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REVIEW ARTICLE

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Linear and profilometric changes of the mucosa following soft tissue augmentation in the zone of aesthetic priority: A systematic review and meta-analysis

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Abstract

Objectives: To assess the outcomes of soft tissue augmentation, in terms of change in level and thickness of mid-buccal mucosa, at implants sites in the zone of the aesthetic priority.

Material and Methods: MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials databases were searched (last search on 1 June 2020). Inclusion criteria were studies reporting outcomes of different materials and timing of grafting in patients undergoing soft tissue augmentation at implant sites in the aesthetic zone with a follow-up of ≥1 year after implant placement. Outcome measures assessed included changes in level and thickness of mid-buccal mucosa, implant survival, peri-implant health and patients' satisfaction.

Results: Eighteen out of 2,185 articles fulfilled the inclusion criteria. Meta-analysis revealed a significant difference in vertical mid-buccal soft tissue change (0.34 mm, 95% CI: 0.13–0.56, $p = .002$) and mid-buccal mucosa thickness (0.66 mm, 95% CI: 0.35–0.97, $p < .001$) following immediate implant placement in favour of the use of a graft versus no graft. Mean difference in mid-buccal mucosa level following delayed implant placement (0.17 mm, 95% CI: 0.01–0.34, $p = .042$) was also in favour of the use of a graft versus no graft. With regard to mucosa thickness, the use of a graft was not in favour compared with no graft following delayed implant placement (0.22 mm, 95% CI: −0.04–0.47, $p = .095$). Observed changes remained stable in the medium term.

Conclusion: Soft tissue augmentation in the zone of the aesthetic priority results in less recession and a thicker mid-buccal mucosa following immediate implant placement and less recession in mid-buccal mucosa following delayed implant placement compared with no graft.

KEYWORDS
aesthetic zone, connective tissue graft, dental implants, meta-analysis, single-tooth restoration, soft tissue augmentation, systematic review

1 | INTRODUCTION

Single-implant treatment in the aesthetic zone has been shown to be a highly reliable treatment for the rehabilitation of a single failing or missing tooth (den Buser et al., 2017; Hartog et al., 2008; Jung et al., 2012; Lang et al., 2012; Slagter et al., 2014). However, with the increasing demand for the most satisfying aesthetic outcome, the focus in research has shifted from implant survival, which has been proven to be very high, towards the ways to enhance and preserve the hard and soft peri-implant tissues (Araújo et al., 2015; Cosyn et al., 2017). This shift in focus originates from the observation that mid-buccal mucosal recession and unpleasing peri-implant mucosa aesthetics are not uncommon (Cosyn et al., 2016; Kan et al., 2018; Tonetti et al., 2017). Several factors, such as limited amount of hard and soft tissues surrounding the osseointegrated implant, incorrect implant positioning and/or poor quality of the prosthetic reconstructions, have been shown to be involved in the aetiology of mucosal recessions (Cosyn et al., 2017).

Current surgical procedures for soft tissue augmentation in the aesthetic region aim to increase the width of keratinized tissue or the volume of the soft tissue at the implant site (Thoma et al., 2018). These procedures include apically positioned split-thickness flaps, vestibuloplasties and soft tissue volume augmentation with the application of autologous tissue or soft tissue substitutes (Wolf et al., 2016). The clinical indications for these procedures include establishment and maintenance of peri-implant tissues, prevention of mucosal recession, compensation for volume deficiencies and facilitation of tissue adaptation on implant placement, all aiming for functional and/or aesthetic improvement.

Thickening of the peri-implant soft tissues with a subepithelial connective tissue graft (SCTG) procedure has been suggested to contribute to soft tissue volume and stability of the mid-buccal mucosal level, although some shrinkage may occur (Lee et al., 2016; Thoma et al., 2014). Over the years, autologous SCTG has been regarded as a gold standard (Lissek et al., 2020). However, to reduce patient morbidity, pain and surgical chair time accompanying connective tissue harvesting, various soft tissue substitutes have been tested as an alternative to replace autologous grafts (Froum et al., 2015; Lorenzo et al., 2012; Sanz et al., 2009; Stefanini et al., 2020; Thoma et al., 2016; Zeltner et al., 2017). Short-term results show that the use of a collagen matrix leads to an increase in peri-implant soft tissue and keratinized mucosa (Cairo et al., 2019; Gargallo-Albiol et al., 2019; Moraschini et al., 2020). Whether this positive effect will hold over time still has to be proven. Aside from the use of the grafting material itself, soft tissue augmentation surgery can also be performed at different time points during implant treatment. The preferable time points for implant placement and soft tissue augmentation are not known yet (Lin et al., 2018).

Previous systematic reviews concluded that there is weak evidence that soft tissue augmentation increases the thickness of the peri-implant soft tissue, thereby improving the aesthetic outcome (Atieh & Alsabeeha, 2020; Esposito et al., 2012; Khzam et al., 2015; Lee et al., 2016), and there is no evidence yet for whether the effect of soft tissue augmentations can be maintained over time (Rotundo et al., 2015). Therefore, the aim of our systematic review was to do a comprehensive analysis of the outcomes of soft tissue augmentation, in terms of change in vertical mid-buccal mucosa level and thickness at implant sites following immediate or delayed implant placement in the zone of aesthetic priority.

2 | MATERIAL AND METHODS

The protocol of this review was registered at the National Institute for Health Research PROSPERO International Prospective Register of Systematic Reviews (CRD42020211690). The reporting of this study complied with the "Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)" statement for systematic reviews (http://prisma-statement.org/) (Moher et al., 2009).

2.1 | Protocol development

A protocol was developed a priori to answer the following question: *What are the outcomes of soft tissue augmentation, in terms of change in level and thickness of mid-buccal mucosa, at implants sites in the zone of aesthetic priority?*

2.2 | Search strategy and study selection

A thorough search of the literature was conducted for studies published until 1 June 2020. The search strategy was developed with the help of a biomedical information specialist according to the syntax rules of each database (Table S1). A literature search of the following electronic databases was conducted: MEDLINE (1964–2020), EMBASE (1947–2020) and the Cochrane Central Register of Controlled Trials (CENTRAL; inception to 2020). The automated search was supplemented by manually searching the references of relevant review articles and eligible studies for additional useful publications. No restriction on language or year of publication was applied.

2.3 | Eligibility criteria

The researchers based the literature search on the PICO index:

2.3.1 | Inclusion criteria

1. Studies reporting the outcome of different materials and timing of grafting in patients undergoing soft tissue augmentation in the maxillary or mandibular aesthetic zone at implant sites.
2. Human subjects included in the studies should be ≥18 years of age.
3. Detailed information should be available on change in mid-buccal mucosa level or thickness or volume; in case of combined data, the required data must be extractable.
4. Follow-up period of at least 1 year after implant placement.

P	*Patients or population*	Patients ≥18 years of age, undergoing single-tooth dental implant therapy in the maxillary or mandibular aesthetic zone (incisor, canine or premolar areas)
I	*Intervention*	Soft tissue augmentation with any kind of grafting material, that is autologous, allogeneic, xenogeneic or synthetic performed: • Before implant placement or • At implant placement or • In the period between placement and abutment Connection/insertion of the reconstruction or • At abutment connection/insertion of the reconstruction or • After insertion of the reconstruction
C	*ComparisonorControl group*	1. No soft tissue augmentation, or 2. Soft tissue augmentation with any kind of material, that is autologous, allogeneic, xenogeneic or synthetic, but different from the material used in the test group or at another time point.
O	*Outcomes*	• Primary outcome: change in mid-buccal mucosa level and thickness at implants sites. • Secondary outcomes: change in mid-buccal mucosa profilometric, implant survival, peri-implant health measured by bleeding on probing or gingival index, probing depth values, papilla height, marginal bone-level changes, patient-reported aesthetic assessments, biological complications, aesthetic outcomes (e.g. Pink Esthetic Score [PES]; White Esthetic Score [WES])
S	*Studies*	Randomized controlled clinical trials (RCTs), non-randomized controlled clinical trials (CCTs) with a minimum sample of 10 patients (five per group or in case of a split-mouth design at least five sites per group), prospective case series >30 patients
T	*Time of outcome assessment*	≥1 year of follow-up after implant placement

2.3.2 | Exclusion criteria

1. Randomized controlled clinical trials or CCTs with <10 patients, <5 sites per group in case of a split-mouth design, prospective case series with <30 patients.
2. Case reports, retrospective studies, experts' opinions, conference abstracts, letters to the editor, animal studies, reviews and systematic reviews.

2.4 | Study eligibility

The studies retrieved after applying the developed literature search strategy in MEDLINE, EMBASE and Cochrane Controlled Trial Register were imported into the RefWorks software (Ex Libris, ProQuest LLC). Duplicates were removed.

The study selection was performed in two consecutive rounds. First, a calibration session was organized on articles not included in this study. Two reviewers (GMR and AK) independently assessed the articles based on titles and abstracts according to the inclusion and exclusion criteria. If an abstract was not available, or in case of doubt, the full text of the article was assessed. In the second round, the full text of the included articles was assessed according to the same inclusion and exclusion criteria. In case of overlapping study populations in publications from the same groups of authors, the publications were considered as one study, or the most recent publication with the longest follow-up was used.

