Periodontal Soft Tissue Root Coverage Procedures: A Systematic Review From the AAP Regeneration Workshop

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Background: This paper aims to create a "bridge" between research and practice by developing a practical, extensive, and clinically relevant study that translates evidence-based findings on soft tissue root coverage (RC) of recession-type defects to daily clinical practice.

Methods: This review is prepared in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement based on the proposed focused questions. A literature search with no restrictions regarding status or the language of publication was performed for MEDLINE and EMBASE databases up to and including June 2013. Systematic reviews (SRs), randomized clinical trials, controlled clinical trials, case series, and case reports evaluating recession areas that were treated by means of RC procedures were considered eligible for inclusion through the three parts of the study (part I, an overview of the base of SRs; part II, an alternative random-effects meta-analyses on mean percentage of RC and sites exhibiting complete RC; and part III, an SR of non-randomized trials exploring other conditions not extensively evaluated by previous SRs). Data on Class I, II, III, and IV recessions, type of histologic attachment achieved with treatment, recipient- and donor-site anatomic characteristics, smoking-related outcomes, root surface conditions, tooth type and location, long-term effectiveness outcomes, unusual conditions that may be reported during conventional daily practice, and patient-centered outcomes were assessed as well.

Results: Of the 2,456 potentially eligible trials, 234 were included. Data on Class I, II, III, and IV gingival recessions, histologic attachment achieved after treatment, recipient- and donor-site anatomic characteristics, smoking-related outcomes, root surface conditions/biomodification, tooth type and location, long-term effectiveness outcomes and unusual conditions that may be reported during conventional daily practice, and patient-centered outcomes (i.e., esthetic, visual analog scale, complications, hypersensitivity, patients perceptions) were assessed. Subepithelial connective tissue (CT)-based procedures and coronally advanced flap plus acellular dermal matrix grafts, enamel matrix derivative, or collagen matrix led to the best improvements of recession depth, clinical attachment level (CAL) gain, and keratinized tissue (KT). Some conditions, such as smoking and use of magnification, may affect RC outcomes.

Conclusions: All RC procedures can provide significant reduction in recession depth and CAL gain for Miller Class I and II recession-type defects. Subepithelial CT graft-based procedures provided the best outcomes for clinical practice because of their superior percentages of mean and complete RC, as well as significant increase of KT. *J Periodontol 2015;86(Suppl.):S8-S51.*

KEY WORDS

Connective tissue; evidence-based dentistry; gingival recession; gingival recession, surgery; gingival recession, therapy; tooth root, surgery.

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Root coverage (RC) periodontal plastic surgery procedures have long been used for the treatment of gingival recession (GR). Esthetics, dental hypersensitivity, and the prevention of caries and non-carious cervical lesions (NCCLs) are considered the main indications reported in the literature.[1-11]

Concomitant to the development of flap and graft-based surgical techniques, more refined and judicious research protocols have also been developed and applied to establish the predictability and best clinical scenarios for each group of procedures.[12-14]

Described in the literature as part of "mucogingival surgery" or "periodontal plastic surgery (PPS),"[15] much information from efficacy trials (i.e., studies performed under ideal conditions)[16] suggest that GR classified as Miller Class I and II[17] may lead to mean RC (MRC) of 80.9% (50% to 97.3%) and complete RC (CRC) of 46.6% (7.7% to 91.6%) ≥6 months after treatment.[4,5] Furthermore, data from other systematic reviews (SRs), including effectiveness trials (i.e., studies performed in clinical practice or in "real-world situations"),[16] support these findings as well.[2,3,6,8]

Evidence is clear that CRC is certainly the definitive clinical outcome expected when an RC procedure is performed.[1-11] It can also be argued that there are few high-quality studies available for many soft tissue RC PPS procedures that have been in clinical use for many years and that some patient-centered outcomes, such as esthetics, patients' preferences, and function, may play an equally important part in the implementation of novel surgical techniques in the future. Additionally, SRs per se may not be clearly designed to translate the current evidence into practical decision guidance for common daily clinical scenarios.[18]

As part of the efforts advanced and highlighted by the 2014 American Academy of Periodontology *Regeneration Workshop*, it is of paramount importance "to build on existing knowledge to determine the best, practical way to treat patients with periodontal regeneration, as well as to prepare solid guidelines and treatment rationale to support decision-making for specific clinical scenarios."

CLINICAL SCENARIOS AND CONSIDERATION OF TREATMENT OPTIONS

During daily practice, clinicians are required to deal with diverse clinical scenarios and to provide the most adequate treatment options for each particular condition based on the best evidence available, the clinician's skills, and the patients' desires. For instance, which treatment options are available for the management of the following conditions? And why are they important?

Clinical Scenario 1: A Complex Case Involving Multiple Recession-Type Defects in Esthetic Areas

Is there sufficient donor tissue to be removed from the palatal vault? Is it safe to use a flap procedure alone, or should other biomaterial be used? What factors will lead to the best choice?

Clinical Scenario 2: Treatment of Miller[17] Class III and IV Recession

How can the odds of achieving a satisfactory result be improved? Is it possible to use a flap procedure alone, or should a graft/biomaterial be used with it? Will a restorative/prosthetic approach be required?

Clinical Scenario 3: Treatment of GRs Not Surgically Treated But Restored With Composites

What is the best technique/material to graft over these previously restored root surfaces? Should the restoration be removed or changed? Is it safe and predictable to surgically treat these areas?

Clinical Scenario 4: Treatment of NCCL Root Surfaces

Should the presence of NCCLs alter the treatment approach? Do these areas need to be restored? If yes, before, during, or after the surgical procedure?

Clinical Scenario 5: Treatment of Carious Root Surfaces

Is it possible to cover carious root surfaces? After removing the caries, it is obvious a restoration will be necessary. How does that change the treatment plan? Similarly to abraded surfaces, do these areas need to be restored before, during, or after the surgical procedure?

Clinical Scenario 6: Lack of Adequate Donor Site (e.g., Small and Shallow Palatal Vault)

What are the risks and benefits associated with the use of allogenic or xenogenic graft substitutes? Do they provide evidence of long-term stability?

Clinical Scenario 7: Most Patients Are Interested Not Only in RC But in Achieving the Best Color and Texture Match

What technique should be used to achieve these goals?

Clinical Scenario 8: Best Treatment Options for the Treatment of Class I and II Recessions

Are the results of therapy stable? What is known about the attachment of the graft/flap to the root and is it important? Is it possible to estimate the outcomes and propose treatment options (i.e., establish a decision tree)? Is it possible to obtain satisfactory results when treating patients who smoke?

Clinical Scenario 9: Other Defect Risk Factors for RC

Are the geometry and the degree of recession important (e.g., narrow and deep versus wide and shallow)?

Is the amount of available keratinized attached gingiva important in the decision-making process? Does the degree of keratinized gingiva in the final outcome affect the long-term stability of cases?

BASIC QUESTIONS TO BE ADDRESSED IN THIS STUDY

Additionally, definitive answers to other important questions remain unclear. For instance, what is the amount of RC that might be anticipated for Class III and IV GR defects? Is it similar to the one achieved by Class I and II defects? What are the long-term (i.e., ≥24 months of follow-up) outcomes of these treatment procedures in clinical practice? Do RC procedures regenerate part of the lost periodontium? Is it important to change the periodontal biotype adjacent to a GR? Does the condition of the exposed root surface play a role in the amount of RC achieved? What are the potential risks associated with RC procedures? Are there safe substitutes for subepithelial connective tissue grafts (SCTGs), and how should the SCTG be used? The exclusion of the aforementioned "effectiveness studies" may not allow a better interpretation (translation) of important findings to daily periodontal practice. Consequently, this paper aims to create a "bridge" between research and practice by developing practical, extensive, and clinically applicable guidance that translates evidence-based findings on soft tissue RC of recession-type defects to daily clinical practice (i.e., translation of efficacy/effectiveness to "manageable" outcomes).

SUMMARY OF WHAT OTHER SRs HAVE EVALUATED

Focused Questions

The following focused questions were addressed. 1) What is the efficacy/effectiveness of RC procedures by the degree of recession?: a) Miller Class I and II;[17] b) Miller Class III or IV.[17] 2) Which factors may influence the expected outcomes (i.e., smoking status and root-surface conditions)? For instance, is it possible to accomplish RC for teeth with NCCL, root caries, or cervical root resorption? 3) What is the anticipated success and attachment apparatus of RC enhancements with autogenous grafts compared with alternative methods and materials? 4) What are the long-term and short-term advantages of root-surface biomodification? 5) What are the relative risks from a patient's viewpoint with the different approaches to RC procedures? 6) Should connective tissue (CT) grafts contain epithelium and/or periosteum? 7) Is there evidence for innovation when treating thin and thick biotypes with existing treatment modalities?

Inclusion and Exclusion Criteria for Papers and/or SRs

The protocol of this study is designed to translate the findings of research to daily practice. It was based on the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses),[19] Cochrane Collaboration,[12] and Check Review[6] checklists. Detailed descriptions of parts of the study protocol (i.e., electronic searching and methodology) used in this review have been published previously.[1-5,7] The subsequent sections give a brief explanation of the detailed protocol of the present study.

To satisfactorily answer the research-focused questions proposed for the present review project, an overview of SRs,[6] an updated set of meta-analysis of randomized clinical trials (RCTs), and an SR review of effectiveness/non-RCTs (i.e., assessment of other conditions not addressed by previous reviews or RCTs) was prepared. For the first part of this work, only SRs evaluating the effect of treatment of patients with a clinical diagnosis of single or multiple recession-type defects (MRTDs) that were surgically treated by means of RC procedures are analyzed. In the second part, the base of RCTs that assessed non-restored, Miller Class I and II recessions[17] with a duration ≥6 months were retrieved and considered eligible for inclusion into the meta-analyses. For the third part, non-randomized studies (controlled clinical trials, case series, and case reports) in which the effectiveness of RC procedures was assessed for conditions that could not be addressed by previous SRs (i.e., Class III and IV, long-term outcomes, histologic findings, etc.) were incorporated into the analyses. Editorials and non-SRs were excluded from this study.

Type of Interventions

The interventions of interest were as follows: 1) free gingival grafts (FGGs); 2) coronally advanced flaps (CAFs) alone or in combination with guided tissue regeneration (GTR), acellular dermal matrix grafts (ADMGs), enamel matrix derivative protein (EMD), xenogenic collagen matrix (CM) grafts, or other biomaterials (e.g., bone substitutes, platelet-rich plasma); 3) laterally positioned flaps (LPFs); and 4) SCTGs alone or in combination with CAFs.

Types of Outcome Measures

The primary outcome measures included CRC and esthetic condition change based on the patient's opinion. The secondary outcome measures included the following: 1) clinical attachment level (CAL) change; 2) keratinized tissue (KT) change; 3) MRC; 4) preference of a patient for a specific PPS procedure; 5) type of histologic healing; 6) occurrence of adverse effects; and/or 7) postoperative complications.

Search Methods for Identification of Studies

The identification of publications included in or considered for this overview study has been based on a comprehensive search strategy reported previously.[1-5,7] Concisely, it was performed via detailed search strategies developed for MEDLINE (for Medical Literature Analysis and Retrieval System Online) and EMBASE (Excerpta Medica Database) without language restriction. Databases were searched up to and including June 30, 2013 using MeSH (Medical Subject Headings) terms, key words, and other free terms, and Boolean operators (OR, AND) were used to combine searches. Detailed search strategies were developed for each database searched based on the search strategy presented in supplementary Figure 1 in online *Journal of Periodontology*. Additionally, reference lists of any potential studies and the databases of four periodontal journals (i.e., *Journal of Periodontology*, *Journal of Clinical Periodontology*, *International Journal of Periodontics and Restorative Dentistry*, and *Journal of Periodontal Research*) were hand searched.

