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Root coverage procedures for treating single and multiple recession-type defects: A Cochrane Systematic Review Updated

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Summary sentence: Subepithelial connective tissue grafts, coronally advanced flaps alone or associated with other allogenous/xenogenous soft tissue substitutes can be used as root coverage procedures for the treatment of recession-type defects

ABSTRACT

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Background: This updated Cochrane systematic review (SR) evaluated the efficacy of different root coverage (RC) procedures in the treatment of single and multiple gingival recessions (GR).

Material and Methods: We included randomized controlled trials (RCTs) only of at least 6 months' duration evaluating Miller's Class I or II GR (≥ 3 mm) treated by means of RC procedures. Five databases were searched up to January 16, 2018. Random effects meta-analyses were conducted thoroughly.

Results: We included 48 RCTs in the SR. The results indicated a greater GR reduction for subepithelial connective tissue grafts (SCTG) + coronally advanced flap (CAF) compared to guided tissue regeneration with resorbable membranes (GTR rm) + CAF (mean difference [MD]: -0.37 mm). There was insufficient evidence of a difference in GR reduction between acellular dermal matrix grafts (ADMG) + CAF and SCTG + CAF or between enamel matrix derivative (EMD) + CAF and SCTG + CAF. Greater gains in the keratinized tissue width (KTW) were found for SCTG + CAF when compared to EMD + CAF (MD: -1.06 mm), and SCTG + CAF when compared to GTR rm + CAF (MD: -1.77 mm). There was insufficient evidence of a difference in KTW gain between ADMG + CAF and SCTG + CAF.

Conclusions: SCTG, CAF alone or associated with another biomaterial may be for treating single or multiple GR. There is also some evidence suggesting that ADMG appear as the soft tissue substitute that may provide the most similar outcomes to those achieved by SCTG.

KEY WORDS (MESH verified): Gingival recession; therapy; surgery; tooth root; surgical flaps.

INTRODUCTION

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Different systematic reviews (SR) have been published focusing on the effect of root coverage (RC) procedures on the treatment of single gingival recessions (GR).[2-7] These authors reported that different surgical techniques led to statistically significant improvements in recession depth (RD), clinical attachment level (CAL) and in the keratinized tissue width (KTW) (when indicated).[2-7] Also, it was recommended for clinical practice that when RC is indicated, subepithelial connective tissue grafts (SCTG), should be considered as the 'gold standard' procedure.[2-7] Moreover, the use of other biomaterials of allogenous (acellular dermal matrix graft [ADMG][8]) or xenogenous (i.e. collagen membranes,[9,10] enamel matrix derivative [EMD][11] and collagen bilayer matrix graft [XCM][12]) origin has been broadly studied since the late 1990s to treat GR.

The previous version of this Cochrane Review[13,14] endorsed these outcomes, and also emphasized the importance of SCTG in improving the KTW. Since its original publication in the *Cochrane Database of Systemtatic Reviews* in 2009[13] and in the *Journal of Periodontology* in 2010,[14] the knowledge on RC procedures and materials have evolved and new randomized clinical trials (RCT) have been published so far. Thus, this updated version of the original Cochrane SR[13,14] evaluated the efficacy of different RC procedures in the treatment of single and multiple GR.

MATERIALS & METHODS

Detailed descriptions of the SR protocol (i.e., criteria for considering studies for the review, search methods for identification of studies, and data collection and analysis) used in this paper have been published previously.[13,14] The following sections provide a brief description of the overall specific methodologic aspects of the 2018 version of the review.[1]

Criteria for considering studies for this review

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Types of studies and participants: RCTs ≥ 6 months' duration and reporting patient-based analysis. Studies were included if they reported the treatment of single or multiple Miller's[15] Class I or II GR (RD ≥ 3 mm), as well as at least 10 participants per group at final examination (with a follow-up < 5 years).

Exclusion criteria: Studies including Miller's[15] Class III and IV and restored root surfaces were not included.

Types of interventions: The interventions of interest were: a) free gingival grafts (FGG); b) laterally positioned flap (LPF); c) CAF; d) SCTG alone or in combination with LPF or CAF; and e) CAF in association with allograft (e.g., ADMG, others), GTR (with resorbabable [rs] or non-resorbable membranes [nrm]), EMD, XCM or other biomaterial. In addition, RCTs comparing variations of the same procedure (e.g. CAF with vertical incisions versus CAF without vertical incisions, etc) were also considered eligible for inclusion in the review.

Outcome measures: Primary outcome measures included aesthetic condition change (ACC) related to patient's opinion, complete root coverage (CRC) and RD change. *Secondary outcome measures were as follows:* CAL change, KTW change, mean root coverage (MRC), patients' preference for a specific RC procedure (in split-mouth trials), occurrence of adverse effects and/or postoperative complications. Outcome measures were separated into short-term (as evaluated 6 months to 12 months following interventions), medium-term (13 months to 59 months) or long-term (≥ 5 years).

Search methods for identification of studies (for details see supplementary Appendix 1 in online *Journal of Periodontology*).

Data collection and analysis

Details regarding data collection until October 2008 were reported previously.[13,14] Identification of studies conducted from November 2008 to January 16, 2018 were performed by two independent reviewers (LC and MASO). Agreement between review authors was assessed calculating Kappa scores. Disagreement between the review authors

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was resolved by discussion with the inclusion of another review author (RR). Risk of bias (low, high, or unclear) of each included study was assessed using the Cochrane domain-based, two-part tool as described in the *Cochrane Handbook for Systematic Reviews of Interventions*.[17]

Data synthesis

Data were collated into evidence tables. Random-effects meta-analyses were used throughout. For continuous data, pooled outcomes were expressed as weighted mean differences (MD) with their associated 95% confidence intervals (CI). For dichotomous data, these were predominately pooled odds ratios (OR) and associated 95% CI. The analyses were conducted using the generic inverse variance statistical method where the MD or log[OR] and standard error (SE) are entered for all studies. Becker-Balagtas method[18] was used to calculate MD and log ORs, as indicated by Curtin et al.[19] to accommodate data pooling from split-mouth and parallel-group studies in a single meta-analysis, and facilitate data synthesis.[18] For split-mouth trials it was assumed a intracluster correlation co-efficient of 0.05, while for parallel trials a co-efficient of zero for the calculation of SE. Statistical heterogeneity was assessed by calculation of the Q statistic. Analyses were performed using RevMan software. [‖]

[‖]Review Manager software, version 5.3; The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark

Variance imputation methods were conducted to estimate appropriate variance estimates in some split-mouth studies, where the appropriate standard deviation of the differences was not included in the trials.[20] The significance of discrepancies in the estimates of the

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treatment effects from the different trials was assessed by means of Cochran's test for heterogeneity and the I^2 statistic.

Presentation of main results: 'Summary of findings' tables for the main comparisons on single GR involving the "gold-standard" procedure (i.e., SCTG-based procedures versus other root coverage procedures) and the currently used alternative approaches (i.e., CAF, CAF + ADMG, CAF + EMD and CAF + XCM)[5,21,22] were produced for the following outcomes: a) CRC; b) GR change; c) CAL change; and d) KTW change. GRADE methods,[23] and the GRADEpro online tool were used for developing 'Summary of findings' tables (www.guidelinedevelopment.org). The quality of the body of evidence was assessed for each comparison and outcome by considering the overall risk of bias of the included studies, the directness of the evidence, the inconsistency of the results, the precision of the estimates, and the risk of publication bias. The quality of each body of evidence was categorised as high, moderate, low, or very low.

RESULTS

Results of the search and included studies

A total of 1714 records were retrieved from the searches (see supplementary Appendix 2 in online *Journal of Periodontology*). After the removal of duplicates, 724 records were screened for eligibility. 530 records were discarded, and the full-texts of 194 articles were assessed. From the 194 papers, 137 did not meet the criteria of eligibility and the reasons for exclusion were reported in the supplementary Appendix 3 in online *Journal*. Kappa scores for the searches conducted from November 2008 to January 2018 for title and/or abstract review, and full texts screening were 0.88 and 0.87, respectively.

Forty-eight studies (reported in 57 papers[8-12,24-75]) were included in the review, with 20 providing data for meta-analyses. Nine RCTs had their data reported in two articles each

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(i.e. according to the follow-up period or type of data (i.e. clinical or patient-reported outcomes).[12,31,32,34,35,44,45,47-51,61-64,66,67] Consequently, the papers with a shorter follow-up period were included under the one study name (e.g. papers with the longer follow-up),[32,35,45,48,50,51,61,67] while one article reporting patient-reported outcomes was included under the name of the clinical outcomes paper.[64] Data on the type of study design, location and country of trial are described in Table 1. Five studies evaluated multiple GR,[25,38,52,53,70] whereas the others single defects. Two studies[32,59] evaluated exclusively outcomes of smokers (i.e. 10 or more cigarettes per day for more than 5 years). In addition, the majority of trials followed participants during a short-term period (6 months to 12 months). Only five publications with medium-term follow-up[11,24,35,61,67] and five with long-term follow-up[45,48,50,51,54] were included. In total, 1227 patients were treated and details on the different treatment modalities are depicted in Table 1.