After each selection round, discrepancies between the two reviewers were resolved in a consensus meeting. A third reviewer (HJAM) was available to give a final judgement in case the disagreement persisted. The percentage of agreement between the reviewers and Cohen's kappa coefficient (κ) were calculated after each round.

2.5 | Data extraction

A standardized, pre-piloted form was used to extract data from the included studies to assess the study quality and for evidence synthesis. Data were extracted independently by GMR and AK.

The extracted information included the following:

- First author and publication year
- Study design
- Study population or treatment setting, that is private practice, tertiary centre
- Number of patients
- Age
- Smoking
- Gender
- Dropouts
- Follow-up
- Implant system
- Number of implants
- Time of implant placement
- Time of soft tissue graft
- Type of soft tissue graft, that is autologous, allogeneic, xenogeneic or synthetic
- Change in mid-buccal mucosa level
- Change in buccal mucosa thickness
- Change in buccal mucosa volume
- Implant survival rate (%)
- Peri-implant health measured by bleeding or gingival index
- Probing pocket depth
- Papilla height
- Marginal bone-level changes (mm)
- Aesthetic assessments using a VAS (patient-reported) and the Pink Esthetic score/White Esthetic Score (PES/WES, professional-reported)
- Occurrence of biological complications.

2.6 | Quality assessment of the included studies

The risk of bias was independently assessed by two reviewers (GMR and HJAM). First, a calibration session was organized on articles not included in this study. In case of RCTs, the risk of bias was assessed using the Cochrane Collaboration's Risk of Bias 2 (RoB2) tool, which is structured in 5 domains to address all important mechanisms by which bias can be introduced into the results of a trial (Sterne et al., 2019). A signalling question was classified as low risk of bias if sufficient information was available, resulting in a positive marker. A signalling question was classified as high risk of bias when no information was available, and a negative marker was attributed. When there was insufficient information and it was not possible to determine the risk of bias, it was classified as presenting "some concerns". The "low risk-of-bias," "some concerns" or "high risk-of-bias" judgements for each domain, based on the answers to signalling questions, were summarized.

The CCTs and prospective case series were assessed with the Newcastle–Ottawa scale (NOS) (Wells et al., 2000), and each article was rated from 0 to 9 stars for each parameter in the scale. Studies scoring ≥6 stars were considered to be high in methodological quality, while <6 stars indicated low quality.

Discrepancies between the two reviewers in assessing the quality of the included studies were resolved in a consensus meeting. A third reviewer (AK) was consulted to give a final judgement in case a disagreement persisted. The percentage of agreement between the reviewers and Cohen's kappa coefficient (κ) were calculated per item/domain of the tool used.

2.7 | Strategy for data synthesis

A qualitative synthesis of the included studies was performed by focusing on changes in mid-buccal mucosa level, soft tissue thickness and volume, implant survival, marginal bone-level changes, patient-reported outcome measures (PROMs) and biological complications. A quantitative synthesis/meta-analysis was carried on the change in mid-buccal mucosa level and thickness if the study groups were sufficiently homogenous (I^2 < 80%.). A subgroup analysis was performed to explore the change in mid-buccal mucosa level and thickness in case of:

- Different types of soft tissue grafts, that is autologous, allogeneic, xenogeneic or synthetic;
- Different time points of soft tissue augmentation, that is before implant placement, at implant placement, in the period between implant placement and abutment connection, at abutment connection/insertion of the reconstruction, or after insertion of the reconstruction.

If ≥10 studies per outcome were available, the likelihood of publication bias was assessed by plotting the log odds ratio against its standard error.

2.8 | Statistical analysis

Inter-observer agreement was calculated with IBM SPSS Statistics 20 (SPSS). Regarding the meta-analyses, a random-effects model with the DerSimonian–Laird estimator was used to calculate the mean differences with 95% confidence intervals (95% CIs) of change-from-baseline mid-buccal mucosa level and thickness after 1-year follow-up between the intervention and control group. Heterogeneity was expressed as I^2 with the corresponding chi-squared test. If >2 studies per outcome were included, 95% prediction intervals (95% PIs) were calculated. The prediction interval incorporates the uncertainty in the mean effect and the between-study heterogeneity, and summarizes the spread of the underlying effects in studies included in the meta-analysis (Higgins et al., 2019; Higgins et al., 2009). If a study did not report the change-from-baseline standard deviations, we calculated these standard deviations assuming a within-patient correlation of 0.5 (Higgins et al., 2019; Smaïl-Faugeron et al., 2014). If two studies included the same control group, we split the sample size of the control group into two equally sized groups and included both studies in the meta-analysis, as recommended (Higgins et al., 2019). The meta-analysis was performed in R (version 4.0.2) using the *meta* package (version 4.15–1; Balduzzi et al., 2019).

3 | RESULTS

3.1 | Study identification and selection

The search resulted in 3,703 potentially eligible papers. After excluding duplicates, 2,185 papers were screened by title and abstract (Figure 1) whereupon 2,158 papers were excluded because they did not meet the inclusion criteria. Disagreements ($n = 2$) were resolved in a consensus meeting. The percentage of agreement between the reviewers and Cohen's kappa coefficient (κ) for the titles and abstracts, according to the inclusion and exclusion criteria, were 99.1 and 0.56, respectively. Three additional records were included after manual search resulting in 30 papers. The full-text articles of these 30 remaining papers were screened for inclusion. The percentage of agreement and Cohen's kappa coefficient were 86.7 and 0.66, respectively. The remaining 18 articles (17 studies) were synthesized qualitatively for this review. There was no need to consult the third reviewer in any phase of the selection of a study. In 2 studies, data were missing on the 1-year results, and these missing data were provided on request (Fenner et al., 2016; Hosseini et al., 2020).

3.2 | Study characteristics

The included articles consisted of 10 RCTs, 7 CCTs and one prospective case series. Their characteristics are presented in Table 1. Five of the RCTs performed immediate implant placement and immediate restoration (Frizzera et al., 2019; Migliorati et al., 2015; van Nimwegen et al., 2018; Yoshino et al., 2014; Zuiderveld et al., 2018).

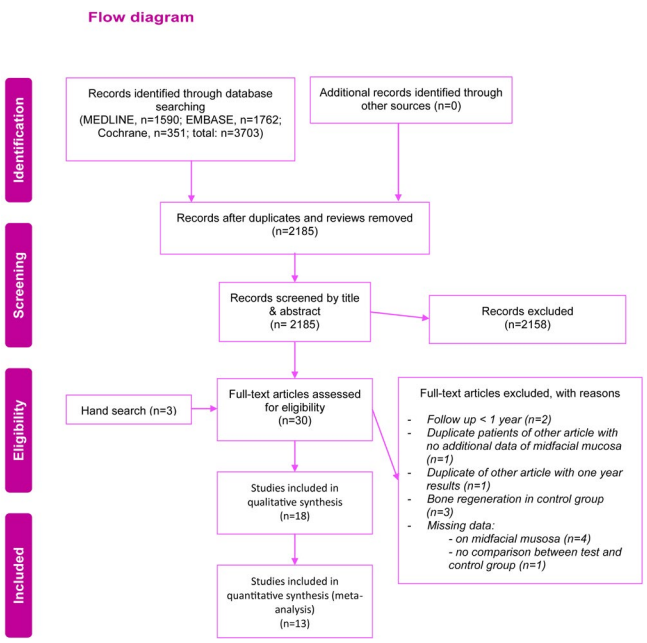

FIGURE 1 Flow chart of study selection procedure

Two of these RCTs assessed the same group of patients, but evaluated different parameters (van Nimwegen et al., 2018; Zuiderveld, Meijer, den Hartog, et al., 2018). The other five RCTs involved delayed implant placement (Liu et al., 2007; Puzio et al., 2018; Rojo et al., 2020; Thoma et al., 2020; Zuiderveld et al., 2018). In all delayed implant placement studies, the implants were placed in healed sites ≥4 months after tooth extraction. Of the 7 included CCTs, 2 reported immediate implant placement and delayed restoration (Tatum et al., 2020) and immediate implant placement and immediate restoration (Cosyn et al., 2016) and 5 reported delayed implant placement (Fenner et al., 2016; Hosseini et al., 2020; Kato et al., 2018; Kobayaski et al., 2020; Zuiderveld et al., 2019). The last study was a prospective case series following alveolar ridge preservation (ARP), delayed implant placement and SCTG (Eghbali et al., 2018). Most studies were performed in a university setting (83%, $n = 15$). One study was performed in a private practice ($n = 1$), whereas the setting was not mentioned in two studies. In total, 594 patients were included of which 54.6% were females. Seven studies included smokers of <10 cigarettes per day and one study included smokers of <5 cigarettes per day ($n = 1$), while the other ten studies excluded smokers. The mean dropout rate ranged from 0% to 37% (8 studies reported a 0% dropout). The follow-up ranged from 1 to 7.2 years with all studies having data available after 1 year of follow-up.