Selection of Studies, Data Extraction, and Assessment of Risk of Bias in Included RCTs

Identification of studies was conducted by one of the authors (LC), who screened the titles, abstracts, and full texts of the articles identified by searching. Data on the following issues were extracted and recorded: 1) citation, publication status, and year of publication; 2) main characteristics of participants; 3) type of interventions; and 4) outcome measures.

As detailed in previous publications,[1,4,5,7] the methodologic quality of the RCTs potentially eligible for inclusion in the meta-analyses (part II) was assessed by focusing on the points described in the Cochrane Collaboration tool for assessing risk of bias and detailed in the *Cochrane Handbook for Systematic Reviews of Interventions* version 5.0.1:[12] The risk of bias in the included studies was categorized as low, unclear, or high (see supplementary Fig. 2 in the online *Journal of Periodontology*).

Data Synthesis

Data were organized into evidence tables describing the characteristics of the publications and results according to the type of study (e.g., SRs or RCTs). Mean percentages of RC (i.e., recession change) and their respective standard deviations from RCTs eligible for inclusion into "head-to-head" (pairwise) meta-analyses were considered for evaluation to balance potential influences of studies reporting exclusively data from GR depth ≥3 mm. After that, random-effects meta-analyses were used for the calculation of pooled estimates for continuous data (expressed as weighted mean differences [MDs] of percentage gain with their corresponding 95% confidence intervals [CIs]) and for dichotomous data (expressed as pooled risk ratios [RRs] and corresponding 95% CIs). For continuous outcomes, these were conducted using the generic inverse variance statistical method in which the MDs and standard errors were entered for all studies to allow the combination of parallel and split-mouth group studies. Variance imputation methods were conducted to estimate appropriate variance values in some studies in which the appropriate standard deviations of the differences were not reported.[20] Also, for dichotomous data, risk difference (RD) and the number needed to treat (NNT) for sites exhibiting CRC were calculated, for which the pooled estimates reached a level of $P < 0.05$. The significance of discrepancies in the estimates of the treatment effects from the different trials was assessed by means of the Cochrane test for heterogeneity and the I^2 statistic.[12] Analyses were performed using a statistical software package.‡

Articles Found and Eliminated

The flowchart of manuscripts, screened through the review process, is depicted in supplementary Figure 3 in online *Journal of Periodontology*. The search methods for identification of studies yielded 2,456 potentially eligible publications, and of them 2,223 were excluded after the title and/or the abstract were evaluated. In total, 19 papers were appraised in part I,[1-5,7-11,21-29] and 215 were evaluated in parts II and III.[30-246]

Part I: Overview of SRs

Nineteen publications described as SRs and/or meta-analyses that reported clinical- and/or patient-centered outcomes on the surgical treatment of GR were published between 2002 and 2013.[1-5,7-11,21-29] Two studies were reported in two publications each, and thus a total of 17 different SRs were included. The majority of reviews specified the type of defects of interest as Miller Class I and II (Table 1), and two were not specifically designed to assess differences between surgical techniques: 1) one assessed the influence of flap thickness,[23] and 2) one assessed the use of RC procedures for the treatment of cervical dentin hypersensitivity.[29]

The authors of these SRs reached a consensus that all RC procedures promote concomitant significant recession depth reduction and CAL gain.[1-5,7-11,21-29] With respect to the KT width, SCTG-, ADMG-, and CM-based procedures led to the most significant gains (Table 1). Another common conclusion reported by these publications relates to the indication of SCTG as the gold standard, irrespective

‡ Review Manager (RevMan) statistical analysis software v.5.2.1, Nordic Cochrane Centre, Cochrane Collaboration, Copenhagen, Denmark.

Table 1.

Characteristics of SRs and/or Meta-Analyses on RC Procedures

Reference	Type of Study and Participants Included	Interventions of Interest	Outcomes Included	Comparisons (as described in the reviews)	Authors' Main Conclusions
Roccuzzo et al.[9]	RCTs, CCTs, and CSs of ≥6 months duration limited to patients with Class I or II[17] GR ≥2 mm	CAF, FGG, GTR, LPF, and SCTG	CAL, CRC, GR, MRC, PBA, and Stab	GTR versus SCTG, GTR versus CAF, and GTR with RS versus GTR with non-RS (ΔGR/ΔCAL)	"Overall, PPS was effective in reducing GRs with a concomitant improvement in attachment levels. Even though no single treatment can be considered superior to all the others, SCTG was statistically significantly more effective than GTR in recession reduction."
Al-Hamdan et al.[21]	All levels of evidence (excluding reviews) of ≥6 months duration limited to patients with GRs	GTR versus any other mucogingival surgery (not specified)	CAL, CRC, GR, MRC, and PD	N/A	"Both conventional mucogingival surgery and GTR-based root coverage can be used to repair GR defects with good success."
Pagliaro et al.,[26] Clauser et al.[25]	RCTs, CCTs, and CSs limited to patients with GRs	CAF, FGG, FGG + CAF, GTR, LPF, and SCTG	CAL, CRC, GR, MRC, and PBA	SCTG versus GTR and individual data meta-analysis	"The meta-analysis of summarized data confirms the fact that surgical root coverage is an effective treatment approach. SCTG appeared to perform better than GTR in terms of CRC."
Oates et al.[8]	RCTs limited to patients with GRs	Not specified	CAL, CRC, GR, KT, PD, MRC, and PBA	GTR/ADMG versus SCTG (ΔGR/ΔKT)	"Soft tissue augmentation procedures are effective means of obtaining root coverage; SCTG techniques appear to have an advantage over GTR."
Gapski et al.[22]	RCTs of ≥3 months duration limited to patients with GRs	ADMG versus CAF or SCTG	CAL, GR, KT, and PD	SCTG versus ADMG (ΔGR/ΔPD/ΔKT) and CAF versus ADMG (ΔGR/ΔPD/ΔCAL/ΔKT)	"ADMG-based mucogingival surgery can be used successfully to repair GR defects and to increase keratinized gingiva."

Table 1. (continued)

Characteristics of SRs and/or Meta-Analyses on RC Procedures

Reference	Type of Study and Participants Included	Interventions of Interest	Outcomes Included	Comparisons (as described in the reviews)	Authors' Main Conclusions
Hwang and Wang[23]	RCTs, cohort/case control studies, and case reports of ≥3 months duration	CAF, CAF + ADMG, CAF + SCTG, GTR with RS, GTR with RS + BS, and EMD associations	CRC, GT, and MRC	Regression analyses for weighted means (CRC/GT/MRC)	"A critical threshold thickness for root coverage success may exist, as suggested by a limited number of investigations, but studies vary significantly in treatment, measurement, and statistical methodology, rendering concrete evidence difficult."
Cheng et al.[24]	RCTs, CCTs, or CSs of 6 to 12 months duration limited to patients with Class I or II[17] GR ≥2 mm	CAF, CAF + EMD, and CAF + RC	CAL, GR, KT, MRC, and PD	N/A	"CAF and CAF + chemical root surface conditioning procedures were unpredictable but became more predictable when the CAF procedure was improved by the modification of adding EMD."
Chambrone et al.[1]	RCTs of ≥6 months duration limited to patients with Class I or II[17] GR ≥2 mm; ≥10 patients per group at the final examination	SCTG versus any RC procedure	CAL, CRC, GR, KT, MRC, and PBA	ADMG versus SCTG, CAF versus SCTG, and GTR with non-RS versus SCTG (ΔGR/ΔCAL/ΔKT); GTR with RS versus SCTG; and (ΔGR/ΔCAL/ΔKT/CRC) GTR with RS + BS versus SCTG (ΔGR/ΔKT)	"SCTG provided significant root coverage, CAL and KT tissue gain."
Cairo et al.[10]	RCTs of ≥6 months duration limited to patients with Class I or II[17] localized GR	CAF alone or combined with ADMG, EMD, HF-DDS, GTR, platelet-rich plasma, or SCTG	CAL, CRC GR, KT, and PBA	CAF + SCTG versus CAF, CAF + EMD versus CAF, CAF + ADMG versus CAF, CAF + GTR with RS versus CAF + SCTG, and CAF + ADMG versus CAF + SCTG (ΔGR/ΔCAL/ΔKT/CRC); CAF + GTR with RS versus CAF (ΔGR/ΔCAL/ΔKT)	"SCTG or EMD in conjunction with CAF enhances the probability of obtaining CRC in Miller Class I and II single gingival recessions."

Table 1. (continued)

Characteristics of SRs and/or Meta-Analyses on RC Procedures

Reference	Type of Study and Participants Included	Interventions of Interest	Outcomes Included	Comparisons (as described in the reviews)	Authors' Main Conclusions
Chambrone et al.[2]	RCTs, CCTs, and CSs of ≥6 months duration limited to patients with Class I or II[17] GR; ≥10 patients per group at the final examination and data from smokers (≥10 cigarettes/d) and non-smokers, recorded separately	ADMG, CAF, FGG, GTR, and SCTG	CAL, CRC, GR, KT, MRC, and Stab	CAF (smokers) versus CAF (non-smokers) and SCTG (smokers) versus SCTG (non-smokers) (ΔGR/ΔCAL/ΔKT/CRC)	"The results of this review show that smoking may negatively influence GR reduction and CAL gain, especially for SCTG. Additionally, smokers may exhibit fewer sites with CRC."
Chambrone et al.[4,5]	RCTs of ≥6 months' duration limited to patients with Class I or II[17] GR ≥3 mm; ≥10 patients per group at the final examination	ADMG, CAF, EMD, FGG, GTR, LPF, and SCTG alone or in combination with LPF or CAF	CAL, CRC, GR, KT, MRC, PBA, and Stab	ADMG versus CAF, ADMG versus SCTG and EMD + CAF versus CAF (ΔGR/ΔCAL/ΔKT); GTR with RS versus GTR with non-RS, GTR with RS + BS versus GTR with RS, and GTR with RS versus SCTG (ΔGR/ΔCAL/ΔKT/CRC); and GTR with RS +BS versus SCTG (ΔGR/ΔKT)	"SCTG, CAF alone or associated with other biomaterial and GTR may be used as root coverage procedures for the treatment of localized recession-type defects. In cases where both root coverage and gain in the KT are expected, the use of SCTG seems to be more adequate."
Chambrone et al.[3]	RCTs, CCTs, and CSs of ≥6 months duration limited to patients with Class I or II[17] multiple GR ≥2 mm	CAF, FGG, GTR, LPF, and SCTG	CAL, CRC GR, KT, and MRC	N/A	"Analysis of the limited information available in the dental literature showed improvements in clinical parameters with all of the PPS procedures."
Chambrone et al.[7]	RCTs of ≥6 months duration limited to patients with Class I or II[17] GR	ADMG, CAF, EMD, FGG, GTR, LPF, and SCTG alone or in combination with LPF or CAF	CRC	Individual data meta-analyses (CRC)	"SCTGs, MGs, and EMD procedures were superior in achieving CRC when compared with CAF alone. Overall, SCTGs showed the best outcomes. The use of RMA did not affect CRC."

