

Efficacy of surgical approaches for peri-implant tissue preservation in immediate implant placement: A systematic review and meta-analysis

Abstract: The preservation of peri-implant tissues after immediate implant placement (IIP), especially in aesthetic zones, is a topic of interest. This systematic review was aimed at investigating the effects of currently available surgical procedures used to improve IIP results, including soft tissue augmentation, bone grafting, the flapless technique, and palatal implant positioning. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement's guidelines were followed, and a search for articles was performed on the PubMed and Cochrane databases with no date restrictions. Only randomised clinical trials that evaluated changes in soft and hard tissues around immediate placed implants were included. Statistical analyses were performed using Review Manager 5.3, and a quality assessment of the studies was performed using the Cochrane Collaboration's tool. Of the fourteen studies that met the inclusion criteria, 11 were analysed in the meta-analysis. The use of connective tissue grafts resulted in a significantly greater improvement of the facial gingival level (MD= -0.51; 95% CI: -0.76 to -0.31; $p < .001$), and the placement of bone grafts significantly reduced the horizontal resorption of the buccal bone (MD= -0.59; 95% CI: -0.78 to -0.39; $p < .001$). Neither the flapless technique nor palatal implant positioning resulted in significant improvements to any parameter investigated.

Keywords: immediate implant; surgical technique; aesthetic zone; systematic review

1. Introduction

Schulte and Heimke first presented post-extraction immediate implant placement (IIP) in 1976 as an alternative to the conventional surgical protocol, which requires a 4- to 6-month healing period (1). This procedure, classified as Type I placement, has become a common clinical therapeutic approach in dental implantology due to its several advantages, such as reduced treatment time, reduced number of surgical procedures, and increased patient satisfaction (2). Despite the high survival rates achieved with this treatment (97-98%) (3,4), obtaining a favourable aesthetic result, particularly in the anterior maxillary region, is challenging (5).

Following tooth extraction, dimensional changes of the alveolar ridge occur, especially within the first 3 months of socket healing (6). Such a reduction in bone volume involves the height and width of the socket walls and is more accentuated at the buccal plate due to its thickness (7,8). Vertical bone losses of 11-22% and horizontal bone losses of 29-63% have been reported in some reviews (9,10).

Contrary to initial suggestions, implant placement into a fresh extraction socket alone does not counteract the physiological remodelling of the alveolar bone, and reduction still occurs in the buccal bony ridge (11,12). The space between the implant surface and alveolar bone tissue or the marginal gap heals through new bone formation from inside the defects and bone resorption of the ridge from outside (13). This is perhaps why a thicker buccal plate might resist bone resorption more effectively (14,15).

The preservation of the alveolar ridge is necessary to peri-implant mucosa stability and aesthetic achievement in teeth replacement (16,17). In fact, missing volume in the horizontal direction at the buccal aspect causes a shadow in the area concerned, which is aesthetically displeasing (18). In the vertical direction, the loss of peri-implant tissue often leads to gingival recession, which can reach approximately 1 mm after 1 year of function (19,20). The extent of these soft tissue alterations, however, has been associated with certain factors. Large U- and W-shaped defects are accompanied by further gingival recession, as reported by Kan et al. (2007) (21). Similarly, the thin tissue biotype is more prone to recession compared to the thick biotype (17,19,22–24).

To counteract morphological changes in peri-implant tissue and attain optimal aesthetic results around immediate placed implants, various surgical strategies have been proposed and tested in numerous clinical studies. These include the flapless technique (25,26), bone grafting (27), soft tissue augmentation (28), and palatal implant positioning (29). However, few systematic reviews have evaluated the benefits of these surgical techniques, and none is based solely on randomised clinical trials (RCTs), which significantly limits the level of evidence. Therefore, the aim of this systematic review was to comprehensively and critically analyse RCTs related to surgical modifications and their influence on hard and soft tissue dimension stability outcomes to improve proper treatment planning and achieve better aesthetic and functional results with IIP.

2. Material and methods

The present systematic review was prepared according the guidelines provided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (30) and the Cochrane Collaboration's recommendations (31).

2.1. Research Question

The focus question was developed according to the Population, Intervention, Comparison, Outcome, and Study (PICOS) criteria. The question was as follows: "Do the available surgical strategies for peri-implant tissue preservation during IIP effectively improve the outcomes of soft and hard tissue conditions?"

P: The participants were systemically healthy patients requiring at least one single immediate postextractive implant in the maxillary aesthetic zone (through the premolars).

I: The surgical approaches were aimed at enhancing or preserving peri-implant tissues in IIP: (a) connective tissue grafts, (b) bone grafts, (c) flapless surgery, and (d) palatal implant positioning.

C: IIP was performed without the aforementioned individual surgical modifications.

O: The primary outcomes of this review were soft and hard tissue changes (in mm), specifically horizontal and vertical changes at facial and interproximal sites. In addition, secondary outcomes employed aesthetic indexes.

2.2. Eligibility criteria

Inclusion criteria

Eligible studies were included if they fulfilled the following inclusion criteria: (a) RCTs with at least 4 months of follow-up after implant placement, (b) studies that included data on peri-implant tissue changes following IIP with or without at least one surgical technique or modification evaluated in the maxillary aesthetic zone (including incisors, canines and premolars), and (c) full text in English.

Exclusion criteria

The exclusion criteria were as follows: (a) non-randomised controlled clinical trials, cohort studies, case-control studies, cross-sectional studies, case series, case reports, animal trials, in vitro, letters to editor, and systematic reviews; (b) studies not related to single IIP procedures or not performed in the maxillary aesthetic zone; (c) studies that lacked sufficient data; and (d) non-English-language articles.

2.3. Search strategy

The search was performed using the PubMed and Cochrane Collaboration Library databases to identify English-language articles published in dental journals through September 2019. The electronic search was complemented by a manual search of the reference lists of all selected articles, as well as reviews and clinical trials related to the topic.

The following search strategy was employed for PubMed: ((“Dental Implants”[Mesh]) OR “Dental Implants, Single-Tooth”[Mesh] OR “Dental Implantation”[Mesh] OR implant*) AND (immediat* OR postextract*) AND (“anterior maxilla” OR “maxillary incisor” OR “maxillary canine” OR “maxillary anterior” OR “maxillary premolar” OR “single maxillary” OR ((aesthetic OR esthetic) AND (zone OR region OR area))). The search strategy for the Cochrane Collaboration Library database used implant* and (immediate or postextract*) and (maxill* or esthetic*).

2.4. Study selection

After the elimination of duplicate articles, the titles and abstracts of the retrieved articles were screened separately by two independent researchers to identify articles that met the review eligibility criteria. When abstracts were unavailable or did not include the required information, the articles' full texts were evaluated before a final decision was made. Disagreement between the reviewers was resolved via discussion or by consulting a senior reviewer.

Next, the same researchers independently studied the full texts of the articles selected during the first screening to establish the final list of articles for review.

2.5. Risk of bias assessment

A quality assessment of the selected RCTs was conducted using the Cochrane Collaboration's tool for assessing bias risk, which includes six domains or questions: random sequence generation, allocation concealment, blinding of outcome assessment, incomplete outcome data, and selective reporting (31). Depending on the descriptions given for each criterion, they were assessed as having low, unclear, or high risk of bias.

