Received: 15 December 2020 | Revised: 3 August 2021 | Accepted: 5 August 2021

DOI: 10.1111/clr.13829

REVIEW ARTICLE

CLINICAL ORAL IMPLANTS RESEARCH WILEY

Influence of soft tissue augmentation procedures around dental implants on marginal bone level changes—A systematic review

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Abstract

Objectives: This systematic review assessed the influence of soft tissue augmentation procedures on marginal bone level changes in partial or fully edentulous patients.

Material and Methods: We identified three relevant PICO questions related to soft tissue augmentation procedures and conducted a systematic search of four major electronic databases for clinical studies in systemically healthy patients receiving at least one dental implant and a minimum follow-up of one year after implant placement. The primary outcome was mean difference in marginal bone levels, and secondary outcomes were clinical and patient-related outcomes such as thickness of peri-implant mucosa, bleeding indices, and Pink Esthetic Score.

Results: We identified 20 publications reporting on 16 relevant comparisons. Studies varied considerably and thus only two meta-analyses could be performed. This systematic review showed that:

Soft tissue augmentation either for augmentation of keratinized mucosa or soft tissue volume inconsistently had an effect on marginal bone level changes when compared to no soft tissue augmentation, but consistently improved secondary outcomes.

The combination soft and hard tissue augmentation showed no statistically significant difference in terms of marginal bone level changes when compared to hard tissue augmentation alone, but resulted in less marginal soft tissue recession as shown by a meta-analysis.

Soft or hard tissue augmentation performed as contour augmentations resulted in comparable marginal bone level changes.

Conclusions: Peri-implant soft and hard tissues seem to have a bidirectional relationship: "*Bone stands hard, but soft tissue is the guard*".

KEYWORDS
alveolar ridge augmentation, bone augmentation, dental implants, guided bone regeneration, guided tissue regeneration, soft tissue augmentation

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1 | INTRODUCTION

Dental implants are considered to be a predictable option to rehabilitate edentulous or partially edentulous patients. The 10-year survival rate of dental implants has been described to be 96.4% (Howe et al., 2019). Retrospective long-term studies document survival rates for dental implants of 92.6% after up to 27 years in function (Balshi et al., 2015). However, often due to tooth-borne pathologies, tissue deficiencies such as horizontal and vertical bone defects and lack of soft tissue quality and quantity are a common finding in future implant sites. To foster a proper site for prosthetically driven implant placement, both soft and hard tissue augmentation procedures are frequently performed mostly in a staged manner prior to implant placement. Augmentation procedures for implant site development have been documented in literature and predictably create an appropriate area for consecutive implant placement (Naenni et al., 2019; Troeltzsch et al., 2016).

These surgical interventions are necessary to establish a site for future implant placement. Further indications for soft and hard tissue augmentation procedures—such as buccal bony contour augmentations or soft tissue volume augmentations—are advocated to improve clinical, biological, and patient-related outcomes. With special emphasis on soft tissue augmentation (STA) procedures, the clinical significance of these surgical interventions is not completely clear in literature.

From a clinical perspective, STA can be performed with two fundamental goals: first to increase attached, keratinized mucosa—that is, to improve oral hygiene procedures and secondly to increase soft tissue volume—that is, to establish a convex architecture of the peri-implant mucosa. These plastic peri-implant procedures have been advocated to establish short- and long-term favorable biological, functional, and esthetic outcomes.

On the other hand, STA has also been advocated to protect marginal bone levels (MBLs) due to an adequate sealing of the peri-implant soft tissue collar. A randomized controlled clinical study comparing thin and thick peri-implant soft tissue heights concluded, that in implants sited surrounded by thin peri-implant soft tissue 1.5 mm of crestal bone loss occurred, while in the thick group only 0.3 mm of crestal bone was lost (Linkevicius et al., 2009). A recent systematic review on the effect of STA on peri-implant health concludes that augmentation of attached keratinized mucosa leads to lower bleeding scores and higher bone levels. It further concludes that augmentation of mucosal thickness using autogenous grafts is associated with less crestal bone loss (Thoma et al., 2018), which might suggest a potential biological advantage for cases with supplementary STA.

However, it is rather unclear whether the direct clinical consequence of STA (increased soft tissue thickness/increased amount of keratinized mucosa or increased soft and hard tissue contour) is able to improve biological parameters such as long-term maintenance of the implant fixture. Therefore, the main objective of this systematic review was to assess the effect of STA (performed at the time of implant placement or as a separate intervention) on peri-implant MBLs. Secondary outcomes of this systematic review were clinical and patient-related outcomes such as soft tissue thickness, soft tissue volume, and esthetic parameters.

2 | METHODS

2.1 | Protocol development and registration

This systematic review aims to identify literature relating to STA on MBL changes and patient-related outcomes minimum of one year after implant placement. In line with current recommendations, the PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analyses) statements' checklist for reporting a systematic review was followed (Moher et al., 2009). For this work and a separate systematic review on related PICO questions, a detailed systematic review protocol was registered a priori with PROSPERO (International Prospective Register of Systematic Reviews, Record ID: CRD42020211689).

2.2 | Eligibility criteria

2.2.1 | Focused research questions

For the purpose of a systematic and comprehensible approach, specific questions following the PICO method were developed and are addressed in this work (Higgins & Green, 2011):

PICO 1. In systematically healthy patients with the need of at least one dental implant [P, population], how does STA (either soft tissue volume augmentation or augmentation of keratinized mucosa) [I, intervention] compared with no augmentative intervention [C, control] affect biological and patient-related parameters [O, outcome measures] a minimum of one year after implant placement [T, time]?

PICO 2. In systematically healthy patients with the need of at least one dental implant [P], how does STA (either soft tissue volume augmentation or augmentation of keratinized mucosa) in combination with hard tissue augmentation [I] compared with only hard tissue augmentative intervention [C] affect biological and patient-related parameters [O] a minimum of one year after implant placement [T]?

PICO 3. In systematically healthy patients with the need of at least one dental implant [P], how does STA (either soft tissue volume augmentation or augmentation of keratinized mucosa) [I] compared with hard tissue augmentation [C] affect biological and patient-related parameters [O] a minimum of one year after implant placement [T]?

2.3 | Inclusion criteria

- Experimental clinical studies (randomized clinical trials [RCT], controlled clinical trials [CCT]).

- Comparative observational studies (e.g., pro- or retrospective cohort studies [OBS]), to ensure all relevant clinical information that was not tested (yet) in experimental studies is captured.
- Studies with systemically healthy adults (≥18 years) in need of a minimum of one dental implant including edentulous or partially dentate patients and including any type of prosthetic suprastructure.
- Studies with a minimum follow-up time of one year following implant placement.
- Studies including the intervention: simultaneous hard and/or simultaneous or staged STA (without or in addition to coagulum stabilizer (e.g., plasma rich in growth factors [PGRFs], hyaluronic acid, and similar).
- Studies with a minimum sample size of 10 participants.
- English or German literature (due to the authors being sufficiently fluent in English and German only).
- Published articles or articles in press.

2.4 | Exclusion criteria

- Reviews, commentaries, perspective articles, non-comparative studies (including case series, case reports, one-armed cohort studies).
- Studies in animals, studies in pre-clinical models/cadavers/mannequins, in-vitro studies.
- Studies with follow-up periods of less than one year.
- Interventions without augmentative procedures.
- Studies in children/adolescents.
- Studies in not systemically healthy patients.
- Studies solely investigating the effect of coagulum stabilizer (e.g., PGRFs, hyaluronic acid, and similar) or tissue expanders without an augmentative procedure.
- Unpublished literature.
- Literature published in another language than German or English.

2.5 | Outcome measures

The primary outcome measure relevant for this systematic review is MBL (in mm). Measure of effect is reported in the mean difference of MBL (mm).

- Secondary outcome measures include following:
- Implant loss rate/Implant survival rate.
- Marginal soft tissue level, thickness [MSTLevel, MSTT].
- Buccal bone thickness [BBT].
- Width of keratinized gingiva [KM].
- Incidence of peri-implantitis [PI].
- Signs of inflammation: Bleeding Scores [BI].
- Peri-implant Probing Depths [PD, mm].
- Pink Esthetic Score [PES].
- Patient related outcome/patient satisfaction.

The measures of effect of the secondary outcomes are reported in mean difference [MD] or (if applicable) odds ratio [OR].

2.6 | Information sources and literature search strategy

The final literature search was primarily conducted on October 29, 2020. Further, an updated search was conducted on December 14, 2020. Following databases were searched electronically:

- Embase.
- MEDLINE (Medical Literature Analysis and Retrieval System Online via PubMed).
- SCOPUS.
- CENTRAL (The Cochrane Central Register of Controlled Trials).Platform-specific search terms can be found in the Supplemental Material (Supplement Table 1).

Hand search was conducted according to following points:

- Reference list on all literature that was deemed eligible after full-text search.
- Following Journals, editions published in the last 20 years: Journal of Dental Research, Journal of Clinical Periodontology, Journal of Periodontology, Clinical Oral Implants Research.
- MetaRegister of Controlled Trials (including ClinicalTrials.gov).

2.7 | Study selection and data extraction

Two independent reviewers (SF, AK) screened titles and abstracts for relevance using pre-established inclusion and exclusion criteria and an initial calibration exercise. Inter-reviewer calibration was conducted on pilot data. The inter-rater reliability was expressed using percentage agreement. Any disagreement was discussed with a third reviewer (MK) as a tie-breaker until a consensus was found. Subsequently, full-text evaluation and rechecking for inclusion eligibility was conducted by two independent reviewers (SF, AK). Disagreements at this stage were mediated by a third reviewer (MK) until a unanimous decision was found. Study characteristics and main findings of eligible literature were extracted independently by two reviewers (SF, AK) using a pre-established and trialed Excel spreadsheet as recommended by the Cochrane Handbook (Higgins & Green, 2011).

2.8 | Quality assessment

To assess study quality and risk of bias of the eligible studies, multiple tools were utilized and recorded by two independent reviewers (SF, AK):

- RoB 2.0 for RCTs (J. A. C. Sterne et al., 2019).

- ROBINS-I for non-randomized trials (J. A. Sterne et al., 2016).
- Newcastle-Ottawa-Scale for observational studies (Wells et al., 2013).Disagreements regarding the assessment of risk of bias were settled by consensus after consultation with a third reviewer (MK).

2.9 | Assessment of heterogeneity

Statistical heterogeneity among studies included in a meta-analysis was measured using Q-test and I2-tests. Heterogeneity was categorized as low (25%–50%), moderate (51%–75%) or high (>75%) (Higgins & Green, 2011;. Higgins et al., 2003).

2.10 | Data analysis

Where appropriate after evaluation of the heterogeneity of the identified evidence following the principles outlined in the Cochrane Manual, study results were summarized using mean values and standard deviations for primary and secondary outcomes in meta-analyses generating weighted mean differences and 95% confidence intervals. Random (for significant/high heterogeneity) models were employed in these meta-analyses. Data analyses were performed using the Cochrane ReviewManager (RevMan, 2020) environment.

3 | RESULTS

The electronic search of the Embase, MEDLINE, SCOPUS, and CENTRAL databases resulted in the identification of 10,193 unique papers (Figure 1). After screening of all titles and abstracts by two independent reviewers, a total of 183 papers were considered for the full-text search. Finally, 20 papers were included in the descriptive analysis (Table 1). A table listing the excluded studies including reasons for exclusion can be found in the supplemental material (supplemental Table 2).

3.1 | Inter-rater agreement

Inter-rater agreement level was assessed during stage one of this systematic review (screening of titles and abstracts). There was an agreement rate of 97.9% on 10193 subjects between the two raters AK and SF.