All seven immediate implant placement articles used SCTG in the test group and no graft in the control group (Cosyn et al., 2016; Frizzera et al., 2019; Migliorati et al., 2015; Nimwegen at al., 2018; Tatum et al., 2020; Yoshino et at., 2014; Zuiderveld, Meijer, den Hartog, et al., 2018). One RCT also applied a type of non-cross-linked porcine collagen matrix (XCM, Mucograft®; Geistlich Pharma AG) (Frizzera et al., 2019). Seven of the 11 delayed implant placement studies used SCTG in the test group and no graft in the control group (Fenner et al., 2016; Hosseini et al., 2020; Kato et al., 2018; Kobayaski et al., 2020; Puzio et al., 2018; Zuiderveld, Meijer, Vissink, et al., 2018; Zuiderveld et al., 2019). XCM or SCTG versus no graft was assessed in two studies (Puzio et al., 2018; Zuiderveld, Meijer, Vissink, et al., 2018). One study compared porcine-derived acellular dermal matrix (ADM; mucoderm®; botiss biomaterials GmbH) with SCTG (Liu et al., 2007). In one study, a type of volume-stable cross-linked porcine collagen matrix (VCMX, Fibro-Gide®; Geistlich Pharma AG) was compared with SCTG (Thoma et al., 2020). All the patients in Zuiderveld, Meijer, Vissink, et al., (2018) study received an alveolar ridge preservation (ARP) after a flapless extraction because of a vertical buccal bone wall defect of >5 mm of the extraction socket, and the implants were placed after 4 months. The control group of Zuiderveld, Meijer, Vissink, et al., (2018) study was also used as the control group in Zuiderveld et al., (2019). The case series patients of another study underwent ARP after flapless extraction too and, then, after 4–6 months, implant placement with SCTG (Eghbali et al., 2018). In one RCT study, the SCTG was harvested from the lateral palate or from the tuberosity area (Rojo et al., 2020). In 3 articles, the SCTG was solely harvested from the tuberosity region (van Nimwegen et al., 2018; Rojo et al., 2020; Zuiderveld, Meijer, den Hartog, et al., 2018) and 1 study did not mention the donor site (Kato et al., 2018). In all the other studies, the SCTG was harvested from the palate. The timing of soft tissue grafting was either before implant placement ($n = 1$), or at implant placement ($n = 10$), or in the period between placement and abutment connection/insertion of the reconstruction ($n = 5$), or abutment connection ($n = 2$) or after insertion of the reconstruction ($n = 2$). In one of those studies, the soft tissue grafting was performed 3 months before and 3 months after implant placement (Puzio et al., 2018), and in another study, the soft tissue grafting was performed 6 or 12 weeks after implant placement (Rojo et al., 2020).

The indications for therapeutic interventions with soft tissue augmentation in the CCTs were reported as follows: to prevent recession and to compensate for volume deficiency (Cosyn et al., 2016); for aesthetic purposes and to compensate for volume deficiencies (Fenner et al., 2016; Hosseini et al., 2020; Kato et al., 2018; Kobayashi et al., 2020); and/or a thin gingival biotype (Hosseini et al., 2020; Tatum et al., 2020).

The studies included in this review applied a variety of implant systems (Table 1). The mean implant survival rate ranged from 95% to 100% (15 of the 18 articles had a survival rate of 100%).

3.3 | Assessment of methodological quality

Cohen's kappa for domains of RoB2 tool for assessing the RCTs ranged between 0.71 and 1.0 (percentage of agreement 90%–100%), with the "Risk of Bias arising from the randomization process" being the domain with the lowest agreement between the reviewers. Cohen's kappa for the domains of the Newcastle–Ottawa tool for assessing the NOS ranged between 0.86 and 1 (percentage

of agreement 85.7%–100%) for all the domains, with "Definition of Controls" and "Comparability of cases and controls on the basis of the design or analysis" being the only two domains not achieving complete agreement between the observers. Table 2 summarizes the results of the quality assessment of the 10 included RCTs. With respect to the CCTs, three studies had 9 scores and four studies had 8 scores (Table 3). The prospective case series was judged as having 8 stars (Eghbali et al., 2018) (Table 4).

3.4 | Outcome measures (Table 5)

In 7 studies, only the change in mid-buccal mucosa level was investigated. The change in mid-buccal mucosa thickness only was measured in 4 studies, and in 6 studies, changes in both level and thickness in mid-buccal mucosa were measured. A variety of measurement methods was applied in the studies, which makes a valid comparison of the results challenging (Table 5).

3.4.1 | Immediate implant placement

Subepithelial connective tissue graft was performed during immediate implant placement (Frizzera et al., 2019; Migliorati et al., 2015; Nimwegen at al., 2018; Tatum et al., 2020; Yoshino et at., 2014; Zuiderveld, Meijer, den Hartog, et al., 2018) or 3 months after implant placement (Cosyn et al., 2016). In the flapless procedure, bone substitutes and/or autologous bone were used to fill the gap between implant and cortical bone. All the immediate implant placement and restoration studies showed that the use of SCTG resulted in significantly less recession of the peri-implant soft tissue at the mid-buccal aspect compared with no SCTG ($p < .01$). Tatum et al., (2020) saw more recession after SCTG and immediate placement, but they had made a full-thickness envelope flap and fabricated the restoration after 3 months. In one RCT study, there was less recession of the peri-implant soft tissue following SCTG than XCM (Frizzera et al., 2019). Two studies reported outcomes for the change in thickness of the labial mucosa whereby SCTG resulted in increased thickness in comparison with no graft or XCM (Frizzera et al., 2019; Migliorati et al., 2015). Two studies reported the outcomes for a follow-up of >1 year (Cosyn et al., 2016; Migliorati et al., 2015). On average, recession of the mid-buccal mucosa increased with 0.1 mm in both groups between 1 and 2 years (Migliorati et al., 2015) and with 0.3 and 0.4 mm between 1 and 5 years (Cosyn et al., 2016) in the SCTG and no graft groups, respectively. The thickness of the mid-buccal mucosa decreased with 0.3 mm and 0.1 mm between 1 and 2 years after using SCTG or no graft, respectively (Migliorati et al., 2015).

3.4.2 | Delayed implant placement

The timing of the graft placement in the studies reporting delayed implant placement is reported in Table 1. There were less recession and gain in thickness of the mid-buccal mucosa after SCTG, compared with no SCTG (Hosseini et al., 2020; Kato et al., 2018; Kobayaski et al., 2020; Puzio et al., 2018; Zuiderveld, Meijer, Vissink, et al., 2018; Zuiderveld et al., 2019). XCM also resulted in an increase in thickness and less change in level of the mid-buccal mucosa versus no SCTG, but the results were less favourable than those for SCTG (Puzio et al., 2018; Zuiderveld, Meijer, Vissink, et al., 2018). There was no significant difference between ADM and SCTG in change in thickness (Liu et a., 2007). The difference between VCMX and SCTG was negligible, and the outcomes were stable in terms of mid-buccal tissue contour, marginal bone levels and aesthetics (Thoma et al., 2020). The studies comparing autologous grafts and soft tissue substitutes were characterized by heterogeneity (time point of implant placement, type of soft tissue graft). However, in the studies a consistent tendency of less recession (2 RCTs) and thicker mid-buccal mucosa (4 RCTs) was shown for autologous grafts. Rojo et al., (2020) compared the soft tissue stability around single implants previously augmented with either SCTG from the lateral palate or SCTG from the tuberosity area. They found similar soft tissue changes after 12 months. Four studies reported the outcomes of a follow-up of >1 year (Eghbali et al., 2018; Fenner et al., 2016; Hosseini et al., 2020; Thoma et al., 2020). One mentioned an increase in mid-buccal mucosal recession and a decrease in the thickness of the mucosa, both equal to 0.07 mm, between 1 and 5 years after using SCTG (Eghbali et al., 2018). After a mean follow-up of 7.2 years, Fenner et al., (2016) reported that the recession of the mid-buccal mucosa had increased with 0.4 mm in the SCTG group, compared with the 1-year follow-up, but had decreased in the no graft group with 0.1 mm. The recession of the mid-buccal mucosa decreased with 0.86 mm between 1 and 5 years when SCTG was used and with 0.18 mm in the no graft group, and the thickness decreased with 0.34 mm in the SCTG group and with 0.06 mm when no graft was used (Hosseini et al., 2020). Thickness of the mid-buccal mucosa had increased between 1 and 3 years with 0.7 mm and 0.8 mm when SCTG or VCMX was used, respectively (Thoma et al., 2020).

3.4.3 | Profilometric changes

Three-dimensional analysis of the *profilometric* changes in the peri-implant tissue showed no significant differences between no graft (-0.49 ± 0.54) and SCTG (-0.68 ± 0.59) after immediate implant placement (van Nimwegen et al., 2018) and between SCTG (-0.2 ± 0.3) and VCMX (-0.3 ± 0.4) after delayed implant placement (Thoma et al., 2020). SCTG from both the palate and tuberosity region demonstrated similar soft tissue stability (Rojo et al., 2020).