2.6. Data collection and analyses

The data from the eligible articles were extracted independently by two reviewers using data extraction tables. Any inter-reviewer disagreement was resolved via discussion aimed at consensus. If there was any doubt or missing data, the articles' corresponding authors were contacted for clarification.

Review Manager (RevMan) Version 5.3 statistical software (The Cochrane Collaboration, Copenhagen, Denmark) was used to perform meta-analyses of comparable studies that reported the same outcome measures. Mean values of primary and secondary outcomes (change-from-baseline or final value scores, when missing initial data) were pooled directly and analysed using mean

differences (MDs) and 95% confidence intervals (CIs). The fixed-effects model was used when appropriate when two or more studies were included in any comparison. However, the random-effects model was used to pool results from more than one study if heterogeneity between studies was detected. Statistical heterogeneity across various studies was assessed using the Cochrane's test for heterogeneity and the I^2 statistic. An I^2 value of $> 75\%$ suggests high heterogeneity (32). The possibility of publication bias was assessed using funnel plots and Egger's tests for small-study effects, which are thought to exist if $p < .05$. A forest plot was created to illustrate the effects of the various studies and global estimation on the meta-analysis. Statistical significance was defined as a p value $< .05$.

3. Results

3.1. Study selection

Figure 1 depicts a flow chart of the article selection process. The electronic database search yielded 1162 studies (PubMed: 746; Cochrane: 416). After eliminating duplicates, 1069 studies were considered during the initial screening of titles and abstracts, and 24 were selected for full-text evaluation. Out of these 24 studies, 10 were excluded for various reasons (Table 1). Therefore, 14 articles fulfilled the established inclusion criteria and were included in the qualitative analysis. Of these, 11 were investigations, and 3 were groups of papers reporting various outcomes or follow-ups derived from a single investigation. The meta-analysis was performed using only 12 of the selected articles.

Table 1. Excluded articles with reasons

Studies	Reasons for exclusion
Bora et al. (33) Cordaro et al. (34) De Angelis et al. (35)	No IIP
Zuffetti et al. (36) Bramanti et al. (37) Cardaropoli et al. (38)	Treatment not performed in maxilla
Mounir et al. (39)	No evaluation of surgical techniques for IIP
Hazzaa et al. (40)	Inadequate control group according to PICO questions
Chen et al. (41)	Inadequate outcome according to PICO questions
Rungcharassaeng et al. (42)	No RCT

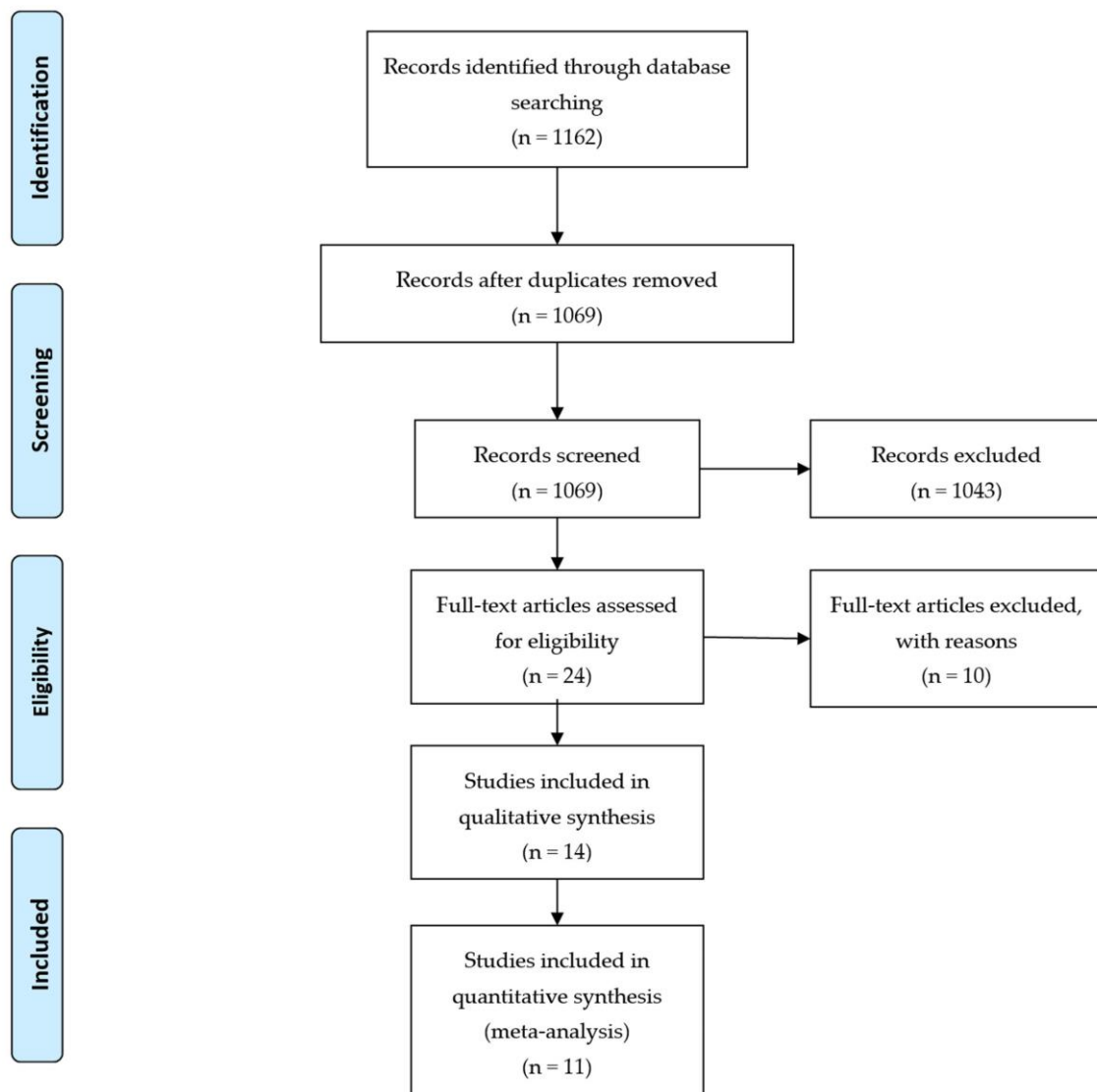


Figure 1. Flow chart depicting the search strategy and selection process.