Risk of bias in included studies

Only one study was considered to be at a low overall risk of bias (Figure 1).[64] According to GRADE methods[23] all evidence was considered to be of low to very low quality, mainly for imprecision and inconsistency (see supplementary Appendix 4 in online *Journal of Periodontology*).

Effects of interventions

ACC, GR change, CAL change and KTW change*:* ACC related to patient's opinion was reported in 10 RCTs[25,29,48,50,51,53,61,72,74,75] (Table 2) Given the heterogeneity of methods/criteria used to assess this outcome and types of procedures compared, formal pooling of data via meta-analysis was precluded. Of the 48 included trials, 18 evaluating single GR[8-11,24,28,35,36,40,41,48,55,56,61,64,65,67,71] and two multiple GR[52,70] were included into 11 sets

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of meta-analyses (Table 3). In addition, data from studies not included in meta-analyses are presented in supplementary Appendix 5 in online *Journal*.

Single GR: With respect to RD change, there was evidence of greater RD reduction for EMD + CAF when compared to CAF alone (short/medium term; P = 0.005, MD: 0.32 mm), for SCTG + CAF when compared to GTR rm + CAF (P = 0.002, MD: -0.37 mm), for GTR rm + CAF associated with bone substitutes compared to GTR rm + CAF (P = 0.02, MD: 0.48 mm) and for XCM + CAF compared to CAF alone (P = 0.006, MD: 0.40 mm). Regarding CAL change, there was evidence of greater reduction of CAL for EMD + CAF when compared to CAF alone (short/medium-term, P = 0.009, MD: 0.35 mm), and for GTR rm + CAF compared to SCTG + CAF (P = 0.02, MD: of 0.35 mm). For KTW change, there was evidence of greater gain in the KTW for EMD + CAF when compared to CAF alone (short-term, P = 0.001, MD: 0.35 mm; short/medium term, P = 0.0005, MD: 0.40 mm), for SCTG + CAF when compared to EMD + CAF (P < 0.00001, MD: -1.06 mm), for SCTG + CAF when compared to GTR rm + CAF (P < 0.0001, mean difference -1.77 mm), for SCTG + CAF when compared to GTR rm + CAF associated with bone substitutes (P < 0.00001, MD: -2.38 mm), and for XCM + CAF when compared to CAF alone (P = 0.03, MD: 0.44 mm). **Multiple GR:** There was evidence of greater reduction of CAL for SCTG + CAF compared to PRF + CAF (P = 0.02, MD: -0.37 mm).

CRC

CRC was reported in 34 studies (Table 2) Among the included RCTs designed to evaluate single GR (excluding the data from Costa et al.[31,32] and Reino et al.[59] who included only heavy smokers), CRC varied from 0%[26] to 91.6%[8] for ADMG; 18.1%[33] to 95.6%[12,51] for SCTG; 25%[24] to 89.5%[47,48] for EMD; 7.7 %[34,35] to 81.8%[73] for CAF; 33.3%[36] to 53.3%[55] for GTR rm; and 28%[10] to 41.6%[9] for GTR nrm. Also, OR analyses of six comparisons did not find statistical differences between procedures (Table 3). For XCM + CAF versus CAF, the

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combined therapy improved the achievement of sites displaying CRC compared to the use of CAF alone (OR of 4.73, 95% CI 2.35 to 9.50).

MRC

All included trials reported the MRC. Within studies evaluating single GR (excluding the data from two RCT[31,32,59] who included heavy smokers), this outcome varied from 50%[41] to 96%[8] for ADMG, 64.7%[29] to 99.3%[12,51] for SCTG, 70.5%[39] to 95.1%[47,48] for EMD, 55.9%[34,35] to 95.4%[73] for CAF, 62.5%[46] to 73.7%[36] for GTR rm, 84.2 %[61,62] to 89.9%[36] for GTR rm associated with bone substitutes, and 80.5%[10] to 82.4%[9] for GTR nrm (Table 2).

Patients' preference for a specific RC procedure in split-mouth trials

This update did not identify additional data to those already publish by the previous version of this SR.[13,14] Details on this outcome are described in supplementary Appendix 6 in online *Journal of Periodontology*.

Occurrence of adverse effects and/or postoperative complications

Occurrence of adverse effects and/or postoperative complications during the postsurgical period was reported in 15 trials,[12,28,36,39,40,42,45,47,49,52,66,71,72,74,75] but restricted to a limited number of patients/cases (see supplementary Appendix 7 in online *Journal*). Overall, the most common adverse outcomes were postsurgical pain/swelling within the first days after surgery, ADMG graft or membrane exposure and postoperative pain in donor site of SCTG.

DISCUSSION

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Summary of main results

The main changes since the last version[13,14] are reported in Figure 2. In spite of aesthetics being considered the primary goal of RC procedures, few studies had evaluated ACC related to patients' opinion.[12,24,29,47-51,53,61,62,72,74,75] In these studies, the majority of the patients were satisfied with the final aesthetic result achieved (Table 2). Also, procedures that make a reduction in the operatory time possible, that eliminate the need for a second surgical site and that use smaller palatal grafts[72,74] were better accepted by the patients. In terms of RD reduction, results from meta-analyses demonstrated evidence that at short-term: SCTG + CAF promoted additional gains to those achieved by GTR rm + CAF; XCM + CAF improved the gains obtained by CAF alone; EMD + CAF led to better stability of the gingival margin after treatment than CAF alone; and GTR rm + bone substitutes + CAF provided better outcomes than GTR rm + CAF (Table 3).

There was a marked variation between procedures in terms of the achievement of CRC at short-term (Table 2): 0% to 95.6%. OR analyses on CRC did not reveal evidence of differences between procedures in none of the available comparisons, except for XCM + CAF versus CAF (i.e. the combined therapy promoted better outcomes). Additionally, some studies showed a decrease in the number of sites displaying CRC over time.[12,33,34,47-51]

With respect to secondary outcomes, four comparisons showed evidence that SCTG + CAF promoted additional gains in the KTW compared to EMD + CAF, GTR rm + CAF, or GTR rm + bone substitutes + CAF. Similarly, the use of EMD + CAF or XCM + CAF promoted additional gains in the KTW compared to the use of CAF alone (Table 3). Regarding CAL changes, there was evidence that SCTG + CAF promoted additional gains to those achieved by platelet-rich fibrin (PRF) + CAF, and that GTR rm + CAF promoted additional gains compared to SCTG + CAF. Also, there was a markedly variation in the amount of RC

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achieved. MRC varied from 44% to 99.3% (Table 2). Furthermore, data from some medium- and long-term trials[12,33,34,47-51] showed that MRC decreased over time.

Patients' preference for a specific RC procedure followed the same pattern as ACC.[9,71,72] Occurrence of an early discomfort with or without pain was related to donor sites of SCTG.[47,48,52,71,72] This aspect may be related to the size of the graft obtained from the palate and the surgical approach used.[72] Moreover, 'bigger grafts' were more associated to shrinkage of the covering flap with graft exposure when compared to 'small grafts'.[72,74] In terms of flap preparation, the removal of the labial submucosal tissue, in the area of lower incisors, led to a reduction in the number of sites experiencing covering flap shrinkage than sites where the submucosal tissue was not removed.[75]

Although 48 RCTs were included in this Cochrane SR, it was difficult to combine data from these trials due to a great variability of comparisons between the various RC procedures and the inexistence of a unique gold standard control group in all studies. Consequently, only 20 trials were incorporated into meta-analyses[8-12,24,28,34-36,40,41,47,48,52,55,56,61-67,70,71] in 11 different group comparisons (Table 3). Few studies reported a follow-up period superior to 12 months.[12,24,34,35,44,45,47-51,54,61,62,66,67] In six of these studies a chronological evaluation of the results evidenced loss in the amount of RC obtained (e.g. MRC and CRC) between the 6 months to 12 months period of evaluation[11,34,35,66,67] and between the first year and 5-and 10-year follow-ups.[12,47-51] This assumption was evidenced by the findings of pooled estimates on EMD + CAF versus CAF (Table 3). Two trials[31,32,59] evidenced the detrimental impact of smoking on root coverage outcomes (i.e. MRC and CRC decrease) within patients who smoke ≥ 10 cigarettes per day for more than 5 years.

Overall, both the individual studies' outcomes (i.e. within-group comparisons reported by each individual trial) and findings of pooled estimates clearly demonstrated that all RC procedures included in this Cochrane Review promoted reduction in the extent of GR and

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concomitant gain in the CAL for both single and multiple GR. Likewise, it was evidenced that KTW augmentation of these sites was associated to the use of SCTG or allogenous (ADMG)/xenogenous (XCM) soft tissue substitutes.

Quality of the evidence

Only one study was considered to be at a low overall risk of bias. GRADE methods[23] were used to assess the quality of the body of evidence of our main comparisons and our assessment is presented in the supplementary Appendix 4 in online *Journal of Periodontology* with all evidence considered to be of low to very low quality, mainly for imprecision and inconsistency.

Potential biases in the review process

In this review, only defects ≥ 3 mm were included in order to minimize heterogeneity between the trials. However, this inclusion criterion could have eliminated data from studies that could be incorporated into meta-analyses.