3.4.4 | Aesthetics

Alveolar ridge preservation and SCTG resulted in favourable clinical and aesthetic outcomes (Eghbali et al., 2018). The Pink Esthetic

TABLE 1 Patient and treatment characteristics of the studies included for analysis

Authors	Setting	Study type	*N* patients (baseline/final)	Dropouts		Mean age (range)	Smoking	Gender F/M
				N	%			
Liu et al. (2007)	U	RCT	22/22	0	0	NR (18–58)	<10	10/12
Yoshino et al. (2014)	U	RCT	20/20	0	0	52.6 (22–87)	0	13/7
Migliorati et al. (2015)	NR	RCT	48/47	1	2	47.5 (22–70)	<5	25/23
Puzio et al. (2018)	U	RCT	57/57	0	0	40.9 (16–65)	<10	34/23
van Nimwegen et al. (2018)	U	RCT	60/50	10	17	46.7 (20.2–75.0)	0	32/28
Zuiderveld, Meijer, den Hartog, et al., (2018)	U	RCT	60/60	0	0	46.7 (19.5–82.2)	0	32/28
Zuiderveld, Meijer, Vissink, et al., (2018)	U	RCT	60/60	0	0	41.9 (18–73)	0	35/25
Frizzera et al. (2019)	U	RCT	24/24	0	0	NR (23–65)	0	17/7
Rojo et al. (2020)	U	RCT	26/21	5	19	54.4 (33–75)	<10	12/14
Thoma et al. (2020)	U	RCT	20/17	3	15	43.8 (NR)	<10	10/7
Cosyn et al. (2016)	U	CCT	22/17	5	23	50 (27–74)	0	10/12
Fenner et al. (2016)	U	CCT	36/28	8	22	48 (27–82)	<10	13/15
Kato et al. (2018)	U	CCT	36/34	2	6	53.6 (32–68)	0	21/13
Zuiderveld et al. (2019)	U	CCT	40/40	0	0	38.6 (18–71)	0	29/11
Hosseini et al. (2020)	U	CCT	19/16	3	12	22 (18–31)	<10	11/8
Kobayashi et al. (2020)	U	CCT	26/26	0	0	51 (19–75)	0	12/14
Tatum et al. (2020)	NR	CCT	41/26	15	37	56.6 (29–79)	<10	NR
Eghbali et al. (2018)	P	Case series	37/32	5	14	38 (18–81)	0	18/19

Abbreviations: ADM, acellular dermal matrix; CCT, case–control trial; F, female; M, male; NR, not reported; P, private practice; RCT, randomized controlled trial; SCTG, subepithelial connective tissue graft; U, university; VCMX, volume-stable collagen matrix; XCM, mucograft.

Score (PES) is mentioned in Table 5. However, soft tissue grafting at implant placement in ARP ridges compared with no soft tissue grafting did not result in a better aesthetic outcome and patient satisfaction or in better peri-implant health, and therefore, SCTG was not recommended as a standard procedure (Zuiderveld, Meijer, Vissink, et al., 2018). In the latter study, the authors did not find a significant difference in change in mid-buccal mucosa level between the groups.

In the cases where immediate implant placement was applied, a better aesthetic outcome of the peri-implant soft tissues according to the Pink Esthetic Score (PES) was achieved when applying a SCGT or XCM compared with no soft tissue grafting (Frizzera et al., 2019; Migliorati et al., 2015; Tatum et al., 2020). Zuiderveld, Meijer, den Hartog, et al., (2018) reported a lower PES after immediate implant placement with SCTG.

3.4.5 | Peri-implant health

There was no significant difference between the groups in mesial and distal papilla changes, bleeding on probing and probing depth over time, including the endpoint values. Mean probing depth was ≤4 mm in all groups. Similar results were reported for marginal

Implant type	Implant system	Implant survival rate (%)	Follow-up (years)	Time of soft tissue grafting	Test group		Control group
					I	II	
Delayed	Straumann	100	1	At implant placement	ADM		SCTG palate
Immediate	Straumann	100	1	At implant placement	SCTG palate		No graft
Immediate	Straumann	100	2	At implant placement	SCTG palate		No graft
Delayed	Camlog	100	1	3 months before implantation (a) and between placement and abutment connection (b)	XCM	SCTG palate	No graft
Immediate	Nobel Biocare	97	1	At implant placement	SCTG tuberosity		No graft
Immediate	Nobel Biocare	97	1	At implant placement	SCTG tuberosity		No graft
Delayed	Nobel Biocare	100	1	At implant placement	SCTG palate	XCM	No graft
Immediate	Flash	100	1	At implant placement	XCM	SCTG palate	No graft
Delayed	Multiple systems	100	1	Between placement and abutment connection (test) and at abutment connection (control)	SCTG tuberosity and palate		SCTG tuberosity and palate
Delayed	NR	100	3	Between placement and abutment connection	VCMX		SCTG palate
Immediate	Nobel Biocare	95	5	After provisional restoration	SCTG palate		No graft
Delayed	Straumann	100	7.2	Between placement and abutment connection	SCTG palate		No graft
Delayed	Nobel Biocare	100	1	At implant placement	SCTG location unknown		No graft
Delayed	Nobel Biocare	100	1	At implant placement	SCTG palate		No graft
Delayed	Astra Tech	100	5	Between placement and abutment connection	SCTG palate		No graft
Delayed	Nobel Biocare	100	1	At abutment connection	SCTG palate		No graft
Immediate	Straumann	100	1	At implant placement	SCTG palate		No graft
Delayed	Nobel Biocare	100	5	After provisional restoration	SCTG palate		

bone-level changes after soft tissue grafting or no graft (Frizzera et al., 2019; Hosseini et al., 2020; Migliorati et al., 2015; Tatum et al., 2020; Thoma et al., 2020; Yoshino et al., 2014; Zuiderveld, Meijer, den Hartog, et al., 2018; Zuiderveld, Meijer, Vissink, et al., 2018; Zuiderveld et al., 2019).

3.4.6 | Complications

Very few complications were reported in the included studies. Two studies noted implant loss (Cosyn et al., 2016; Zuiderveld, Meijer, den Hartog, et al., 2018). ADM caused the gums to swell during the first week and decreased after 2 weeks (Liu et al., 2007). Two cases of peri-implantitis were reported (Eghbali et al., 2018; Puzio et al., 2018). The patients generally described the treatment as highly satisfactory, and the approaches for professional evaluation between the groups were similar (Frizzera et al., 2019; Rojo et al., 2020; Tatum et al., 2020; Thoma et al., 2020; Zuiderveld, Meijer, den Hartog, et al., 2018; Zuiderveld, Meijer, Vissink, et al., 2018; Zuiderveld et al., 2019). Standardized approaches for professional evaluation (PES/WES) were not frequently used, thus impairing a possible meta-analysis.

TABLE 2 Risk-of-bias assessment of the randomized studies

Study	D1	D2	D3	D4	D5	Overall
Liu (2007)	Some concerns	Some concerns	Low	Low	Low	High
Yoshino (2014)	Some concerns	Low	Low	Low	Low	Some concerns
Migliorati (2015)	Low	Low	Low	Low	Low	Low
Puzio (2018)	Low	Low	Low	Low	Low	Low
van Nimwegen (2018)	Low	Low	Low	Low	Low	Low
Zuiderveld, Meijer, den Hartog, et al., (2018)	Low	Low	Low	Low	Low	Low
Zuiderveld, Meijer, Vissink, et al., (2018)	Low	Low	Low	Low	Low	Low
Frizzera (2019)	Low	Low	Low	Low	Low	Low
Rojo (2020)	Low	Low	Low	Low	Low	Low
Thoma (2020)	Low	Low	Low	Low	Low	Low

Note: Domains:
D1: Bias arising from the randomization process.
D2: Bias due to deviations from intended intervention.
D3: Bias due to missing outcome data.
D4: Bias in measurement of the outcome.
D5: Bias in selection of the reported result.
Green: low risk-of-bias.
Yellow: some concerns in risk-of-bias.
Red: high risk-of-bias.

3.5 | Meta-analysis

The meta-analysis was performed on studies reporting outcomes after 1 year of follow-up ($n = 13$). Two studies included in the qualitative synthesis had evaluated the same group of patients, and therefore, one study was not included in the meta-analyses (van Nimwegen et al., 2018). Four studies were excluded because they did not have a control group without graft (Eghbali et al., 2018; Liu et a., 2007; Rojo et al., 2020; Thoma et al., 2020). A meta-analysis on studies reporting medium-term outcomes ($n = 5$) was not performed due to the high heterogeneity of follow-up period.

3.5.1 | Immediate implant placement

The mean difference in the mid-buccal mucosa level after 1 year was 0.34 mm (95% CI: 0.13–0.56, $p = .002$, $I^2 = 14\%$, 95% PI: −0.07 to 0.76, Figure 2a) in favour of the use of graft versus no graft. A subgroup analysis showed a significant mean difference in the mid-buccal mucosa level after 1 year of 0.38 mm (95% CI: 0.12–0.64, $p = .005$, $I^2 = 39\%$, 95% PI: −0.30 to 1.06, Figure 2b) in favour of the use of SCTG versus no graft.