3.2 | Included studies: overview, risk of bias, and heterogeneity

Table 1 gives an overview of the included studies, describing study designs and baseline characteristics. Generally, the studies showed a high level of heterogeneity in several aspects of the study design. Sample sizes varied from 10 to 63 included patients per study arm. Basic baseline [T0] and population characteristics (e.g., age distribution, gender distribution) were not reported in various articles. A total of 20 publications reporting on 16 relevant comparisons were identified. Eleven studies were RCTs, and 9 studies were observational studies. The results of the studies including listings of conflict of interest statements and funding sources—if reported—can be found in Table 2. Overall, only 2 publications reporting on two observational studies were judged to have a low risk of bias. All other studies—including all RCTs—revealed at least some risk of bias concerns.

After review of all eligible studies, we have conducted one meta-analysis referring to a primary outcome and one to a secondary outcome in PICO 2. Even though there were multiple studies reporting on the same outcome within one PICO-scenario, the overwhelming heterogeneity of the study designs, utilized methodologies, outcome definitions, and differing observation periods did not allow additional meta-analyses.

PICO 1. In systematically healthy patients with the need of at least one dental implant [P, population], how does STA (either soft tissue volume augmentation or augmentation of keratinized mucosa) [I, intervention] compared with no augmentative intervention [C, control] affect biological and patient-related parameters [O, outcome measures] a minimum of one year after implant placement [T, time]? (Tables 3, 4, and 5).

Seven publications reporting on six trials met the inclusion criteria (Bianchi & Sanfilippo, 2004; Linkevicius et al., 2015; Park et al., 2017; Puisys & Linkevicius, 2015; Roccuzzo et al., 2016; Wiesner et al., 2010). Two studies were RCTs (Oh et al., 2017; Wiesner et al., 2010), while five studies were observational cohort studies (Bianchi & Sanfilippo, 2004; Linkevicius et al., 2015; Park et al., 2017; Puisys & Linkevicius, 2015; Roccuzzo et al., 2016). One observational study (Linkevicius et al., 2015) is a secondary analysis of the same patient population (Puisys & Linkevicius, 2015).

Six studies (reported in seven publications) were judged with a medium risk of bias (some concerns) (Bianchi & Sanfilippo, 2004; Linkevicius et al., 2015; Park et al., 2017; Puisys & Linkevicius, 2015; Roccuzzo et al., 2016; Wiesner et al., 2010).

Overall, three studies used STA to improve the amount of keratinized mucosa [KM] around dental implants (Oh et al., 2017; Park et al., 2017; Roccuzzo et al., 2016) and four studies used STA to improve soft tissue volume around dental implants (Bianchi & Sanfilippo, 2004; Linkevicius et al., 2015; Puisys & Linkevicius, 2015; Wiesner et al., 2010).

Overall, with respect to the primary outcome of this systematic review MBL changes, one study showed that sites grafted with free gingival grafts [FGG] revealed less bone loss when compared to non-grafted sites (Oh et al., 2017) while two studies did not show any differences in MBLs (Park et al., 2017; Roccuzzo et al., 2016). With respect to the secondary outcomes of this systematic review all included studies showed that FGG significantly improved bleeding indices (such as GI) and revealed less mucosal inflammation

TABLE 1 List of included studies included in the analysis

Author		Study Type	Setting	Group	Intervention
PICO 1 - STA vs. NOA					
Oh et al. 2017		RCT	university	test	STA
				control	NOA
Wiesner et al. 2010		RCT	private practice	test	STA
				control	NOA
Bianchi and Sanfilippo 2004		OBS prospective cohort	NI	test1	STA
				test2	STA
				test3	STA
				control	NOA
Park et al. 2017		OBS retrospective cohort	private practice	test	STA
				control	NOA
Roccuzzo et al. 2016		OBS retrospective cohort	private practice	test	STA
				control1	NOA
				control2	NOA
Linkevicius et al. 2015	These publications report on the same study.	OBS prospective cohort	private practice	test1	STA
Puisys and Linkevicius 2015				control1	NOA
				control2	NOA
PICO 2 - HTA and STA vs. HTA					
Migliorati et al. 2015		RCT	university	test	HTA and STA
				control	HTA
Yoshino et al. 2014		RCT	university	test	HTA and STA
				control	HTA
van Nimwegen et al. 2018	These publications report on the same study.	RCT	NI	test	HTA and STA
Zuiderveld et al. 2020, Zuiderveld et al. 2018a				control	HTA
Zuiderveld et al. 2018b		RCT	NI	test1	HTA and STA
				test2	HTA and STA
				control	HTA

Details	Implant placement	Gap	Type of restoration	Number of patients (implants)	Age ([years] mean, SD)	Gender distribution (% males)
FGG	augmentation after implantation	Single unit implants	Single crowns	15 (23)	65 (5)	28.57
NOA	augmentation after implantation			15 (22)	63 (9)	35.71
CTG	delayed/late	Single unit implants	Single crowns	10 (10)	39 (range: 25–60)	30
NOA	delayed/late			10 (10)	39 (range: 25–60)	30
CTG, 0–3 years observation	immediate	Single unit implants	Single crowns	32 (32)	NI	NI
CTG, 3–6 year observation	immediate			42 (42)	NI	NI
CTG, 6–9 year observation	immediate			22 (22)	NI	NI
NOA	immediate			20 (20)	NI	NI
FGG	delayed/late	NI	NI	11 (21)	NI	NI
NOA	delayed/late	NI	NI	11 (21)	NI	NI
FGG	augmentation after implantation	not specified	not specified	11 (11)	NI	NI
NOA (implant in KM)	delayed/late	not specified	not specified	63 (63)	NI	NI
NOA (implant in AM)	delayed/late	not specified	not specified	24 (24)	NI	NI
XCM (Alloderm), thin tissue biotype	delayed/late	Single unit implants	Single crowns	35 (35)	NI	NI
thin tissue biotype	delayed/late			34 (34)	NI	NI
thick tissue biotype	delayed/late			34 (34)	NI	NI
gap fill with BioOss, CTG	immediate	Single unit implants	Single crowns	24 (24)	NI	NI
gap fill with BioOss	immediate			24 (24)	NI	NI
gap fill with BioOss, CTG	immediate	Single unit implants	Single crowns	10 (10)	NI	NI
gap fill with BioOss	immediate			10 (10)	NI	NI
gap fill with BioOss and autogenous bone, CTG	immediate, simultaneous augmentation	Single unit implants	Single crowns	30 (30)	45.5 (15.5)	43.33
gap fill with BioOss and autogenous bone	immediate, simoultaneous augmentation			30 (30)	47.8 (16.5)	50
socket preservation with autologous bone and spongious bone substitute, XCM	delayed, implant placement simultaneous XCM	Single unit implants	Single crowns	20 (20)	45.4 (17.0)	35
socket preservation with autologous bone and spongious bone substitute, CTG	delayed, implant placement simultaneous CTG			20 (20)	38.2 (16.7)	55
socket preservation with autologous bone and spongious bone substitute	delayed/late			20 (20)	42.0 (15.7)	35

(Continues)

TABLE 1 (Continued)

Author		Study Type	Setting	Group	Intervention
Hosseini et al. 2020		OBS prospective cohort	university	test	HTA and STA
				control	HTA
Kobayashi et al. 2020		OBS prospective cohort	university	test	HTA and STA
				control	HTA
Noelken et al. 2018		OBS retrospective cohort	private practice	test	HTA and STA
				control	HTA
Tatum et al. 2020		OBS prospective cohort	NI	test	HTA and STA
				control	HTA
PICO 3 - HTA vs STA					
Bruyckere et al. 2020a Bruyckere et al. 2020b, Bruyckere et al. 2018	These publications report on the same study.	RCT	university and two private practices	test	STA
				control	HTA

Abbreviations: AM, alveolar mucosa; APF, apically positioned flap; CCT, controlled clinical trial; CM, collagen membrane; CTG, connective tissue graft; DBBM, deproteinized bovine bone mineral;FGG, free gingival graft; GBR, guided bone regeneration; HTA, hard tissue augmentation; KM, keratinized mucosa; NI, no information; NOA, no augmentation procedure; OBS, observational study; RCT, randomized controlled trial; SD, standard deviation; STA, soft tissue augmentation; VP, vestibuloplasty; XCM, xenogeneic collagen matrix.

and pocket depth following grafting with FGG when compared to a control group (Oh et al., 2017; Park et al., 2017; Roccuzzo et al., 2016).

One study reported about STA with subepithelial connective tissue grafts (CTG) at the time of immediate implant placement (Bianchi & Sanfilippo, 2004) and one study used CTG in delayed or late implant placement scenarios (Wiesner et al., 2010). Two publications used collagen matrices [CM] to augment soft tissue volume at the time of delayed implant placement (Linkevicius et al., 2015; Puisys & Linkevicius, 2015). MBLs were not influenced using CTG at the time of immediate or delayed implant placement, although one study reported a trend toward more stable MBLs over time in the augmented group. With respect to the secondary outcomes of this systematic review, CTG-grafting significantly improved gingival thickness when compared to the control group and also showed significantly higher esthetic parameters than the control group (Bianchi & Sanfilippo, 2004; Wiesner et al., 2010).

Two studies (Linkevicius et al., 2015; Puisys & Linkevicius, 2015), describing the same patient population, evaluated the use of a CM at the time of delayed implant placement for soft tissue thickening. They reported statistically significant less marginal bone loss when CM was used.

PICO 2. In systematically healthy patients with the need of at least one dental implant [P], how does STA (either soft tissue volume augmentation or augmentation of keratinized mucosa) in combination with hard tissue augmentation [I] compared to only hard tissue augmentative intervention [C] affect biological and patient-related parameters [O] a minimum of one year after implant placement [T]? (Tables 6–9).

Ten publications met the inclusion criteria (Hosseini et al., 2020; Kobayashi et al., 2020; Migliorati et al., 2015; Noelken et al., 2018; Tatum et al., 2020; van Nimwegen et al., 2018; Yoshino et al., 2014; Zuiderveld, Meijer, Vissink, & Raghoebar 2018b; Zuiderveld et al., 2018; Zuiderveld et al., 2020). Three publications reported about the same patient population (van Nimwegen et al., 2018; Zuiderveld, Meijer, den Hartog, Vissink, & Raghoebar 2018a; Zuiderveld et al., 2020). Four studies (reported in 6 publications) were randomized CCTs (Migliorati et al., 2015; van Nimwegen et al., 2018; Yoshino et al., 2014; Zuiderveld et al., 2018a; Zuiderveld et al., 2018b; Zuiderveld et al., 2020), while three studies were prospective cohort

Details	Implant placement	Gap	Type of restoration	Number of patients (implants)	Age ([years] mean, SD)	Gender distribution (% males)
GBR (BioOss and BioGide), CTG	delayed/late	Single unit implants	Single crowns	4 (4)	20 (range: 18–23)	25
				6 (6) splitmouth	splitmouth 22 (range: 19–31)	splitmouth 16.6
GBR (BioOss and BioGide)	delayed/late			9 (17)	23 (range: 20–31)	64.7
				6 (6) splitmouth	splitmouth 22 (range: 19–31)	splitmouth 16.6
GBR (BioOss and BioGide), CTG	delayed/late with GBR, second stage CTG	NI	NI	12 (12)	50 (range: 24–68)	41.66
GBR (BioOss and BioGide)	delayed/late with GBR	NI	NI	14 (14)	52 (range: 19–75)	64.28
autologous bone graft, CTG	immediate, simultaneous augmentation	Single unit implants	Single crowns	13 (13)	NI	NI
autologous bone graft	immediate, simultaneous augmentation			13 (13)	NI	NI
bone allograft and BioGide, CTG	immediate, simultaneous augmentation	Single unit implants	Single crowns	12 (12)	51.6 (14.5)	NI
bone allograft and BioGide	immediate, simoltaneous augmentation			14 (14)	61.6 (14.5)	NI
CTG, contour augmentation	delayed/late, simultaneous augmentation	Single unit implants	Single crowns	21 (21)	48 (15)	57.14
BioOss and Creos, contour augmentation	delayed/late, simultaneous augmentation			21 (21)	51 (13)	47.61

studies (Hosseini et al., 2020; Kobayashi et al., 2020; Tatum et al., 2020) and one study was a retrospective cohort study (Noelken et al., 2018).