3.2. Quality assessment

Figure 2 summarises the results of the quality assessment of the included studies after applying the checklist from the Cochrane Collaboration's bias risk assessment tool. Only one study had a low risk of bias for all six analysed fields, whereas 8 studies had a low risk of bias for the five main criteria. The remaining studies had a high or unclear risk of bias in two or more fields.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)
Chen 2007	?	?	?	?	+	+
Esposito 2018	+	+	-	+	+	+
Esposito 2019	+	+	-	+	-	+
Frizzera 2019	?	?	-	+	+	+
Girlanda 2019	+	+	+	+	+	+
Grassi 2019	+	+	-	+	+	+
Mastrangelo 2018	+	+	-	+	?	+
Migliorati 2015	+	-	-	+	+	-
Nimwegen 2018	+	+	-	+	+	+
Paknejad 2017	+	-	-	?	+	+
Sanz 2017	+	+	-	+	-	+
Stoupel 2016	+	+	-	+	+	+
Yoshino 2014	+	-	-	-	+	+
Zuiderveld 2018	+	+	-	+	+	+

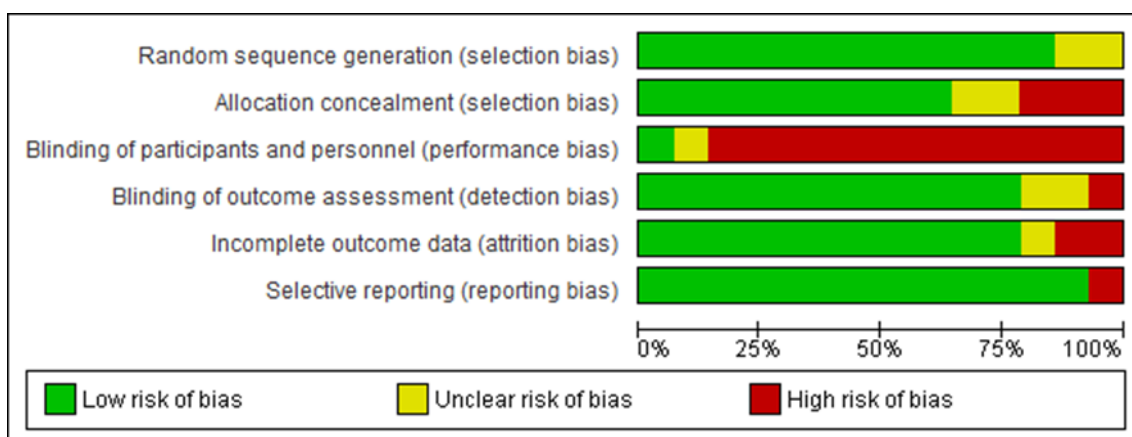


Figure 2. Risk of bias graph.

3.3. Description of studies

The main features of the included studies are summarised with details in Table 2. Of the 18 studies selected, 5 evaluated the use of connective tissue grafts (43–47), 6 investigated the use of bone

grafts (48–53), 2 compared flap and flapless surgeries (53,54), and 2 evaluated 3D positioning (55,56). Only 1 study addressed more than one of the previous topics (53). All studies were published between 2005 and 2019. The observation period and data reported in the studies were at least 12 months after implant placement, except in studies evaluating bone grafts, in which 4 months was the minimum follow-up period.

Table 2. General characteristics of included studies

Author (year), country	No. of patients (excluded)	No. of implants analysed	Inclusion/exclusion criteria	Intervention (test vs control)	Mean follow-up, mo.	Study outcomes
Zuiderveld et al. (2018), Netherlands (43)	60(2)	29 T 29 C	Non-smoking patients >18 yrs. with a single failing tooth between 15 and 25 and a bony defect of <5 mm (vertical)	<ul style="list-style-type: none"> • Connective tissue graft (tuberosity) • No connective tissue graft 	15	GL, PL, PES, MBL
Nimwegen et al. (2017), Netherlands (44)	60(10)	25T 25C	Non-smoking patients >18 yrs. with a single failing tooth between 15 and 25 and intact facial bone wall	<ul style="list-style-type: none"> • Connective tissue graft (tuberosity) • No connective tissue graft 	15	GL, GT, PES
Yoshino et al. (2014), USA (45)	20(0)	10 10	Non-smoking patients >18 yrs. with a single failing tooth between 15 and 25	<ul style="list-style-type: none"> • Connective tissue graft (palate) • No connective tissue graft 	12	GL, MBL
Migliorati et al. (2013), Italy (46)	48(1)	24 23C	Patients >21 yrs. with a single failing tooth between 15 and 25 and intact facial wall or with vertical defect <3 mm	<ul style="list-style-type: none"> • Connective tissue graft (palate) • No connective tissue graft 	27-28	GL, PL, GT, MBL.
Frizzera et al. (2019), Brazil (47)	24	8 8	Non-smoking patients >18 yrs. with a single failing maxillary incisor presenting alveolar facial wall dehiscence	<ul style="list-style-type: none"> • Connective tissue graft (palate) • No connective tissue graft 	12	GL, PL, PES, GT, HFB
Chen et al. (2006), Australia (48)	20	10 10	Patients with failing tooth between 15 and 25	<ul style="list-style-type: none"> • Gap filled with xenograft • No bone graft, no membrane 	6	HFB, VFB
Paknejad et al. (2017), Iran (49)	20(5)	14T 13C	Non-smoking patients between 18 and 50 years with failing tooth between 15 and 25, and intact buccal bone plate	<ul style="list-style-type: none"> • Gap filled with xenograft • No bone graft 	4-6	VFB
Sanz et al. (2016), Spain, Sweden, Italy (50)	91(5)	43T 43C	Patients >18 yrs. with failing tooth between 15 and 25, and intact extraction socket	<ul style="list-style-type: none"> • Gap filled with xenograft • No bone graft 	4	VFB, HFB, HPB
Girlanda et al. (2019), Brazil (51)	30 (8)	11 11	Non-smoking patients >18 yrs. with failing maxillary incisor	<ul style="list-style-type: none"> • Gap filled with xenograft • No bone graft 	6	GL, PL, HB
Mastrangelo et al. (2018), Italy (52)	108(6)	51 51	Patients >18 yrs. with one or more failing tooth between 15 and 25	<ul style="list-style-type: none"> • Gap filled with xenograft • No bone graft 	12 36	MBL, PES

Grassi et al. (2019), Italy (53)	45(1)	15T1 15T2 14C	Patients >18 yrs. with failing tooth in maxillary premolar area with vertical defect <3 mm	<ul style="list-style-type: none"> • Open flap and gap filled with xenograft • Open flap, no grafting • Flapless, no grafting 	6	HFB, VFB
Stoupe et al. (2016), USA (54)	39(3)	16T 20C	Patients >18 yrs. with failing tooth between 15 and 25, and intact buccal alveolar crest	<ul style="list-style-type: none"> • Flap • Flapless 	12	GL, PL, HFB
Esposito et al. (2018), Spain (55)	30(4)	12T 14C	Patients >18 yrs. with failing tooth between 15 and 25	<ul style="list-style-type: none"> • Natural positioning • Palatal positioning 	12	MBL, PES
Esposito et al. (2019), Spain (56)	20(6)	6T 6C	Patients aged >18 yrs. with failing tooth between 15 and 25	<ul style="list-style-type: none"> • Natural positioning • Palatal positioning 	36	MBL, PES

Facial gingival level (GL), interproximal papilla levels (PL), gingival tissue thickness (GT), marginal bone level (MBL), vertical facial bone dimension (VFB), horizontal facial bone dimension (HFB), pink aesthetic score (PES)

3.4. Results for connective tissue grafts

Five RCTs (43–47) reported the effect of connective tissue grafts (CTGs). They included 152 patients with a mean age of 48.9 (± 3.2) years. Sixty percent of patients were female. A thin biotype was registered in 46% and 48% of patients in the test and control groups, respectively. Four studies reported the inclusion of sites with facial dehiscence (up to 5 mm), and one was performed exclusively under these circumstances (47). In addition, in all these studies, flapless surgery was performed, the gap was filled with xenograft, and the implants were immediately provisionalised (Table 3).