Agreements and disagreements with other studies or reviews

Important aspects already described in both the previous[13,14] and current versions of this Cochrane SR are depicted in supplementary Appendix 8 in online *Journal*. The current version of this SR evidenced that both patients and clinicians seem to agree that, in terms of aesthetic perception, CRC is perceived as the primary 'successful outcome' of a RC procedure.[76] However, it is important to highlight that patients' perception of buccal recessions is not high (approximately half of the patients with one gingival recession do not perceive them), as well as that the majority of those defects do not lead to functional or aesthetic concerns.[77]

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It has been demonstrated by an individual patient data meta-analysis of 602 Miller Class I and II recession defects[4] that the greater the baseline RD, the smaller the chance of CRC. It should also be noted that the inclusion of studies with recession defects ≥ 4 mm tends to show greater differences between baseline and follow-up means (i.e. outcome change), a factor that may influence the calculation of meta-analyses.[4,13,14] Another couple of studies[78,79] demonstrated that sites in which the gingival margin was sutured at the level of the cemento-enamel junction the achievement of CRC was inferior to those sites where a trapezoidal flap was sutured coronal (approximately 1 mm to 2 mm) (i.e. the more apical the gingival margin after surgery, the smaller the chance of CRC). Moreover, other anatomic aspects related to the interproximal dental papillae were already described previously[13,14] (see supplementary Appendix 8 in online *Journal of Periodontology*). Consequently, all these factors make comparisons and combination of data from different trials a critical issue.

It has been shown that smoking can affect the results obtained by RC procedures.[5] Two RCTs[31,32,59] evaluated only patients who smoked ≥ 10 cigarettes per day for at least 5 years, and their results showed that heavy smokers may be benefited by RC therapy, as well. However, MRC and CRC were clearly inferior to the outcomes achieved by trials evaluating non-smokers (Table 2). Eight trials[29,30,40,12,51,73-75] reported the inclusion of smokers who smoked less than 10 cigarettes per day. None of them performed comparisons between smokers and non-smokers. Zucchelli et al.[10] commented only that patients who smoke more than 10 cigarettes a day presented the worst percentage of RC. This is in line with included RCTs on smokers[31,32,59] and the data from other studies that have assessed the amount of RC obtained by smokers and non-smokers through CAF and SCTG.[5,3,14]

The present version of this Cochrane Review is completely in line with data from the recent American Academy of Periodontology Regeneration Workshop SR[5] that concluded that: 1) “all RC procedures can provide significant reduction in RD and CAL gain without alteration of

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probing depth for Miller Class I and II single GR, but multiple GR seems to be benefit as well despite the reduced quantity of information available;" 2) "SCTG-based procedures provided the best outcomes for clinical practice because of their superior percentages of MRC and CRC and the significant increase of KTW when compared with most of the other procedures" (as reported by the individual studies' outcomes, Table 2); 3) "the use of CAF with ADMG, EMD, and XCM also provided gains, many of them similar to SCTG-based procedures, and thus these may be considered as adequate substitute treatment approaches"; and 4) "smoking may decrease the expected results".[5]

It is also important to highlight that recent evidence from three long-term non-randomized studies, that followed patients for at least 20 years, found that GR relapse appears to be associated to sites lacking an attached KT band of at least 2mm.[80-82] Similarly, a recent SR[83] evaluating the long-term outcomes of untreated buccal GR (in terms of associated reported aesthetic and functional alterations and factors influencing the progression/worsening of dental and periodontal tissue conditions) found that: a) untreated GR in individuals with good oral hygiene are highly likely to experience RD increase during long-term follow-up (78% of the defects displayed clinical worsening); and b) the presence of KTW and/or greater KTW decrease the chance of RD increase or the development of new recessions. Nonetheless, individual data from some of the studies included in the present SR suggest that SCTG promoted better stability of the gingival margin/some degree of creeping attachment over time, compared to other surgical approaches.[12,24,40,51,70]

CONCLUSIONS

- All the analyzed RC procedures led to RD reduction and CAL gain and thus can be used in clinical practice. However, there was a great variability in the percentages of CRC and MRC.
- The available evidence base indicates that the most suitable options for RC of single GR, in terms of clinical outcomes and cost-to-benefit ratio, are: (1) SCTG plus CAF; (2) ADMG

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plus CAF; (3) EMD + CAF; (4) XCM + CAF; and (5) CAF alone. Despite of the restricted number of studies on multiple GR included in this SR, this 'hierarchy criterion' may be applied for the treatment of such defects, as well.

- GTR could be used to treat single GR, but most the information on these procedures were obtained from studies published up to the early 2000'0.
- Individual studies' outcomes and the available pooled estimates suggest that SCTG plus CAF may be considered as 'gold standard' procedure for the treatment of single and multiple GR. Moreover, evidence suggests that SCTG promoted better stability of the gingival margin/some degree of creeping attachment over time, compared to other surgical approaches.
- ADMG (primarily) and XCM (secondly) may be considered as alternative soft tissue grafting materials.
- Outcome measures of the evaluated surgical techniques were not improved by the use of root modification agents or the type of mechanical root scaling during surgery.
- The incidence of adverse effects, such as discomfort with or without pain, was mainly related to donor sites of SCTG. However, these conditions occurred mainly within the first week after surgery and did not influence on RC outcomes.

Implications for research

• Limited data exist on ACC related to patient's opinion, thus further RCTs are still required to evaluate this primary outcome variable. The use of the VAS (or other 'standardized scales') will allow more precise evaluations of patient-based outcomes.

• Future split-mouth trials should focus on patients' preference for a specific RC procedure.

• The inclusion of baseline and final individual defect measurements will allow more precise evaluations, as well as subgroup evaluations (e.g. patients presenting similar defects) and future comparisons via meta-analyses. These outcome measures should include GR depth and width, CAL, KTW and thickness, and root surface conditions (i.e. presence of caries, abrasions or restorations). Also, in order to draw more robust conclusions about treatment of

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sites lacking attached gingiva: a) the number of Miller Class I and II should be balanced and equally distributed in the study groups (i.e., test and control); and b) the differences in response to treatment between these sites should be considered.

• Comparisons between different operators (i.e. with respect to the degree of operator's experience) remain necessary to evaluate differences in the expected outcome measures.

• Considering the proposed inclusion criteria, no data were available for LPF and there is limited information for FGG and platelet-rich fibrin. These procedures might be evaluated by future research.

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Figure legends.

Figure 1 - Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

Figure 2 - ‘What’s new’ table - changes since the last version.

Table 1 - Characteristics of included studies

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Study	Methods	Participants	Interventions	Outcomes	Notes
Abolfazli et al.[24]	RCT, split-mouth design, 2 treatment groups, 24 months' duration	12 individuals, 8 females, aged 28 to 51 years, with 2 bilateral Miller Class I buccal gingival recessions of at least 3 mm	1. EMD + CAF 2. SCTG + CAF	GRC*(2), CALC*(2), KTC*(2), SCRC, PCRC*(2), MRC*(2) (Manual probe)	Practice-based (Iran)
Ahmedbeyli et al.[25]	RCT, parallel design, 2 treatment groups, 12 months' duration	24 individuals, 12 females, aged 22 to 40 years, with Miller Class I multiple buccal gingival recessions of at least 3 mm	1. ADMG + CAF 2. CAF	ACC, GRC*(1), CALC*(1) KTC*(1), SCRC, PCRC, MRC (Manual probe)	University/hospital-based (Turkey)
Ayub et al.[26]	RCT, split-mouth design, 2 treatment groups, 6 months' duration	15 individuals, number of females not reported, aged 20 to 56 years, with 2 bilateral Miller Class I or II buccal gingival recessions of at least 3 mm	1. ADMG (positioned 1 mm apical to the cemento-enamel junction) + CAF (extended flap) 2. ADMG + CAF (extended flap)	GRC*(1), CALC*(1), KTC, SCRC, PCRC, MRC (Automated controlled force probe and manual probe)	University/hospital-based (Brazil) and supported by the State of São Paulo Research Foundation and BioHorizons Inc
Babu et al.[27]	RCT, split-mouth design, 2 treatment groups, 6 months' duration	10 individuals, number of females not reported, age not reported, with 2 Miller Class I or II buccal gingival recessions of at least 3 mm	1. GTR + CAF (collagen membrane - Bioproducts Lab) 2. SCTG + CAF	GRC, CALC, KTC, MRC (Manual probe)	University/hospital-based (India)
Barros et al.[28]	RCT, split-mouth design, 2 treatment groups,	15 individuals, 10 females, aged 23 to 54 years, with 2 bilateral Miller Class	1. ADMG + CAF (extended flap) 2. SCTG + CAF (extended flap)	GRC, CALC, KTC, MRC (Automated controlled force probe - 0.50 N)	University/hospital-based (Brazil)