Five RCTs were judged at a medium risk of bias (Migliorati et al., 2015; van Nimwegen et al., 2018; Zuiderveld et al., 2018a; Zuiderveld et al., 2018b; Zuiderveld et al., 2020), and one RCT was judged with a high risk of bias due to allocation and standardization of measurements (Yoshino et al., 2014). Two prospective cohort studies were judged at a low risk of bias (Hosseini et al., 2020; Kobayashi et al., 2020). One retrospective cohort study and one prospective cohort study were judged at a medium risk of bias (Noelken et al., 2018; Tatum et al., 2020). Two studies (Noelken et al., 2018; Zuiderveld et al., 2020) reported about data from CBCT analysis, while the other publications reported on peri-apical radiographs.

Five studies (data reported in six publications (Migliorati et al., 2015; Noelken et al., 2018; Tatum et al., 2020; van Nimwegen et al., 2018; Yoshino et al., 2014; Zuiderveld et al., 2018a; Zuiderveld et al., 2020)) used immediate implant placement in conjunction with bone grafting and buccal STA using subepithelial CTG versus bone grafting alone. Of these, one study showed that additional STA improved MBLs around immediate implants (Noelken et al., 2018), two studies showed a tendency of improved bone levels (Migliorati et al., 2015; Yoshino et al., 2014), while one study failed to show any effect of STA on MBLs (Tatum et al., 2020). One study (study population used in three publications (Zuiderveld et al., 2018a; Zuiderveld et al., 2020)) showed that additional STA around immediately placed and grafted implants significantly increase midfacial marginal bone loss when compared to bone grafting alone. With respect to the secondary outcomes of this systematic review, all included studies using immediately placed and grafted implants showed that an additional STA with SCTG improves esthetic parameters such as midfacial recession.

One study reported about delayed implant placement following ridge augmentation/preservation and additional STA with subepithelial CTG or collagen matrix versus no additional STA (Zuiderveld et al., 2018b). This study showed with respect to the primary outcomes of this review that soft tissue grafting using SCTG additional to a previous HTA procedure had no significant influence on MBLs when compared to hard tissue grafting alone. Also, in this study, additional soft tissue grafting did not improve esthetic or biological parameters such as midfacial recession, PES, or incidence of peri-implantitis.

Two studies reported about delayed implant placement with bone augmentation using the GBR-technique and additional STA with subepithelial CTG versus bone grafting alone (Hosseini et al., 2020;

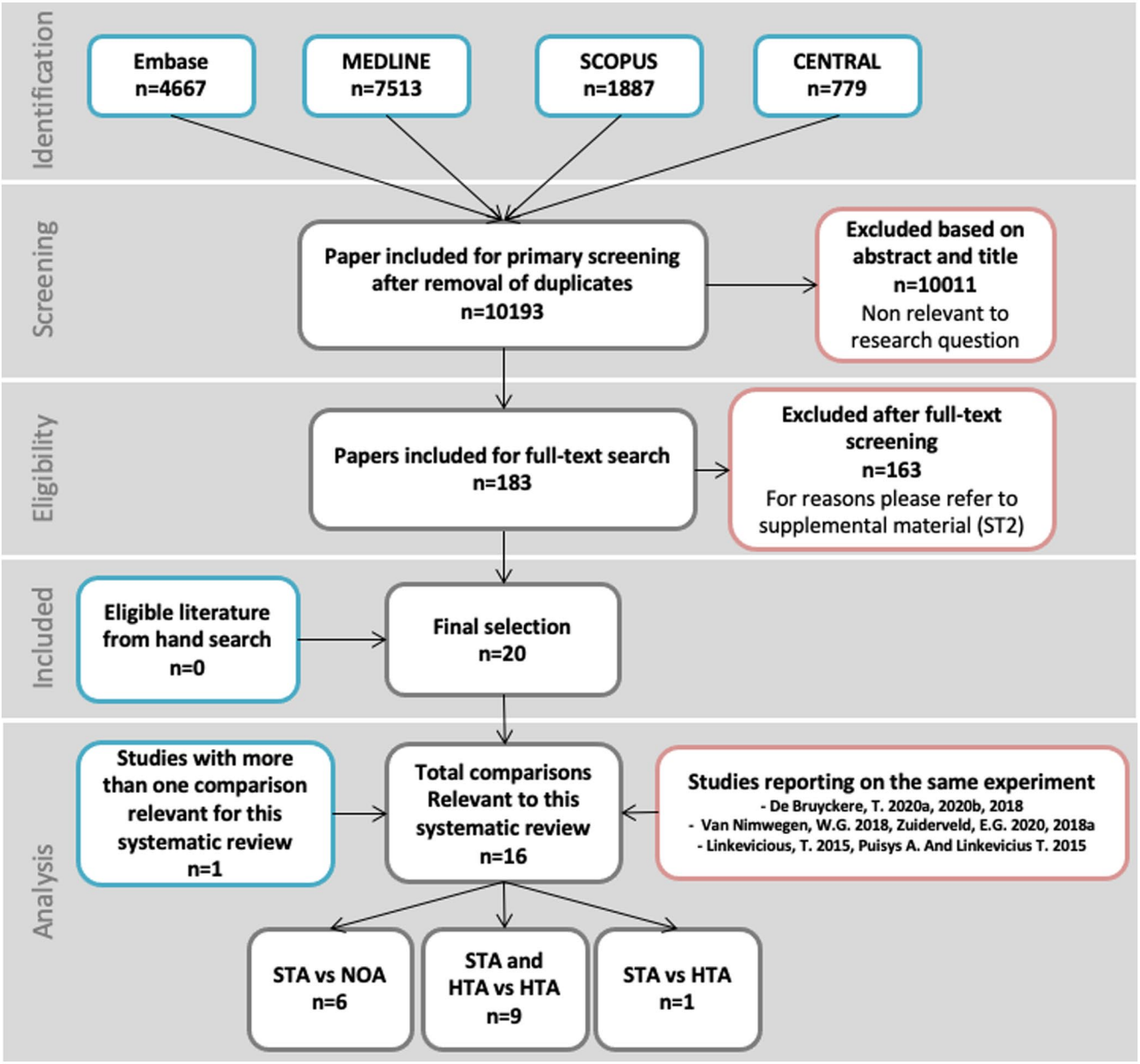

FIGURE 1 Flow chart of literature search and study selection

Kobayashi et al., 2020). One study reported that additional STA had no significant influence on MBLs (Hosseini et al., 2020), while the other study indicated that additional STA was able to limit marginal bone loss (Kobayashi et al., 2020). However, both studies showed that additional STA improved the secondary outcomes of this review such as less facial tissue recession or better soft tissue color match.

Our meta-analysis showed no significant differences on MBL changes in sites treated with a combination of hard and STA when compared to hard tissue augmentation alone (Figure 2). One study (Hosseini et al., 2020) was excluded from this analysis due to increased observation time (36 months versus 12 months in all other studies). High levels of heterogeneity were observed in this analysis ($I2 = 84\%$).

Due to the amount of data on marginal soft tissue levels (MSTL) and MSTL-changes, we were able to conduct a meta-analysis on this secondary outcome including results from the included RCTs reporting on MSTL relevant to PICO 2 (Figure 3). Concomitant soft and hard tissue augmentations resulted in significantly less marginal soft tissue recession when compared to hard tissue augmentation only ($p = .003$). Low levels of heterogeneity between the studies included in the meta-analysis were observed, leading to a $I2$ of 0%.

PICO 3. In systematically healthy patients with the need of at least one dental implant [P], how does STA (either soft tissue volume augmentation or augmentation of keratinized mucosa) [I] compared with hard tissue augmentation [C] affect biological and patient-related parameters [O] a minimum of one year after implant placement [T]? (Table 10).

Three publications, reported about the same patient population (De Bruyckere, Cabeza, et al., 2020; De Bruyckere, Cosyn,

TABLE 2 Risk of bias assessment results of all included publications

Author	Year	Conflict of Interest [CoI] reported	RoB judgment
PICO 1 - STA vs. NOA			
Oh; S. L.	2017	authors declared no CoI	some concerns (RoB 2)
Wiesner; G.	2010	authors declared no CoI	some concerns (RoB 2)
Bianchi; A. E. and Sanfilippo; F.	2004	authors declared no CoI, self-funded	some concerns (NOS)
Park; W. B.	2017	authors declared no CoI	some concerns (NOS)
Roccuzzo; M.	2016	NI	some concerns (NOS)
Linkevicius; T.	2015	NI	some concerns (NOS)
Puisys; A. and Linkevicius; T.	2015	NI	some concerns (NOS)
PICO 2 - HTA and STA vs. HTA			
Migliorati; M.	2015	NI	some concerns (RoB 2)
Yoshino; S.	2014	authors declared no CoI, project partially funded by Straumann USA	high risk (RoB 2)
van Nimwegen; W. G.	2018	authors declared no CoI, supported by an unrestricted grant from Nobel Biocare Services AG, Gothenburg, Sweden	some concerns (RoB 2)
Zuiderveld; E. G.	2020		some concerns (RoB 2)
Zuiderveld; E. G.	2018a		some concerns (RoB 2)
Zuiderveld; E. G.	2018b	authors declared no CoI	some concerns (RoB 2)
Hosseini; M.	2020	authors declared no CoI, financially supported by KOF/Calcin Foundation of The Danish Dental Association	low risk (NOS)
Kobayashi; T.	2020	authors declared no CoI	low risk (NOS)
Noelken; R.	2018	authors declared no CoI	some concerns (NOS)
Tatum; C. L.	2020	authors declared no CoI, study partially funded by International Team of Implantology (ITI)	some concerns (NOS)
PICO 3 - HTA vs. STA			
De Bruyckere; T.	2020a	authors declared no CoI; dental implants and prosthetic components supplied free of charge by Nobel Biocare Services AG (Kloten, Switzerland); Prof. Cosyn has collaboration agreements with Nobel Biocare (Kloten, Switzerland) and Straumann (Basel, Switzerland)	some concerns (RoB 2)
De Bruyckere; T.	2020b		some concerns (RoB 2)
De Bruyckere; T	2018		some concerns (RoB 2)

Abbreviation: NI, no information provided.

et al., 2020; De Bruyckere et al., 2018), met the inclusion criteria. Therefore, only one study—performed as a RCT—was included in the analysis. All three publications describing one study population were judged at a medium risk of bias (De Bruyckere, Cabeza, et al., 2020; De Bruyckere, Cosyn, et al., 2020; De Bruyckere et al., 2018). Both studies were randomized CCTs.