Facial gingival changes were evaluated in all five studies, and measurements were made using calibrated intra-oral photographs (43,44,47) and calibrated study cast photographs (46) or made directly in casts (45). The meta-analysis revealed statistically significant differences favouring CTGs at all periods except at 24 months,

Table 3. Comparison of selected studies

	Demographic factors		Anatomic factors			Clinical factors			
	Mean age (months)	Gender (% female)	Dehiscence sites	Thin biotype (% Test/Control)	CTG Donor site	Gap filling	Flap elevation	Immediate loading	Implant positioning
Zuiderveld et al., 2018	46.6 (19.5–82.2)	53.33	Yes (3-5 mm vertical)	66.66/50	Tuberosity	Bio-Oss + Autogenous bone (1:1)	No (control) Partial envelope (test)	Yes	3 mm apical UAC Palatine
Nimwegen et al., 2018	46.6 (19.5–82.2)	53.33	Yes (3-5 mm)	66.66/50	Tuberosity	Bio-Oss + Autogenous bone (1:1)	No (control) Partial envelope (test)	Yes	3 mm apical UAC Palatine
Yoshino et al., 2014	52.6 (27-87)	65	-	0/30	Palate	Bio-Oss	No (control) Total envelope (test)	Yes	3 mm apical MG Palatine
Migliorati et al., 2013	47.5 (22-70)	52.08	Yes (< 3 mm)	58.3/52.2	Palate	Bio-Oss Collagen	No (control) Partial envelope (test)	Yes	Palatine
Frizzera et al., 2019	23-65	70.83	Yes (all cases)	62.5/62.5	Palate	Bio-Oss Collagen +Bio-Gide	No	Yes	4 mm apical MG Palatine

when a moderate heterogeneity was obtained due to the differences in gingival biotype and the small sample size. The differences were more pronounced at 12-15 months (MD= -0.51; 95% CI: -0.76 to -0.31; $p < .001$; $I^2=23\%$) (Figure 3).

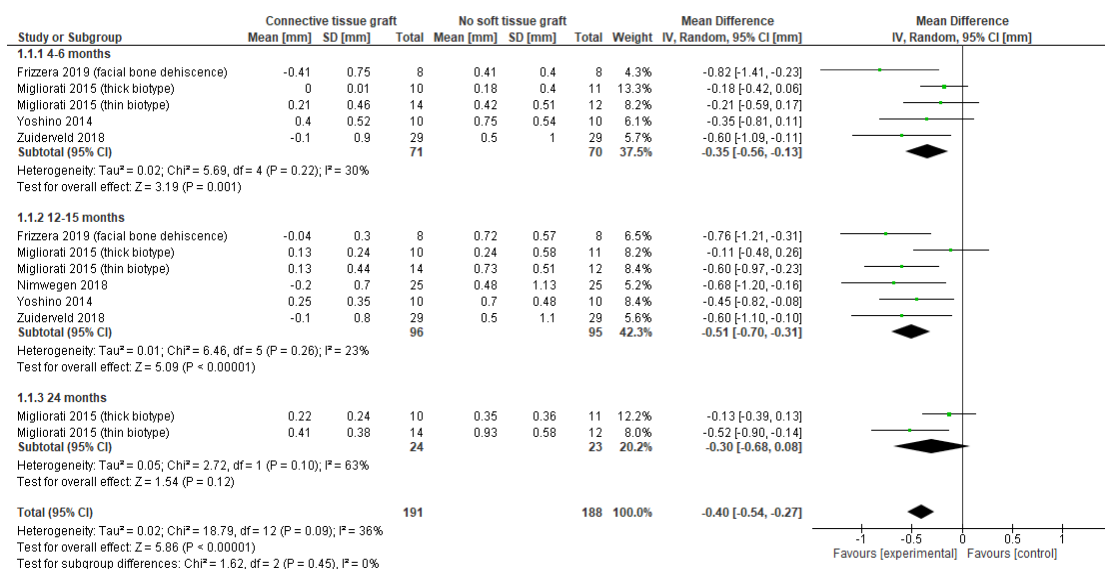


Figure 3. Comparison: IIP with vs without CTGs. Outcome: Facial gingival level changes at 4-6, 12-15, and 24 months.

Linear changes in mesial and distal interproximal gingiva were assessed in two studies (43,47), although one reported on final values (46). The meta-analysis showed no statistically significant differences between the groups in relation to the mesial and distal papilla during all follow-up periods (MD= -0.06; 95% CI: -0.17 to -0.06; $p < .32$; $I^2=0\%$) (Figure 4).

One study evaluated gingival thickness changes (44), and two reported on final values (46,47). In the first study, no significant differences were observed at 1 year between sites with or without CTGs based on a meta-analysis of mucosal volume loss (MD= 0.19; 95% CI: -0.12 to 0.5; $p = 0.23$). Statistically significant differences were noted for final gingival thickness in favour of the CTG group (MD= -0.77; 95% CI: -1.09 to -0.45; $p < .001$; $I^2=0\%$) for the same period. The overall meta-analysis results indicated high heterogeneity among the trials ($\chi^2=21.65$; $df=3$; $P<.0001$; $I^2=86\%$) (Figure 5). The funnel plot showed relative asymmetry on visual inspection, and the Egger test was significant ($t=2.2719$, $P = .023$). Thus, the presence of publication bias could not be ruled out (Figure 6).