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	12 months' duration	I or II buccal gingival recessions of at least 3 mm			
Bouchard et al.[29]	RCT, parallel design, 2 treatment groups, 6 months' duration	30 individuals, 24 females, aged 21 to 62 years, with 1 Miller Class I or II buccal gingival recession of at least 3 mm	1. SCTG + CAF + CA (graft without epithelial collar) 2. SCTG (graft with epithelial collar)	ACC, GRC,CALC, KTC, SCRC, PCRC, MRC (Automated controlled force probe - 0.50 N)	Practice-based (France)
Bouchard et al.[30]	RCT, parallel design, 2 treatment groups, 6 months' duration	30 individuals, 25 females, aged 21 to 70 years, with 1 Miller Class I or II buccal gingival recession of at least 3 mm	1. SCTG + CAF + TTC-HCl 2. SCTG + CAF + CA	GRC, CALC, KTC, SCRC, PCRC, MRC (Automated controlled force probe - 0.50 N)	Practice-based (France)
Costa et al.[31,32]	RCT, split-mouth design, 2 treatment groups, 6 months' duration	20 individuals (heavy smokers - > 10 cigarettes/day for over 5 years), 12 females, aged 30 to 50 years, with 2 bilateral Miller Class I or II buccal gingival recessions of at least 3 mm	1. ADMG + EMD + CAF (extended flap) 2. ADMG + CAF (extended flap)	GRC*(1), CALC, KTC, SCRC, PCRC, MRC (Automated controlled force probe and compass)	University/hospital-based (Brazil)
Da Silva et al.[33]	RCT, split-mouth design, 2 treatment groups, 6 months' duration	11 individuals, 5 females, aged 18 to 43 years, with 2 bilateral Miller Class I or II buccal gingival recessions of at least 3 mm	1. SCTG + CAF 2. CAF	GRC, CALC, KTC*(1), SCRC, PCRC, MRC (Automated controlled force probe)	University/hospital-based (Brazil) Unpublished data were included following contact with author

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De Queiroz et al.[34,35]	RCT, split-mouth design, 2 treatment groups, 24 months' duration	13 individuals, 7 females, mean age 32.8 years, with 2 bilateral Miller Class I buccal gingival recessions of at least 3 mm	1. ADMG + CAF 2. CAF	GRC, CALC, KTC, SCRC, PCRC, MRC (Manual probe)	University/hospital-based (Brazil)
Del Pizzo et al.[11]	RCT, split-mouth design, 2 treatment groups, 24 months' duration	15 individuals, 11 females, aged 18 to 56 years, with 2 bilateral Miller Class I or II buccal gingival recessions of at least 3 mm	1. EMD + CAF 2. CAF	GRC, CALC, KTC*(1), SCRC, PCRC, MRC (Manual probe)	University/hospital-based (Italy)
Dodge et al.[36]	RCT, split-mouth design, 2 treatment groups, 12 months' duration	12 individuals, 8 females, aged 23 to 51 years, with 2 Miller Class I or II buccal gingival recessions of at least 3 mm	1. GTR (polylactic acid membrane - Guidor) + TTC-HCl + DFDBA 2. GTR (polylactic acid membrane - Guidor) + TTC-HCl	GRC, CALC*(1), KTC*(1), SCRC PCRC, MRC (Manual probe)	Practice-based (USA)
Henderson et al.[37]	RCT, split-mouth design, 2 treatment groups, 12 months' duration	10 individuals, 5 females, aged 24 to 68 years, with 2 Miller Class I or II buccal gingival recessions of at least 3 mm	1. ADMG (connective tissue side against the tooth) + CAF 2. ADMG (basement membrane side against the tooth) + CAF	GRC, CALC, KTC, MRC (Manual probe)	University/hospital-based (USA) and supported by Lifecore Biomedical
Jaiswal et al.[38]	RCT, parallel design, 2 treatment groups, 6 months' duration	20 individuals, 8 females, aged 25 to 56 years, with Miller Class II multiple buccal gingival recessions of at least 3 mm	1. EMD + CAF 2. CAF	GRC*(1), CALC*(1), KTC, MRC (Automated controlled force probe - 15g)	University/hospital-based (India)

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Jankovic et al.[39]	RCT, split-mouth design, 2 treatment groups, 12 months' duration	20 individuals, 12 females, aged 21 to 48 years, with bilateral Miller Class I and II maxillary buccal gingival recessions of at least 3 mm	1. Platelet-rich fibrin + CAF 2. EMD + CAF	GRC, KTC*(2), SCRC, PCRC, MRC (Manual probe)	University/hospital-based (Serbia)
Jepsen et al.[40]	RCT, split-mouth design, 2 treatment groups, 6 months' duration	35 individuals, age > 18 years, with 2 Miller Class I or II buccal gingival recessions of at least 3 mm	1. XCM + CAF 2. CAF	GRC*(1), CALC, KTC*(1), SCRC, PCRC, MRC (Manual probe)	University/hospital-based (German, Italy, Sweden and Spain) and supported by Geistlich Pharma AG
Joly et al.[41]	RCT, split-mouth design, 2 treatment groups, 6 months' duration	10 individuals, 4 females, aged 24 to 68 years, with 2Miller Class I or II maxillary buccal gingival recessions of at least 3 mm	1. ADMG + CAF (flap without vertical incisions) 2. SCTG + CAF (flap without vertical incisions)	GRC*(2), CALC*(2), KTC, MRC (Manual probe)	University/hospital-based (Brazil)
Keceli et al.[42]	RCT, parallel design, 2 treatment groups, 12 months' duration	40 individuals, 30 females, aged 18 to 60 years, with 1Miller Class I or II buccal gingival recession of at least 3 mm. 36 individuals completed the study	1. SCTG + platelet-rich plasma + CAF 2. SCTG + CAF	GRC, CALC, KTC, SCRC, PCRC, MRC (Manual probe)	University/hospital-based (Turkey) and supported by The Research Foundation of Hacettepe University
Keceli et al.[43]	RCT, parallel design, 2 treatment groups, 6 months' duration	40 individuals, 27 females, aged 22 to 50 years, with 1Miller Class I or II buccal gingival recession of at least 3 mm	1. SCTG + platelet-rich fibrin + CAF 2. SCTG + CAF	GRC, CALC, KTC, SCRC, PCRC, MRC*(1) (Manual probe)	University/hospital-based (Turkey)

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Leknes et al.[44,45]	RCT, split-mouth design, 2 treatment groups, 72 months' duration	20 individuals, 10 females, mean age 38.4 years, with 2MillerClass I or II buccal gingival recessions of at least 3 mm. 11 individuals completed the study	1. GTR (polylactic acid membrane - Guidor) 2. CAF	GRC, CALC, KTC, SCRC, PCRC, MRC (Automated controlled force probe and manual probe)	University/hospital-based (Norway) and membranes provided by Guidor AB Unpublished data were included following contact with author
Matarasso et al.[46]	RCT, parallel design, 2 treatment groups, 12 months' duration	20 individuals, 8 females, aged 18 to 42 years, with 1 Miller Class I or II buccal gingival recession of at least 3 mm	1. GTR (polylactic acid membrane - Guidor) + double papilla flap 2. GTR (polylactic acid membrane - Guidor) + CAF	GRC, CALC, KTC, MRC (Manual probe)	University/hospital-based (Italy) Unpublished data were included following contact with author
McGuire et al.[47,48]	RCT, split-mouth design, 2 treatment groups, 5 years' duration	20 individuals, 10 females, aged 23 to 62 years, with 2 Miller Class II maxillary buccal gingival recessions of at least 4 mm. 19 individuals completed the 6-month follow-up, 17 completed the 12-month follow-up, and 9 the 5-year follow-up	1. EMD + CAF 2. SCTG + CAF	GRC, CALC, KTC*(2), PCRC, MRC (Manual probe)	Practice-based (USA) and supported by BIORA AB (currently Straumann) Unpublished data were included following contact with author
McGuire et al.[49,50]	RCT, split-mouth design, 2 treatment groups, 5 years' duration	30 individuals, 26 females, aged 18 to 70 years, with 2 Miller Class II buccal gingival recessions of at least 3 mm. 30 individuals completed the 6	1. Beta-tricalcium phosphate (b-TCP) + recombinant human platelet-derived growth factor-B with a bioabsorbable collagen wound-healing dressing + CAF 2. SCTG + CAF	ACC, GRC*(2), CALC, KTC*(2), SCC, PCRC, MRC (Manual probe)	Practice-based (USA) and supported by Osteohealth Unpublished data were included following contact with author

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		months follow-up, whereas 20 the 5 years follow-up			
McGuire et al.[12,51]	RCT, split-mouth design, 2 treatment groups, 5 years' duration	25 individuals, 17 females, aged 18 to 70 years, with 2 Miller Class II buccal gingival recessions of at least 3 mm. 23 individuals completed the 12 months follow-up, whereas 17 the 5 years follow-up	1. XCM + CAF 2. SCTG + CAF	ACC, GRC*(2), CALC*(2), KTC, SCC, PCRC, MRC (Manual probe)	Practice-based (USA) and supported by Giestlich Pharma AG Unpublished data were included following contact with author Data from earlier article were reported as part of this trial
Öncü et al.[52]	RCT, split-mouth design, 2 treatment groups, 6 months' duration	20 individuals, 11 females, age > 18 years, with maxillary bilateral multiple Miller Class I or II buccal gingival recession of at least 3 mm	1. Platelet-rich fibrin + CAF without vertical incisions 2. SCTG + CAF without vertical incisions	GRC, CALC, KTC*(2), SCRC, PCRC, MRC (Manual probe)	University/hospital-based (Turkey)
Ozenci et al.[53]	RCT, parallel design, 2 treatment groups, 12 months' duration	20 individuals, 13 females, aged 22 to 42 years, with Miller Class I multiple buccal gingival recessions of at least 3 mm	1. ADMG + Tunnel (CAF) 2. ADMG + CAF	ACC*(2), GRC*(2), CALC*(2), KTC*(2), SCC, PCRC, MRC (Manual probe)	University/hospital-based (Turkey)
Paolantonio et al.[54]	RCT, parallel design, 2 treatment groups, 60 months' duration	70 individuals, 38 females, aged 25 to 48 years, with 1 Miller Class I or II buccal gingival recession of	1. SCTG + double papilla flap 2. FGG	GRC*(1), KTC, SCRC, PCRC, MRC (Manual probe)	Practice-based (Italy) Unpublished data were included following contact with author