The included study reported about delayed implant procedures in the anterior maxilla with adequate amount of bone for implant placement. A subepithelial CTG was used to increase soft tissue thickness in one treatment group and HTA using the GBR-technique with bovine bone mineral and collagen membranes was utilized to perform contour augmentation in the other treatment group. The study showed no difference between both treatment groups with respect to MBL changes 12 months after surgery (De Bruyckere, Cabeza, et al., 2020; De Bruyckere, Cosyn, et al., 2020; De Bruyckere et al., 2018). With respect to the secondary outcomes of this systematic review, the study reported no statistically significant differences regarding postoperative mucosal recessions between the study groups. All other secondary outcomes such as PROMS, incidence of peri-implantitis or PES were either not reported or did not show significant differences between both treatment groups.

4 | DISCUSSION

This systematic review analyzes the scientific literature to identify the influence of STA procedures around dental implants on biological parameters such as MBL changes and secondary outcomes after a minimum of one year following implant placement. Based on 20

TABLE 3 Primary Outcomes PICO 1: STA versus NOA

Author	Group	Intervention	Follow-up	loss to or (partially) not included in ≥12m follow-up	MBLevel (mm)		MBLevel-Change (mm)	Conclusion
					T0 mean (SD)	12m mean (SD)	T0 to 12m mean (SD)[a]	
Oh et al., 2017	test	STA (FGG)	6m, 12m, 18m	NI	NI	NI	**significantly less bone loss**	Less MBL change in test group
	control	NOA	6m, 12m, 18m	NI	NI	NI	**significantly more bone loss**	Less GI in test group, no difference in PD, PI
Wiesner et al., 2010	test	STA (CTG)	12m	NI	0.35 (0.24)	1.14 (0.29)	−1.14 (0.29)	No difference in MBL
	control	NOA	12m	NI	0.44 (0.16)	1.06 (0.41)	−1.06 (0.41)	Thicker soft tissues and better PES in test group
Bianchi and Sanfilippo 2004	test1	STA (CTG)	0–3 years	NI	implant shoulder to first bone contact	1-3y: PD values ≤3.5mm: 59% PD values >3.5mm: 41%	NI	No difference in MBL Tendency for more stability of MBL
	control	NOA	0–3 years	NI		1-3y: PD values ≤3.5mm: 60% PD values >3.5mm: 40%	NI	Mucosa less stable in control group
Roccuzzo et al. 2016	test	STA (FGG)	10 years	NI	NI	NI	10y: −0.56 (0.39)	
	control1	NOA (KM)	10 years	NI	NI	NI	10y: −0.34 (0.38)	
	control2	NOA (AM)	10 years	NI	NI	NI	10y: −0.50 (0.38)	
Park et al. 2017	test	STA (FGG)	15y	NI	NI	NI	15y: −2.13 (0.93)	No difference in MBL
	control	NOA	15y		NI	NI	15y: −2.10 (0.83)	Lower modified bleeding in test group No difference in PI and PD
Puisys and Linkevicius 2015	test	STA (CM)	2m, 12m	NI	NI	NI	**mesial −0.24 (0.06)distal −0.20 (0.06)**	Less MBL in Test group
Linkevicius et al. 2015	control	NOA	2m, 12m	NI	NI	NI	**mesial −1.22 (0.08)distal −1.14 (0.07)**	No information about secondary outcomes

Note: **Bold** flags areas, where the authors have reported statistically significant differences between test and control group(s).

Abbreviations: 1,2,3,6,12,18m, 1-, 2-, 3-, 6-, 12-, 18-month examination; 1-3y, 1- to 3-year observation period; 15y, 15-year examination; CM, collagen matrix; CTG, connective tissue graft; FGG, free gingival graft; GBR, guided bone regeneration; HTA, hard tissue augmentation; IQR, interquartile range; MBLevel, marginal bone level; NI, no information provided; NOA, no augmentation procedure; SD, standard deviation; STA, soft tissue augmentation; T0, baseline; VP, vestibuloplasty.

[a]Negative value indicate loss, positive indicate gain.

TABLE 4 Secondary Outcomes PICO 1: STA versus NOA

			SR [%]	BSTT [mm]		BSTT-change [mm]	MSTLevel [mm]		KM [mm]		KM-Change [mm]
Author	Group	Intervention	12m	T0 mean (SD)	12m mean (SD)	change T0 to 12m	T0 mean (SD)	12m mean (SD)	T0 mean (SD)	12m mean (SD)	T0 to 12m mean (SD)
Oh et al. 2017	test	STA (FGG)	NI	NI	NI	NI	not significantly different	**significantly higher than control**	not significantly different	**significantly higher than control**	NI
	control	NOA	NI	NI	NI	NI	not significantly different	**significantly lower than test**	not significantly different	**significantly lower than test**	NI
Wiesner et al. 2010	test	STA (CTG)	NI	2.00 (0.47)	**3.20 (0.42)**	**1.20 (0.63)**	NI	NI	NI	NI	NI
	control	NOA	NI	2.05 (0.50)	**1.90 (0.32)**	**−0.15 (0.34)**	NI	NI	NI	NI	NI
Bianchi and Sanfilippo 2004	test1	STA (CTG)	100	NI	NI	NI	NI	NI	NI	NI	NI
	control	NOA	100	NI	NI	NI	NI	NI	NI	NI	NI
Roccuzzo et al. 2016	test	STA (FGG)	NI	NI	NI	NI	NI	NI	NI	NI	NI
	control1	NOA (KM)	NI	NI	NI	NI	NI	NI	NI	NI	NI
	control2	NOA (AM)	NI	NI	NI	NI	NI	NI	NI	NI	NI
Park et al. 2017	test	STA (FGG)	NI	NI	**15y: 2.66 (0.55)**	NI	NI	NI	**15y: 4.33 (0.94)**	**15y: 3.64 (1.27)**	**15y: 0.69 (0.95)**
	control	NOA	NI	NI	**15y: 1.84 (0.68)**	NI	NI	NI	**15y: 2.86 (0.92)**	**15y: 1.64 (1.48)**	**15y: 1.21 (0.96)**
Puisys and Linkevicius 2015	test	STA (CM)	100	NI	NI	NI	NI	NI	NI	NI	NI
Linkevicius et al. 2015	control	NOA	100	NI	NI	NI	NI	NI	NI	NI	NI

Note: **Bold** flags areas, where the authors have reported statistically significant differences between test and control group(s).

Abbreviations: 12m, 12-month examination; 15y, 15-year examination; BSTT, buccal/marginal soft tissue thickness; CM, collagen matrix; CTG, connective tissue graft; FGG, free gingival graft; GBR, guided bone regeneration; HTA, hard tissue augmentation; KM, width of keratinized mucosa; MSTLevel, marginal soft tissue level; NI, no information provided; NOA, no augmentation procedure; SD, standard deviation; SR, survival rate; STA, soft tissue augmentation; T0, baseline; VP, vestibuloplasty.

Negative value indicate loss, positive indicate gain.

TABLE 5 Secondary Outcomes PICO 1: STA vs NOA continued

			Rec [mm]	PD [mm]		PAL [mm]	PI [%]
Author	Group	Inter-vention	12m mean (SD)	T0 mean (SD)	12m mean (SD)	12m mean (SD)	T0 mean (SD)
Oh et al. 2017	test	STA (FGG)	NI	m: 3.2 (1.2) b: 3.0 (1.2) d: 3.0 (1.4)	m: 3.4 (1.4) b: 3.0 (1.2) d: 3.5 (1.6)	NI	not significantly different
	control	NOA	NI	m: 3.3 (1.1) b: 2.6 (1.0) d: 3.5 (1.5)	m: 3.2 (1.3) b: 3.2 (1.4) d: 3.4 (1.2)	NI	not significantly different
Wiesner et al. 2010	test	STA (CTG)	NI	NI	NI	NI	NI
	control	NOA	NI	NI	NI	NI	NI
Bianchi and Sanfilippo 2004	test1	STA (CTG)	NI	NI	1-3y: PD values ≤3mm: 47% PD values >3mm: 53%	1-3y: PD values ≤2.5mm: 53% PD values >2.5mm: 47%	NI
	control	NOA	NI	NI	1-3y: PD values ≤3mm: 49% PD values >3mm: 51%	1-3y: PD values ≤3mm: 52% PD values >2.5mm: 48%	NI
Roccuzzo et al. 2016	test	STA (FGG)	**10y1.27 (1.17)**	NI	10y 2.95 (0.80)	NI	NI
	control1	NOA (KM)	**10y0.16 (0.39)**	NI	10y 3.13 (0.59)	NI	NI
	control2	NOA (AM)	**10y2.08 (0.71)**	NI	10y 2.77 (0.70)	NI	NI
Park et al. 2017	test	STA (FGG)	15y: 0.52 (0.95)	NI	NI	NI	mPI 15y: 1.20 (0.15)
	control	NOA	15y: 0.74 (0.99)	NI	NI	NI	mPI 15y: 1.31 (0.19)
Puisys and Linkevicius 2015 Linkevicius et al. 2015	test	STA (CM)	NI	NI	NI	NI	NI
	control	NOA	NI	NI	NI	NI	NI

Note: **Bold** flags areas, where the authors have reported statistically significant differences between test and control.

Rec—recession, PD—probing depth, PAL—probing attachment level, PI—Plaque Index, GI—gingiva index, PES—pink esthetic score, PapS—papilla score, PtSat—patient satisfaction, T0—baseline, SD—standard deviation, 12m—12-month examination, 15y—15-year examination, 1-3y—1 to 3 years observation period, STA—soft tissue augmentation, FGG—free gingival graft, CTG—connective tissue graft, NOA—no augmentation procedure, NI—no information provided, VP—vestibuloplasty

publications reporting on 16 relevant comparisons, the following conclusions can be drawn:

(i)STA (to increase keratinized mucosa or augment tissue volume) showed a limited effect on MBL changes when compared to no STA.
(ii) Clinically relevant parameters (BOP, PD) and plaque control were improved by keratinized mucosa augmentation.
(iii) Procedures to augment tissue volume using CTGs have a beneficial effect on esthetic parameters (PES, MSTL).
(iv) Sites treated with a combination of hard and STA showed no statistically significant difference in terms of MBL changes when compared to hard tissue augmentation alone.
(v) Concomitant soft and hard tissue augmentations resulted in less marginal soft tissue recession when compared to hard tissue augmentation only.
(vi) Based on one single RCT, including 42 patients and 42 implants, both soft and hard tissue augmentation procedures resulted in comparable MBL changes.

In total, three different PICO questions formed the basis of this systematic review and the results of this analysis are discussed in the following:

4.1 | PICO1

This PICO question addresses the effect of STA procedures around dental implants either for augmentation of keratinized mucosa or soft tissue volume. Based on nine included publications, the results of this present systematic review reveal that augmentation of keratinized mucosa using FGG or CM does not improve MBLs around

	GI [%]		BI [%]		PES	PapS (Jemt's Index)	PtSat
12m mean (SD)	T0 mean (SD)	12m mean (SD)	T0 mean (SD)	12m mean (SD)	12m mean (SD)	12m mean (SD)	12m mean (SD)
not significantly different	not significantly different	**significantly lower than control**	1.7 (0.8)	1.4 (1)	NI	NI	NI
not significantly different	not significantly different	**significantly higher than test**	1.7 (1.3)	2.1 (0.8)	NI	NI	NI
NI	NI	NI	NI	NI	**11.32 (1.63)**	NI	patients significantly preferred test site
NI	NI	NI	NI	NI	**8.45 (1.46)**	NI	1 patient unsatisfied
NI	NI	NI	NI	NI	NI	NI	NI
NI	NI	NI	NI	NI	NI	NI	NI
10y: 27.3 (26.1)	NI	NI	NI	10y 27.3 (26.1)	NI	NI	Soreness in 1 patient
10y: 21.0 (20.2)	NI	NI	NI	10y: 23.4 (18.4)	NI	NI	**Soreness in 0 patients**
10y: 37.5 (27.6)	NI	NI	NI	10y: 33.3 (25.2)	NI	NI	**Soreness in 5 patients**
mPI 15y: 1.42 (0.25)	NI	NI	**mBI 15y: 0.46 (0.16)**	**mBI 15y: 0.71 (0.23)**	NI	NI	NI
mPI 15y: 1.50 (0.25)	NI	NI	**mBI 15y: 0.65 (0.26)**	**mPI 15y: 0.83 (0.16)**	NI	NI	NI
NI	NI	NI	NI	NI	NI	NI	NI
NI	NI	NI	NI	NI	NI	NI	NI

dental implants but has a significant influence on secondary outcomes such as bleeding indices, mucosal inflammation, and pocket depths. Furthermore, augmentation of soft tissue volume showed a limited effect on MBL changes around dental implants but improves secondary outcomes such as gingival thickness or patient-related outcomes such as PES.