Table 1. (continued)

Characteristics of SRs and/or Meta-Analyses on RC Procedures

Reference	Type of Study and Participants Included	Interventions of Interest	Outcomes Included	Comparisons (as described in the reviews)	Authors' Main Conclusions
Hofmänner et al.[27]	Articles of at least 6 months' duration limited to patients with Class I, II, or III[17] GR; ≥5 patients included in the study	Not specified	CRC and MRC	N/A	"In Miller Class I and Class II multiple GRs, CAF or modified CAF with or without SCTG may lead to predictable CRC."
Oliveira and Muncinelli[28]	RCTs limited to patients with Class I or II[17] GR ≥3 mm	Not specified	CDH, GR, KT, MRC, and PD	N/A	"All mucogingival surgery approaches achieved a high rate of success in terms of root coverage. None of the RMA protocols reviewed produced any advantage to justify their use in root coverage procedures."
Douglas de Oliveira et al.[29]	RCTs limited to patients with Class I or II[17] GR	Not specified	CDH	Frequency and magnitude of CDH before and after surgery	"There is not enough evidence to conclude that surgical root coverage procedures predictably reduce CDH."
Buti et al.[11]	RCTs of at least 6 months' duration limited to patients with Class I or II[17] localized GR	CAF alone or combined with ADMG, EMD, HF-DDS, GTR, platelet-rich plasma, or SCTG	CAL, CRC, GR, and KT	Bayesian network meta-analyses (ΔGR, ΔCAL, ΔCRC, and ΔKT)	"CAF+SCTG was the most effective procedure for root coverage in terms of GR reduction and CAL gain and could be considered the gold standard in the treatment of Miller Class I and II GRs."

BS = associated with bone substitutes; CCT = controlled clinical trial; CDH = cervical dentin hypersensitivity; CS = case series; HF-DDS = living tissue-engineered human fibroblast-derived dermal substitute; MG = matrix grafts; N/A = not available; PBA = patient-based outcomes; RMA = root modification agent; RS = resorbable membranes; Stab = long-term stability; Δ = mean change from baseline.

of the flap procedure approach performed (Table 1), not only because of the better aforementioned outcomes but also because of the significant number of sites exhibiting CRC, better cost-effectiveness, and superior long-term stability when compared with CAF, CAF + GTR, LPF, and FGG. The association of EMD to CAF appears also as an interesting and safe approach superior to the use of CAF alone, despite the additional costs related to biomaterial.[1,4,5,7,10,11]

Two reviews reporting data exclusively on multiple recessions[3,27] suggested that both CAF + SCTG and CAF alone may promote an adequate reestablishment of aesthetics with concomitant decrease in dental hypersensitivity. However, none of them could combine in pooled estimates the outcomes of included individuals because of the lack of adequate data, and thus the effects of treatment of these defects clearly seem to remain partially explored.

Moreover, some specific factors influencing RC gain were also discussed, such as the effect of root modification agents (RMAs),[5,6,9,28] baseline recession characteristics and potential confounders,[7] and smoking.[2] Regarding the use of RMAs, there was also a consensus that these agents did not modify the response rate of any surgical procedure.[5,6,9,28] For tobacco smoking, smokers may benefit from treatment of GR via PPS, but the use of SCTGs seems to be less effective in smokers than in nonsmokers in terms of recession reduction and CAL gain, whereas no significant differences were found for smokers treated with CAFs.[2]

It could be seen that most comparisons between procedures were conducted using pairwise models (i.e., direct comparisons between only two procedures); however, many direct comparisons are not available.[7,11] Three SRs used Bayesian network or individual data approaches to assess indirect comparisons.[7,11,25,26] These statistical models, applied when there were no "head-to-head" trials and to improve the power of analysis (to detect any authentic difference between treatments), also give support to the achievement of improved results when SCTGs were used.[7,11,25,26]

Part II: Random-Effects Meta-Analyses of RCTs: Mean Percentage of RC and Sites Exhibiting CRC

A total of 101 articles[30-131] with 94 RCTs potentially eligible for inclusion into the pooled estimates were identified in the base of evidence, and their main characteristics (i.e., number and age of participants, interventions, follow-up period, number of sites exhibiting CRC, MRC [percentage], use of RMAs, randomization, allocation concealment, masking of examiners, completeness of the follow-up period, and risk of bias) are depicted in Table 2.[30-131] Seven studies were reported in two articles each, and their data were reported under one study name.[37,38,57,58,65,66,83,84,90,91,110,111,115,116]

Of the 94 trials included in Table 2, 52 were included in the following sets of meta-analyses: 1) ADMG/CM + CAF versus SCTG-based procedures;[31,66,76,97,102,114] 2) ADMG/CM + CAF versus CAF;[57,58,86,125] 3) BS + GTR with resorbable membranes (RS) + CAF versus GTR with RS + CAF;[62,63,78,101] 4) EMD + CAF versus CAF;[51,53,59,71,94,103,115,116] 5) EMD + CAF versus SCTG + CAF;[30,32,90,91] 6) GTR with RS + CAF versus CAF;[36,83,84] 7) GTR (all types of membrane) + CAF versus SCTG-based procedures;[35,43,55,74,96,101,107,109,117,122,123,126] 8) SCTG-based procedures versus CAF;[40,41,54,56,80] 9) SCTG + CAF versus SCTG (epithelial collar);[44,47] 10) SCTG-based procedures, micro versus macro procedures;[42,46] and 11) SCTG-based procedures versus FGG.[70,100] All of the comparisons were performed using studies reporting data on single defects, except for one comparison on EMD + CAF versus CAF[53,71] that could also be conducted using data on multiple recessions. Primary analyses were performed based on the follow-up evaluation at 6 months (or the minimum one available), but secondary analyses were also performed using longer-term data when these were reported by the individual studies. The full report of all analyses is depicted in Figures 1 and 2 and supplementary Figures 4 through 13 in online *Journal of Periodontology*.

With respect to GR change (MRC), there was a statistically significantly greater MRC for ADMG + CAF compared with CAF ($P = 0.04$), EMD + CAF compared with CAF (shorter-term [$P = 0.001$] and longer-term [$P < 0.001$] comparisons), SCTG-based procedures compared with GTR + CAF (Fig. 1A [$P < 0.001$]), SCTG + CAF compared with CM + CAF ($P = 0.002$), SCTG + CAF compared with EMD + CAF (longer-term comparisons [$P = 0.03$]), SCTG-based procedures compared with CAF (Figs. 2A [$P = 0.006$] and 2B and 2C [$P = 0.004$]), for SCTG-based micro procedures compared with macro procedures ($P = 0.01$), and for SCTG-based procedures compared with FGG ($P < 0.001$). Additionally, the unique meta-analysis on multiple recessions failed to demonstrate significant differences in mean percentage of RC (5.01, 95% CI = –0.38 to 10.39; $P = 0.07$; $I^2 = 0\%$).

Regarding the sites with CRC, significant differences were found for EMD + CAF compared with CAF (see supplementary Figs. 7E [$P = 0.02$] and 7F [$P = 0.01$] in online *Journal of Periodontology*), for GTR + CAF compared with SCTG-based procedures (Fig. 1B [$P = 0.009$]), for SCTG-based procedures compared with CAF (Figs. 2D [$P = 0.004$], 2E [$P < 0.001$], and 2F [$P < 0.001$]), for SCTG-based micro procedures compared with macro procedures

Table 2.

RCTs Evaluating Class I and II GR Treated With RC Procedures Alone

Study	Participants (n)/Age (y)	Interventions	Follow-Up	SCRC (%)	MRC (%)	RMA	MR	AC	BE	CF	RB
Abolfazli et al.[30]	12 (NS)/28 to 51	EMD + CAF	12 mo	NR/12	77.7	Yes	U	U	Yes	Yes	U
			24 mo	3/12 (25.0)	76.9						
		SCTG + CAF	12 mo	NR/12	83.4	No					
			24 mo	8/12 (66.6)	93.1						
Aichelmann-Reidy et al.[31]	22 (NS)/24 to 67	ADMG + CAF	6 mo	7/22 (31.8)	65.9	No	A	U	Yes	Yes	U
		SCTG + CAF	6 mo	11/22 (50.0)	74.1	No					
Alkan and Parlar[32]	12 (NS)/23 to 42	EMD + CAF	6 mo	NR/12	90.6	Yes	A	U	U	Yes	U
			12 mo	9/12 (75.0)	90.6						
						Yes					
		SCTG + CAF	6 mo	NR/12	88.5						
			12 mo	7/12 (58.3)	88.5						
Aroca et al.[33]	20/22 to 47 MGR	PRF + CAF	6 mo	35/67 (52.2)	80.7	No	A	U	No	Yes	H
		CAF	6 mo	50/67 (74.6)	91.5	No					
Aroca et al.[34]	22 (NS)/≥18 MGR	CM + CAF (tunnel)	12 mo	5/22s (22.7)	71.0	No	A	U	Yes	Yes	U
		SCTG + CAF (tunnel)	12 mo	13/22s (59.1)	90.0	No					
Babu et al.[35]	10/NR	GTR with RS + CAF	6 mo	NR/10p	84.0	No	U	U	U	Yes	U
		SCTG + CAF	6 mo	NR/10p	84.8	No					
Banihashemrad et al.[36]	7 (NS)/35 to 65	GTR with RS + CAF	6 mo	2/11 (18.2)	67.9	No	A	U	Yes	Yes	U
		CAF	6 mo	2/11 (18.2)	57.8	No					
Barros el al.[37,38]	14 (NS)/22 to 46	ADMG mod + CAF	6 mo	3/16 (18.7)	79.0	Yes	A	U	U	Yes	U
			12 mo	3/16 (18.7)	82.5						
		ADMG + CAF	6 mo	1/16 (6.2)	63.9	Yes					
			12 mo	1/16 (6.2)	62.3						
Berlucchi et al.[39]	14 (NS)/20 to 45	EMD + SCTG + CAF	6 mo	11/13 (84.6)	93.6	Yes	A	U	U	Yes	U
		EMD + CAF	6 mo	10/13 (76.9)	94.0	Yes					
Bittencourt et al.[40,41]	17 (NS)/21 to 52	SCTG	6 mo	13/17 (76.5)	96.1	No	A	U	Yes	Yes	U
			30 mo	15/17 (88.2)	96.8						
		CAF (semilunar)	6 mo	9/17 (52.9)	90.0	No					
			30 mo	10/17 (58.8)	89.2						
Bittencourt et al.[42]	24 (NS)/18 to 55	SCTG + CAF (micro)	12 mo	21/24 (87.5)	98.0	No	A	U	Yes	Yes	U
		SCTG + CAF (macro)	12 mo	14/24 (58.3)	88.3	No					

Table 2. (continued)

