surgical time and patients' comfort in alternatives (Thoma, Buranawat, et al., 2014; Thoma, Muhlemann et al., 2014), autograft (FGG, SCTG) remains the gold standard for soft tissue augmentation in terms of KTW, tissue thickness, esthetic and long-term volume stability (Fu et al., 2012; Park, 2006). Hence, the present review focused on the autogenous soft tissue graft-related studies.

Surprisingly, different baseline values of KTW can end up with different change 1 year later. For example, the weighted mean KTW change was 0.55 mm in ≥2 mm group and 2.56 mm in <2 mm group. The result of this review implied the predictability of soft tissue augmentation in sites with baseline KTW <2 mm. On the contrary, the

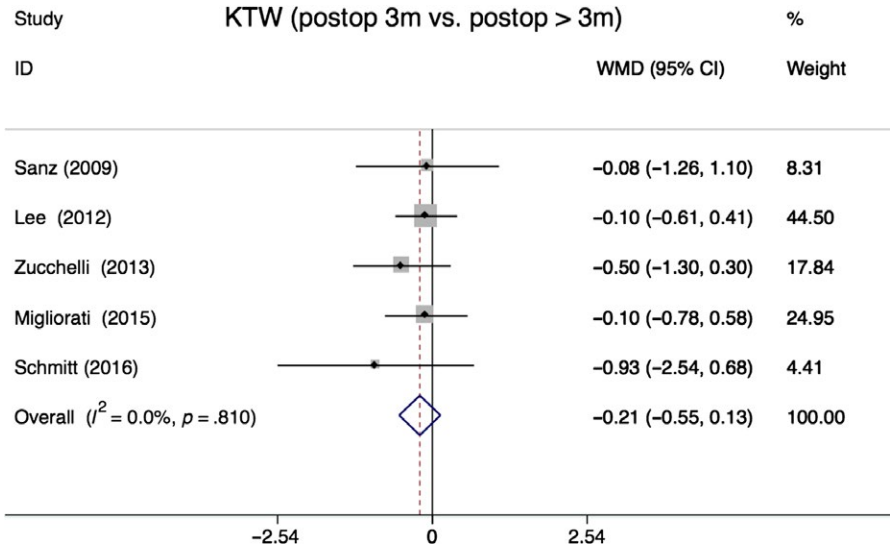

FIGURE 3 Meta-analysis was performed to examine keratinized tissue width (KTW) change at 3 months and 3 months later after surgery