The mean difference in mid-buccal mucosa thickness after 1 year was 0.66 mm (95% CI: 0.35–0.97, $p < .001$, $I^2 = 28\%$, Figure 3a) in favour of the use of graft versus no graft. Subgroup analysis showed a significant mean difference of mid-buccal mucosa thickness after 1 year of 0.87 mm (95% CI: 0.62–1.12, $p < .001$, $I^2 = 0\%$, Figure 3b) in favour of the use of SCTG versus no graft.

All studies evaluating the mid-buccal mucosa level, except Cosyn et al., (2016), reported on soft tissue grafting at implant placement; therefore, no further analysis was performed. Since the change in thickness was reported by all the studies with grafting at implant placement, further analysis was not performed.

3.5.2 | Delayed implant placement

The mean difference in the mid-buccal mucosa level after 1 year was 0.17 mm (95% CI: 0.01–0.34, $p = .042$, $I^2 = 55\%$, 95% PI: −0.29 to 0.64, Figure 4a) in favour of the use of graft versus no graft. The subgroup analysis showed a significant mean difference in the mid-buccal mucosa level after 1 year of 0.20 mm (95% CI: 0.04–0.35, $p = .011$, $I^2 = 44\%$, 95% PI: −0.20 to 0.59, Figure 4b) in favour of the use of SCTG versus no graft.

The mean difference in mid-buccal mucosa thickness after 1 year between any graft versus no graft was 0.22 mm (95% CI: −0.04 to 0.47, $p = .095$, $I^2 = 31\%$, 95% PI: −0.62 to 1.05, Figure 5a). The mean difference in mid-buccal mucosa thickness after 1 year between SCTG versus no graft was 0.28 mm (95% CI: −0.09 to 0.66, $p = .143$, $I^2 = 66\%$, 95% PI: −1.28 to 1.84, Figure 5b).

The mean difference in the mid-buccal mucosa level after grafting at implant placement was 0.11 mm (95% CI 0.00–0.22, $I^2 = 0\%$, 95% PI: −0.58 to 0.81), between placement and abutment connection −0.02 mm (95% CI −0.39 to 0.34, $I^2 = 0\%$), and at abutment connection 0.55 mm (95% CI 0.27–0.83, single study). Subgroup analysis showed no significant difference between grafting at implant placement and between placement and abutment connection ($p = .49$, $I^2 = 0\%$). Thus, regarding mid-buccal mucosa level, current evidence is insufficient for a recommendation for a preferable time point for soft tissue augmentation.

TABLE 3 Risk-of-bias assessment of the non-randomized studies

	Selection				Comparability		Exposure			
Study	Case definition	Representativeness of the cases	Controls	Definition of controls	Most important factor	Additional factor	Ascertainment of exposure	Same method of cases and controls	Non-response rate	Total score[a]
Fenner (2016)	★	★	★		★	★	★	★	★	8
Cosyn (2016)	★	★	★		★	★	★	★	★	8
Kato (2018)	★	★	★	★	★	★	★	★	★	9
Hosseini (2020)	★	★	★		★	★	★	★	★	8
Tatum (2020)	★	★	★	★	★	★	★	★	★	9
Zuiderveld (2019)	★	★	★	★	★	★	★	★	★	9
Kobayashi (2020)	★	★	★		★	★	★	★	★	8

[a]Studies with ≥6 stars are considered to be high in methodological quality, and <6 stars indicate a low quality.

TABLE 4 Risk-of-bias assessment of the case series

	Selection				Comparability		Outcome			
Study	Exposed cohort	Non-exposed cohort	Ascertainment of exposure	Outcome of interest	Most important factor	Additional factor	Assessment of outcome	Length of follow-up	Adequacy of follow-up	Total score[a]
Eghbali (2018)	★		★	★	★	★	★	★	★	8

[a]Studies with ≥6 stars are considered to be high in methodological quality, and <6 stars indicate a low quality.

TABLE 5 Outcome measures at final assessment

	Number of implants baseline		Number of implants final		Change in midfacial mucosa height (mm)			Change in mucosal thickness (mm)		
					Test			Test		
Authors	Test	Control	Test	Control	I	II	Control	I	II	Control
Liu et al. (2007)	10	12	10	12	NR		NR	1.9 ± 1.33		1.7 ± 1.13
Yoshino et al. (2014)	10	10	10	10	−0.25 ± 0.35		−0.7 ± 0.48	NR		NR
Migliorati et al. (2015)	24	24	24	23	−0.4 ± 1.2		−0.7 ± 1.2	0.4 ± 0.7		−0.2 ± 0.5
Puzio et al. (2018)	Ia: 15 Ib: 15 IIa: 15 IIb: 15	15	Ia: 15 Ib: 15 IIa: 15 IIb: 15	15	NR	NR	NR	Ia: 1.16 ± 0.7 Ib: 0.89 ± 0.6	IIa: 1.76 ± 0.7 IIb: 1.52 ± 1.0	0.7 ± 0.8
van Nimwegen et al. (2018)	30	30	25	25	Zuiderveld, Meijer, den Hartog, et al., (2018)		Zuiderveld, Meijer, den Hartog, et al., (2018)	NR		NR
Zuiderveld, Meijer, den Hartog, et al., (2018)	30	30	29	29	0.1 ± 0.8		−0.5 ± 1.1	NR		NR
Zuiderveld, Meijer, Vissink, et al., (2018)	Test I: 20 test II: 20	20	Test I: 20 test II: 20	20	−0.03 ± 0.2	−0.16 ± 0.2	−0.15 ± 0.2	NR	NR	NR
Frizzera et al. (2019)	Test I: 8 Test II: 8	8	Test I: 8 Test II: 8	8	−0.42 ± 0.6	0.04 ± 0.3	−0.72 ± 0.57	1.12 ± 0.33	2.06 ± 0.32	1.11 ± 0.42
Rojo et al. (2020)	10	16	8	13	NR			0.04 ± 0.19		0.0 ± 0.21
Thoma et al. (2020)	10	10	8	9	NR		NR	0.44 ± 1.1		1.1 ± 1.5
Cosyn et al. (2016)	7	15	5	12	−0.50		−0.63	NR		NR
Fenner et al. (2016)	14	22	13	15	−0.92 ± 1.2		−0.23 ± 0.75	NR	NR	
Kato et al. (2018)	12	12	12	12	0		−0.1	0	0	
Zuiderveld et al. (2019)	20	20	20	20	0.07 ± 0.29		−0.15 ± 0.23			
Hosseini et al. (2020)	10	23	8	20	0.68 ± 0.77		−0.05 ± 0.57	0.30 ± 0.71	−0.08 ± 0.93	
Kobayashi et al. (2020)	14	12	14	12	−0.09 ± 0.30		−0.64 ± 0.42	0.05 ± 0.32	−0.09 ± 0.56	
Tatum et al. (2020)	20	21	12	14	−0.20 ± 1.14		0.01 ± 1.56	NR	NR	
Eghbali et al. (2018)	37		32		−0.12 ± 0.36			0.9 ± 0.5		

Abbreviation: NR, not reported.

4 | DISCUSSION

Dimensional changes, including mid-buccal mucosal recession and loss of buccal soft tissue, could result in unpleasing peri-implant mucosa aesthetics (Cosyn et al., 2016; Kan et al., 2018; Tonetti et al., 2017). This systematic review aimed to assess the effect of soft tissue grafts regarding changes in the mid-buccal mucosa when applied for immediate or delayed implant placement in the maxillary

Change in mucosal volume (mm)		Probing pocket depth final measurement (mm)			Marginal bone-level changes (mm)			PES		
		Test			Test			Test		
Test	Control	I	II	Control	I	II	Control	I	II	Control
NR	NR	NR		NR	NR		NR	NR		NR
NR	NR	NR		NR	−0.01 ± 0.27		−0.14 ± 0.53	NR		NR
NR	NR	3.4		3.2	−0.06		0.16	8		6.65
NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
−0.68 ± 0.59	−0.49 ± 0.54	2.28		2.44	NR		NR	11.28		11.36
NR	NR	2.3 ± 0.9		2.5 ± 1.2	Mesial: −0.04 Distal: 0.02		Mesial: −0.06 Distal: 0.03	6.4 ± 1.5		6.8 ± 1.5
NR	NR	3.3 ± 1.2	2.8 ± 1.6	2.7 ± 1.1	Mesial: −0.3 median Distal: −0.5 median	Mesial: −0.9 median Distal: −0.7 median	Mesial: −0.3 median Distal: −0.3 median	7.0 ± 2.4	6.1 ± 1.7	6.6 ± 1.5
NR	NR	NR		NR	Less than 1.5 mm			10 ± 1.3	10.75 ± 1.38	9.87 ± 1.64
NR	NR	2.4 ± 0.5		2.6 ± 0.4	NR		NR	8.25 ± 2.18		9.78 ± 2.39
−0.3 ± 0.4	−0.2 ± 0.3	2.8 ± 0.3		2.9 ± 0.3	−0.9 ± 1.0		−0.3 ± 0.3	9.1 ± 2.4		10.0 ± 2.3
NR	NR	Overall 3.1			Overall 0.19			Overall 11.18		
NR	NR	4.09		3.97	2.50		2.20	NR		NR
NR	NR	NR		NR	NR		NR	NR		NR
NR	NR	3.0 ± 0.8		2.9 ± 1.3	Mesial: −0.06 ± 0.5 distal: 0.01 ± 0.4		Mesial: −0.03 ± 0.4 distal: −0.13 ± 0.5	6.60		6.55
NR	NR	NR		NR	−0.11 ± 0.45		−0.12 ± 0.33	NR		NR
NR	NR	NR		NR	NR		NR	NR		NR
NR	NR	1.92 ± 0.79		3.21 ± 1.58	Mesial: −0.06 ± 0.12 distal: −0.01 ± 0.12		Mesial: 0.00 ± 0.13 distal: −0.08 ± 0.15	6.19 ± 2.19		5.88 ± 1.63
NR		3.00 ± 0.75			−0.47 ± 0.4			11.17 ± 1.91		