RCTs Evaluating Class I and II GR Treated With RC Procedures Alone

Study	Participants (n)/Age (y)	Interventions	Follow-Up	SCRC (%)	MRC (%)	RMA	MR	AC	BE	CF	RB
Borghetti et al.[43]	14/20 to 55	GTR with RS + CAF	6 mo	4/14 (28.5)	70.2	No	U	U	No	Yes	H
		SCTG + CAF	6 mo	4/14 (28.5)	76.0	No					
Bouchard et al.[44]	30/21 to 62	SCTG + CAF	6 mo	3/15 (20.0)	69.7	Yes	U	U	No	Yes	H
		SCTG (epithelial collar) + CAF	6 mo	5/15 (33.2)	64.7	No					
Bouchard et al.[45]	30/21 to 70	SCTG + CAF (TH)	6 mo	6/15 (40.0)	79.3	Yes	U	U	No	Yes	H
		SCTG + CAF + (CA)	6 mo	8/15 (53.3)	84.0	Yes					
Burkhardt and Lang[46]	10 (NS)/32 to 44	SCTG + DPF (micro)	6 mo	6/8 (75.0)	98.0	No	A	U	No	Yes	H
			12 mo	5/8 (62.5)	98.0						
		SCTG + DPF (macro)	6 mo	2/8 (25.0)	89.7	No					
			12 mo	2/8 (25.0)	89.9						
Byun et al.[47]	20 (NS)/20 to 60	SCTG + CAF	6 mo	9/10 (90.0)	89.1	No	I	I	Yes	Yes	H
		SCTG (epithelial collar) + CAF	6 mo	7/10 (70.0)	97.5	No					
Caffesse et al.[48]	36/18 to 65	SCTG + CAF	6 mo	NR	94.6	Yes	A	U	U	Yes	U
		SCTG + CAF	6 mo	NR	85.3	No					
Cardaropoli and Cardaropoli[49]	16 (NS)/18 to 54	BS + GTR with RS + CAF	6 mo	7/10 (70.0)	93.3	No	A	U	U	Yes	U
		CAF	6 mo	6/10 (60.0)	92.5	No					
Cardaropoli et al.[50]	18 (NS)/21 to 59	CM + CAF	12 mo	8/11 (72.7)	94.2	No	A	U	Yes	Yes	U
		SCTG + CAF	12 mo	9/11 (81.8)	96.9	No					
Castellanos et al.[51]	22 (NS)/28 to 71	EMD + CAF	6 mo	NR/11	89.9	Yes	I	U	U	Yes	H
			12 mo	NR/11	88.6						
		CAF	6 mo	NR/11	62.7	No					
			12 mo	NR/11	62.2						
Cheung and Griffin[52]	18/NR	PCG + CAF	8 mo	NR (60.0)	80.0	No	A	U	U	Yes	U
		SCTG + CAF	8 mo	NR (65.5)	95.0	No					
Cordaro et al.[53]	10/18 to 60	EMD + CAF	6 mo	9/29 (31.0)	82.8	Yes	U	U	Yes	Yes	U
			24 mo	13/29 (44.8)	74.8						
	MGR	CAF	6 mo	5/29 (17.2)	80.7	No					
			24 mo	7/29 (24.1)	71.0						
Cortellini et al.[54]	85/≥18	SCTG + CAF	6 mo	25/42 (59.5)	83.3	No	A	A	Yes	Yes	L
		CAF	6 mo	16/43 (37.2)	77.7	No					

Table 2. (continued)

RCTs Evaluating Class I and II GR Treated With RC Procedures Alone

Study	Participants (n)/Age (y)	Interventions	Follow-Up	SCRC (%)	MRC (%)	RMA	MR	AC	BE	CF	RB
Çetiner et al.[55]	22 (NS)/22 to 58	GTR with RS (collagen) + CAF	12 mo	NR/20	74.3	No	A	U	U	Yes	U
		GTR with RS (dura mater) + CAF	12 mo	NR/20	69.6	No					
		SCTG + CAF	12 mo	NR/20	86.3	No					
da Silva et al.[56]	11 (NS)/18 to 43	SCTG + CAF	6 mo	2/11 (18.1)	75.3	No	A	U	No	Yes	H
		CAF	6 mo	1/11 (9.0)	68.8						
de Queiroz Côrtes et al.[57,58]	13 (NS)/32.8	ADMG + CAF	6 mo	3/13 (23.0)	76.0	No	A	U	U	Yes	U
			12 mo	2/13 (15.3)	71.0						
			24 m	01/13 (7.7)	68.4						
		CAF	6 mo	03/13 (23.0)	71.0	No					
			12 mo	02/13 (15.3)	66.7						
			24 mo	01/13 (7.7)	55.9						
Del Pizzo et al.[59]	15 (NS)/18 to 56	EMD + CAF	6 mo	11/15 (73.3)	94.0	Yes	A	U	Yes	Yes	U
			12 mo	12/15 (80.0)	93.7						
			24 mo	11/15 (73.3)	90.7						
		CAF	6 mo	11/15 (73.3)	93.0	Yes					
			12 mo	10/15 (66.7)	88.3						
			24 mo	9/15 (60.0)	86.7						
Dilsiz et al.[60]	17 (NS)/21 to 49	SCTG + CAF (Nd:YAG)	6 mo	3/17 (17.6)	31.6	Yes	U	U	U	Yes	U
		SCTG + CAG	6 mo	11/17 (64.7)	75.7	No					
Dilsiz et al.[61]	12 (NS)/18 to 42	SCTG + CAF (Er:YAG)	6 mo	9/12 (75.0)	79.8	Yes	U	U	U	Yes	U
		SCTG + CAF	6 mo	8/12 (66.7)	85.9	No					
Dodge et al.[62]	12/23 to 51	BS + GTR with RS + CAF	12 mo	6/12 (50.0)	89.9	Yes	A	U	Yes	Yes	U
		GTR with RS + CAF	12 mo	4/12 (33.3)	73.7	Yes					
Duval et al.[63]	14/NR	BS + GTR with RS + CAF	6 mo	NR/8	81.6	No	I	U	U	Yes	H
		GTR with RS + CAF	6 mo	NR/9	90.1	No					
Felipe et al.[64]	15 (NS)/22 to 54	ADMG +CAF extend	6 mo	5/15 (33.3)	69.0	Yes	A	U	U	Yes	U
		ADMG + CAF extend + VRI	6 mo	9/15 (60.0)	84.8	Yes					
Haghighati et al.[65]/Moslemi et al.[66]	16 (NS)/24 to 45	ADMG + CAF	6 mo	11/16 (68.7)	85.4	No	A	A	Yes	Yes	L
			60 mo	3/15 (20.0)	54.6						
		SCTG + CAF	6 mo	5/16 (31.2)	69.0	No					
			60 mo	2/15 (13.3)	39.8						

Table 2. (continued)

RCTs Evaluating Class I and II GR Treated With RC Procedures Alone

Study	Participants (n)/Age (y)	Interventions	Follow-Up	SCRC (%)	MRC (%)	RMA	MR	AC	BE	CF	RB
Henderson et al.[67]	10 (NS)/24 to 68	ADMG mod + CAF	12 mo	7/10 (70.0)	94.9	No	U	U	Yes	Yes	U
		ADMG + CAF	12 mo	8/10 (80.0)	95.5	No					
Huang et al.[68]	24 (NS)/24 to 63	PRP + CAF	6 mo	7/11 (63.6)	81.0	No	A	U	Yes	Yes	U
		CAF	6 mo	7/12 (58.3)	83.5	No					
Ito et al.[69]	6/22 to 58	GTR with non-RS + CAF	6 mo	NR	81.3	Yes	U	U	U	Yes	U
			12 mo	NR	73.9						
	MGR	FGG	6 mo	NR	76.3	Yes					
			12 mo	NR	86.2						
Jahnke et al.[70]	10/16 to 51	SCTG (envelope)	6 mo	5/9 (55.5)	78.6	Yes	A	U	No	Yes	H
		FGG	6 mo	1/9 (11.1)	37.9	Yes					
Jaiswal et al.[71]	20/25 to 46 MGR	EMD + CAF	6 mo	NR/22	86.3	Yes	A	U	U	Yes	U
		CAF	6 mo	NR/24	79.6	Yes					
Jankovic et al.[72]	20 (NS)/21 to 48	PRF + CAF	12 mo	12/20 (60.0)	72.1	No	A	U	Yes	Yes	U
		EMD + CAF	12 mo	13/20 (65.0)	70.5	Yes					
Jankovic et al.[73]	15/19 to 47	PRF + CAF	6 mo	NR (75.8)	88.7	No	A	U	Yes	Yes	U
		SCTG + CAF	6 mo	NR (79.6)	91.9	No					
Jepsen et al.[74]	15/20 to 62	GTR with non-RS + CAF	12 mo	7/15 (46.6)	87.1	Yes	U	U	U	Yes	U
		SCTG	12 mo	7/15 (46.6)	86.9	Yes					
Jepsen et al.[75]	45/20 to 73	CM + CAF	6 mo	16/45 (35.5)	75.3	Yes	A	A	Yes	Yes	L
		CAF	6 mo	14/45 (31.1)	72.7	Yes					
Joly et al.[76]	10/20 to 68	ADMG + CAF	6 mo	NR	50.0	No	A	U	No	Yes	H
		SCTG + CAF	6 mo	NR	79.5	No					
Keceli et al.[77]	40/16 to 60	PRF + SCTG	12 mo	06/17 (35.3)	86.4	No	I	U	Yes	Yes	H
		SCTG	12 mo	08/19 (42.1)	86.4	No					
Kimble et al.[78]	20/21 to 69	BS + GTR with RS + CAF	6 mo	NR/8	74.3	No	I	U	No	Yes	H
		GTR with RS + CAF	6 mo	NR/10	68.4	No					

Table 2. (continued)

RCTs Evaluating Class I and II GR Treated With RC Procedures Alone

Study	Participants (n)/Age (y)	Interventions	Follow-Up	SCRC (%)	MRC (%)	RMA	MR	AC	BE	CF	RB
Koudale et al.[79]	10 (NS)/18 to 40 MGR	ADMG + CAF	6 mo	4/5s (80.0)	94.3	No	A	U	U	Yes	U
		SCTG + CAF	6 mo	4/5s (80.0)	96.6	No					
Kuis et al.[80]	37 (NS)/20 to 52	SCTG + CAF	6 mo	53/57 (93.0)	97.2	No	A	U	Yes	Yes	U
			12 mo	53/57 (93.0)	97.2						
			24 mo	51/57 (89.5)	94.6						
			60 mo	47/57 (82.5)	92.3						
		CAF	6 mo	45/57 (78.9)	91.9	No					
			12 mo	42/57 (73.7)	90.9						
			24 mo	38/57 (66.7)	86.5						
			60 mo	34/57 (59.6)	82.7						
Kuru and Yildirim[81]	21 (NS)/15 to 50	FGG (marginal to tooth)	8 mo	4/8 (50.0)	91.6	No	A	U	U	Yes	U
		FGG	8 mo	0/9 (0.0)	67.0	No					
Köseoglu et al.[82]	11 (NS)/19 to 41	GTR with RS + GF + CAF	6 mo	NR/11	72.4	No	A	U	U	Yes	U
			12 mo	NR/11	69.6						
		GTR with RS + CAF	6 mo	NR/11	51.3	No					
			12 mo	NR/11	38.3						
Leknes et al.[83]/Amarante et al.[84]	20/38.4	GTR with RS + CAF	6 mo	5/20 (25.0)	51.2	No	A	U	Yes	Yes	U
			12 mo	4/20 (20.0)	51.2						
			72 mo	2/11 (18.2)	35.0						
		CAF	6 mo	10/20 (50.0)	63.8	No					
			12 mo	6/20 (30.0)	61.2						
			72 mo	1/11 (9.1)	34.2						
Lins et al.[85]	10 (NS)/25 to 55	GTR with non-RS + CAF	6 mo	1/10 (10.0)	60.0	Yes	U	U	U	Yes	U
		CAF	6 mo	1/10 (10.0)	45.5	Yes					
Mahajan et al.[86]	14 (NS)/16 to 40	ADMG + CAF	6 mo	NR/7	97.1	No	A	U	U	Yes	U
		CAF	6 mo	NR/7	77.4	No					
Mahajan et al.[87]	20 (NS)/16 to 40	Periosteal graft + CAF	12 mo	8/10 (80.0)	92.6	No	A	U	Yes	Yes	U
		SCTG + CAF	12 mo	7/10 (70.0)	88.5	No					
Matarasso et al.[88]	20/18 to 42	GTR with RS + DPF	12 mo	1/10 (10.0)	73.0	No	U	U	No	Yes	H
		GTR with RS + CAF	12 mo	1/10 (10.0)	62.5	No					
Mazzocco et al.[89]	20 (NS)/21 to 57	SCTG + CAF mod	6 mo	20/25 (80.0)	97.0	No	A	U	No	Yes	H
		SCTG + CAF	6 mo	17/27 (62.9)	95.0	No					