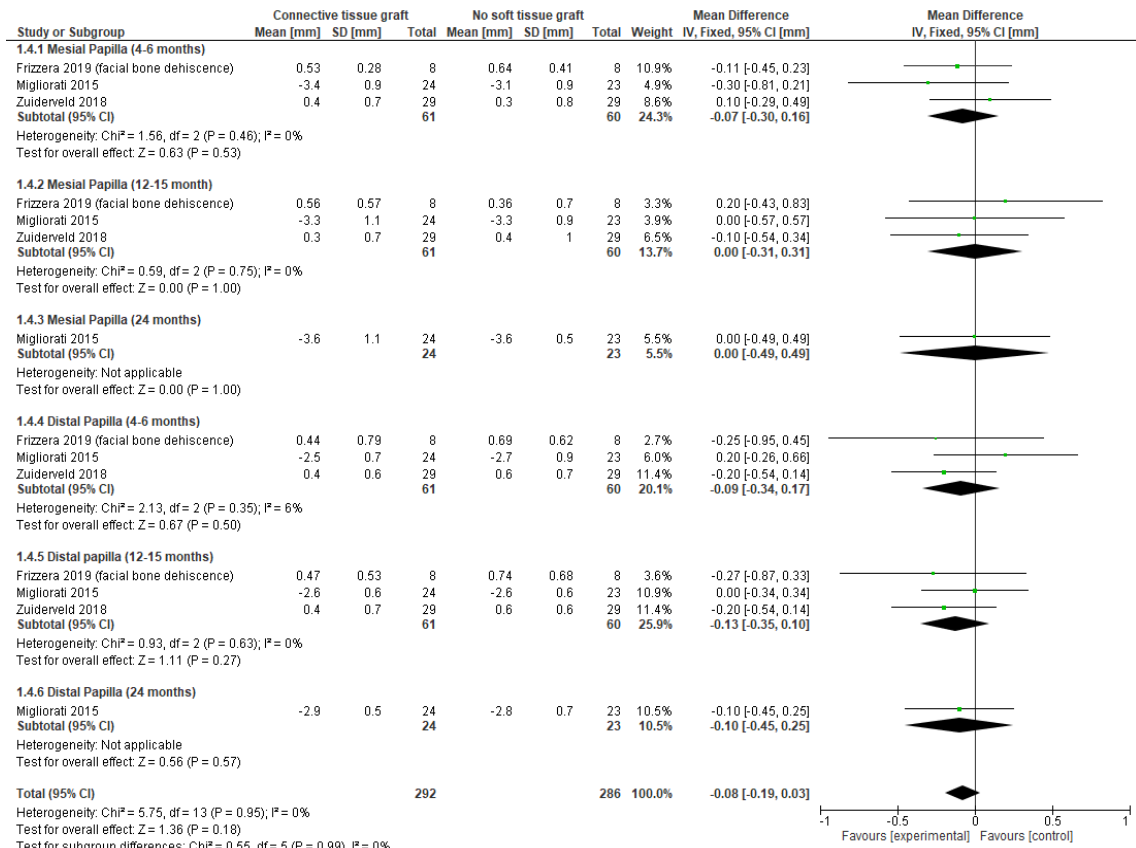


Figure 4. Comparison: IIP with vs without CTGs. Outcome: Mesial and distal papilla level changes at 4-6, 12-15, and 24 months.

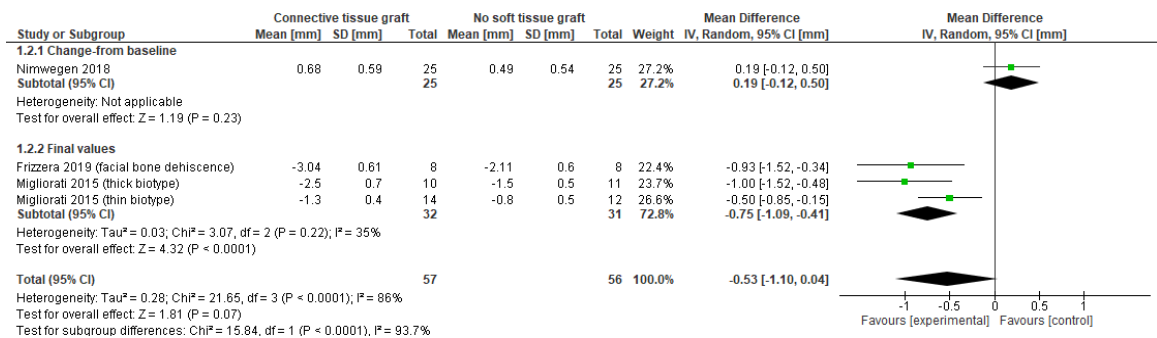


Figure 5. Comparison: IIP with vs without CTGs. Outcome: Gingival tissue thickness (change from baseline and final values) at 12-15 months.

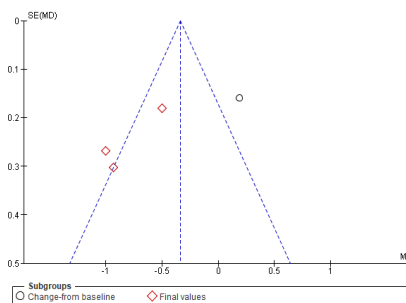


Figure 6. Funnel plot of meta-analysis of gingival tissue thickness among selected studies.

Marginal bone level changes were reported in two studies (45,46). An additional study (43) only reported the final mesial and distal values, so it was not included in the meta-analysis. The meta-analysis revealed significant differences between the investigated groups for change in marginal bone level (MBL) values in favour of the CGT group (MD= 0.11; 95% CI: -0.14 to -0.08; p= < .001; I²=0%) in all follow-up periods (Figure 7). Zuiderveld et al. (43) found no significant differences in marginal bone level at the mesial and distal sites.

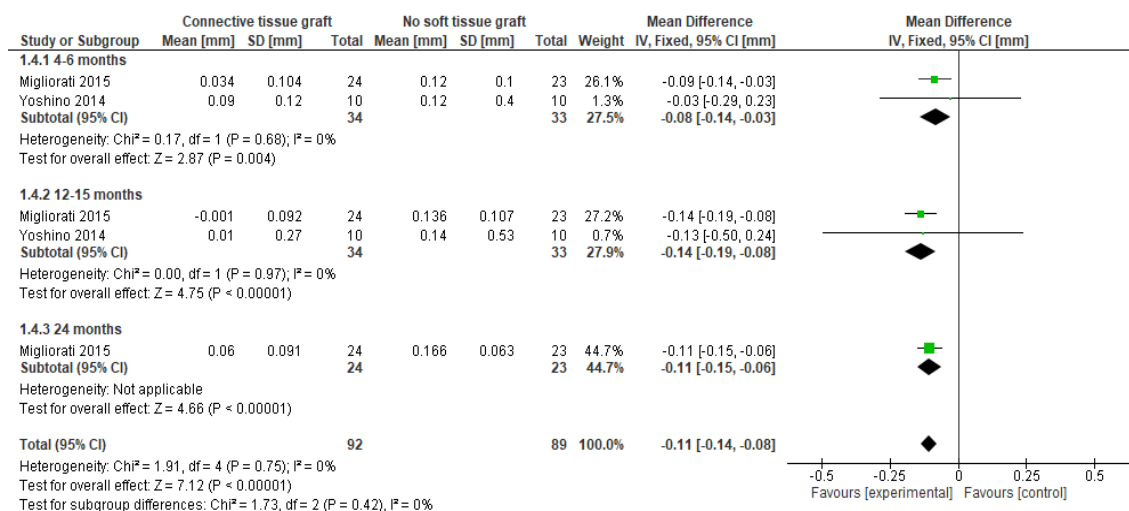


Figure 7. Comparison: IIP with vs without CTGs. Outcome: Marginal bone level changes at 4-6, 12-15, and 24 months.

The aesthetics of the peri-implant mucosa were assessed using the pink esthetic scale (PES) described by Belser et al. (57) and are summarized in Figure 8. Three studies (43,46,47) were included, and the random-effects meta-analysis model was used (heterogeneity test, p =.0008). The results showed no significant difference (p =.05) between groups. However, corroborating the correlation analysis performed by Migliorati et al. (46), a selective analysis of studies in which the CTGs contributed to increased gingival volume resulted in a statistically significant difference (MD= 1.44; 95% CI: 0.87 to 2; p= < .001; I²=0%), and the test group had a higher score (Figure 9).