and mandibular aesthetic zone. Meta-analysis on studies reporting outcomes after 1 year of follow-up revealed a significant difference in change in mid-buccal mucosa level (0.34 mm) and mid-buccal mucosa thickness (0.66 mm) following immediate implant placement in favour of the use of a graft versus no graft. Mean difference in vertical mid-buccal mucosa level (0.17 mm) following delayed implant placement was also in favour of the use of a graft versus no graft. With regard to mucosa thickness, the use of a graft was not in

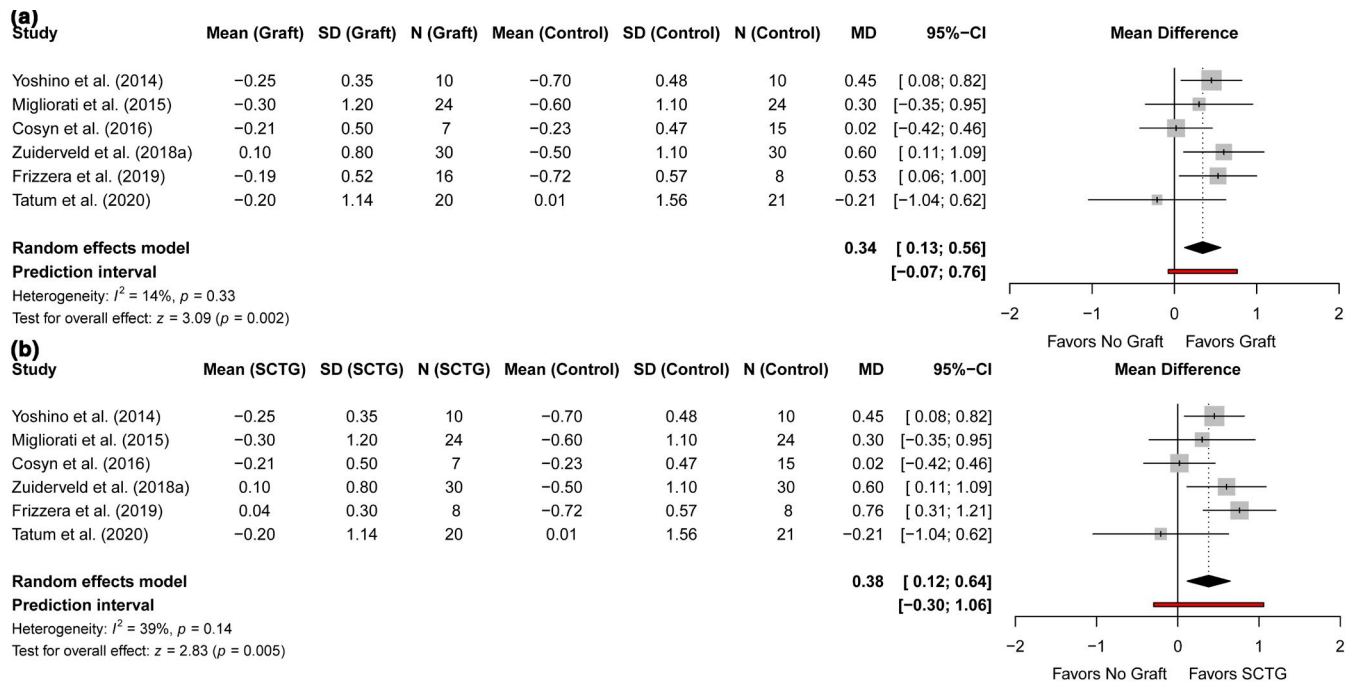

FIGURE 2 Forest plot of the mean difference (mm) in the mid-buccal mucosa level after 1 year after immediate implant placement. (a) Soft tissue augmentation with all grafts versus no graft. (b) Soft tissue augmentation with SCTG versus no graft. Abbreviations: *SD*, standard deviation; MD, mean difference; 95% CI, 95% confidence interval; SCTG, subepithelial connective tissue graft

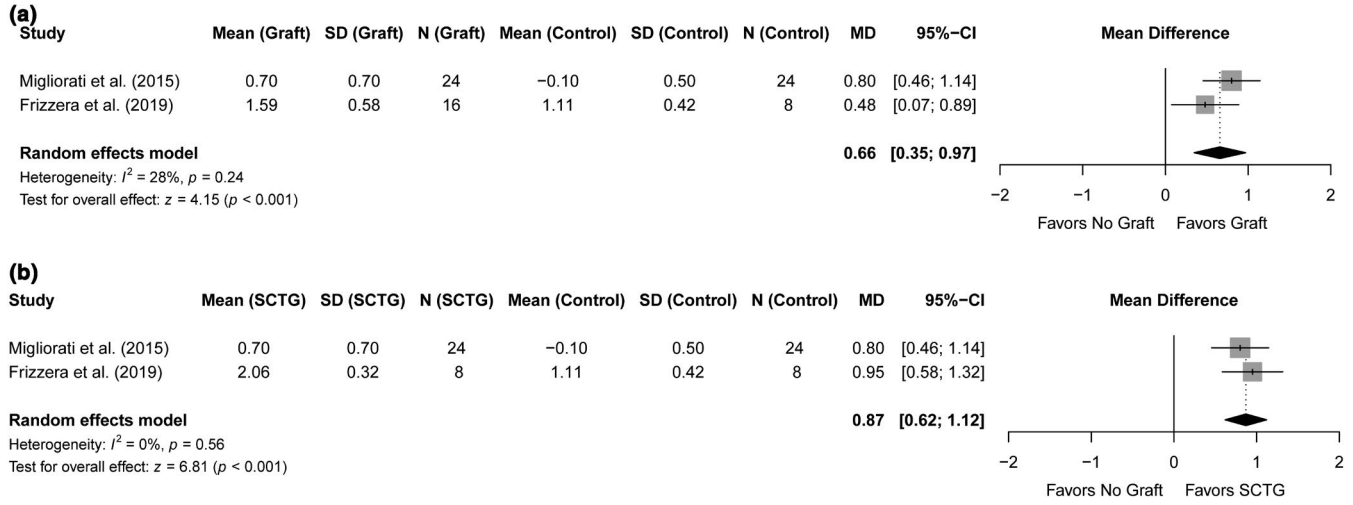

FIGURE 3 Forest plot of the mean difference (mm) of mid-buccal mucosa thickness after 1 year after immediate implant placement. (a) Soft tissue augmentation with all grafts versus no graft. (b) Soft tissue augmentation with SCTG versus no graft. Abbreviations: *SD*, standard deviation; MD, mean difference; 95% CI, 95% confidence interval; SCTG, subepithelial connective tissue graft

favour compared with no graft following delayed implant placement. The observed changes remained stable in the medium term, while evidence remains insufficient for a recommendation for a preferable time point for soft tissue augmentation, and between using autologous grafts and soft tissue substitutes.