Table 2. (continued)

RCTs Evaluating Class I and II GR Treated With RC Procedures Alone

Study	Participants (n)/Age (y)	Interventions	Follow-Up	SCRC (%)	MRC (%)	RMA	MR	AC	BE	CF	RB
McGuire and Nunn[90]/McGuire et al.[91]	20/23 to 62	EMD + CAF	12 mo	17/19 (89.5)	95.1	Yes	A	A	Yes	Yes	L
			10 y	5/9 (55.6)	83.3						
		SCTG + CAF	12 mo	15/19 (79.0)	93.8	Yes					
			10 y	7/9 (77.8)	89.8						
McGuire and Scheyer[92]	25 (NS)/18 to 70	CM + CAF	6 mo	15/25 (60.0)	83.5	Yes	A	U	U	Yes	U
			12 mo	17/23 (73.9)	88.5						
		SCTG + CAF	6 mo	23/25 (92.0)	97.0	Yes					
			12 mo	22/25 (88.0)	99.3						
McGuire et al.[93]	30 (NS)/18 to 70	β-TCP + CD with rhPDGF-BB + CAF	6 mo	NR	90.8	Yes	U	A	Yes	Yes	U
		SGTG + CAF	6 mo	NR	98.6	Yes					
Modica et al.[94]	12 (NS)/20 to 50	EMD + CAF	6 mo	9/14 (64.3)	91.2	Yes	A	U	Yes	Yes	U
		CAF	6 mo	7/14 (50.0)	80.9	Yes					
Nazareth and Cury[95]	15 (NS)/22 to 47	BS + CAF	6 mo	10/15 (66.6)	85.6	No	A	U	Yes	Yes	U
		CAF	6 mo	11/15 (73.3)	90.0	No					
Nickles et al.[96]	16/18 to 60	GTR with RS + CAF	6 mo	1/9 (11.1)	47.4	No	U	U	Yes	Yes	U
			10 y	0/7 (0.0)	1.9						
		SCTG (envelope)	6 mo	2/7 (28.6)	72.7	No					
			10 y	1/7 (14.3)	43.7						
Novaes et al.[97]	9 (NS)/23 to 53	ADMG + CAF	6 mo	5/15 (33.3)	66.5	No	A	U	Yes	Yes	U
		SCTG + CAF	6 mo	6/15 (40.0)	64.9	No					
Ozcelic et al.[98]	43/22 to 48 MGR	CAF + orthodontic button	6 mo	66/77(85.7)	96.2	Yes	A	A	Yes	Yes	L
		CAF	6 mo	47/ 78(60.2)	89.1	Yes					
Ozturan et al.[99]	10 (NS)/34	CAF + LILT	12 mo	7/10s (70.0)	90.8	No	A	U	Yes	Yes	U
		CAF	12 mo	3/10s (30.0)	74.9	No					
Paolantonio et al.[100]	70/25 to 48	SCTG + DPF	60 mo	17/35 (48.6)	85.2	No	A	U	No	Yes	U
		FGG	60 mo	3/35 (8.6)	53.2	No					
Paolantonio[101]	45/27 to 51	GTR with RS + CAF	12 mo	6/15 (40.0)	81.0	No	A	U	No	Yes	U
		BS + GTR with RS + CAF	12 mo	8/15 (53.3)	87.1	No					
		SCTG + DPF	12 mo	9/15 (60.0)	90.0	No					
Paolantonio et al.[102]	30/29 to 51	ADMG + CAF	12 mo	4/15 (26.6)	83.3	No	A	U	Yes	Yes	U
		SCTG + CAF	12 mo	7/15 (46.6)	88.8	No					

Table 2. (continued)

RCTs Evaluating Class I and II GR Treated With RC Procedures Alone

Study	Participants (n)/Age (y)	Interventions	Follow-Up	SCRC (%)	MRC (%)	RMA	MR	AC	BE	CF	RB
Pilloni et al.[103]	30 (NS)/19 to 67	EMD + CAF	18 mo	13/15 (86.6)	93.8	Yes	U	U	Yes	Yes	U
		CAF	18 mo	5/15 (33.3)	66.5	No					
Pini Prato et al.[104]	10/NR	CAF + polishing	14 y	5/9 (55.5)	NR	No	U	U	No	Yes	H
		CAF + SRP	14 y	3/9 (33.3)	NR	No					
Pourabbas et al.[105]	15 (NS)/26 to 63	EMD + ADMG + CAF	6 mo	NR	84.9	Yes	A	U	Yes	Yes	U
		ADMG + CAF	6 mo	NR	89.5	Yes					
Rasperini et al.[106]	56 (NS)/35.5	EMD + SCTG + CAF	12 mo	16/26 (61.5)	90.7	Yes	A	A	U	Yes	U
		SCTG + CAF	12 mo	14/30 (46.6)	76.6	Yes					
Ricci et al.[107]	NR	GTR with non-RS + CAF	12 mo	NR/18	80.8	No	U	U	U	Yes	U
		SCTG + CAF	12 mo	NR/18	77.1	No					
Roccuzzo et al.[108]	12 (NS)/21 to 31	GTR with RS + CAF	6 mo	5/12 (41.6)	82.4	No	A	U	Yes	Yes	U
		GTR with non-RS + CAF	6 mo	5/12 (41.6)	82.4	No					
Romagna-Genon[109]	21/21 to 54	GTR with RS + CAF	6 mo	NR/21	74.6	No	A	U	U	Yes	U
		SCTG	6 mo	NR/21	84.8	No					
Rossetti et al.[110,111]	12 (NS)/25 to 60	BS + GTR with RS + CAF	6 mo	2/12 (25.0)	76.4	Yes	U	U	Yes	Yes	U
			18 mo	3/12 (25.0)	84.2						
			30 mo		87.0						
		SCTG + CAF	6 mo	8/12 (66.7)	95.0	Yes					
			18 mo	8/12 (66.7)	95.7						
			30 mo		95.5						
Santana et al.[112]	22 (NS)/18 to 47	CAF (semilunar)	6 mo	2/22 (9.0)	41.8	No	A	U	Yes	Yes	U
		CAF	6 mo	14/22 (63.6)	82.8	No					
Santana et al.[113]	36 (NS)/34.0	LPF	6 mo	15/18 (83.3)	95.5	No	A	U	Yes	Yes	U
		CAF	6 mo	16/18 (88.8)	96.6	No					
Shori et al.[114]	20/29.7	ADMG + CAF	6 mo	NR/10	86.9	No	A	U	U	Yes	U
		SCTG + CAF	6 mo	NR/10	84.7	No					
Spahr et al.[115]/Hägewald et al.[116]	37/22 to 62	EMD + CAF	6 mo	NR/30	80.0	Yes	A	U	Yes	Yes	U
			12 mo	NR/30	80.0						
			24 mo	NR/30 (53.3)	84.0						
		Placebo + CAF	6 mo	NR/30	79.0	Yes					
			12 mo	NR/30	79.0						
			24 mo	NR/30 (23.3)	67.0						

Table 2. (continued)

RCTs Evaluating Class I and II GR Treated With RC Procedures Alone

Study	Participants (n)/Age (y)	Interventions	Follow-Up	SCRC (%)	MRC (%)	RMA	MR	AC	BE	CF	RB
Tatakis and Trombelli[117]	12 (NS)/22 to 48	GTR with RS + CAF SCTG + CAF	6 mo 6 mo	7/12 (58.3) 10/12 (83.3)	81.0 96.0	Yes Yes	A	U	Yes	Yes	U
Tözüm et al.[119]	31/16 to 59	SCTG + MTP SCTG + CAF	6 mo 6 mo	NR NR	96.4 77.1	No No	A	U	No	Yes	H
Trabulsi et al.[118]	26 (NS)/20 to 65	EMD + GTR with RS + CAF GTR with RS + CAF	6 mo 6 mo	NR/13 NR/13	63.0 75.0	Yes Yes	A	U	U	Yes	U
Trombelli et al.[120]	15/25 to 51	Fibrin glue + CAF CAF	6 mo 6 mo	1/11 (9.1) 2/11 (18.2)	63.1 52.9	Yes Yes	U	U	Yes	Yes	U
Trombelli et al.[121]	8/25 to 57	GTR with non-RS + CAF GTR with non-RS + fibrin + CAF	6 mo 6 mo	1/8 (12.5) NR/8	66.6 61.4	No Yes	U	U	Yes	Yes	U
Trombelli et al.[122]	12/23 to 58	GTR with RS + CAF SCTG + CAF	6 mo 6 mo	1/12 (8.3) 6/12 (50.0)	51.6 83.3	Yes Yes	A	U	U	Yes	U
Wang et al.[123]	16/30 to 54	GTR with RS + CAF SCTG + CAF	6 mo 6 mo	7/16 (43.8) 7/16 (43.8)	73.0 84.0	No No	A	U	Yes	Yes	U
Wilson et al.[124]	13/38 to 60	TEHG + CAF SCTG + CAF	6 mo 6 mo	1/10 (10.0) 1/10 (10.0)	56.7 64.5	No No	A	A	Yes	Yes	L
Woodyard et al.[125]	24 (NS)/34.6	ADMG + CAF CAF	6 mo 6 mo	11/12 (91.6) 4/12 (33.3)	96.0 67.0	Yes Yes	A	U	Yes	Yes	U
Zucchelli et al.[126]	54/23 to 33	GTR with RS + CAF GTR with non-RS + CAF SCTG + CAF	12 mo 12 mo 12 mo	7/18 (39.0) 5/18 (28.0) 12/18 (66.0)	85.7 80.5 93.5	No No No	U	U	Yes	Yes	U
Zucchelli et al.[127]	15/18 to 35	SCTG (Redgraft) + CAF SCTG + CAF	12 mo 12 mo	13/15 (86.7) 12/15 (80.0)	97.3 94.7	No No	A	U	Yes	Yes	U
Zucchelli et al.[128]	32/22 to 46 MGR	CAF without VRI CAF	12 mo 12 mo	42/47 (89.3) 35/45 (77.7)	97.3 92.6	Yes Yes	A	A	Yes	Yes	L

Table 2. (continued)
RCTs Evaluating Class I and II GR Treated With RC Procedures Alone

Study	Participants (n)/Age (y)	Interventions	Follow-Up	SCRC (%)	MRC (%)	RMA	MR	AC	BE	CF	RB
Zucchelli et al.[129]	11/18 to 40	CAF + ultrasonic	6 mo	6/11 (54.5)	84.2	No	A	U	Yes	Yes	U
		CAF + curets	6 mo	9/11 (81.8)	95.4	No					
Zucchelli et al.[130]	50/21 to 50	SCTG + CAF (FGG dep)	12 mo	21/25 (84.0)	96.2	No	A	A	Yes	Yes	L
		SCTG + CAF	12 mo	18/25 (72.0)	92.3	No					
Zucchelli et al.[131]	50/20 to 45 Molar teeth	LMCAF	12 mo	1/24 (4.0)	74.2	No	A	A	Yes	Yes	L
		SCTG + CAF	12 mo	12/25 (48.0)	88.8	No					

A = adequate; AC = allocation concealment; BE = blindness of examiners; BS = bone substitute; CA = citric acid; CD = collagen dressing; CF = completeness of follow-up; CM = xenogenic CM graft; dep = deepithelialized graft; DPF = double papilla flap; Er:YAG = erbium:yttrium-aluminum-garnet; extend = extended incision; GF = autologous gingival fibroblasts; H = high; I = inadequate; L = low; LILT = low-intensity laser therapy; LMCAF = laterally moved coronally advanced flap; mod = modified; macro = macrosurgery; micro = microsurgery; MGR = multiple gingival recession; MR = method of randomization; MTP = modified tunnel procedure; Nd:YAG = neodymium:yttrium-aluminum-garnet; NR = not reported; NS = non-smokers; p = patients; PCG = platelet-concentrate graft; PRF = platelet-rich fibrin; PRP = platelet-rich plasma; RB = risk of bias; Redgraft = graft size equal to the size of bone dehiscence; RS = resorbable membranes; s = sites (more than one GR per site); SCRC = sites with CRC; TEHG = tissue-engineered human graft; TH = tetracycline hydrochloride; U = unclear; VRI = vertical releasing incisions.