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		at least 3 mm			
Paolantonio[55]	RCT, parallel design, 3 treatment groups, 12 months' duration	45 individuals, 31 females, aged 27 to 51 years, with 1Miller Class I or II buccal gingival recession of at least 3 mm	1. GTR (polylactic acid membrane - Guidor) 2. GTR (polylactic acid membrane - Paroguide) + hydroxyapatite/collagen/chondroitin sulfate graft 3. SCTG + double papilla flap	GRC, CALC, KTC*(3), SCRC, PCRC, MRC (Manual probe)	University/hospital-based (Italy) and supported by ItalianMinistry of University and Scientific Research Unpublished data were included following contact with author
Paolantonio et al.[56]	RCT, parallel design, 2 treatment groups, 12 months' duration	30 individuals, 19 females, aged 29 to 51 years, with 1Miller Class I or II buccal gingival recession of at least 3 mm	1. ADMG + CAF 2. SCTG + CAF	GRC, CALC, KTC*(2), SCRC, PCRC, MRC (Automated controlled force probe - 20 g and calliper)	University/hospital-based (Italy) and supported by ItalianMinistry of University and Scientific Research Unpublished data were included following contact with author
Pendor et al.[57]	RCT, parallel design, 2 treatment groups, 6 months' duration	20 individuals, 6 females, aged 25 to 46 years, with 1 Miller Class I or II buccal gingival recession of at least 3 mm	1. SCTG + double pedicle flap 2. SCTG + CAF	GRC, CALC, KTC, SCRC, PCRC, MRC (Automated controlled force probe - 15 g and calliper)	University/hospital-based (India)
Rasperini et al.[58]	RCT, parallel design, 2 treatment groups, 12 months' duration	56 individuals, 39 females, mean 35.5 years, with 1 Miller Class I or II buccal gingival recession of at least 3 mm	1. EMD + SCTG + CAF 2. SCTG + CAF	GRC, CALC, KTC, SCRC, PCRC, MRC (Manual probe)	University/hospital-based (Italy)
Reino et al.[59]	RCT, split-mouth design, 2 treatment groups, 6 months'	12 individuals (heavy smokers - ≥ 20 cigarettes per day for more than 5 years), 10 females,	1. SCTG + CAF (extended flap) 2. SCTG + CAF	SCRC, PCRC, MRC (Automated controlled force probe and manual probe)	University/hospital-based (Brazil) and supported by the State of São Paulo Research Foundation, São Paulo, Brazil

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	duration	aged 35 to 50 years, with 2 bilateral Miller Class I or II buccal gingival recessions of at least 3 mm			
Reino et al.[60]	RCT, split-mouth design, 2 treatment groups, 6 months' duration	20 individuals, 14 females, aged 26 to 46 years, with 2 bilateral Miller Class I or II buccal gingival recessions of at least 3 mm	1. XCM + CAF (extended flap) 2. XCM + CAF	GRC*(1), CALC, KTC, MRC (Automated controlled force probe and calliper)	University/hospital-based (Brazil) and supported by the State of São Paulo Research Foundation, São Paulo, Brazil and Geistlich Pharma AG
Roccuzzo et al.[9]	RCT, split-mouth design, 2 treatment groups, 6 months' duration	12 individuals, 3 females, aged 21 to 31 years, with 2 Miller Class I or II buccal gingival recessions of at least 4 mm	1. GTR (polylactic acid membrane - Guidor) 2. GTR (ePTFE membrane - Gore-Tex)	GRC, CALC, KTC, SCRC, PCRC, MRC (Manual probe)	University/hospital-based (Italy)
Rossetti et al.[61,62]	RCT, split-mouth design, 2 treatment groups, 30 months' duration	12 individuals, 9 females, aged 25 to 60 years, with 2 Miller Class I or II buccal gingival recessions of at least 3 mm	1. GTR (collagen membrane) + TTC-HCl + DFDBA 2. SCTG + HCl	ACC, GRC, CALC, KTC*(2), MRC (Manual probe)	University/hospital-based (Brazil) and supported by Brazilian National Council for Scientific and Technologic Development
Sangiorgio et al.[62,64]	RCT, parallel design, 4 treatment groups, 6 months' duration	68 individuals, aged 18 to 60 years, with 1 maxillary Miller Class I or II buccal gingival recession of at least 3 mm	1. XCM + CAF 2. EMD + CAF 3. XCM + EMD + CAF 4. CAF	ACC, GRC*(Groups 1, 2 and 3 were superior to 4), CALC, KTC SCRC, PCRC*(Groups 2 and 3 were superior to 4), MRC* (Groups 1, 2 and 3 were superior to 4) (Manual probe and digital	University/hospital-based and supported by the State of São Paulo Research Foundation, São Paulo, Brazil

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				calliper)	
Shori et al.[65]	RCT, parallel design, 2 treatment groups, 6 months' duration	20 individuals, aged 18 to 50 years, with 1 Miller Class I or II buccal gingival recessions of at least 3 mm	1. ADMG + CAF 2. SCTG + CAF	GRC, CALC, KTC*(2), SCR, PCRC, MRC (Automated controlled force probe)	University/hospital-based (India)
Spahr et al.[66,67]	RCT, split-mouth design, 2 treatment groups, 24 months' duration	37 individuals, 17 females, aged 22 to 62 years, with 2 Miller Class I or II buccal gingival recessions of at least 3 mm. 30 individuals completed the study	1. EMD + CAF 2. Placebo (propylene glycol alginate) + CA	GRC, CALC, KTC, PCRC, MRC (Automated controlled force probe, calliper and manual probe)	University/hospital-based (Germany)and supported by BIORA AB (currently Straumann)
Tözum et al.[68]	RCT, parallel design, 2 treatment groups, 6 months' duration	31 individuals, 21 females, aged 16 to 59 years, with 1 Miller Class I or II buccal gingival recession of at least 3 mm	1. SCTG + modified tunnel procedure 2. SCTG + CAF	GRC*(1), CALC*(1), MRC (Manual probe)	University/hospital-based (Turkey) Unpublished data were included following contact with author
Trombelli et al.[69]	RCT, split-mouth design, 2 treatment groups, 6 months' duration	15 individuals, 3 females, aged 25 to 51 years, with 2 Miller Class I or II maxillary buccal gingival recessions of at least 3 mm	1. CAF (fibrin glue + TTC-HCl) 2. CAF (TTC-HCl)	GRC, CALC, KTC, SCRC, PCRC, MRC (Manual probe)	University/hospital-based (Italy) and supported by Italian Ministry of University and Scientific Research

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Tunali et al.[70]	RCT, split-mouth design, 2 treatment groups, 12 months' duration	10 individuals, 6 female, aged 25 to 52 years, with 2 Miller Class I or II multiple buccal gingival recessions of at least 3 mm	1. Leukocyte- and platelet-rich fibrin + CAF 2. SCTG + CAF	GRC, CALC, KTC, SCRC, PCRC, MRC (Manual probe)	University/hospital-based (Italy) Unpublished data were included following contact with author
Wang et al.[71]	RCT, split-mouth design, 2 treatment groups, 6 months' duration	16 individuals, 10 females, aged 30 to 54 years, with 2 Miller Class I or II buccal gingival recessions of at least 3 mm	1. GTR (reabsorbable double thickness collagen membrane - Sulzer Dental Inc) 2. SCTG + CAF	ACC, GRC, CALC, KTC, MRC (Manual probe)	University/hospital-based (USA) and supported by Sulzer Calcitek Inc
Woodyard et al.[8]	RCT, parallel design, 2 treatment groups, 6 months' duration	24 individuals, 14 females,mean age 34.6 years, with 1 Miller Class I or II buccal gingival recession of at least 3 mm	1. ADMG + CAF 2. CAF	GRC*(1), CALC*(1), KTC, SCRC, PCRC, MRC (Manual probe)	University/hospital-based (USA)
Zucchelli et al.[10]	RCT, parallel design, 3 treatment groups, 12 months' duration	54 individuals, 29 females, aged 23 to 33 years, with 1 Miller Class I or II buccal gingival recession of at least 3 mm	1. GTR (polylactic acid membrane - Guidor) 2. GTR (ePTFE membrane - Gore-Tex) 3. SCTG + CAF	GRC, CALC, KTC*(3), SCRC, PCRC, MRC (Manual probe)	University/hospital-based (Italy)
Zucchelli et al.[72]	RCT, split-mouth design, 2 treatment groups, 12 months' duration	15 individuals, aged 18 to 35 years, with 2 Miller Class I or II maxillary buccal gingival recessions of at least 3 mm	1. SCTG (graft size equal to the bone dehiscence) + CAF 2. SCTG (graft size 3 mm greater than the bone dehiscence) + CAF	ACC, GRC, CALC*(1), KTC*(2), SCRC, PCRC, MRC (Manual pressure sensitive probe)	University/hospital-based (Italy)
Zucchelli et al.[73]	RCT, split-mouth design, 2	11 individuals, aged 18 to 40 years, with 2 Miller	1. Ultrasonic instrumentation - CAF 2. Hand instrumentation – CAF	GRC, CALC, KTC, SCRC, PCRC, MRC (Manual	University/hospital-based (Italy)