The finding that STA with FGG improves peri-implant health in terms of bleeding indices and mucosal inflammation is in accordance with several previously published systematic review articles. Lin et al. showed that a lack of adequate keratinized mucosa around endosseous dental implants is associated with more plaque accumulation, tissue inflammation, mucosal recession and attachment loss (Lin et al., 2013). Gobbato et al. concluded in a systematic review that reduced keratinized mucosa around dental implants appear to be associated with increased peri-implant inflammation and poor oral hygiene (Gobbato et al., 2013).

The finding that STA with keratinized mucosa is not associated with improvements in MBLs when compared to non-augmented controls is in accordance with a systematic review by Tavelli et al. (Tavelli et al., 2020) who failed to find strong evidence regarding a positive effect of apically positioned flaps in conjunction with FGG on MBLs. On the other hand, Thoma et al. showed that STA with keratinized mucosa is associated with improvements of bleeding indices and higher MBLs (Thoma et al., 2018). In this present systematic review, we could only identify three studies dealing with STA in terms of KM (2 RCTs, 2 prospective observational studies) meeting the inclusion criteria of at least 10 patients per treatment group, systemically healthy participants and at least one year of follow-up (Oh et al., 2017; Park et al., 2017; Roccuzzo et al., 2016). Of these, only one study showed that FGG-grafted sites revealed less bone loss when compared to non-grafted sites (Oh et al., 2017) and two studies could not show any differences in terms of MBLs. Park

TABLE 6 Primary outcomes PICO 2: STA and HTA versus HTA

Author	Group	Intervention	Follow-up	loss to or (partially) not included in ≥12m follow-up
Migliorati et al. 2015	test	HTA (gap fill with BioOss), STA (CTG)	12m, 24m	NI
	control	HTA (gap fill with BioOss)	12m, 24m	NI
Yoshino et al. 2014	test	HTA (gap fill with BioOss), STA (CTG)	3m, 6m, 12m	NI
	control	HTA (gap fill with BioOss)	3m, 6m, 12m	NI
Zuiderveld et al. 2018a, Zuiderveld et al. 2020	test	HTA (gap fill with BioOss and autogenous bone), STA (CTG)	12m	1 (loss due to failed osseointegration)
van Nimwegen et al. 2018	control	HTA (gap fill with BioOss and autogenous bone)	12m	1 (loss due to failed osseointegration)
Zuiderveld et al. 2018b	test1	HTA (autologous bone and spongious bone substitute), STA (XCM)	12m	0
	test2	HTA (autologous bone and spongious bone substitute), STA (CTG)	12m	0
	control	HTA (autologous bone and spongious bone substitute)	12m	0
Hosseini et al. 2020	test	HTA (GBR with BioOss and BioGide), STA (CTG)	6m, 12m, 36m, 60m	n < 10 at 36m and 60m
	control	HTA (GBR with BioOss and BioGide)	6m, 12m, 36m, 60m	60m: 1 PI case
Kobayashi et al. 2020	test	HTA (GBR with BioOss and BioGide), STA (CTG)	12m	0
	control	HTA (GBR with BioOss and BioGide)	12m	0
Noelken et al. 2018	test	HTA, STA (GBR, CTG)	45m	NI
	control	HTA (GBR)	45m	NI
Tatum et al. 2020	test	HTA, STA (allograft, BioGide, CTG)	12m	NI
	control	HTA (allograft, BioGide)	12m	NI

Note: **Bold** flags areas, where the authors have reported statistically significant differences between test and control group(s)

Abbreviations: 12m, 12-month examination; 12m, 12-month examination; 36m, 3-year examination; 3m, 3-month examination; CTG, connective tissue graft; GBR, guided bone regeneration; HTA, hard tissue augmentation; IQR, interquartile range; MBLevel, marginal bone level; NI, no information provided; SD, standard deviation; STA, soft tissue augmentation; T0, baseline; XCM, xenogeneic collagen matrix.

Negative value indicate loss, positive indicate gain.

et al., 2017; Roccuzzo et al., 2016). It should also be kept in mind that the study showing a statistically significant effect of soft tissue grafting on MBLs was judged at a medium risk of bias. Furthermore, this study included 41 single unit implants from five different implant manufacturers (Oh et al., 2017). Studies have shown that rough collar implants have lower MBL changes than machined collar

MBLevel [mm]			MBLevel-Change [mm]	
	T0 mean (SD)	12m mean (SD)	T0 to 12m mean (SD) buccal/facial[a]	Conclusion
NI	NI	NI	0.001 (0.092)	No difference in MBLevel-Change
NI	NI	NI	−0.136 (0.107)	Better esthetic outcome and better tissue stability in test groups
MBLevel - distance to reference line	−0.06 (0.19)	−0.07 (0.16)	−0.01 (0.27)	No difference in MBLevel-Change Facial gingival level better in test group
	−0.17 (0.25)	−0.31 (0.41)	−0.14 (0.53)	
median (IQR) mesial distal	1m 0.8 (0.0–1.5) 0.3 (0.0–1.1)	0.9 (0.4–1.2) 0.8 (0.0–1.1)	1m to 12m mesial: −0.06 (0.42) distal: 0.03 (0.38)	No difference in MBLevel-Change Less midfacial recession in test group
	1m 0.9 (0.2–1.2) 0.5 (0.0–1.2)	0.8 (0.5–1.2) 0.8 (0.0–1.1)	1m to 12m mesial: −0.04 (0.46) distal: 0.02 (0.37)	
median (IQR) mesial distal	1m 0.7 (0.3–1.6) 0.6 (0.0–1.1)	0.9 (0.3–1.3) 0.7 (0.1–1.0)	median (IQR) 1m to 12m mesial: 0.00 (−0.21–0.27) distal: 0.00 (−0.08–0.15)	No difference in MBLevel-Change No difference in esthetic result or peri-implant health
	1m 0.3 (0.0–0.9) 0.5 (0.0–1.0)	0.3 (0.0–1.1) 0.5 (0.0–1.1)	median (IQR) 1m to 12m mesial: 0.00 (−0.13–0.01) distal: 0.00 (−0.29–0.06)	
	1m 0.5 (0.0–0.9) 0.4 (0.0–1.1)	0.3 (0.0–0.9) 0.3 (0.0–0.8)	median (IQR) 1m to 12m mesial: 0.00 (−0.18–0.00) distal: 0.00 (−0.02–0.39)	
NI	NI	NI	Baseline to 5 year −0.11 (0.45)	No difference in MBLevel-change Better mucosal match and facial mucosa in test group
NI	NI	NI	Baseline to 5 year −0.12 (0.33)	
NI	platform-level		platform-level	Less facial bone resorption in test group Less facial soft tissue recession in test group
	1.73 (1.09)	1.59 (1.02)	**−0.13 (0.16)**	
NI	platform-level		platform-level	
	1.38 (1.40)	0.73 (1.13)	**−0.65 (0.53)**	
36m in relation to reference level	−5.5 (4.1)	−0.9 (0.6)	6.4 (4.2)	Less bone loss in test group Better facial soft tissue level in test group
	−2.4 (2.2)	−0.3 (0.9)	2.2 (2.6)	
distance implant shoulder to first bone-to-implant contact	mesial 0.04 (0.11) distal 0.11 (0.20)	mesial 0.11 (0.17) distal 0.12 (0.23)	**mesial −0.06 (0.12)distal −0.01 (0.12)**	No difference in MBLevel change Addition of CTG leads to situation comparable to thick biotype
	mesial 0.08 (0.12) distal 0.33 (0.52)	mesial 0.09 (0.18) distal 0.24 (0.45)	**mesial 0.00 (0.13)distal 0.08 (0.15)**	

implants (Messias et al., 2019). Therefore, data from various implant manufacturers should be analyzed with caution regarding bone level alterations.

STA for volume augmentation has been assessed in four included studies (Bianchi & Sanfilippo, 2004; Linkevicius et al., 2015; Puisys & Linkevicius, 2015; Wiesner et al., 2010). The results are difficult

TABLE 7 Secondary outcomes PICO 2: STA and HTA versus HTA

Author	Group	Intervention	Complications	SR [%]	SuccR [%]	BSTT [mm]	
				12m	12m	T0 mean (SD)	12m mean (SD)
Migliorati et al. 2015	test	HTA (gap fill with BioOss), STA (CTG)	NI	NI	NI	1.1 (0.6)	1.8 (0.8)
	control	HTA (gap fill with BioOss)	NI	NI	NI	1.5 (0.5)	1.1 (0.5)
Yoshino et al. 2014	test	HTA (gap fill with BioOss), STA (CTG)	NI	100	100	NI	NI
	control	HTA (gap fill with BioOss)	NI	100	100	NI	NI
Zuiderveld et al. 2018a, Zuiderveld et al. 2020 van Nimwegen et al. 2018	test	HTA (gap fill with BioOss and autogenous bone), STA (CTG)	NI	96.7	96.7	NI	NI
	control	HTA (gap fill with BioOss and autogenous bone)	NI	96.7	96.7	NI	NI
Zuiderveld et al. 2018b	test1	HTA (autologous bone and spongious bone substitute), STA (XCM)	NI	100	100	NI	NI
	test2	HTA (autologous bone and spongious bone substitute), STA (CTG)	NI	100	100	NI	NI
	control	HTA (autologous bone and spongious bone substitute)	NI	100	100	NI	NI
Hosseini et al. 2020	test	HTA (GBR with BioOss and BioGide), STA (CTG)	NI	NI	NI	NI	NI
	control	HTA (GBR with BioOss and BioGide)	36m: 1 mucosal discoloration	NI	NI	NI	NI
Kobayashi et al. 2020	test	HTA (GBR with BioOss and BioGide), STA (CTG)	NI	100	100	alveolar bone crest level	
			NI			**4.46 (0.67)**	**4.41 (0.74)**
			NI			platform level	
			NI			**2.73 (0.84)**	**2.78 (0.82)**
	control	HTA (GBR with BioOss and BioGide)	NI	100	100	alveolar bone crest level	
			NI			**3.19 (0.41)**	**2.98 (0.62)**
			NI			platform level	
			NI			**1.99 (0.69)**	**1.91 (0.64)**
Noelken et al. 2018	test	HTA, STA (GBR, CTG)	NI	100	100	NI	NI
	control	HTA (GBR)	5 implants showed >1mm bone loss apical to reference level	100	38.7	NI	NI