(P = 0.01), and for SCTG-based procedures compared with FGG (P < 0.001).

In addition, the RD (that is, the difference between the proportions of sites exhibiting CRC in the two groups) and NNT for comparisons that reached significant RR were calculated; the results were as follows: 1) EMD + CAF compared with CAF: see supplementary Figures 7E (RD = 0.29; 95% CI = 0.12 to 0.47; P = 0.001; NNT = 4) and 7F (RD = 0.30; 95% CI = 0.12 to 0.47; P = 0.001; NNT = 4) in online *Journal of Periodontology*; 2) SCTG-based procedures compared with GTR: RD = –0.19; 95% CI = –0.31 to –0.07; P = 0.002; NNT = 6; 3) SCTG-based procedures compared with CAF: see Figures 2D (RD = 0.16; 95% CI = 0.07 to 0.16; P <0.001; NNT = 7), 2E (RD = 0.22; 95% CI = 0.12 to 0.32; P <0.001; NNT = 5), and 2F (RD = 0.22; 95% CI = 0.11 to 0.32; P <0.001; NNT = 5); 4) SCTG-based micro procedures compared with macro procedures: RD = 0.31; 95% CI = 0.10 to 0.52; P = 0.004; NNT = 4); and 5) SCTG-based procedures compared with FGG: RD = 0.41; 95% CI = 0.24 to 0.58; P <0.001; NNT = 3).

Part III: SR of Efficacy Trials and Conditions Not Judgmentally Explored by Previous SRs

Effect of treatment of Miller[17] Class III GRs. A group of studies that mainly assessed the treatment of Class I or II GR has already included Class III defects. Regarding exclusively these defects, their reported outcomes can be found as follows. 1) For Miller,[132] of the 21 Class III mandibular defects treated with FGG (recession depth range, 4 to 9 mm), 19 (90.5%) reached CRC (an outcome inferior to those reported for Class I defects [100% CRC or 13 of 13] and superior to Class II ones [87.9% CRC or 58 of 66). Overall, an MRC of 98.1% was reported for Class III defects. 2) For Barker et al.,[133] eight Class III defects were assigned to one of the groups testing two types of ADMG + CAF; the MRC for the four defects included in the conventional ADMG were 62.5% and 61.3% for the "alternative" ADMG. 3) For Boltchi et al.,[134] seven (50.0%) of 14 Class III defects treated with GTR with RS achieved CRC. 4) For Carney et al.,[135] 16 Class III defects were treated with ADMG + CAF (n = 8) or recombinant human platelet-derived growth factor (rhPDGF) + ADMG + CAF (n = 8) in this RCT, and MRCs of 60.8% and 51.5% were found for these GRs 6 months after treatment, respectively. 5) For Cueva et al.,[136] in their RCT that assessed EMD + CAF (test) versus CAF (control), CRC was achieved in three (42.8%) of the seven Class III GRs (2 of 3 [test] and 1 of 4 [control]). 6) For Jepsen et al.,[137] in none of the eight Class III defects was CRC accomplished after the use of RS. 7) For Nart

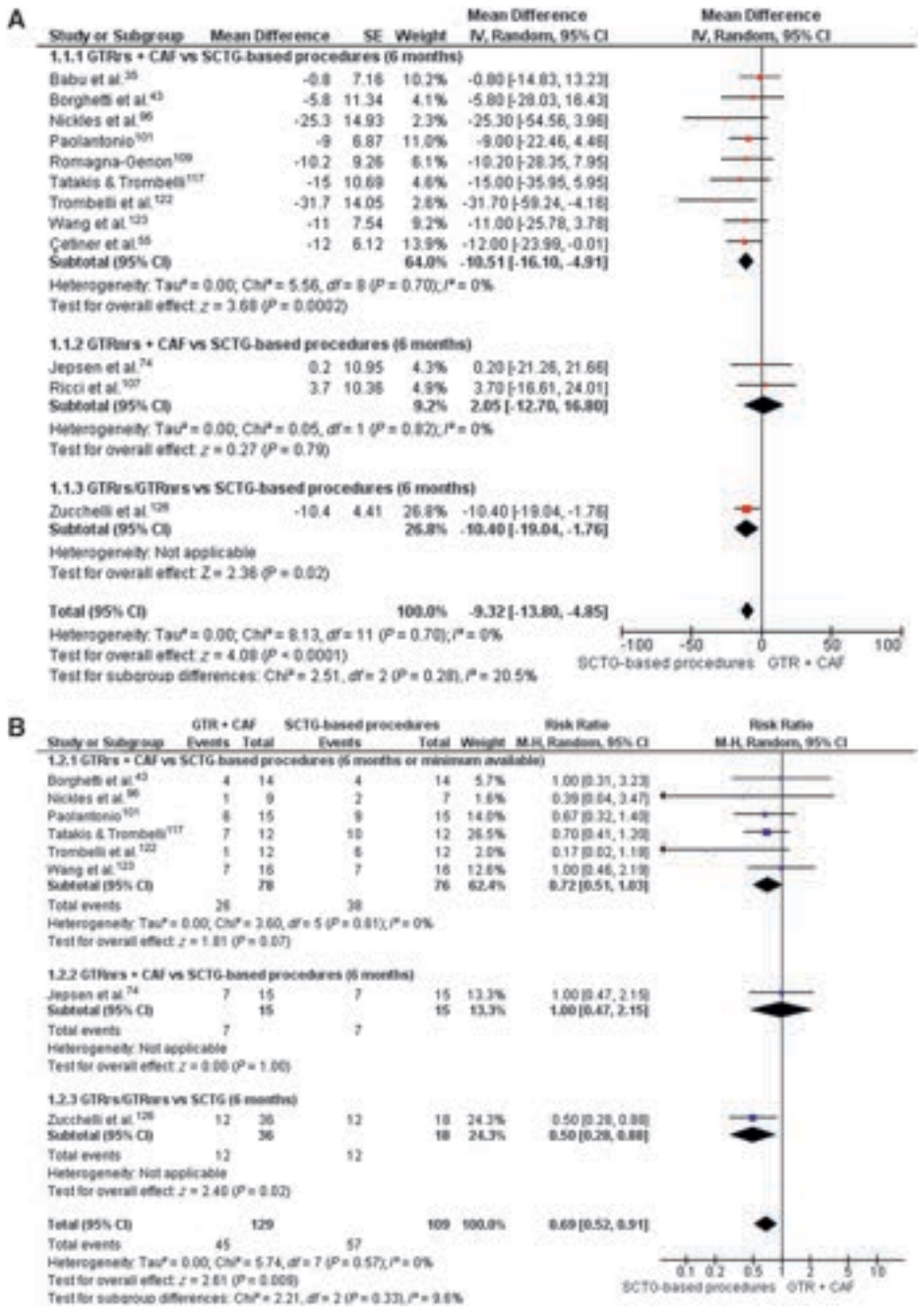

Figure 1.
Forest plots of random-effects meta-analysis comparing GTR + CAF and SCTG-based procedures. IV = inverse variance; nRS = non-resorbable membrane; M-H = Mantel-Haenszel; Tau² = Kendall τ test; z = z test. ***A)*** *Difference in the percentage of recession reduction.* ***B)*** *Difference in the number of sites exhibiting CRC.*

et al.[138], within seven Class III defects on mandibular incisors treated with SCTG + CAF, mean recession depth decreased from 5.1 to 0.8 mm (86.4%), with concomitant mean CAL and KT gains of 5 and 3 mm, respectively. CRC was achieved in three recessions (42.8%). When compared with the Class II defects included in the same study, no significant differences were observed (P >0.05).

Additionally, three other RCTs evaluated specifically Class III defects. 1) Aroca et al.[139] evaluated 139 Class III GRs in a group of 20 patients treated with a modified tunnel/SCTG procedure with or without the addition of EMD in sites of MRTDs. Despite the significant changes within groups recorded for recession reduction and CAL at the 12-month exam, the use of EMD did not lead to significant improvements between groups (MRC of 82% and CAL gain of 2.9 mm for the EMD group, and MRC of 83% and CAL gain of 2.8 mm for the control group). 2) Henriques et al.[140] also compared the outcomes of SCTG + CAF with (test group) or without (control group) the addition of EMD, in a split-mouth study comprising 12 individuals. Twelve months after treatment, significant recession reductions of GR of 2.5 mm (70.0%) and 1.7 mm (54.8%) were found for the test and control groups, respectively (P = 0.01). CAL and KT were also improved (for test, 3.0 and 0.8 mm, respectively; and for control, 1.2 and 0.6 mm, respectively). 3) The study by Cairo et al.[141] assessed the use of SCTG + CAF and CAF for the treatment of Class III GRs (i.e., with interdental clinical attachment loss [AL] less than or equal to the buccal AL). Of the 15 patients treated with SCTG + CAF, 57% presented CRC, whereas 64% of the 14 treated with CAF showed a similar outcome. The MRC was 2.6 mm (85.0%) for the combined approach and 2.0 mm (69.0%) for the use of flap alone, and both treatments reported similar esthetic outcomes (as measured by a visual analog scale [VAS]).[141] According to the authors, the following could be concluded: A) SCTGs lead to an increase in the number of sites with CRC up to >80% of the sites when the baseline amount of interdental clinical AL was ≤3 mm; B) more sites treated with CAF experienced