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	treatment groups, 6 months' duration	Class I maxillary buccal gingival recessions of at least 3 mm		pressure sensitive probe)	
Zucchelli et al.[74]	RCT, parallel design, 2 treatment groups, 12 months' duration	60 individuals, aged > 18 years, with 1 Miller Class I or II maxillary buccal gingival recession of at least 3 mm	1. SCTG (de-epithelialized free gingival graft: graft height equal to the depth of bone dehiscence and thickness ≥ 2 mm) + CAF 2. SCTG (de-epithelialized free gingival graft: graft height of 4 mm thickness < 2 mm) + CAF	ACC, GRC, CALC, KTC, SCRC, PCRC, MRC (Manual probe)	University/hospital-based (Italy)
Zucchelli et al.[75]	RCT, parallel design, 2 treatment groups, 12 months' duration	50 individuals, 28 females, age > 18 years, with 1 Miller Class I or II gingival recession of at least 3 mm at the buccal aspect of lower incisors	1. SCTG + CAF - with removal of the labial submucosal tissue 2. SCTG + CAF - without removal of the labial submucosal tissue	ACC*(1), GRC*(1), CALC, KTC*(2), SCRC, PCRC, MRC (Manual probe and calliper)	University/hospital-based

ACC: aesthetic condition change; ADMG: acellular dermal matrix graft; CA: citric acid; CAF: coronally advanced flap; CALC: clinical attachment change; DFDBA: demineralized freeze-dried bone allograft; EMD: enamel matrix derivative; ePTFE: expanded polytetrafluorethylene; FGG: free gingival graft; GRC: gingival recession change; GTR: guided tissue regeneration; KTC: keratinized tissue change; MRC: mean root coverage; PCRC: percentage of complete root coverage; RCT: randomized controlled trial; SCRC: sites with complete root coverage; SCTG: subepithelial connective tissue graft; TTC-HCl: tetracycline hydrochloride; XCM - xenogeneic collagen matrix.
*statistically significant between-groups (superior group).

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Table 2 - Root coverage outcomes (i.e., complete root coverage and mean root coverage) and aesthetic condition change

Study	Interventions	SCRC	PCRC	MRC	ACC
Abolfazli et al.[24] (single GR)	EMD + CAF (12 months)	NR	NR	77.7	NR
	SCTG + CAF (12 months)	NR	NR	83.4	
	EMD + CAF (24 months)	3/12	25.0	76.9	
	SCTG + CAF (24 months)	8/12	66.6	93.1	
Ahmedbeyli et al.[25] (multiple GR)	ADMG + CAF	11/12	83.3	94.8	The authors asked each patient about different patient-reported outcomes (i.e. root coverage attained, color of gums, shape and contour of gums), and both procedures were rated equally in all aspects
	CAF	6/12	50.0	74.9	
Ayub et al.[26] (single GR)	ADMG (1 mm apical to the CEJ) + CAF (extended flap)	4/15	26.6	88.4	NR
	ADMG + CAF (extended flap)	0/15	0	65.8	
Babu et al.[27] (single GR)	GTR (collagen membrane) + CAF	NR	NR	84.0	NR
	SCTG + CAF	NR	NR	84.8	
Barros et al.[28] (single GR)	ADMG + CAF (extended flap)	NR	NR	80.7	NR
	SCTG + CAF (extended flap)	NR	NR	78.7	
Bouchard et al.[29] (single GR)	SCTG + CAF + citric acid (graft without epithelial collar)	3/15	20.0	69.7	Aesthetic evaluation was performed by 2 independent examiners who were blinded to the given treatment. Additionally, the authors commented that no patient was dissatisfied with the aesthetical results obtained
	SCTG (graft with epithelial collar)	5/15	33.3	64.7	
Bouchard et al.[30] (single GR)	SCTG + CAF + tetracycline hydrochloride	6/15	40.0	79.3	NR
	SCTG + CAF + citric acid	8/15	53.3	84.0	
Costa et al.[31,32] (single GR)	ADMG + EMD + CAF (6 months)	3/19	15.8	55.4	NR
	ADMG + CAF (6 months)	1/19	5.3	44.0	
	ADMG + EMD + CAF (12 months)	3/19		59.7	
	ADMG + CAF (12 months)	1/19		52.8	

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da Silva et al.[33] (single GR)	SCTG + CAF	2/11	18.1	75.3	NR
	CAF	1/11	9.0	68.8	
de Queiroz et al.[34,35] (single GR)	ADMG + CAF (6 months)	3/13	23.0	76.0	NR
	CAF (6 months)	3/13	23.0	71.0	
	ADMG + CAF (12 months)	2/13	15.3	71.0	
	CAF (12 months)	2/13	15.3	66.7	
	ADMG + CAF (24 months)	1/13	7.7	68.4	
	CAF (24 months)	1/13	7.7	55.9	
Del Pizzo et al.[11] (single GR)	EMD + CAF	11/15	73.3	90.7	NR
	CAF	9/15	60.0	86.7	
Dodge et al.[36] (single GR)	GTR (polylactide membrane - Guidor) + tetracycline hydrochloride + DFDBA + CAF	6/12	50.0	89.9	NR
	GTR (polylactide membrane - Guidor) + tetracycline hydrochloride + CAF	4/12	33.3	73.7	
Henderson et al.[37] (single GR)	ADMG (basement membrane side against the tooth) + CAF	7/10	70.0	94.9	NR
	ADMG (connective tissue side against the tooth) + CAF	8/10	80.0	95.5	
Jaiswal et al.[38] (multiple GR)	EMD + CAF	NR	NR	86.3	NR
	CAF	NR	NR	79.6	
Jankovic et al.[39] (single GR)	Platelet-rich fibrin + CAF	12/20	60.0	72.1	NR
	EMD + CAF	13/20	65.0	70.5	
Jepsen et al.[40] (single GR)	XCM + CAF	29/35	82.8	72.0	NR
	CAF	17/35	48.6	66.2	
Joly et al.[41] (single GR)	ADMG + CAF (without vertical incisions)	NR	NR	50.0	NR
	SCTG + CAF (without vertical incisions)	NR	NR	79.5	
Keceli et al.[42] (single GR)	SCTG + platelet-rich plasma + CAF	6/17	35.3	86.4	NR
	SCTG + CAF	8/19	42.1	86.4	
Keceli et al.[43] (single GR)	SCTG + platelet-rich fibrin + CAF	11/20	55.0%	89.6	NR
	SCTG + CAF	7/20	35.0%	79.9	

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Leknes et al.[44,45] **(single GR)**	GTR (polylactide membrane - Guidor) (6 months) + CAF	5/20	25.0	51.2	NR
	CAF (6 months)	10/20	50.0	63.8	
	GTR (polylactide membrane - Guidor) (12 months) + CAF	4/20	20.0	51.2	
	CAF (12 months)	6/20	30.0	61.1	
	GTR (polylactide membrane - Guidor) (72 months) + CAF	2/11	18.2	35.0	
	CAF (72 months)	1/11	9.1	34.2	
Matarasso et al.[46] **(single GR)**	GTR (polylactide membrane - Guidor) + double papilla flap	NR	NR	73.9	NR
	GTR (polylactide membrane - Guidor) + CAF	NR	NR	62.5	
McGuire et al.[47,48] **(single GR)**	EMD + CAF (6 months)	17/19	89.5	95.1	Ten years after surgery patients were asked to respond to questions related to aesthetic satisfaction. Six patients had no preference for a particular type of treatment, two favored aesthetic results with the test treatment (i.e. EMD + CAF), and one favored results with the control treatment (SCTG + CAF) (P = 0.564).
	SCTG + CAF (6 months)	15/19	79.0	93.8	
	EMD + CAF (10 years)	5/9	55.6	83.3	
	SCTG + CAF (10 years)	7/9	77.8	89.8	
McGuire et al.[49,50] **(single GR)**	B-TCP + CD with rhPDGF-BB + CAF (6 months)	NR	NR	90.8	At 6 months, patients aesthetic rating by 10 cm visual analogue scale did not identify differences in the clinical rating of color/texture of the tissues observed between the treatments. At 5 years, of the 20 test and 20 control sites, "14 sites for each were rated as 'very satisfied.' In the test group, 4 sites were rated as 'satisfied,' 1 as 'unsatisfied,' and 1 as 'very unsatisfied.' In the control group, the remaining 6 sites were rated as 'satisfied'
	SCTG + CAF (6 months)	NR	NR	98.6	
	B-TCP + CD with rhPDGF-BB + CAF (5 years)	12/20	60.0	74.1	
	SCTG + CAF (5 years)	15/20	75.0	89.3	