BSTT-Change [mm]	MSTLevel [mm]	MSTLevel-Change [mm]		BBT [mm]		BBT-Change [mm]	Dim-Change [mm]
T0 to 12m mean (SD)[a]	T0 mean (SD)	12m mean (SD)	T0 to 12m mean (SD)[a]	T0 mean (SD)	12m mean (SD)	T0 to 12m mean (SD)[a]	T0 to 12m mean (SD)[a]
NI	NI	NI	NI	NI	NI	NI	NI
NI	NI	NI	NI	NI	NI	NI	NI
NI	NI	NI	**−0.25 (0.35)**	NI	NI	NI	NI
NI	NI	NI	**−0.7 (0.48)**	NI	NI	NI	NI
−0.49 (0.54)	NI	NI	***0.1 (0.8)***	NI	NI	**−0.84 (0.61)**	NI
−0.68 (0.59)	NI	NI	***−0.5 (1.1)***	NI	NI	**−0.46 (0.54)**	NI
NI	NI	NI	−0.17 (1.3)	NI	NI	NI	NI
NI	NI	NI	−0.04 (1.1)	NI	NI	NI	NI
NI	NI	NI	−0.48 (1.5)	NI	NI	NI	NI
NI	NI	NI	NI	NI	NI	NI	D1: 0.95 (0.59) **D2: 1.35 (0.56)D3: 1.50 (0.70)**
NI	NI	NI	NI	NI	NI	NI	D1: 0.72 (0.52) **D2: 0.78 (0.88)D3: 0.78 (1.50)**
alveolar bone crest level	alveolar bone crest level		alveolar bone crest level	platform level		platform level	NI
−0.05 (0.38)	3.32 (0.73)	3.33 (0.82)	0.01 (0.33)	2.26 (1.32)	2.18 (1.29)	−0.08 (0.28)	
platform level	platform level		platform level				
0.05 (0.32)	5.07 (1.06)	**4.98 (0.88)**	**−0.09 (0.30)**				
alveolar bone crest level	alveolar bone crest level		alveolar bone crest level	platform level		platform level	NI
−0.21 (0.41)	3.11 (0.95)	3.06 (0.64)	−0.06 (0.44)	1.72 (1.07)	1.48 (1.12)	−0.24 (0.48)	
platform level	platform level		platform level				
−0.09 (0.56)	4.46 (0.93)	**3.81 (0.81)**	**−0.64 (0.42)**				
NI	NI	NI	NI	1mm: 0.1 (0.2) 3mm: 0.2 (0.2) 6mm: 0.3 (0.5)	36m 1mm: 1.8 (1.0) 3mm: 1.7 (0.7) 6mm: 1.4 (0.7)	T0 to 36m 1mm: 1.8 (0.9) 3mm: 1.6 (0.7) 6mm: 1.1 (0.8)	NI
NI	NI	NI	NI	1mm: 0.2 (0.3) 3mm: 0.4 (0.4) 6mm: 0.6 (0.7)	36m 1mm: 1.4 (1.3) 3mm: 1.7 (1.4) 6mm: 1.9 (1.4)	T0 to 36m 1mm: 1.2 (1.4) 3mm: 1.3 (1.5) 6mm: 1.3 (1.1)	NI

(Continues)

TABLE 7 (Continued)

Author	Group	Intervention	Complications	SR [%]	SuccR [%]	BSTT [mm]	
				12m	12m	T0 mean (SD)	12m mean (SD)
Tatum et al. 2020	test	HTA, STA (allograft, BioGide, CTG)	12m	NI	NI	NI	NI
	control	HTA (allograft, BioGide)	12m	NI	NI	NI	NI

Note: **Bold** flags areas, where the authors have reported statistically significant differences between test and control group(s).

Bold-italic are multiple reports across interrelated publications—values reporting on 12m (or closest to 12m examination) or with highest samples size were chosen.

Abbreviations: 12m, 12-month examination; 12m, 12-month examination; 36m, 3-year examination; 3m, 3-month examination; BBT, buccal bone thickness; BSTT, buccal/marginal soft tissue thickness; CTG, connective tissue graft; Dim, dimensional; GBR, guided bone regeneration; HTA, hard tissue augmentation; MSTLevel, marginal soft tissue level; NI, no information provided; SD, standard deviation; SR, survival rate; STA, soft tissue augmentation; SuccR, success rate; T0, baseline; XCM, xenogeneic collagen matrix.

Negative value indicate loss, positive indicate gain.

TABLE 8 Secondary outcomes PICO 2: STA and HTA vs HTA continued (part 2)

Author	Group	Intervention	KM [mm]		Rec [mm]		PD [mm]
			T0 mean (SD)	12m mean (SD)	T0 mean (SD)	12m mean (SD)	T0 mean (SD)
Migliorati et al. 2015	test	HTA (gap fill with BioOss), STA (CTG)	3.3 (1.2)	3.0 (1.2)	NI	NI	3.4 (0.7)
	control	HTA (gap fill with BioOss)	4.3 (1.1)	3.7 (1.1)	NI	NI	3.2 (0.4)
Yoshino et al. 2014	test	HTA (gap fill with BioOss), STA (CTG)	NI	NI	NI	NI	NI
	control	HTA (gap fill with BioOss)	NI	NI	NI	NI	NI
Zuiderveld et al. 2018a, Zuiderveld et al. 2020 van Nimwegen et al. 2018	test	HTA (gap fill with BioOss and autogenous bone), STA (CTG)	NI	NI	NI	NI	***m: 2.8 (0.9)b: 2.2 (0.9)d: 2.9 (1.0)p: 2.6 (1.6)***
	control	HTA (gap fill with BioOss and autogenous bone)	NI	NI	NI	NI	***m: 2.6 (0.9)b: 2.6 (1.4)d: 2.5 (1.1)p: 2.2 (1.0)***
Zuiderveld et al. 2018b	test1	HTA (autologous bone and spongious bone substitute), STA (XCM)	NI	NI	NI	NI	NI
	test2	HTA (autologous bone and spongious bone substitute), STA (CTG)	NI	NI	NI	NI	NI
	control	HTA (autologous bone and spongious bone substitute)	NI	NI	NI	NI	NI

BSTT-Change [mm]	MSTLevel [mm]	MSTLevel-Change [mm]		BBT [mm]		BBT-Change [mm]	Dim-Change [mm]
T0 to 12m mean (SD)[a]	T0 mean (SD)	12m mean (SD)	T0 to 12m mean (SD)[a]	T0 mean (SD)	12m mean (SD)	T0 to 12m mean (SD)[a]	T0 to 12m mean (SD)[a]
NI	NI	NI	0.20 (1.14)	NI	NI	NI	NI
NI	NI	NI	−0.01 (1.56)	NI	NI	NI	NI

	PD Change [mm]	PI [%]		BoP [%]		Papilla Height [mm]			
12m mean (SD)	T0 to 12m mean (SD)	T0 mean (SD)	12m mean (SD)	T0 mean (SD)	12m mean (SD)	mesial T0 mean (SD)	mesial 12m mean (SD)	distal T0 mean (SD)	distal 12m mean (SD)
3.3 (0.4)	NI	mPL: 0.1 (0.2)	mPL: 0.1 (0.2)	0.2 (0.4)	0.4 (0.3)	2.8 (1.3)	3.3 (0.9)	2.1 (1.2)	2.6 (0.6)
3.1 (1.0)	NI	mPL: 0.1 (0.3)	mPL: 0.1 (0.2)	0.4 (0.4)	0.4 (0.4)	2.8 (0.9)	3.3 (1.1)	2.3 (0.7)	2.6 (0.6)
NI	NI	mPI 3m 0: 4 1: 5 2: 1	mPI 0: 8 1: 2	mBI 3m 0: 4 1: 4 2: 2	mBI 0: 7 1: 3	NI	NI	NI	NI
NI	NI	mPI 3m 0: 4 1: 6	mPI 0: 8 1: 2	mBI 3m 0: 9 1: 1	mBI 0: 10	NI	NI	NI	NI
m: 2.8 (1.1)b: 2.3 (0.9)d: 2.9 (0.9)p: 2.2 (0.7)	NI	NI	NI	NI	NI	NI	NI	NI	NI
m: 3.0 (0.9)b: 2.5 (1.2)d: 2.9 (1.4)p: 2.3 (0.8)	NI	NI	NI	NI	NI	NI	NI	NI	NI
NI	m: 3.0 (1.9) **b: 2.3 (1.0)**d: 3.2 (1.2) **p: 2.4 (0.7)**	NI	NI	NI	NI	NI	NI	NI	NI
NI	m: 3.0 (1.3) **b: 3.1 (1.2)**d: 3.0 (1.2) **p: 2.4 (0.5)**	NI	NI	NI	NI	NI	NI	NI	NI
NI	m: 2.9 (1.3) **b: 2.9 (0.9)**d: 3.3 (1.1) **p: 1.9 (0.8)**	NI	NI	NI	NI	NI	NI	NI	NI

(Continues)

TABLE 8 (Continued)

Author	Group	Intervention	KM [mm]		Rec [mm]		PD [mm]
			T0 mean (SD)	12m mean (SD)	T0 mean (SD)	12m mean (SD)	T0 mean (SD)
Hosseini et al. 2020	test	HTA (GBR with BioOss and BioGide), STA (CTG)	NI	5years 5.34 (1.7)	NI	NI	NI
	control	HTA (GBR with BioOss and BioGide)	NI	5years 5.43 (1.9)	NI	NI	NI
Kobayashi et al. 2020	test	HTA (GBR with BioOss and BioGide), STA (CTG)	NI	NI	NI	NI	NI
	control	HTA (GBR with BioOss and BioGide)	NI	NI	NI	NI	NI
Noelken et al. 2018	test	HTA, STA (GBR, CTG)	3.3 (1.1)	3.9 (0.9)	2.3 (0.7)	0.3 (0.4)	NI
	control	HTA (GBR)	4.1 (1.0)	4.4 (1.1)	1.8 (0.6)	0.8 (0.7)	NI
Tatum et al. 2020	test	HTA, STA (allograft, BioGide, CTG)	NI	NI	NI	NI	**m: 2.50 (1.24)d: 2.33 (0.49)b: 1.75 (0.75)p: 2.00 (0.85)**
	control	HTA (allograft, BioGide)	NI	NI	NI	NI	**m: 3.17 (0.77)d: 3.43 (0.85)b: 2.93 (1.14)p: 2.64 (0.50)**

Note: ***Bold-italic*** are multiple reports across interrelated publications—values reporting on 12m (or closest to 12m examination) or with highest samples size were chosen.

Abbreviations: 12m, 12-month examination; 3m, 3-month examination; BoP, Bleeding on Probing; CTG, connective tissue graft; d, distal; db, distobuccal; do, disto-oral; GBR, guided bone regeneration; HTA, hard tissue augmentation; KM, width of keratinized mucosa; m, mesial; mb, mesiobuccal; mo, mesio-oral; NI, no information provided; o, oral; p, palatal; PD, probing depth; PI, Plaque Index; Rec, recession; SD, standard deviation; STA, soft tissue augmentation; T0, baseline; XCM, xenogeneic collagen matrix.