4.1 | Immediate implant placement

This study indicates that soft tissue grafting results in significantly less recession of the mid-buccal mucosa than when no grafting is used. In this review, "recession" is used as the apical displacement of the supracrestal peri-implant soft tissue (Burkhardt et al., 2008). SCTG results in less recession of the mid-buccal mucosa and a thicker mid-buccal mucosa and has a favourable effect on PES for at least up to 1 year after grafting. The soft tissue changes are minor in vertical and horizontal direction, but nevertheless they may be clinically relevant, especially in cases where there is already a recession and/or volume deficit on the buccal side of the failing tooth. It is, however, not yet set whether applying SCTG combined with immediate implant placement is favourable in the long run. Van Nimwegen et al., (2018) showed that the gain in soft tissue volume 1 year after applying a SCTG was followed by

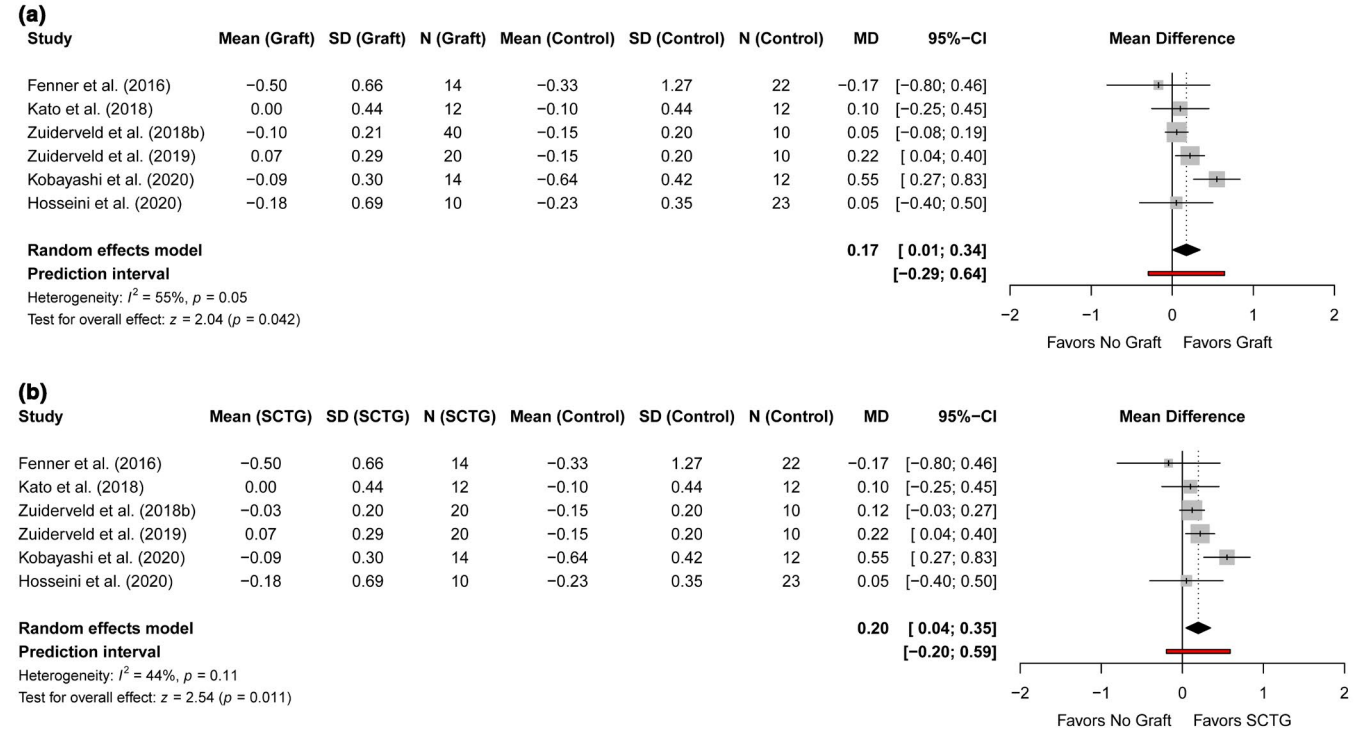

FIGURE 4 Forest plot of the mean difference (mm) of the mid-buccal mucosa level after 1 year after delayed implant placement. (a) Soft tissue augmentation with all grafts versus no graft. (b) Soft tissue augmentation with SCTG versus no graft. Abbreviations: *SD*, standard deviation; MD, mean difference; 95% CI, 95% confidence interval; SCTG, subepithelial connective tissue graft

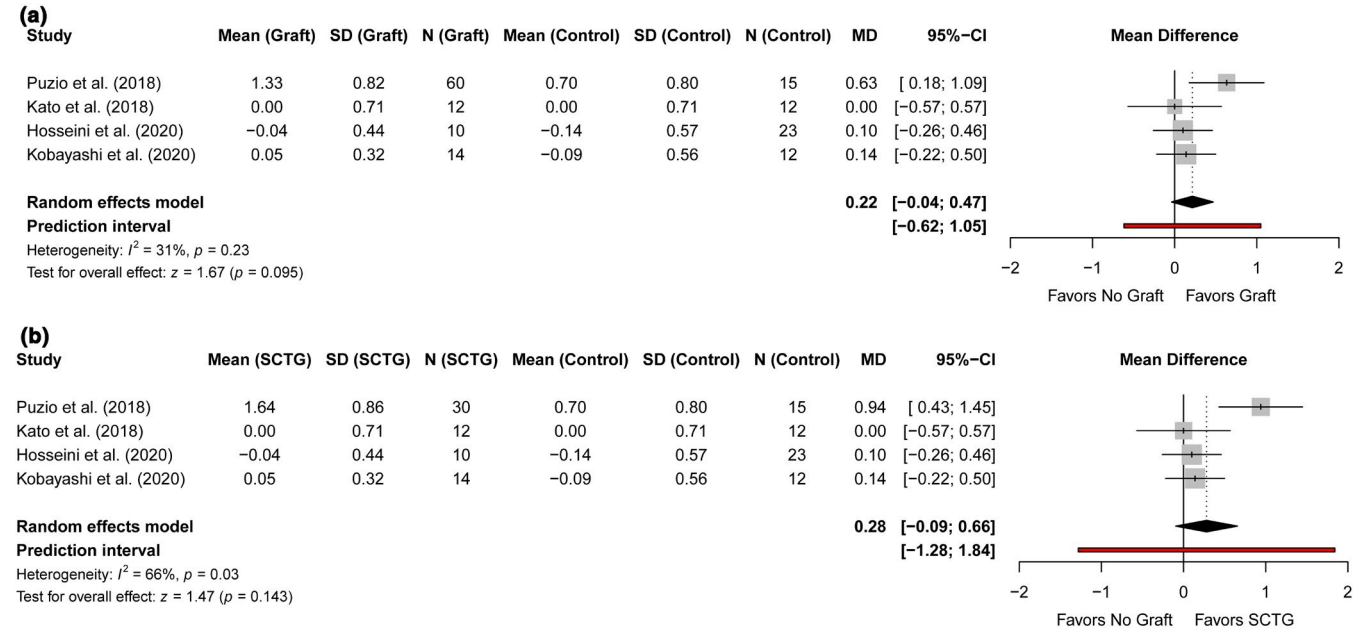

FIGURE 5 Forest plot of the mean difference (mm) of mid-buccal mucosa thickness after 1 year after delayed implant placement. (a) Soft tissue augmentation with all grafts versus no graft. (b) Soft tissue augmentation with SCTG versus no graft. Abbreviations: *SD*, standard deviation; MD, mean difference; 95% CI, 95% confidence interval; SCTG, subepithelial connective tissue graft

a decrease in volume with time and the volume loss was larger than when immediate implant placement was used without the appliance of a SCTG. Apparently, the use of a SCTG cannot fully compensate for the mid-buccal mucosal volume loss caused by underlying bone loss of the buccal bone wall following immediate implant placement (van Nimwegen et al., 2018). This assumption is supported by the observation from cone-beam computed tomographic (CBCT) analyses that a SCTG combined with immediate implant placement resulted in more buccal bone loss than when no SCTG was applied (Zuiderveld et al., 2020). A possible explanation for this phenomenon is that the surgical intervention used to position the SCTG submucosally might induce additional bone loss by compromising the vascularization of the mucosa and bone in that area. The disruption in the blood supply, together with the bone remodelling process after tooth extraction (Araújo et al., 2006; Vignoletti et al., 2012), could have induced further loss of mid-buccal bone (Mazzocco et al., 2017).

It is not yet set whether the use of alternative techniques such as a flapless approach, palatinal/lingual implant position, filling the bone gap between the implant and buccal alveolar wall, abutment configuration and crown design might be better approaches to limit the degree of recession of the mucosa (Grunder, 2011; Kan et al., 2018; Lee et al., 2016; Lin et al., 2014; Raes et al., 2011). A prospective multicentre case series in which a flapless immediate implant placement approach was applied to 100 patients without additional SCTG reported very favourable aesthetic outcomes after 1 year (Groenendijk et al., 2020). Latter authors showed an improvement in mucosal level and a stable contour of the alveolar process the first year after treatment.

A major limitation of most studies is the lack of long-term results. Such data are needed to show whether the buccal bone thickness remains stable and whether the mid-buccal mucosa level can indeed be preserved with this approach. The conclusion, though, is that SCTG with immediate implant placement seems to be able to limit recession and to increase the thickness of the mid-buccal mucosa to some extent. The lack of data, since only 1 study was available, means it is not possible to make any definitive statements yet about alternative materials for soft tissue grafting (Frizzera et al., 2019).