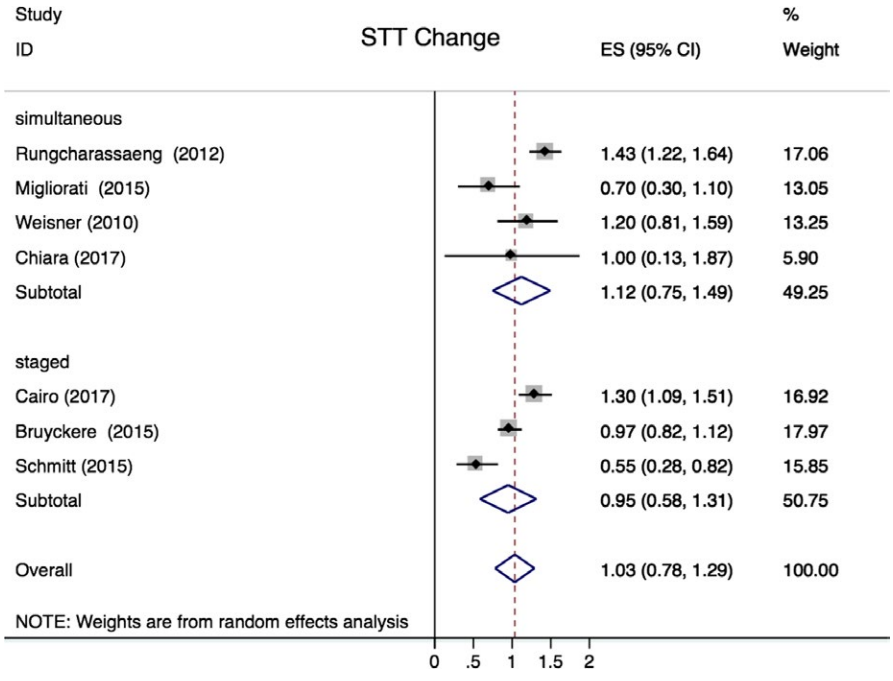

FIGURE 4 Meta-analysis was conducted to examine soft tissue thickness change at different time points

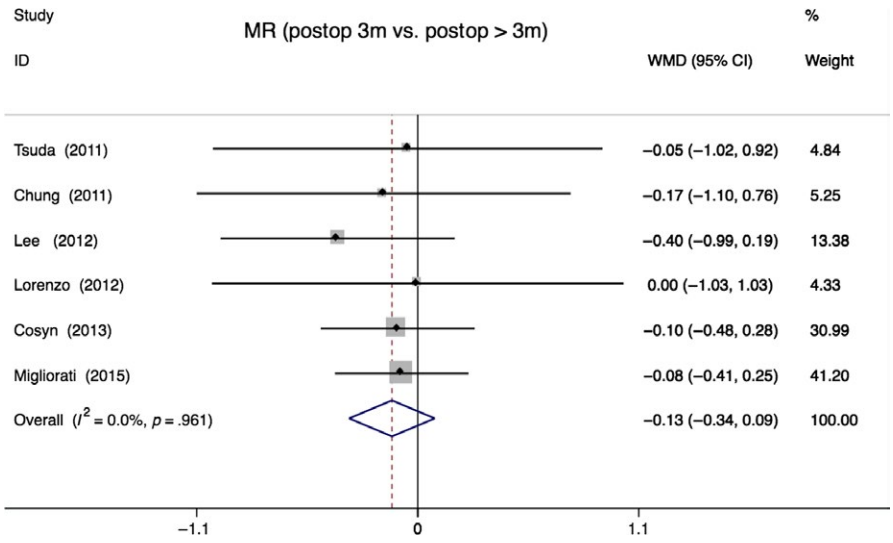

FIGURE 5 Meta-analysis of mucosal recession changes at 3 months and 3 months later after surgery

necessity of additional soft tissue graft might not be needed in sites of ≥2 mm due to limited KTW augmentation.

4.2 | Soft tissue thickness

Soft tissue volume comprises two parts in different directions: BW and STT (Thoma, Buranawat, et al., 2014; Thoma, Muhlemann et al., 2014). According to previous studies, BW has been known as the vertical part of soft tissue around implants, which also permits a safe zone for the bone underneath (Abrahamsson, Berglundh, & Lindhe, 1997; Berglundh & Lindhe, 1996; Berglundh et al., 1991). On the other hand, STT is the horizontal part of soft tissue often known as biotype. Interestingly, one theory suggested that adequate STT around implant could prevent the crestal bone loss (Linkevicius, Puisys, Linkeviciene, Peciuliene, & Schlee, 2015); however, the 2 mm threshold of thickness was measured at the crestal portion of flap. In other words, STT in that article was more likely to reference biotype instead of BW. It is because of the different views of STT in various articles that precautions must be taken when interpreting this result.

Different methods/tools were used for soft tissue assessment, which include but are not limited to sounding with stopper, ultrasonic device, cast-superimposed technique, and three dimension image based on intraoral photos (Zeltner et al., 2017). To minimize the possible bias, the meta-analysis of STT merely included the data from sounding (D'Elia et al., 2017; Wiesner et al., 2010; Zucchelli et al., 2013) and ultrasonic measurement (De Bruyckere et al., 2015). To be more specific, the details in STT change for ultrasonic device could be up to 0.01 mm, which is more accurate than the conventional tools (endodontic ruler, caliper, or periodontal probe). Additionally, the location of MGJ can only be found by both a functional test and the staining method, so the determination of KT border might have some impacts on measurement errors. Aside from STT and KTW, the various measurement methods and different reference lines in MR should be mentioned in related articles. Hence, these different assessment tools might explain some of the discrepancies noted among studies, and the data extracted from different articles should be interpreted with cautions as well.