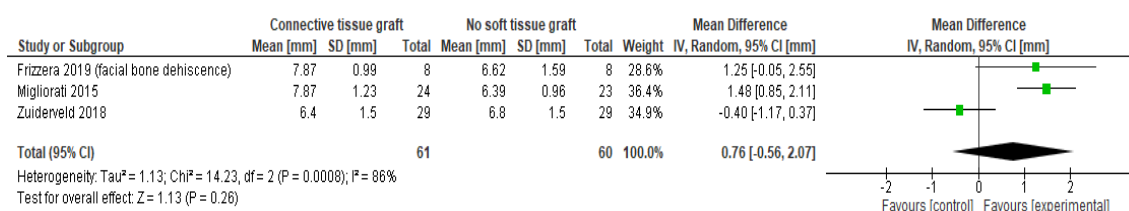


Figure 8. Comparison: IIP with vs without CTGs. Outcome: PES at 12-15 months

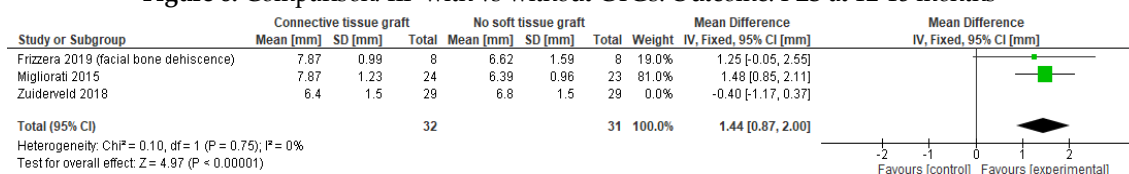


Figure 9. Comparison: IIP with vs without CTGs. Outcome: PES at 12-15 months after selective analysis.

3.5. Results for bone grafts

Regarding bone grafts, six articles were included, all evaluating the use of various xenografts (48–53). They included 314 patients with a mean age of 43.82 (± 3.61) years (Table 4). Sixty-three percent of the patients were females. Dehiscence sites included in three studies were less than 3 mm (50,53) and up to 10 mm (48). The mean gaps in the test and control groups were 2.35 and 2.25 mm, respectively. One study combined the use bone grafts with a membrane (52), as in one group of another study (48). In two studies, the procedure was conducted without flaps (49,51), whereas in the remaining studies, a flap was raised. Implant-supported temporary restoration was used immediately after implant placement in only one study (51).

Soft tissue assessment was performed only by Girlanda et al. (51), and measurements were made using individual stents and periodontal probes. At 6 months, no statistically significant differences were found between groups regarding soft tissue height at the buccal site ($p < .05$). However, mesial and distal sites showed significant differences, and the test group presented lower height reduction at these sites ($p < .05$).

Three studies reported on horizontal crestal bone changes (48,50,53) measured from the implant surface to the external surface of the bone crest. When these were pooled, the meta-analysis revealed significant differences between investigated groups, with less horizontal resorption in grafted groups 4-6 months after implant placement (MD= -0.59; 95% CI: -0.78 to -0.39; $p < .001$; $I^2=0\%$) (Figure 10).

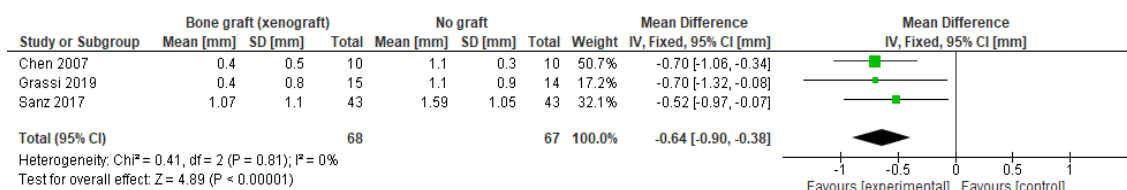


Figure 10. Comparison: IIP with vs without bone graft. Outcome: Horizontal crestal bone changes at 4-6 months.

Vertical crestal bone changes from the top of the crest to the implant platform were recorded in four studies (48–50,53). The meta-analysis revealed no significant differences between the grafted and control groups regarding vertical resorption at 4-6 months after immediate implantation (no grafting) (MD= -0.01; 95% CI: -0.34 to 0.37; $p=.94$; $I^2=0\%$) (Figure 11).

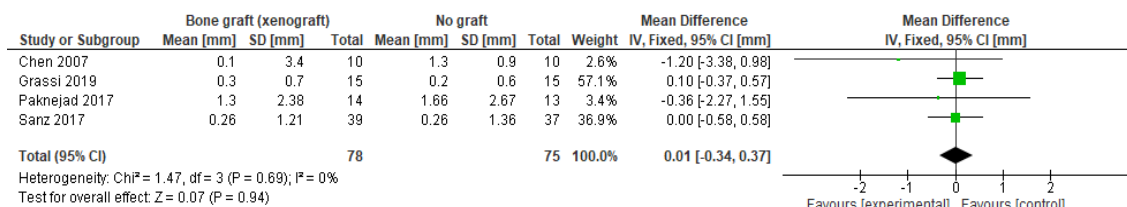


Figure 11. Comparison: IIP with vs without bone graft. Outcome: Vertical crestal bone changes at 4-6 months.

Table 4. Comparison of selected studies

	Demographic factors		Anatomic factors				Clinical factors			
	Mean age (months)	Gender (% female)	Dehiscence sites	Thin biotype (% test/control)	Gap size (mean, test/control)	Type of bone graft (test)	Flap elevation	Connective tissue graft	Immediate loading	Implant positioning
Chen et al. (2006)	45.2 (10.1)	66.7	Yes (< 10mm)	NR	1.9/1.9	BioOss	Yes	No	No	2-3 mm apical bucco-gingival margin
Paknejad et al. (2017)	38.8 (37-57)	85	No	NR	NR	CompactBone@ B	No	No	No	1-2 mm apical buccal bone
Sanz et al. (2016)	NR	49	Yes (< 3 mm)	NR	NR	Bio-Oss Collagen	Yes	No	No	NR
Girlanda et al. (2019)	21-58	81.81	No	NR	2.55/2.45	Bio-Oss Collagen	No	No	Yes	3 mm apical adjacent palatal teeth
Grassi et al. (2019)	47.3 (12.9)	57.77	Yes (< 3 mm)	66.66/64.28	2.6/2.4	Bio-Gen	Yes	No	No	1 mm apical palatal bone
Mastrangelo et al. (2018)	44 (6.7)	38.23	NR	NR	NR	BioOss	Yes	No	No	1-2 mm apical palatal bone

Table 5. Comparison of selected studies

	Demographic factors			Anatomic factors			Clinical factors			
	Mean age (months)	Gender (% female)	Dehiscence sites	Thin biotype (% test/control)	Gap size (mean, test/control)	Gap filling	Flap elevation	Connective tissue graft	Immediate loading	Implant positioning
Stoupel et al. (2016)	50 (33-70)	64.1	No	NR	2.3/3.1	No		No	Yes	Level buccal and palatal crest
Grassi et al. (2019)	47.3 (12.9)	57.77	Yes (< 3 mm)	66.66/64.28	2.6/2.4	No		No	No	1 mm apical palatal bone

Marginal bone changes were evaluated by Mastrangelo et al. (52), who reported 3-year outcomes. No significant differences were found between the grafted and ungrafted groups (MD= -0.03, 95% CI: -0.160 to 0.105; p=0.42).