	PD Change [mm]	PI [%]		BoP [%]		Papilla Height [mm]			
12m mean (SD)	T0 to 12m mean (SD)	T0 mean (SD)	12m mean (SD)	T0 mean (SD)	12m mean (SD)	mesial T0 mean (SD)	mesial 12m mean (SD)	distal T0 mean (SD)	distal 12m mean (SD)
NI	NI	NI	mPI (5years) 0: 50% 1: 50%	NI	mBI (5years) 0: 87.5% 1: 12.5%	NI	NI	NI	NI
NI	NI	NI	mPI (5years) 0: 80% 1: 20%	NI	mBI (5years) 0: 55% 1: 40% 2: 5%	NI	NI	NI	NI
NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
NI	NI	NI	NI	NI	NI	NI	NI	NI	NI
36m mb: 3.0 (1.0) b: 2.5 (0.9) db: 2.8 (0.7) mo: 2.7 (0.4) o: 2.2 (0.4) do: 3.0 (0.6)	NI	NI	NI	NI	NI	NI	NI	NI	NI
36m mb: 3.0 (1.0) b: 2.5 (0.9) db: 2.8 (0.7) mo: 2.7 (0.4) o: 2.2 (0.4) do: 3.0 (0.6)	NI	NI	NI	NI	NI	NI	NI	NI	NI
m: 2.42 (1.31)d: 2.42 (0.51)b: 1.92 (0.79)p: 1.75 (0.97)	NI	mPI m: 0.42 (1.00) d: 0.17 (0.58) b: 0.08 (0.29) **p: 0.00 (0.00)**	mPI **m: 0.00 (0.00)**d: 0.08 (0.29) **b: 0.00 (0.00)**p: 0.00 (0.00)	mSBI **m: 0.00 (0.00)**d: 0.17 (0.58) b: 0.25 (0.62) p: 0.00 (0.00)	mSBI m: 0.08 (0.29) d: 0.17 (0.39) **b: 0.00 (0.00)p: 0.00 (0.00)**	NI	NI	NI	NI
m: 3.29 (0.83)d: 3.36 (1.01)b: 3.21 (1.58)p: 2.21 (0.70)	NI	mPI m: 0.29 (0.61) d: 0.36 (0.50) b: 0.14 (0.36) **p: 0.36 (0.50)**	mPI **m: 0.50 (0.76)**d: 0.29 (0.61) **b: 0.29 (0.61)**p: 0.21 (0.58)	mSBI **m: 0.43 (0.65)**d: 0.29 (0.47) b: 0.64 (0.93) p: 0.29 (0.47)	mSBI m: 0.29 (0.47) d: 0.29 (0.47) **b: 0.64 (0.93)p: 0.29 (0.47)**	NI	NI	NI	NI

TABLE 9 Secondary outcomes PICO 2: STA and HTA vs HTA continued (part 3)

Author	Group	Intervention	PES		WES
			T0 mean (SD)	12m mean (SD)	12m mean (SD)
Migliorati et al. 2015	test	HTA (gap fill with BioOss), STA (CTG)	NI	24m ≥8: 66.6% 7: 12.5% 6: 20.8%	no significant results
	control	HTA (gap fill with BioOss)	NI	24m ≥8: 17.3% 7: 21.7% 6: 48.5% ≤5: 17.3%	no significant results
Yoshino et al. 2014	test	HTA (gap fill with BioOss), STA (CTG)	NI	NI	NI
	control	HTA (gap fill with BioOss)	NI	NI	NI
Zuiderveld et al. 2018a, Zuiderveld et al. 2020 van Nimwegen et al. 2018	test	HTA (gap fill with BioOss and autogenous bone), STA (CTG)	NI	***6.4 (1.5)***	***6.9 (1.9)***
	control	HTA (gap fill with BioOss and autogenous bone)	NI	***6.8 (1.5)***	***7.4 (1.3)***
Zuiderveld et al. 2018b	test1	HTA (autologous bone and spongious bone substitute), STA (XCM)	NI	6.1 (1.7)	8.3 (1.6)
	test2	HTA (autologous bone and spongious bone substitute), STA (CTG)	NI	7.0 (2.4)	8.9 (1.2)
	control	HTA (autologous bone and spongious bone substitute)	NI	6.6 (1.5)	8.7 (0.9)
Hosseini et al. 2020	test	HTA (GBR with BioOss and BioGide), STA (CTG)	NI	NI	NI
	control	HTA (GBR with BioOss and BioGide)	NI	NI	NI
Kobayashi et al. 2020	test	HTA (GBR with BioOss and BioGide), STA (CTG)	NI	NI	NI
	control	HTA (GBR with BioOss and BioGide)	NI	NI	NI
Noelken et al. 2018	test	HTA, STA (GBR, CTG)	8.7 (2.6)	12.0 (0.9)	NI
	control	HTA (GBR)	10.3 (1.5)	12.4 (1.2)	NI
Tatum et al. 2020	test	HTA, STA (allograft, BioGide, CTG)	NI	6.19 (2.19)	11.64 (3.22)
	control	HTA (allograft, BioGide)	NI	5.88 (1.63)	12.07 (2.87)

Note: ***Bold-italic*** are multiple reports across interrelated publications—values reporting on 12m (or closest to 12m examination) or with highest samples size were chosen.

Abbreviations: 12m, 12-month examination; 1m, 1-month examination; 24m, 24-month examination; CTG, connective tissue graft; GBR, guided bone regeneration; HTA, hard tissue augmentation; IQR, interquartile range; NI, no information provided; OHIP, Oral Health Impact Profile; PES, pink esthetic score; PIS, papilla index score; PtSat, patient satisfaction; SD, standard deviation; STA, soft tissue augmentation; T0, baseline; WES, white esthetic score; XCM, xenogeneic collagen matrix.

PIS				Match Change		PtSat (OHIP)	
T0 mean (SD)		12m mean (SD)		mucosal color	mucosal lightness	T0 mean (SD)	12m mean (SD)
NI	NI	NI	NI	NI	NI	NI	NI
NI	NI	NI	NI	NI	NI	NI	NI
mesial 0: 40% 1: 10% 2: 20% 3: 30%	distal 0: 30% 1: 20% 2: 20% 3: 30%	mesial 0: 10% 1: 20% 2: 30% 3: 40%	distal 0: 10% 1: 10% 2: 30% 3: 50%	NI	NI	NI	NI
mesial 0: 20% 1: 30% 2: 10% 3: 40%	distal 0: 20% 1: 40% 2: 10% 3: 30%	mesial 0: 0% 1: 10% 2: 40% 3: 50%	distal 0: 0% 1: 30% 2: 50% 3: 20%	NI	NI	NI	NI
mesial 0: 0% 1: 13.8% 2: 37.9% 3: 48.3%	distal 0: 3.4% 1: 6.9% 2: 34.5% 3: 55.2%	mesial 0: 0% 1: 6.9% 2: 27.6% 3: 65.5%	mesial 0: 0% 1: 6.9% 2: 24.1% 3: 69.0%	NI	NI	median (IQR) 10.0 (6.0–16.0)	median (IQR) 2.0 (1.0–5.0)
mesial 0: 3.6% 1: 17.9% 2: 39.3% 3: 39.3%	distal 0: 3.6% 1: 14.3% 2: 46.4% 3: 35.7%	mesial 0: 0% 1: 10.3% 2: 41.4% 3: 48.3%	distal 0: 0% 1: 6.9% 2: 27.6% 3: 65.5%	NI	NI	median (IQR) 10.0 (5.3–19.8)	median (IQR) 2.0 (0.0–6.0)
mesial 1m 0: 0% 1: 15% 2: 25% 3: 60%	distal 1m 0: 0% 1: 20% 2: 35% 3: 45%	mesial 0: 0% 1: 10% 2: 35% 3: 55%	distal 0: 0% 1: 10% 2: 50% 3: 40%	NI	NI	median (IQR) 25.5 (22.3–40.0)	median (IQR) 15.0 (14.0–19.8)
mesial 1m 0: 0% 1: 0% 2: 15% 3: 85%	distal 1m 0: 0% 1: 5% 2: 35% 3: 60%	Mesial 0: 0% 1: 0% 2: 15% 3: 85%	Distal 0: 0% 1: 0% 2: 25% 3: 75%	NI	NI	median (IQR) 31.0 (25.0–37.8)	median (IQR) 16.0 (15.0–22.3)
mesial 1m 0: 0% 1: 5% 2: 65% 3: 30%	distal 1m 0: 0% 1: 5% 2: 35% 3: 40%	mesial 0: 0% 1: 0% 2: 45% 3: 55%	distal 0: 0% 1: 0% 2: 55% 3: 45%	NI	NI	median (IQR) 24.5 (21.3–41.0)	median (IQR) 15.0 (14.0–21.3)
NI	NI	NI	NI	−0.41 (3.48)	1.24 (3.39)	NI	NI
NI	NI	NI	NI	0.84 (3.26)	−0.43 (3.95)	NI	NI
NI	NI	NI	NI	NI	NI	NI	NI
NI	NI	NI	NI	NI	NI	NI	NI
NI	NI	NI	NI	NI	NI	NI	NI
NI	NI	NI	NI	NI	NI	NI	NI
NI	NI	NI	NI	NI	NI	NI	NI
NI	NI	NI	NI	NI	NI	NI	NI

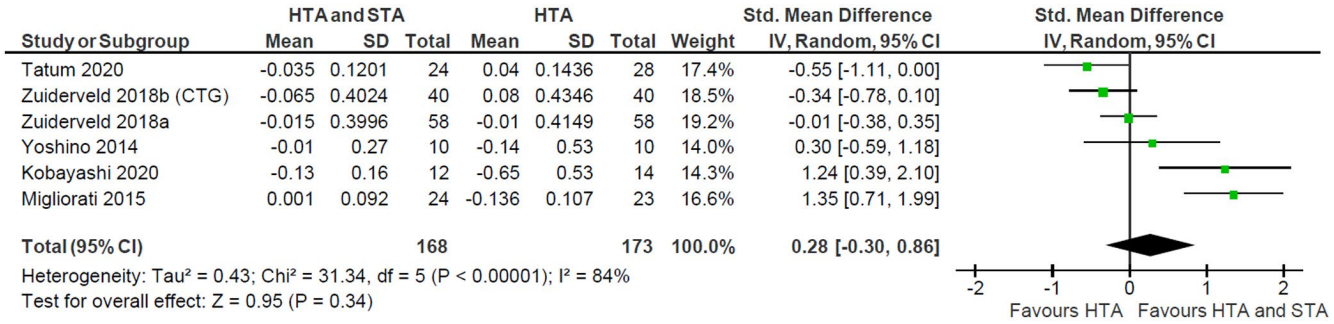

FIGURE 2 Forest plot on marginal bone level changes in PICO 2. CTG, connective tissue graft; HTA, hard tissue augmentation; SD, standard deviation; STA, soft tissue augmentation

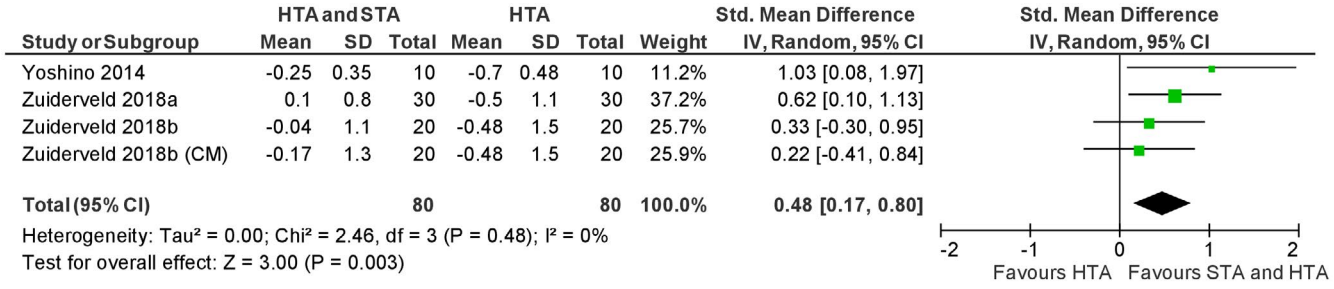

FIGURE 3 Forest plot on marginal soft tissue level changes in PICO 2. CM, collagen matrix; CM, collagen matrix; HTA, hard tissue augmentation; SD – standard deviation; SD, standard deviationaugmentation; STA, soft tissue augmentation

to interpret, as two studies could not show any significant influence of soft tissue grafting on MBLs, one study showed a tendency to more bone level stability over long term in CTG-grafted groups and two publications (analyzing the same population) showed a significant influence of CM-grafting on MBLs. Furthermore, one study, reporting on CTG-grafting versus non-grafted controls had to be excluded in this systematic review because of additional bone augmentation in selected cases (Puzio et al., 2020). This study also showed that CTG-grafted cases revealed a tendency to lower MBL and determined a critical value of peri-implant soft tissue thickness of 2.88 mm (Puzio et al., 2020). This is in accordance with the included studies by Linkevicius et al. and Puysis et al., showing that initially thick peri-implant soft tissues (>2mm) or thickened peri-implant soft tissues with CM led to significantly less marginal bone loss when compared to thin soft tissues (<2mm) (Linkevicius et al., 2015; Puisys & Linkevicius, 2015).