To facilitate evaluation the effect of timing on soft tissue augmentation outcomes, we subdivided the assessment into two groups (simultaneous or staged). Data from this review showed 0.95 and 1.12 mm of STT gain in staged and simultaneous groups, respectively. However, no significant difference was found. Soft tissue graft during implant treatment could definitely be considered to improve the contour and esthetics, especially in thin biotype. Interestingly, the soft tissue stability on simultaneous soft tissue graft remains a concern among many clinicians (Bassetti et al., 2016; Thoma, Buranawat, et al., 2014; Thoma, Muhlemann et al., 2014), however, both groups achieved comparable STT gain. Additionally, Thoma et al. regarded soft tissue augmentation after final restoration as a procedure with less predictability and is often used as a rescue approach. Yet, four articles included in staged approach group showed favorable outcomes, which might attribute to limited defect size (single implant) (Lorenzo et al., 2012; Roccuzzo et al., 2014; Sanz et al., 2009; Zucchelli et al., 2013). In summary, soft tissue augmentation during implant therapy can be applied in different timing with predictability.

Results from this review showed soft tissue graft prevents mid-facial MR during implant therapy. Furthermore, there is no statistically significant difference in MR between 3 months after soft tissue augmentation and 1-year follow-up. This is in agreement with one review that showed flapless, bone graft in bone gap, and SCTG placement were able to prevent mid-facial MR (Lin et al., 2013). The flapless approach often leads to less recession when compared to flapped ones (Raes, Cosyn, Crommelinck, Coessens, & De Bruyn, 2011). The bone graft in the gap can provide the foundation support for soft tissue in-growth and autogenous soft tissue graft results in coronal movement of mucosal level, that is, all to minimize MR. Nevertheless, autograft placement can increase KTW but at the cost of 0.5 mm recession of flapping opening (Esposito et al., 2012). In present review, the overall mean value from baseline was 0.13 mm with the range from −0.34 mm to ~0.09 mm, which was in line with the values in the previous studies.

The favorable outcome noted in our article may be largely due to autogenous soft tissue grafts being the only ones assessed. This is in agreement with the systematic review paper that discussed soft tissue graft with implant therapy. In this paper, authors only extracted data from articles with least 6-month follow-up. They found shrinkage of soft tissue ranged from 0.34 to 6.8 mm with the highest reduction observed at first month to 3–6 months (Bassetti et al., 2016).

Data from this paper showed techniques used for harvesting autogenous soft tissue did not affect the outcomes. This can be explained by the minimal-invasive (envelope, pouch, and tunnel) harvesting technique employed in most of these papers. On the contrary, APF with graft was preferred in articles with multiple implants and soft tissue augmentation after final restoration in single implant, because these approaches can significantly increase the amount of STT and KTW.

The limitations of this review should be acknowledged. (i) Most of the included studies had small sample sizes and short follow-up periods; (ii) there were inconsistencies in methodologies with various treatment modalities; (iii) the present review includes only English language publications, which may have introduced selection bias. Therefore, there is a need for a better RCT with longer follow-up, larger sample size, and clearer study design that compares simultaneous and staged soft tissue augmentation.

5 | CONCLUSION

This review revealed that the stability of soft tissue, in terms of KTW and mid-buccal MR, can be obtained 3 months after surgery. There is no difference between simultaneous and staged soft tissue augmentations during implant treatment, and both procedures significantly enhance KT width and STT.

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CONFLICT OF INTEREST

The authors report no conflict of interest.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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