The PES score (57) was also investigated in this same study, and the findings indicated that sites treated with the addition of an inorganic bone substitute achieved better aesthetics than sites treated only with implant placement (MD= 1.56, 95% CI: 0.782 to 2.328; p<0.001).

3.6. Results for flapless surgery

Regarding the effect of not raising a flap during surgery, two studies (53,54) were included; these reported outcomes on a cohort of 81 patients. The mean age was 48.65 (SD 1.9), and 61% of patients were females. Grassy et al. (53) reported the inclusion of sites with facial dehiscence of up to 3 mm. In the test and control groups, the mean gaps were 2.45 and 2.75 mm, respectively. In both cases, the procedure was conducted without filling the gaps, and the implants were immediately provisionalised in only one (54) (Table 5).

One study evaluated per-implant soft tissue, including the level of the mucosal margin and the papilla (54). After 12 months of follow-up, no significant differences were observed between sites with or without flap raising in terms of the mean longitudinal recession of the gingival margin at buccal (0.22 vs 0.42), mesial (0.09 vs 0.22), and distal (0.06 vs 0.28) points.

Buccal ridge changes in the horizontal plane were assessed in two studies, and one evaluated the change on the vertical plane (53). As for the first, the meta-analysis revealed no significant differences between the flapless and flap groups during an observation period of 6 months (MD= -0.07; 95% CI: -0.51 to 0.37; p= < .74; I²=0%). Similarly, vertical resorption did not differ significantly between the groups during the same period (MD= -0.10; 95% CI: -0.55 to 0.35; p= < .66).

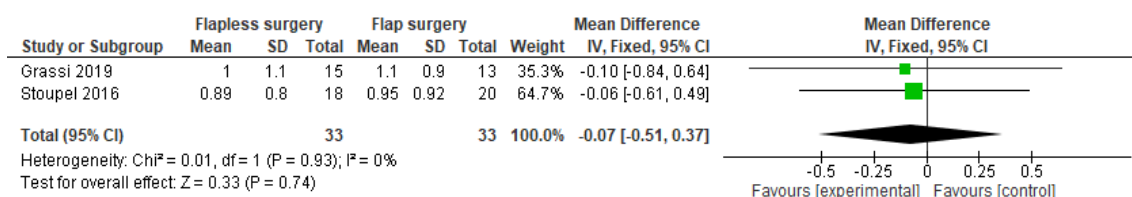


Figure 12. Comparison: IIP with vs without flap elevation. Outcome: Horizontal crestal bone changes at 6 months.

3.7. Results for implant positioning

Regarding implant positioning, two multicentre studies (55,56) derived from the same investigation reported the one- and three-year outcomes of 30 patients who were initially allocated to receive either implants in the natural position (control group) or approximately 3 mm more palatally (test group). The surgery was performed with flap elevation and applying xenografts buccally to the implants; these were left to heal submerged during 4 months. The authors found no statistically significant differences between the two procedures for peri-implant marginal bone level changes at 1 year and 3 years after implant loading. PES scores (58) were also comparable between the groups, although statistical significant differences were observed between centres at 1 year.

4. Discussion

This is a systematic review and meta-analysis based only on RCTs that evaluate the efficacy of various surgical techniques associated with IIP in the preservation of hard and soft peri-implant tissues. Fourteen studies were identified and divided into four main groups: (1) studies comparing the use and non-use of CTGs, (2) studies evaluating the use and non-use bone graft placement in the gap, (3) studies investigating flap and flapless surgery, and (4) studies comparing palatal and natural implant positioning. In the first group, CTGs significantly reduced facial gingival margin recession and did not significantly improve the position of the interdental papillae. In addition, the increase in gingival thickness was associated with reduced marginal bone loss and improved PES. In the second

group, the application of bone graft resulted in reduced horizontal resorption of the buccal bone plate and no significant improvement with respect to the vertical bone resorption. In the third group, flapless surgery did not significantly reduce the horizontal and vertical resorption of the buccal plate and did not significantly influence the level of the gingival contour. In the fourth group, the palatal position of the implant offered no advantages over the natural position in terms of marginal bone loss or aesthetic index.

Connective tissue grafts

The efficacy of CTGs in soft tissue augmentation around implants has been reported in numerous studies (59). It has been studied to a certain extent in immediate implantology, as until recently, reviews could not obtain definitive conclusions due to the lack of sufficient randomized clinical trials (60,61). In the present review, we included five RCTs on the use of CTGs simultaneous to IIP with very similar methodological characteristics.

One of the primary results, evaluating changes in soft tissues around implants, showed a significantly less apical migration of the facial gingival margin following CTGs, especially in those cases at high risk of recession, such as the presence of the thin biotype or facial bone dehiscence. The statistical analysis included samples exclusively with these conditions or consisting mostly of patients with these characteristics. Thus which even with small sample sizes, we were able to detect statistically significant differences. Until now, treatment in compromised post-extraction sockets has been considered unpredictable even after soft and hard tissue corrections (62), so in these cases, delayed implant placement has always been recommended (63).

In contrast, CTG did not significantly improve the position of the interdental papillae, which could be explained by the buccal and central insertion of the graft in studies that barely involved the interproximal areas and used horizontal sutures almost exclusively for stabilization. Furthermore, the variability and unpredictability observed in the various studies, as well as in the investigated groups, validates the hypothesis that the implant papilla is dictated by the height of the alveolar ridge in the interproximal areas (64,65) and influenced by the gingival morphology of the prosthesis and its emergence profile (66–68).

The use of autogenous CTGs for increased gingival thickness around implants is considered the treatment of choice for soft tissue volume augmentation (69,70). CTGs can induce keratinization of the overlying epithelium, especially if mostly composed of lamina propria and collagen fibres. In fact, the location of the donor site may affect the quality and composition of the graft. A CTG from the deep palate does not appear to have the same potential to induce keratinization as one from the superficial palate or the tuberosity because of its large amount of adipose and glandular tissue and little lamina propria. It appears that submucosal tissue can act as a barrier to plasma diffusion and impair revascularization during the early healing phase, leading to a trend of graft contraction over time and reduced volume gain (71). This theory contradicts the results obtained in one of the studies included in the present review, the only one in which no significant differences were obtained regarding gingival thickness and in which a tuberosity graft was used. The explanation of these results is unclear, as CTGs from the tuberosity are known to resemble more fibrotic tissue with a tendency to exhibit a hyperplastic response (72). Furthermore, the digital volumetric measurements used in this study were used successfully in several other studies on augmentations around implants (18,73). The lack of data on the graft's thickness, whether its dimensions were standardized, and the description of its placement greatly hinders interpretation. On the other hand, in the present review, average gingival thickness, taking into account only the final values, was 2.28 mm with the use of CTG; it was lower than those obtained in other studies: 2.98 mm (74), 2.5 mm (75), and 3.4 mm (76). This might have occurred because, in these studies, the implants were placed in healed alveolar ridges.