4.2 | Delayed implant placement

There was significant difference in recession of the mid-buccal mucosa in favour of soft tissue grafting whether SCTG was used or not, while the use of a graft resulted in no thicker mid-buccal mucosa compared with no graft. Five-year data show that the thickness of the buccal contour remains rather stable over time after soft tissue grafting (Eghbali et al., 2018; Hanser & Khoury, 2016; Hosseini et al., 2020). Such a gain in soft tissue could be particularly clinically relevant if there is a volume deficit before implant placement. Another possibility to increase the buccal contour when delayed implant placement is applied is guided bone regeneration (GBR). In a RCT, it was shown that both GBR and SCTG are effective in restoring the buccal soft tissue profile (De Bruyckere et al., 2020). As an alternative to SCTG, VCMX and XCM were introduced for soft tissue grafting (Sanz et al., 2009; Thoma et al., 2016). These materials are promising, although the gain in volume of the mid-buccal mucosa is less than when a SCTG is applied (Cairo et al., 2019; Moraschini et al., 2020). Nevertheless, both substitutes have a favourable effect and are accompanied by a lower morbidity. VCMX seems even to be more promising than XCM as the latter degrades earlier than VCMX (Moraschini et al., 2020; Naenni et al., 2020). These substitute materials may be suitable for sites, which only require minor thickening of the mucosa, for patients who are pain-sensitive and for patients who do not consent to the harvesting of soft tissues (Lissek et al., 2020). Moreover, these materials may also be an alternative for professionals who are not trained to or are uncomfortable with harvesting connective tissue grafts.

Grafting of the peri-implant soft tissues can be performed at different time points, such as before implant placement, simultaneously with implant placement, during the phase of osseointegration of the implant, or after prosthetic reconstruction (Lin et al., 2018). According to the results gleaned from the current systematic review, there is no evidence for a preferable time point for soft tissue augmentation. Soft tissue grafting simultaneously with immediate implant placement was reported in all the study groups, except Cosyn et al., (2016), and showed less recession and increase thickness of the mid-mucosa. Before installation of the final restoration, SCTG has been considered to be of added value in case of advanced mid-buccal recession (≥1 mm) and/or obvious alveolar process deficiency during the healing period after implant placement, or during the temporary implant crown phase (Cosyn et al., 2016; Fenner et al., 2016; Hosseini et al., 2020; Kobayashi et al., 2020). This treatment approach is accompanied by stable clinical, aesthetic and radiographical long-term outcomes after 10 years when immediate implant placement was combined with SCTG (Seyssens et al., 2020). Strikingly, the latter paper, based on the same patient material as Cosyn et al., (2016), observed that when adding SCTG to treat a recession during the healing phase was of added value. In cases where no graft was used, in about one third of the patients (33%) the recession progressed (Seyssens et al., (2020). This percentage was substantially higher than the 11% described in a systematic review by Khzam et al., (2015). Latter review, however, evaluated short-term effects only. It has to be noted that the clinical relevance of a change in mucosa level and thickness resulting from SCTG may be minor in the short term but may gain in importance after a longer follow-up period. Finally, in the study of Bienz et al., (2017) a connective tissue graft was applied in healed sites for aesthetic reasons. This graft was applied 3–4 months after implant placement and 4–6 weeks before abutment connection. They reported favourable outcomes after SCTG grafting compared with non-grafted implant sites for their 5-year follow-up. The *profilometric* and linear changes were minimal, and the peri-implant parameters were stable. That finding is in line with the results in this review.

During the first 3 months after the soft tissue augmentation, substantial shrinkage of the graft occurs, resulting in a decrease in soft tissue volume. The shrinkage proceeded during remaining of the

first year at a lower rate (Poskevicius et al., 2017). In the present systematic review, the mid-buccal mucosa showed a slight decrease in level and thickness after the first year of applying soft tissue grafting. Therefore, the effect of soft tissue grafting was considered stable in the medium term. Stability was considered when changes are <0.5 mm (Thoma et al., 2020). As most of the observed changes are <0.5 mm, the change in soft tissue volume was considered as clinically negligible. Translating this observation to a clinical environment means that loss of 0.5 mm in the medium term can be considered as clinically acceptable in the aesthetic region, keeping in mind that such minimal changes may not be perceived by the naked eye (Bienz et al., 2017). When the level and/or thickness of the mid-buccal mucosa continue to decrease further over time, which is not yet known, these changes can become clinically bothersome.

A systematic review concluded that, until now, no appropriate moment can be indicated for soft tissue grafting and that further studies with accurate evaluation methods need to be performed (Poskevicius et al., 2017). However, a recent study reported that soft tissue augmentation after implant placement may result in higher marginal bone loss compared with pre-surgical soft tissue augmentation (Puzio et al., 2020). Other studies showed that when soft tissue grafting is applied after placement of the final implant crown to compensate for soft tissue loss, such an approach is often more difficult to perform and accompanied by a less favourable outcome (Burkhardt et al., 2008; Thoma et al., 2014).

4.2.1 | Secondary outcomes

Besides the favourable primary outcomes of soft tissue grafting on the stability of the mid-buccal mucosal level, the peri-implant tissues were healthy, the loss of marginal bone was minor and the PES was favourable. The PES showed significantly higher scores after immediate implant placement with SCTG (Frizzera et al., 2019; Migliorati et al., 2015; Tatum et al., 2020). This observation contradicts Zuiderveld, Meijer, den Hartog, et al., (2018) findings, who reported better PES scores when no SCTG was applied. A possible explanation for this discrepancy in the latter study could be that the surgical envelope technique used to place the SCTG resulted in more mucosal deformation and scarring of the peri-implant soft tissues. In delayed implant placement cases, it was reported that applying SCTG resulted in higher PES scores than when no SCTG, XCM or VCMX grafting was applied (Thoma et al., 2020; Zuiderveld, Meijer, Vissink, et al., 2018; Zuiderveld et al., 2019).

Soft tissue thickness seems to play an important role in maintaining or improving peri-implant health (Cairo et al., 2019; Thoma et al., 2018). A factor often mentioned as an indication to apply soft tissue grafting is a thin gingival biotype (Hosseini et al., 2020; Kan et al., 2018; Puzio et al., 2020; Tatum et al., 2020). In the studies that were considered eligible for the current review, the biotype was not shown to be a significant factor with regard to changes observed in the level of the mid-buccal mucosa after applying a SCTG, or not (Zuiderveld, Meijer, den Hartog, et al., 2018; Zuiderveld, Meijer, Vissink, et al., 2018). The latter study supported the conclusion of a previous systematic review indicating that the preoperative tissue biotype does not influence soft tissue and aesthetic outcomes (Khzam et al., 2015).

When implants are placed in preserved alveolar ridges, there is no need to apply SCTG because it does not result in a better aesthetic outcome (PES), higher patient satisfaction or better peri-implant health (Zuiderveld, Meijer, Vissink, et al., 2018; Zuiderveld et al., 2019). When augmentation surgery of the extraction socket was combined with sealing the socket using a mucosa graft, these conditions might already have provided sufficient soft tissue volume for preserving a stable mid-buccal mucosal level (Raghoebar et al., 2009).

4.2.2 | Limitations

The conclusions drawn in this systematic review need to be interpreted with caution because of the large heterogeneity in study designs and the limited number of eligible studies/study groups per topic. As an example, the methods used to analyse soft tissues over time include intra-oral photographs, transmucosal probing (endodontic instruments), ultrasonography, non-invasive profilometrics, CBCTs and *profilometric* measurements based on casts and optical scans (Eghbali et al., 2018; Frizzera et al., 2019; Kato et al., 2018; Kobayashi et al., 2020; Migliorati et al., 2015; Puzio et al., 2018; Rojo et al., 2020; Thoma et al., 2020). As most of these methods score a three-dimensional change two-dimensionally, the true volume thickening effect of a connective tissue graft may have even been underestimated. Thus, the true effect of soft tissue grafting with respect to the change in the volume of peri-implant soft tissues needs further investigation, preferably by using digital imaging technology to facilitate three-dimensional measurements. Information about the three-dimensional position of the implant is important because buccal implant shoulder position has been associated with mid-buccal recession (Seyssens et al., 2020). Furthermore, there is a need for better designed RCTs with longer follow-ups, larger sample sizes and uniform analytic methods to reduce methodological bias. In addition, all the studies should preferably report both clinical and patient-reported outcomes as most papers lack such a combination of outcomes.

5 | CONCLUSIONS

Soft tissue augmentation in the zone of the aesthetic priority results in less recession (0.34 mm) and a thicker mid-buccal mucosa (0.66 mm) following immediate implant placement when compared with no grafting after 1 year. Also, for delayed implant placement soft tissue augmentation results in less recession of the mid-buccal mucosa (0.17 mm) when compared with no grafting after 1 year. At medium-term follow-up, based on the few studies ($n = 5$) that are available, the outcomes of soft tissue augmentation seem to

be stable. Evidence remains insufficient for a recommendation for a preferable time point for soft tissue augmentation and between using autologous grafts and soft tissue substitutes. However, a consistent tendency of less recession (2 RCTs) and thicker mid-buccal mucosa (4 RCTs) was shown for autologous grafts compared with soft tissue substitutes. The rather limited number of studies, and the high clinical and methodological heterogeneity of studies, suggests that the results of this systematic review should be interpreted with caution.

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CONFLICT OF INTEREST

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AUTHOR CONTRIBUTIONS

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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