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McGuire et al.[12,51] **(single GR)**	XCM + CAF (6 months)	15/25	60.0	83.5	Patients rated equivalent aesthetic changes from baseline to 6 months for XCM + CAF versus SCTG + CAF (overall, "for both test and control treatments, > 90% of subjects recorded improvement"). Similarly, approximately 90% of patients (15 XCM + CAF and 16 SCTG + CAF) remained "satisfied or very satisfied" 5 year after root coverage therapy and no statistical difference in satisfaction was reported
	SCTG + CAF (6 months)	23/25	92.0	97.0	
	XCM + CAF (12 months)	17/23	73.9	88.5	
	SCTG + CAF (12 months)	22/23	95.6	99.3	
	XCM + CAF (5 years)	9/17	52.9	77.6	
	SCTG + CAF (5 years)	15/17	88.2	95.5	
Öncü et al.[52] **(mutiple GR)**	Platelet-rich fibrin + CAF (6 months)	15/30(t)	50.0	77.1	NR
	SCTG + CAF (6 months)	18/30(t)	60.0	84.0	
Özenci et al.[53] **(multiple GR)**	ADMG + CAF (tunnel)	12/31(t)	37.4(t)	75.7	A similar overall patient satisfaction was recorded for patients with multiple recession-type defects treated by ADMG + coronally advanced tunnel flap or ADMG + CAF (without vertical releasing incisions) (P > 0.05)
	ADMG + CAF (without vertical realising incisions)	23/27(t)	85.0(t)	93.8	
Paolantonio et al.[54] **(single GR)**	SCTG + double papilla flap	17/35	48.6	85.2	NR
	FGG	3/35	8.6	53.2	
Paolantonio[55] **(single GR)**	GTR (polylactide membrane - Guidor) + CAF	6/15	40.0	81.0	NR
		8/15	53.3	87.1	
	GTR (polylactic acid membrane - Paroguide) + hydroxyapatite/collagen/chondroitin-sulphate graft + CAF	9/15	60.0	90.0	
	SCTG + double papilla flap				
Paolantonio et al.[56] **(single GR)**	ADMG + CAF	4/15	26.6	83.3	NR
	SCTG + CAF	7/15	46.6	88.8	

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Pendor et al.[57] (single GR)	SCTG + double papilla flap	6/10	60.0	88.0	NR
	SCTG + CAF	6/10	60.0	84.7	
Rasperini et al.[58] (single GR)	SCTG + EMD + CAF	16/26	61.5	90.7	NR
	SCTG + CAF	14/30	46.6	76.6	
Reino et al.[59] (single GR)	SCTG + CAF (extended flap)	2/20	10.0	44.5	NR
	SCTG + CAF	0/20	0	43.2	
Reino et al.[60] (single GR)	XCM + CAF (extended flap)	NR	NR	81.9	NR
	XCM + CAF	NR	NR	62.8	
Roccuzzo et al.[9] (single GR)	GTR (polylactic acid membrane - Guidor) + CAF	5/12	41.6	82.4	NR
	GTR (ePTFE membrane - Gore-Tex) + CAF	5/12	41.6	82.4	
Rosetti et al.[61,62] (single GR)	GTR (collagen membrane) + tetracycline hydrochloride + DFDBA + CAF (18 months)	NR	NR	84.2	Aesthetical evaluation was performed by five examiners who were not participating in the study. In this study, the authors have mentioned only that the patient satisfaction survey indicated that all patients were satisfied with the aesthetic results achieved by both procedures at 18 months post-surgery. In addition, no significant differences were identified between the 18 and 30 months assessments.
		NR	NR	95.6	
	SCTG + tetracycline hydrochloride (18 months)	NR	NR	87.0	
		NR	NR	95.5	
	GTR (collagen membrane) + tetracycline hydrochloride + DFDBA + CAF (30 months)				
	SCTG + tetracycline hydrochloride (30 months)				
Sangiorgio et al.[63,64] (single GR)	XCM + CAF	9/17	52.9	87.2	The reported the results of root coverage aesthetics and overall aesthetic results evaluated by each patient with the assistance of a VAS. In terms of root coverage aesthetics both treatment approaches showed evidence of similar improvements between baseline and 6-month
	EMD + CAF	12/17	70.6	88.8	
	XCM + EMD + CAF	10/17	58.8	91.6	
	CAF	4/17	23.5	68.0	

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					evaluation. Regarding overall aesthetic results following treatment, there was evidence of equivalent outcomes for all groups (i.e. similar aesthetics).
Shori et al.[65] (single GR)	ADMG + CAF	NR	NR	86.9	NR
	SCTG + CAF	NR	NR	84.7	
Spahr et al.[66,67] (single GR)	EMD + CAF (6 months)	NR	NR	80.0	NR
	Placebo (propylene glycol alginate) + CAF (6 months)	NR	NR	79.0	
	EMD + CAF (12 months)	NR	NR	80.0	
	Placebo (propylene glycol alginate) + CAF (12 months)	NR	NR	79.0	
	EMD + CAF (24 months)	NR	53.0	84.0	
	Placebo (propylene glycol alginate) + CAF (24 months)	NR	23.0	67.0	
Tozum et al.[68] (single GR)	SCTG + modified tunnel procedure	NR	NR	96.4	NR
	SCTG + CAF	NR	NR	77.1	
Trombeli et al.[69] (single GR)	CAF + fibrin glue + tetracycline hydrochloride	1/11	9.1	63.1	NR
	CAF + tetracycline hydrochloride	2/11	18.2	52.9	
Tunali et al.[70] (multiple GR)	Leukocyte- and platelet-rich fibrin + CAF (6 months)	4/22(t)	18.2	74.6	NR
	SCTG + CAF (6 months)	2/22(t)	9.1	74.1	
	Leukocyte- and platelet-rich fibrin + CAF (12 months)	3/22(t)	13.6	76.6	
	SCTG + CAF (12 months)	4/22(t)	18.2	77.4	
Wang et al.[71] (single GR)	GTR (reabsorbable double thickness collagen membrane - Sulzer Dental Inc) + CAF	7/16	43.8	73.0	NR
	SCTG + CAF	7/16	43.8	84.0	
Woodyard et al.[8] (single GR)	ADMG + CAF	11/12	91.6	96.0	NR
	CAF	4/12	33.3	67.0	

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Zucchelli et al.[10] **(single GR)**	GTR (polylactic acid membrane - Guidor) + CAF	7/18	39.0	85.7	NR
	GTR (ePTFE membrane - Gore-Tex) + CAF	5/18	28.0	80.5	
	SCTG + CAF	12/18	66.0	93.5	
Zucchelli et al.[72] **(single GR)**	SCTG (graft size equal to the bone dehiscence) + CAF	13/15	86.7	97.3	The results obtained at the 12-month follow-up visit showed that patients were more satisfied with the appearance of test-treated recessions (i.e. graft dimension equal to the depth of the bone dehiscence), as well as, less satisfied with poor color blending and excessive thickness of the control-treated recessions (i.e. graft dimension 3 mm greater than the depth of the bone dehiscence
	SCTG (graft size 3 mm greater than the bone dehiscence) + CAF	12/15	80.0	94.7	
Zucchelli et al.[73] **(single GR)**	Ultrasonic scaling + CAF	6/11	54.5	84.2	NR
	Manual/hand scaling + CAF	9/11	81.8	95.4	
Zucchelli et al.[74] **(single GR)**	SCTG (de-epithelialized FGG (graft height of 4 mm and thickness < 2 mm)) + CAF	25/30	83.3	96.3	Based on a visual analogue scale, the authors did not identify differences in terms of patient root coverage aesthetic assessment 12 months after surgery between sites treated with SCTG (de-epithelialized FGG (graft height of 4 mm and thickness < 2 mm)) + CAF versus SCTG (de-epithelialized FGG (graft height > 4 mm and thickness $\geq$ 2 mm)) + CAF. Overall, both procedures led to high aesthetic results, but color match scores were higher for patients receiving reduced size grafts ($P < 0.01$)
	SCTG (de-epithelialized FGG (graft height > 4 mm and thickness $\geq$ 2 mm)) + CAF	24/30	80.0	96.7	
Zucchelli et al.[75] **(single GR)**	SCTG + CAF (removal of the labial submucosal tissue)	22/25	88.0	97.8	The outcomes achieved with a visual analogue scale did
		12/25	48.0	82.8	

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	SCTG + CAF	not show differences between procedures in terms of root coverage, but color match was identified by patients as better when the labial submucosal tissue was removed

ADMG: acellular dermal matrix graft; B-TCP: Beta-tricalcium phosphate; CAF: coronally advanced flap; CEJ: cemento-enamel junction; DFDBA: demineralized freeze-dried bone allograft; EMD: enamel matrix derivative; ePTFE: expanded polytetrafluorethylene; FGG: free gingival graft; GTR: guided tissue regeneration; MRC: mean root coverage; NR: not reported; PCRC: percentage of complete root coverage; rhPDGF-BB: recombinant human platelet-derived growth factor-BB; SCRC: sites with complete root coverage; SCTG: subepithelial connective tissue graft; t: teeth; XCM: xenogeneic collagen matrix;