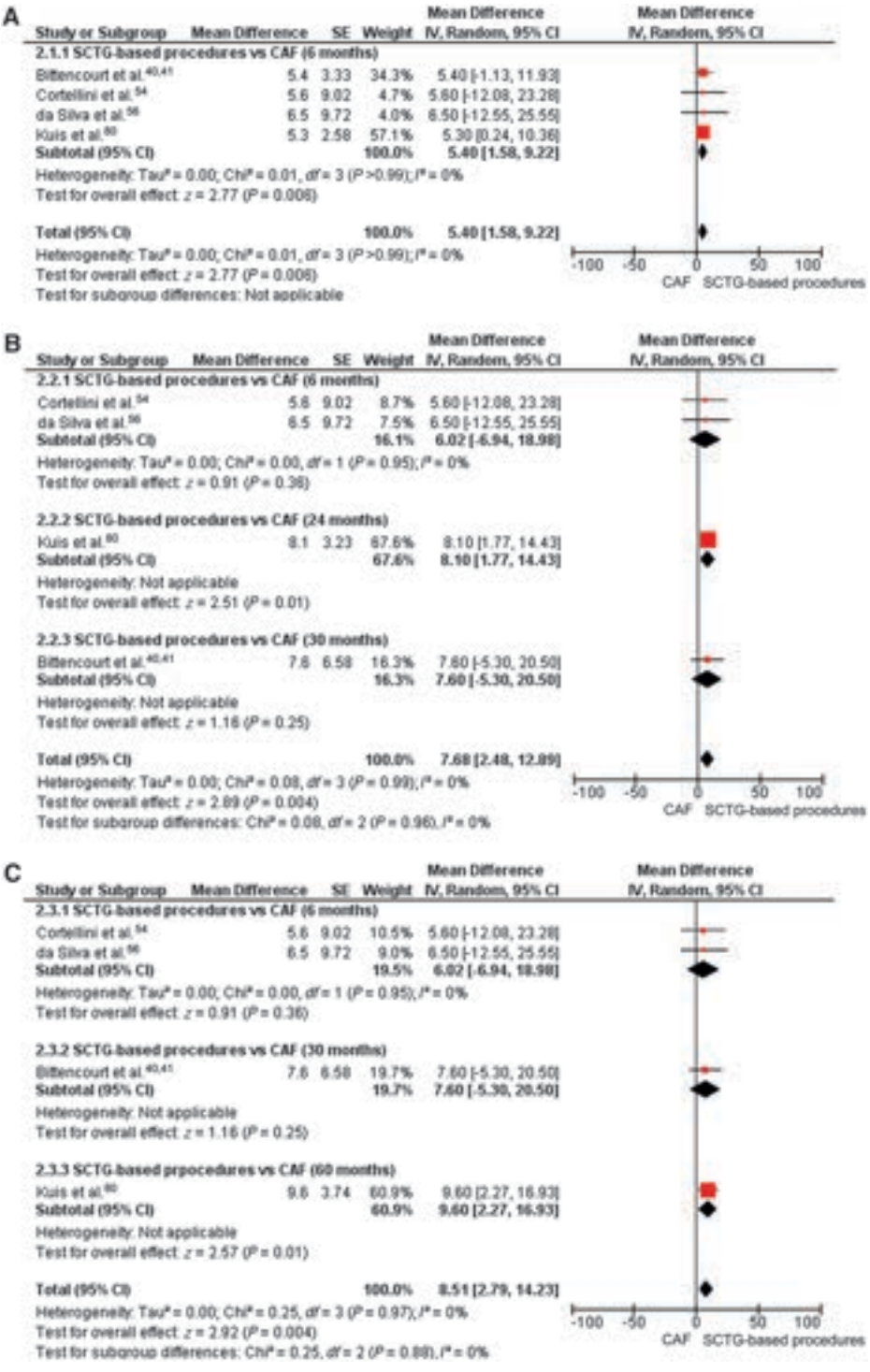

Figure 2.
Forest plots of random-effects meta-analysis comparing SCTG-based procedures and CAF. IV = inverse variance; M-H = Mantel-Haenszel; Tau² = Kendall τ test; z = z test. ***A through C)*** *Difference in the percentage of recession reduction (according to the different follow-up periods).* ***D through F)*** *Difference in the number of sites exhibiting CRC (according to the different follow-up periods).*

soft tissue contraction in the early healing phase; and C) SCTG + CAF was associated with longer chair time and stronger perception of the surgical procedure, leading to greater postoperative discomfort.

Effect of treatment of Miller[17] Class IV GRs. With respect to the outcomes achieved after the treatment of Class IV recession defects, six publications could be identified and included, but the entire base of evidence is formed exclusively by case reports[142-146] or case series.[147] In total, the outcomes of 21 Class IV recessions treated by coronally positioned FGG + citric acid,[142] the association of CAF + SCTG,[143,145] CAF + SCTG + autogenous bone graft,[144] LPF,[146] and SCTG (envelope technique)[147] have been reported. The major amount of information is from the case series by Vergara and Caffesse,[147] who presented data on 12 defects ranging from 2 to 10 mm (mean recession reduction of 5.1 mm) within a group of patients aged >40 years. Six months after treatment, the authors reported a mean recession reduction of 3.2 mm (62.7%, range of 2 to 10 mm), but CRC was achieved only in 16% of the cases. Overall, all other publications reported partial RC and CAL gain similar to these findings,[142-147] but they all also stated that the amount of RC could not be anticipated. In three case reports,[144-146] additional restorative procedures were necessary to complete treatment and improve patients' esthetics.

Histologic Attachment and Re-Entry Assessment

The human histologic findings of GRs treated by ADMG, CM,

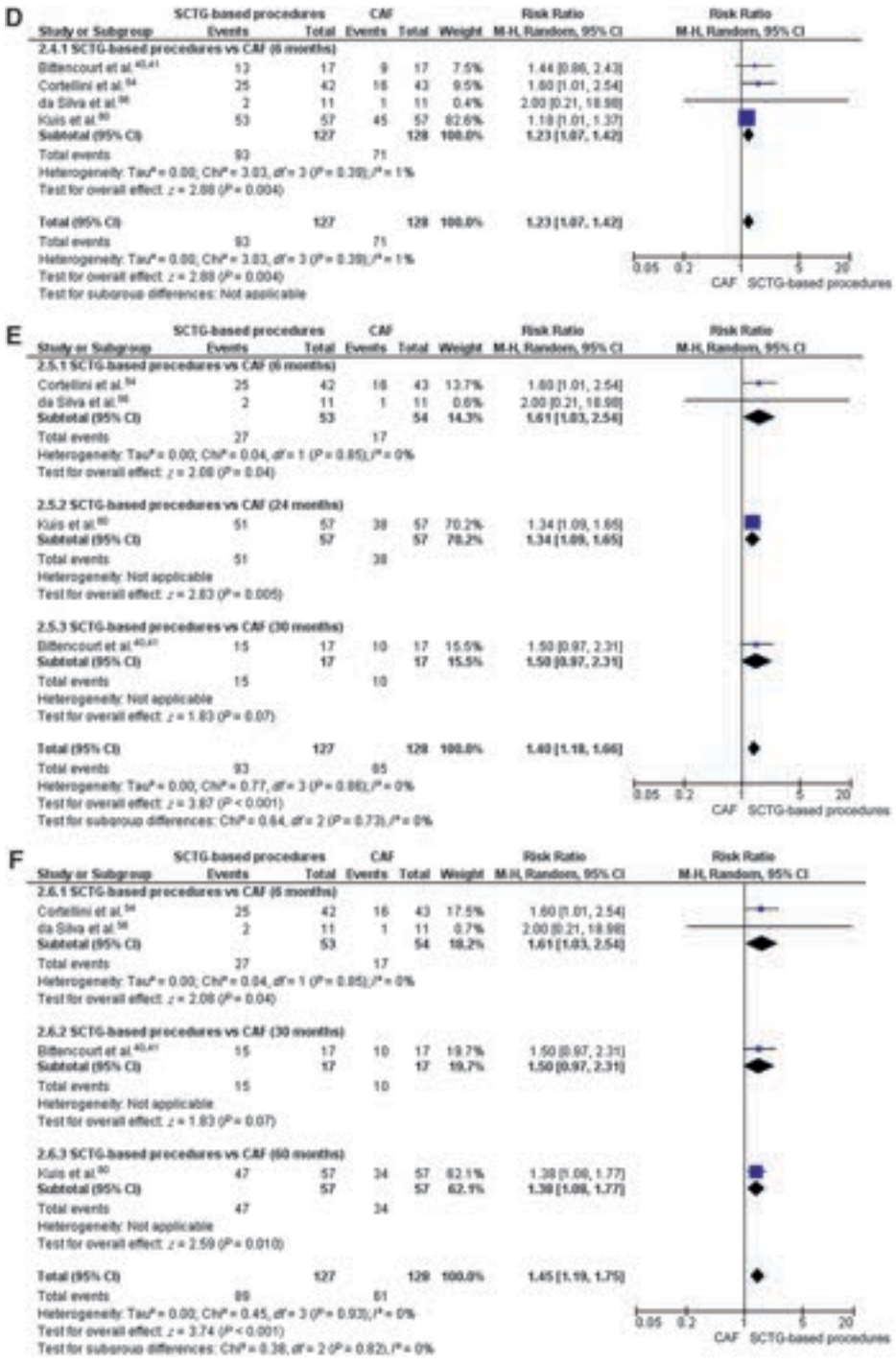

Figure 2.
Continued.

EMD, FGG, GTR, LPF, SCTG, and growth factors have been described by a group of case publications.[51,93,148-163] These are mainly derived from teeth already scheduled for extraction for orthodontic,[51,93,148-156] periodontal,[157,158] or prosthetic reasons.[159-162]

When GTR with non-resorbable membranes (non-RS) is performed, new CT attachment with newly formed cementum and crestal bone may be formed at least 180 days after treatment.[155,156] Conversely, the use of GTR with RS has shown contrasting results. Whereas Harris[161] described the formation of a long junctional epithelium without regeneration of periodontal tissues, Vicenzi et al.[151] showed that the use of RS can promote periodontal regeneration by forming "a coronal area of CT attachment and an apical area of bone fibers and cementum." Regarding reentry assessments, data on 11 GRs treated with RS showed a mean gain of 2.0 mm (range of 1.5 to 2.5 mm) or ≈44% of the mean baseline CAL.[164] For non-RS, 3.1 mm of newly formed tissue over the root surfaces could be seen (i.e., 57.7% of the baseline mean recession depth).[107]

Despite not being published in an English-language journal, a PhD thesis by Chambrone[157] assessed the histologic healing of six molar teeth presenting GR (to the apex of the mesial root) treated with LPF. Three months after surgery, long junctional epithelium and CT attachment with collagen fibers running parallel to the root surface covering the major part of the root surface were found. Sharpey fibers inserted into new cellular cementum could also be found in the most apical area of the previously exposed root surface (close to the original periodontal ligament [PDL]). Regarding the use of CAF alone, Cummings et al.[163] also described the presence of a long junctional epithelium with the underlying gingival CT presenting collagen fibers in a parallel arrangement with the root 6 months after surgery. For the treatment of deep recessions with thick FGGs, it has been reported that a long junctional epithelium,

as well as the development of new CT attachment, new cementum with perpendicular inserting CT fibers (deposited on old cementum), and new bone growth, may occur at deep portions of the previously denuded root surfaces.[148]

Some authors described different types of attachment after the use of SCTGs. Histologic data retrieved ≥5 months after surgery showed the following: 1) some degree of periodontal regeneration at the base of the recession defect (i.e., formation of new bone,[149,153,159,163] cementum,[149,150,153,159,163] and PDL;[149,159]) and 2) major portions of the root covered by CT attachment (mostly parallel to the root surface)[149,150,153,154,158-160,163] and/or long junctional epithelium.[149,153,154,158-160] It has also been suggested that the formation of new attachment may be associated with the use of SCTGs, including the palatal periosteum, and its potential "barrier effect" when the graft is placed with periosteum facing the root surface.[150] A similar assumption was already proposed by another case report.[159] Histologic evidence of RC above the original free gingival margin was found associated with the use of SCTG.[158]

Regarding the use of CM, histologic and microcomputed tomography analysis showed the formation of a long junctional epithelium attachment and CT adhesion without areas of regeneration 120 days after surgery.[152] For ADMG,[163] there was an evident disposition of dense collagen arranged parallel to the root surface, the presence of some CT fibers inserted perpendicularly into the root surface (in 25% of the sample), and some bone/cement apposition (in 50% of the sample). Harris[165] used 2-mm punch biopsies removed from interproximal areas (including soft tissue only) of GRs treated with ADMG and SCTG and showed that both grafts were incorporated by the tissues into the surgical sites and presented similar structures (i.e., cellular components) 3 to 7 months after surgery, respectively, but elastin fibers may also be present at ADMG sites.