The heterogeneity of the results with respect to the effect of soft tissue grafting on MBLs is in accordance with three systematic reviews and meta-analysis showing that thick peri-implant soft tissue have less marginal bone loss (Diaz-Sanchez et al., 2019; Suarez-Lopez Del Amo et al., 2016; Thoma et al., 2018), while one systematic review could not find sufficient evidence to answer this question (Akcali et al., 2017). Furthermore, only the studies by Linkevicius et al. and Puysis et al. stratified the included patients with respect to the initial thickness of the peri-implant mucosa (Linkevicius et al., 2015; Puisys & Linkevicius, 2015). In all other included studies, the control group without STA may also have had a thick biotype from baseline mitigating the effect of STA in the test group. Therefore, to underline the trend seen in this present systematic review and others, RCTs with strict inclusion criteria regarding initial soft tissue thickness are needed.

4.2 | PICO2

This PICO question addressed the effect of combined soft and hard tissue augmentation around immediate, delayed, and late implant when compared to bone grafting alone. Overall, meta-analysis revealed that a sites treated with a combination of hard and STA showed no statistically significant difference in terms of MBL changes when compared to hard tissue augmentation alone. With respect to the secondary outcomes of this systematic review, concomitant soft and hard tissue augmentations resulted in less marginal soft tissue recession when compared to hard tissue augmentation only.

Of ten identified publications, five studies (data reported in 6 publications (Migliorati et al., 2015; Noelken et al., 2018; Tatum et al., 2020; van Nimwegen et al., 2018; Yoshino et al., 2014; Zuiderveld et al., 2018a; Zuiderveld et al., 2020)) used immediate implant placement in conjunction with bone grafting and buccal STA using subepithelial CTG versus bone grafting alone. With respect to MBL changes, a high heterogeneity of study results could be witnessed as one study showed that additional STA improved bone levels around immediate implants (Noelken et al., 2018), two studies

TABLE 10 Primary outcomes PICO 3: STA vs HTA

Author	Group	Intervention	Follow-up	loss to or (partially) not included in ≥12m follow-up	MBLevel [mm] 12m mean (SD)	Conclusion
Bruyckere et al. 2018, Bruyckere et al. 2020a, Bruyckere et al. 2020b	test	STA (CTG, contour augmentation)	12m	1. No volumetric analysis, as cast was lost, but other parameters were recorded	0.78 (0.88)	No difference in MBLevel Change No difference between groups in secondary outcomes
	control	HTA (BioOss and Creos, contour augmentation)	12m	2. (intervention discontinued due to financial restrictions, therefore no esthetic or volumetric data)	0.42 (0.36)	

Abbreviations: 12m, 12-month examination; CTG, connective tissue graft; HTA, hard tissue augmentation; MBLevel, marginal bone level; NI, no information provided; SD, standard deviation; STA, soft tissue augmentation.

showed a tendency of improved bone levels (Migliorati et al., 2015; Yoshino et al., 2014), while one study failed to show any effect of STA on MBLs (Tatum et al., 2020) and one study (study population used in three publications (Zuiderveld et al., 2018a; Zuiderveld et al., 2020)) showed that additional STA around immediately placed and grafted implants significantly increase midfacial marginal bone loss when compared to bone grafting alone.

These heterogeneous findings can be seen in accordance with a recent systematic review, addressing STA around immediately placed implants. The authors conclude that STA using CTG did not reveal significant differences in terms of MBL change, but significantly contributed to midfacial soft tissue stability following immediately placed implants (Seyssens et al., 2020). The finding, that additional STA is beneficial for soft tissue stability around immediately placed implants is clinically relevant, as midfacial recession has become a concern following immediately placed implants (Chen & Buser, 2014; Cosyn et al., 2012; Kan et al., 2011; Khzam et al., 2015). However, it is not clear in literature, if only delicate clinical indications (such as thin periodontal biotypes) benefit from additional soft tissue grafting. Clinical studies suggest that in a particular group of patients with a thin periodontal biotype, midfacial recession occurs more frequently and that these patients would benefit more from additional soft tissue grafting (Bittner et al., 2020; Kan et al., 2011; Migliorati et al., 2015; Tatum et al., 2020). Most recently Tatum et al. performed a controlled clinical study, where patients with a thin periodontal biotype additionally to bone augmentation received a CTG to boost soft tissue volume at time of immediate implant placement. Consistently with the data of this review and previous reviews, MBLs were not influenced by additional soft tissue grafting. In terms of secondary outcomes, augmented thin periodontal biotypes showed similar results when compared with initially thick periodontal biotypes in terms midfacial soft tissue height (Tatum et al., 2020).

In the present review, two studies were included, reporting about delayed implant placement with bone augmentation using the GBR-technique and additional STA with subepithelial CTG versus bone grafting alone (Hosseini et al., 2020; Kobayashi et al., 2020). One study reported that additional STA had no significant influence on MBLs (Hosseini et al., 2020), while the other study indicated that additional STA was able to limit marginal bone loss (Kobayashi et al., 2020). However, both studies showed that additional STA improved the secondary outcomes of this review such as less facial tissue recession or better soft tissue color match.

It is important to note that the studies of Kobayashi et al., Noelken et al., and Zuiderveld et al. performed cone-beam computed tomography to determine the facial bone resorption (Kobayashi et al., 2020; Noelken et al., 2018; Zuiderveld et al., 2020). Kobayashi et al. and Noelken et al. concluded that CTG may be effective in both reducing labial bone resorption and reducing the recession of the soft tissues (Kobayashi et al., 2020; Noelken et al., 2018). Zuiderveld et al. confirmed that CTG is effective in reducing the midfacial recession, but in opposite is also accompanied with more loss of buccal bone thickness (Zuiderveld et al., 2020).

This finding might point into the direction that thin peri-implant soft tissue situations might induce bone resorption as documented by a series of clinical trials (Linkevicius et al., 2010, 2015; Puisys & Linkevicius, 2015). Also, recent systematic reviews implement that thin soft tissues possible induced bone remodeling (Suarez-Lopez Del Amo et al., 2016; Thoma et al., 2018). On the other hand, flap elevation—either full-thickness or partial thickness—might induce bone remodeling (Fickl et al.,2008, 2011).

The findings should be interpreted with caution, as most of the studies used periapical radiographs to determine MBL changes. Nevertheless, the available scientific data lead to the conclusion that on one side a certain height and thickness of peri-implant bone supports the overlying peri-implant soft tissues (Chappuis et al., 2018), but also a certain amount of peri-implant soft tissues are necessary to protect the peri-implant bone (Thoma et al., 2018). However, the exact dimensions of soft and hard tissues for this bidirectional connection are not clarified today.

4.3 | PICO3

Three publications, reported about the same patient population (De Bruyckere, Cabeza, et al., 2020; De Bruyckere, Cosyn, et al., 2020; De Bruyckere et al., 2018), were included in this systematic review. This study population showed no significant differences between both treatment groups with respect to MBL alterations 12 months after surgery (De Bruyckere, Cabeza, et al., 2020; De Bruyckere, Cosyn, et al., 2020; De Bruyckere et al., 2018). With respect to secondary outcomes, the included patient population showed no statistically significant differences with respect to postoperative mucosal recessions between test and control groups. All other secondary outcomes such as PROMS, incidence of peri-implantitis or PES were either not reported or did not show significant differences between both treatment groups.

The results must be analyzed with caution due to the heterogeneity and the limited sample size. Interesting additional valuable information can be drawn from the study by De Bruyckere et al. (De Bruyckere et al., 2018). They showed that 58% of the patients treated with GBR only still demonstrated slight alveolar process deficiency at 1-year follow-up. Following CTG grafting only 38% of the patients failed to show perfect soft tissue convexity at the buccal aspect. This may imply that the combination of soft and hard tissue augmentation is needed in most cases. This was confirmed by Schneider et al., demonstrating that a combined soft and hard tissue augmentation was effective in completely augmenting tissue volume and achieve tissue stability over a 1-year follow-up (Schneider et al., 2011). As already described above, a bidirectional relationship between peri-implant soft and hard tissue seems to exist. The underlying peri-implant bone supports the soft tissue height and thickness, and the peri-implant soft tissue protects the underlying bone from resorption. This may at least partially explain, why the results from combined soft and hard tissue grafting were on secondary outcomes such as tissue volume, peri-implant soft tissue height and esthetics were superior to either soft or hard tissue grafting procedures alone.

This systematic review has some limitations. First, with respect to the primary outcome of this review, most of the studies used periapical radiographs to determine MBLs. However, STA procedures are mostly performed on the buccal aspect due to the horizontal resorption profile of the ridge following tooth extraction. The majority of the included studies report on peri-apical radiographs, while only few studies present CBCT-data to analyze changes of buccal bone thickness. Therefore, the results of this analysis must be used with caution.

Secondly, a countless number of different materials/techniques/combinations have been used. It is obvious that different techniques, that is, harvesting techniques of CTG might have an influence on long-term stability of the grafted site. Furthermore, varying soft tissue substitutes are difficult to compare to autologous soft tissue. Third, various implant systems have been used in the included studies. It has also been documented that varying implant micro- and macrotopography can lead to different behavior of peri-implant soft and hard tissue over short- and long term. Finally, the Risk of Bias was different between the studies and only few of the included studies were judged at a low risk of bias.

5 | CONCLUSION

Overall, the results of this systematic review and two meta-analyses suggest that peri-implant MBLs are not influenced by STA aiming to increase the width of keratinized mucosa or the amount of soft tissue volume. With respect to secondary parameters such as bleeding indices, midfacial recession or tissue volume, STA are beneficial. Peri-implant soft and hard tissues seem to have a bidirectional relationship: “Bone stands hard, but soft tissue is the guard.”

ACKNOWLEDGEMENTS

This review was supported only by institutional funds from the authors’ institutions.

CONFLICT OF INTEREST

Prof Fickl has received lecture fees from Geistlich Pharma AG & Straumann AG, Prof Kebschull has received lecture fees from Geistlich Pharma AG, outside the submitted work. Prof Dietrich reports Personal fees from Orthocell, outside the submitted work.

The authors report no conflict of interest regarding this systematic review.

AUTHOR CONTRIBUTIONS

SF and AK performed literature research and systematic review. MK supervised the literature research and systematic research and performed the statistical analysis of the meta-analysis. TD contributed to the systematic research and paper writing. SF wrote the paper. All authors agreed on the final version of this manuscript.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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How to cite this article: Fickl, S., Therese Kröger, A., Dietrich, T., & Kebschull, M. (2021). Influence of soft tissue augmentation procedures around dental implants on marginal bone level changes—A systematic review. *Clinical Oral Implants Research*, 32(Suppl. 21), 108–137. https://doi.org/10.1111/clr.13829