The idea that gingival augmentation procedures could also achieve a biological effect such as minimizing marginal bone loss was only proposed recently (77). Data from two studies included in the meta-analysis showed a beneficial effect of CTGs in terms of greater marginal bone preservation observed in the experimental groups. Likewise, in another recent systematic review reported similar

results regarding the use of CTG (70). In contrast, in the study by Zuideverld et al. (43), which was also included in this review, no significant differences were found between the groups regarding the final values of mesial and distal marginal bone loss, possibly due to the lack of volumetric gain reported in this study after the use of CTGs.

From an aesthetic perspective, the study by Migliorati et al. (46) contained a direct correlation between gingival thickness and the pink esthetic score (PES). This was also confirmed in the present meta-analysis, which initially showed great heterogeneity, but resulted in a high statistical significance in favour of the experimental groups regarding PES when excluding the study by Zuiderverld et al. (43). The importance of soft tissue thickening in obtaining more predictable aesthetic results is justified by the role that it plays in compensating for volume deficiencies caused by dental extraction, as well as in controlling the gingival recession and reducing unsightly gingival transparencies. Previously, the Cochrane Systematic Review (78) found weak evidence suggesting improved aesthetics when using CTGs with implants.

Bone grafts

The effects of various materials on regenerative therapies combined with immediate implantation was evaluated in several animal and clinical human studies. In many, as in the studies included in this review, xenograft were the most widely used bone substitutes. The data based on the present meta-analysis reveal a significant reduction in buccal bone loss at 4-6 months of follow-up with the use of xenografts. The horizontal reduction rate was 50% less than in the control groups. Because graft-associated membranes can improve tissue preservation and increase the cost of the procedure, groups in which they were used were excluded from the statistical analysis for a more adequate evaluation of the biomaterial effect *per se*. In contrast, the most recent systematic review data is controversial and could not fully support this surgical technique in preserving peri-implant hard tissues (79,80).

However, a remarkable aspect of the various included studies is the lack of useful information regarding morphological changes in the soft tissues around the implants. Only in one of them, in which a flapless surgery was performed in addition to filling the gap with a bone graft, was the height of the gingival margin at the buccal and interproximal levels reported, demonstrating better results in the grafted group at 3 and 6 months in the mesial and distal interproximal areas. The relevance of this type of data must be emphasized because, as previously seen, bone resorption after tooth extraction could alter the stability of the peri-implant mucosa, causing advanced recessions (81). A study evaluating the effects of bone grafts on recession as a secondary outcome found no effect of the addition of this biomaterial on recession in immediate implants (82), which might agree with the results obtained in this review regarding the vertical resorption of the ridge. On the other hand, a series of cases published by Cardaropoli et al. (83) documented changes in soft tissue contour after placing 26 immediately provisionalised post-extraction implants in which the space between the implant and bone was grafted with mineralized bovine bone mineral. This study found no significant differences between the state before and after treatment and concluded that this surgical protocol is capable of maintaining the contour and aesthetics of soft tissues.

The use of bone grafting might indirectly affect aesthetics by limiting the horizontal collapse of the socket after extraction, thus minimizing the formation of aesthetically unfavourable shadows.

Flapless approach

Whether or not to elevate the flap is an issue in implant therapy that has always been the subject of debate and controversy. Authors who advocate flapless surgery defend the approach because it causes less trauma to the peri-implant tissues by not having to separate the periosteum from the underlying bone, which causes vascular disruption and consequent bone resorption or gingival recession (7,25,26,84,85). However, when placing implants with a flapless procedure, the surgeon works blindly, and bone dehiscence or fenestration is more likely (78,86). Furthermore, in cases of bone gap filling, it is easier to remove the material from its place when it is not covered by a membrane or CTG. In the present review, based on two studies, no better results were demonstrated at the hard or soft tissue levels to support this approach. However, the interpretation of this

observation might be compromised because the sample sizes were quite small. Even so, it is noteworthy that bone grafting was used in none of the evaluated groups, which is an advantage for comparison and facilitates better estimation of the technique's effect. Similarly, a systematic review by Lee et al. (87) also failed to show significant differences in alveolar ridge preservation after IIP when comparing surgeries conducted with or without flaps – in this case, in prospective cohort studies. Regarding changes in soft tissues, in another systematic review that evaluated the immediate implantation and restoration of implants, no significant benefit was obtained from flapless surgery (88).

Implant position

The influence of the position of immediately placed implants in post-extraction sockets has been associated with changes at the hard and soft tissue levels (17,19). Specifically, implants with a vestibular platform position exhibited retraction levels three times greater than those of implants with a palatal platform position (19). Furthermore, leaving a gap when performing IIP minimized the compression of the facial bone wall when inserting the implant and allowed bone regeneration in the space created, leading to a thicker facial bone (17). Ferrus et al. found that a gap greater than 2 mm had less vertical resorption of the buccal bone compared to gaps of less than 1 mm. In fact, the current trend, which is recommended by almost all clinicians, is placing implants somewhat more palatally to achieve a better aesthetic result. Contrary to this way of thinking, the two articles included in this review failed to demonstrate an aesthetic advantage by placing implants 3 mm towards the palatal side at one and three years of follow-up; instead, results indicated better trends for implants in the natural position. In line with these results, at the time of this writing, a recently published RCT reported that, when analysing the influence of implant position, the greater the horizontal gap, the greater the changes observed in the facial aspect at the soft tissue level and the greater the variation in buccal table thickness (89). However, in both cases, the sample sizes were limited to establish definitive conclusions. Consequently, future clinical trials should confirm whether palatal placement are within certain ranges to ensure predictable results.

Limitations of the systematic review

Although the studies' comparability was high, the small number of results eligible for meta-analysis, as well as the small number of cases, sometimes complicated the adequate interpretation of the techniques' effects on some of the variables studied. This was even more limiting when only one study was included in the evaluation of a certain variable. In addition, the inclusion of only publications in English could have introduced selection bias.

More studies with larger sample sizes and a longer follow-up periods that include the largest number of variables related to changes in hard and soft peri-implant tissues are necessary to confirm the results and elucidate others that remain unclear.

5. Conclusions

Given this review's limitations, the following conclusions can be drawn in relation to IIP:

1. The use of CTGs prevents recession of the facial gingival tissue and seems to be especially beneficial in high-risk cases (fine biotype and facial dehiscence defects). The presence of CTGs does not influence the height of the interproximal papillae. When associated with increased gingival thickness, it prevents marginal bone loss and improves aesthetic outcomes.
2. The placement of bone replacement grafts in the gap reduces the horizontal resorption of the buccal bone but does not influence bone changes in vertical direction. The resulting aesthetics could be improved.
3. There is no evidence that flapless surgery and palatal implant positioning improve the preservation of peri-implant soft and hard tissues.
4. RCTs with high patient number and longer follow-up periods that evaluate hard and soft tissues are recommended.

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