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Table 3 – Summary of meta-analyses

Comparison	Outcome	Statistical method	Effect size	Chi^2	P value (Q)	I^2 (%)
ADMG + CAF versus SCTG + CAF[28,41,56,65] (single GR)	GR depth change	MD 95% CI	-0.36 (-1.03, 0.30)	15.06	0.002	80.0
	CAL change	MD 95% CI	-0.53 (-1.14, 0.08)	9.73	0.02	69.0
	KT width change	MD 95% CI	-0.59 (-1.27, 0.10)	17.17	0.0007	83.0
	SCRC	OR 95% CI	0.43 (0.13, 1.37)	0.00	0.96	0
ADMG + CAF versus CAF[8,35] (single GR)	GR depth change	MD 95% CI	0.61 (-0.52, 1.73)	7.45	0.006	87.0
	CAL change	MD 95% CI	0.51 (-0.25, 1.27)	2.32	0.13	57.0
	KT width change	MD 95% CI	0.28 (-0.08, 0.64)	0.30	0.59	0
	SCRC	OR 95% CI	3.97 (0.20, 80.50)	5.03	0.02	80.0
EMD + CAF versus CAF[11,64,67] (*) (single GR)	GR depth change	MD 95% CI	0.07 (-0.25, 0.40)	5.62	0.06	64.0
	CAL change	MD 95% CI	0.22 (-0.02, 0.45)	1.57	0.46	0
	KT width change	MD 95% CI	0.35 (0.13, 0.56)	0.64	0.73	0
EMD + CAF versus CAF (2)[11,64,67] (**) (single GR)	GR depth change	MD 95% CI	0.32 (0.10, 0.55)	2.10	0.35	5.0
	CAL change	MD 95% CI	0.35 (0.09, 0.61)	1.25	0.53	0
	KT width change	MD 95% CI	0.40 (0.17, 0.62)	1.63	0.44	0
EMD + CAF versus SCTG + CAF[24,48] (single GR)	GR depth change	MD 95% CI	-0.39 (-1.27, 0.48)	25.79	<0.00001	96.0
	CAL change	MD 95% CI	-0.25 (-0.69, 0.20)	2.95	0.09	66.0
	KT width change	MD 95% CI	-1.06 (-1.36, -0.76)	2.47	0.12	59.0
	SCRC	OR 95% CI	0.61 (0.05, 7.86)	7.86	0.005	87.0
GTR rm + CAF versus SCTG + CAF[10,55,71] (single GR)	GR depth change	MD 95% CI	-0.37 (-0.60, -0.13)	0.25	0.88	0
	CAL change	MD 95% CI	0.35 (0.06, 0.63)	0.93	0.63	0
	KT width change	MD 95% CI	-1.77 (-2.66, -0.89)	15.84	0.0004	87.0
	SCRC	OR 95% CI	0.61 (0.30, 1.24)	2.01	0.37	0
GTR rm + CAF versus GTR nrm + CAF[9,10] (single GR)	GR depth change	MD 95% CI	0.23 (-0.22, 0.68)	1.59	0.21	37.0
	CAL change	MD 95% CI	0.12 (-0.37, 0.60)	0.28	0.60	0
	KT width change	MD 95% CI	0.12 (-0.23, 0.48)	0.03	0.86	0
	SCRC	OR 95% CI	1.33 (0.46, 3.85)	0.21	0.65	0
GTR rm associated with bone substitutes + CAF versus SCTG + CAF[55,61] (single GR)	GR depth change	MD 95% CI	-0.82 (-2.13, 0.49)	9.92	0.002	90.0
	CAL change	MD 95% CI	-0.52 (-1.34, 0.30)	2.72	0.10	63.0
	KT width change	MD 95% CI	-2.38 (-2.84, -1.92)	1.86	0.17	46.0
GTR rm associated with bone substitutes + CAF versus GTR rm + CAF[36,55] (single GR)	GR depth change	MD 95% CI	0.48 (0.09, 0.88)	0.10	0.76	0
	CAL change	MD 95% CI	0.76 (-0.01, 1.54)	2.83	0.09	65.0
	KT width change	MD 95% CI	0.23 (-0.21, 0.68)	1.63	0.20	39.0
	SCRC	OR 95% CI	1.87 (0.75, 4.64)	0.03	0.87	0
XCM + CAF versus CAF[40,64] (single GR)	GR depth change	MD 95% CI	0.40 (0.11, 0.68)	0.86	0.35	0
	CAL change	MD 95% CI	0.37 (-0.09, 0.83)	1.70	0.19	41.0
	KT width change	MD 95% CI	0.44 (0.04, 0.85)	1.16	0.28	14.0
	SCRC	OR 95% CI	4.73 (2.35, 9.50)	0.16	0.69	0
PRF + CAF versus SCTG + CAF[52,70] (multiple GR)	GR depth change	MD 95% CI	-0.01 (-0.89, 0.86)	14.71	0.0001	93.0
	CAL change	MD 95% CI	-0.37 (-0.69, -0.06)	0.58	0.45	0
	KT width change	MD 95% CI	-0.26 (-0.98, 0.45)	13.41	0.0003	93.0

ADMG: acellular dermal matrix graft; CAF: coronally advanced flap; CAL: clinical attachment level; CI: confidence interval; EMD: enamel matrix derivative; GR: gingival recession; GTR rm: guided tissue regeneration resorbable membrane; GTR nrm: guided tissue regeneration non-resorbable membrane; KT: keratinized tissue; MD: mean difference; OR: odds ratio; PRF: platelet-rich fibrin; SCRC: sites with complete root coverage; SCTG: subepithelial connective tissue graft; XCM: xenogeneic collagen matrix.

Authors' Note: Analyses were performed according to the follow-up evaluation (i.e. short term (6 months follow-up preferably) in the majority of comparisons, except for two comparisons: EMP + CAF versus CAF where the data were derived from short-term (6 months[64])* and medium-term (24 months[11,67])** measurements; and EMP + CAF versus SCTG + CAF where the data from mean changes from baseline (i.e. gingival recession, clinical attachment level and keratinized tissue width) were derived from short-term measurements, whereas sites with complete root coverage the data were derived from 6-month[48] and 24-month[24] measurements.

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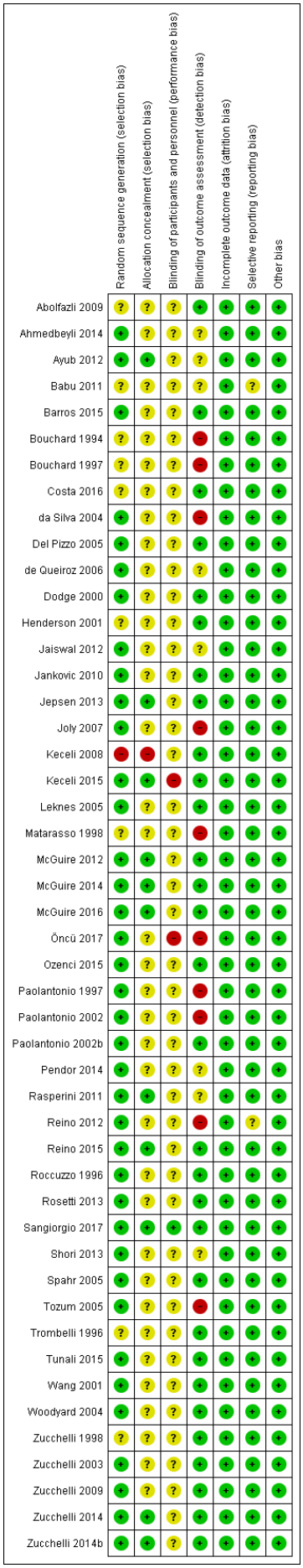

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Figure 2: ‘What’s new’ table - changes since the last version.

Description
• Changes to the original protocol • Title: Inclusion of 'multiple' defects • Objectives: 'effectiveness' was changed to 'efficacy' • Type of interventions: Assessment of CAF + different biomaterial • Type of outcomes: 'number/percentage of sites achieving complete root coverage' became a primary outcome • Type of outcomes: studies with follow-up >12 months and ≤60 months were considered as medium-term trials, whereas RCT with follow-up > 60 months of long-term. • Search methods for identification of studies: Searches were updated up to January 16, 2018 • Assessment of risk of bias in included studies: Risk of bias assessment was updated to follow the current version of the Cochrane Handbook • GRADE methods were used to assess the quality of the body of evidence of our main comparisons (i.e., SCTG-based procedures versus other root coverage procedures and CAF versus other biomaterials) • Inclusion of 24 new RCTs (50% of the total number of included studies) • Outcomes on smokers were provided by two RCTs • Data from 20 RCTs were included into the meta-analyses • Inclusion of outcomes from multiple recession-type defects and data from xenogeneic collagen matrix • Three new comparisons added; EMD + CAF versus SCTG + CAF and XCM + CAF versus CAF for the treatment of single gingival recessions and PRF + CAF versus SCTG + CAF for the treatment of multiple recession-type defects

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