Additionally, the healing response of biologic mediators associated with CAF procedures was evaluated as well. Histologic evaluation of CAF + EMD indicates the formation of new cementum, organizing PDL fiber running parallel between cementum and areas of condensing bone.[51,158] When an SCTG was added to the CAF + EMD procedure, a longer junctional epithelium (≈1.2 mm) and a zone of CT with fibers running parallel to the root surface could be seen at the coronal half of the recession defect, whereas partial regeneration of periodontal supporting tissues was observed at the apical half of the recession area.[162]

Likewise, it has been found that the treatment of GR with CAF + collagen dressing saturated with recombinantly produced PDGF-BB placed on β-tricalcium phosphate (β-TCP) and collagen wound dressing matrices can promote alveolar bone, cellular cementum, and PDL (inserted into bone and cementum) regeneration.[93,154]

Recipient- and Donor-Site Anatomic and Surgical Characteristics

The importance of flap thickness was studied in a case series of 19 patients treated by CAF, in which it was suggested that flap thickness >0.8 mm is associated with the achievement of CRC of shallow GRs.[166] Berlucchi et al.[167] found that the baseline recession depth and flap thickness were associated with the degree of success achieved by EMD + CAF. It was shown that 19 patients presenting recession depth <4 mm achieved significant (P = 0.009) MRC of 94.7% (CRC = 89.5%) when compared with 11 patients with recession depth ≥4 mm, which reached 85.8% MRC (CRC = 36.4%). Also, this study demonstrated that the higher the distance between the cemento-enamel junction (CEJ) and bone crest and the thinner the flap thickness (≤1 mm for GR ≥4 mm), the smaller the chance of achieving CRC at 12-month follow-up. Another prospective study containing 21 Class I GRs submitted to CAF found that an initial gingival thickness (GT) >1.1 mm was related to 100% RC 6 months after treatment.[168] An RCT on CAF (not included in part II because of its 3-month follow-up period) showed that the higher the flap tension, the lower the recession reduction (i.e., flap tension of 6.5 g led to 78% MRC and 18% CRC, whereas flaps sutured almost without flap tension [0.4 g] achieved 87% MRC and 45% CRC).[169] Moreover, comparisons between conventional CAF versus semilunar-design CAF showed that these procedures may reach MRC ranging from 57.8%[36] to 93.0%[59] and CRC ranging from 9.0%[56] to 78.9%[80] and MRC varying from 41.8%[112] to 90.0%[40] and CRC varying from 9.0%[112] to 52.9%[40] 6 months after surgery, respectively.

The practice-based study by Pini Prato et al.[170] reported that, among a group of 60 patients, each with one localized Class I recession treated with CAF, 33 (55%) presented with hypersensitivity, and of them, in 11 (33.3% of those with hypersensitivity or 18.3% of the total number of patients) this condition was still present at the 6-month follow-up. Besides sites in which the gingival margin was sutured at the level of the CEJ that did not reach 100% coverage at the final evaluation, other factors, such as baseline recession depth (i.e., deeper defects) and the amount of flap displacement over the CEJ (i.e., greater coronal displacements), were allied with greater recession decrease.[170] Authors of the same Italian research group[171] using a Bayesian network analysis with data from the same GRs found

that the accomplishment of CRC may be prejudiced by the post-surgical position of the gingival margin (the more apical the gingival margin after surgery, the smaller the chance of CRC) and, secondarily, by the baseline recession depth (i.e., deeper defects were associated with a more apical location of the gingival margin after surgery). In addition, the influence of baseline recession outcomes are in line with data from the individual patient data meta-analysis of 602 Miller Class I and II recession defects described by Chambrone et al.,[7] who showed that the greater the baseline recession depth, the smaller the chance of achieving CRC.

Some specific factors related to SCTGs have also been studied, such as the cellular composition of these grafts, the use of grafts with epithelial collar, the maximum graft dimensions that could be safely taken from the palatal vault, clinical predictability of teeth treated with grafts removed from a donor area used previously (i.e., removed from the same donor site at different time periods), and change in tissue thickness (i.e., biotype change) after treatment. For instance, in the case series by Harris,[172] trimmed samples of 30 SCTGs removed from the palate with the parallel incision method (using a scalpel with parallel blades designed by the author) were histologically assessed. It could be found that epithelium remained in 80% of the specimens and that two thirds of the graft were composed of the lamina propria and one third by submucosa. Despite these features, it was reported that all grafts (placed in 28 localized and two multiple GRs) functioned well clinically.[172]

Two studies have compared the outcomes of SCTGs with or without an epithelial collar. In the study by Bouchard et al.,[44] a mean GR decrease of 2.9 mm for both types of grafts (P >0.05) and a significant gain of KT for grafts with an epithelial collar (comparison between groups, P <0.005) were reported. Similarly, Byun et al.[47] did not find significant differences between groups in terms of MRC, CRC, or KT gain. Regarding the maximum available tissue graft obtained from the palatal vault, Monnet-Corti et al.,[173] after examining 198 maxillary plaster models of periodontally healthy individuals using a Boley gauge, reported a mean length of the harvesting area of 31.7 mm (31.1 mm [range of 24 to 45 mm] for females and 33.0 mm [range of 26 to 46 mm] for males) and a mean height ranging from 12.1 mm (midpalatal aspect of the canine) to 16.2 mm (interproximal palatal area between the second premolar and the first molar). The authors considered that the palatal vault has adequate dimensions to allow safe and adequate SCTG removal.[173]

Another practice-based case series[174] described the clinical outcomes of SCTGs removed from the same donor site at different times from 60 consecutively treated patients. A total of 176 GR defects were evaluated (85 were treated by the first graft removed and 91 by the second), and both groups presented similar clinical improvements in recession depth, CAL, and KT.[174] The MRC obtained with the second SCTG (98.2%) was statistically significantly better than with the first (95.4%), but no additional donor-site postoperative problems were observed related to the second graft than those related to the first.[174] The authors also described that a minimum timeframe of 2 months seems to be enough to allow tissue restructuring between the removal of first and the second grafts.[174] Concerning the change in tissue thickness after various procedures, a mean increase of 0.45 mm[41,56] was described when SCTGs of 1.0-[41] to 1.3-mm[56] thickness were combined with CAF. For CAF alone, there were no changes in the periodontal biotype.[41,56]

In addition, no significant differences were observed whether the SCTG was obtained via conventional graft harvesting techniques (e.g., trap door, parallel incision method) or by epithelialized gingival graft harvesting technique (i.e., deepithelialized FGG) in terms of SCTG dimensions, postoperative pain, or bleeding.[130] Conversely, conventional harvesting techniques were associated with increased surgical chair time and better outcomes on "postoperative inability to chew- and stress-related visual analog scale values."[130]

Smoking-Related Outcomes

In addition to the data reported by the included SR[2] that compared the clinical outcomes of smokers and non-smokers, additional information on the role of tobacco smoking on the short- and long-term clinical parameters, gingival crevicular fluid (GCF) markers, graft vascularization, and comparisons between different procedures among smokers could be retrieved from three recent studies[175-177] and one paper assessed previously.[178]

The long-term stability of GRs treated with SCTG + CAF was assessed within a sample of 30 non-smoking and 25 smoking patients followed for 36 months.[175] At the 12-month evaluation, the authors reported MRC of 92.6% for non-smokers and 89.0% for smokers; however, after 36 months, these rates decreased to 81.5% and 68%, respectively (P <0.05). For CRC, a similar pattern of recession increase was equally observed at 12 and 36 months for both smokers (62.1% and 12.5%, respectively) and non-smokers (72.5% and 42.5%, respectively). It could be also observed that smoking patients testing positive for interleukin-1 gene polymorphism were at an increased risk of periodontal breakdown after RC procedures.[175]

Regarding the influence of smoking and GCF markers on CAF results, Kaval et al.,[176] after treating 30 patients (15 smokers and 15 non-smokers, each group composed of 18 GRs) separated according to the baseline cotinine levels, did not detect significant differences between these patients in terms of clinical variables or biochemical content in GCF markers 6 months after surgery. Conversely, GRs with GT ≥0.95 mm were 100% covered in non-smokers, whereas for some smokers it did not happen.[176]

The unique RCT available in the literature tested the association of EMD + ADMG + CAF versus ADMG + CAF in a group of 19 heavy smokers (≥10 cigarettes/d >5 years) with bilateral Miller Class I or II GRs of ≥3 mm depth.[177] After a 6-month follow-up period, it could be found that both groups benefited from these therapies, but defects also treated with EMD presented better clinical outcomes.[177]

A final important characteristic not evaluated by the smoking SR[2] but reported by a previous study[178] relates to the histologic and histomorphometric assessment of SCTGs. Trimmed specimens from 30 grafts (half from smokers) used to treat localized GRs showed that donor sites of smokers present less vascularization (i.e., blood vessels) than the palatal vault of non-smokers.[178]

Furthermore, updated meta-analyses including the data from recent studies[175,176] in addition to those used originially[2,170,178-181] showed that non-smokers may be benefiting from an additional mean coverage of 17.49% (P = 0.01; I^2 = 74%) and a superior number of sites achieving CRC (RR = 0.36; P = 0.04; I^2 = 61%) when compared with smokers when SCTG was the treatment of choice (Fig. 3). The significant heterogeneity (I^2) found for these comparisons was directly associated with the data of the late study,[175] because the original analysis reported 0% of heterogeneity.[2] Also, based on the significant difference of sites with CRC, the RD and NNT calculated were –0.35 (95% CI = –0.50 to –0.20; P <0.001) and 3, respectively. For CAF, the lack of significance between groups in terms of sites exhibiting CRC (RR = 0.87; 95% CI= 0.50 to 1.51; P = 0.62; I^2 = 42%) and MRC (–8.87%; 95% CI = –21.65 to 3.91; P = 0.07; I^2 = 62%) remained at 6 months after surgery (see supplementary Fig. 13 in online *Journal of Periodontology*).

Root Surface Conditioning

Three RCTs[182-186] that investigated the role of combined restorative–surgical approaches in the treatment of GR associated with NCCLs and their detailed outcomes have been explored by a recent publication in *Clinical Advances in Periodontics*.[187] In this best-evidence topic paper, these trials assessed the combination of restorative procedures + CAF[182-184] or SCTG + CAF[185,186] procedures. Two of them reported not only short-term outcomes (6 months) but long-term results (24 months) as well.[183-186] Overall, the included studies showed that both procedures provided significant recession reduction and CAL gain, independently of whether the NCCL was restored or not (i.e., combined restorative–surgical approaches were as safe, predictable, and effective as the single use of the surgical procedures).[182-187] None of these included RCTs have evaluated the esthetic outcomes by a standardized scale.[182-186]

With respect to the long-term stability of results achieved with RC procedures, there was an increase in recession depth between short- and long-term assessments for GRs treated with CAF (independently of whether cervical lesions were restored or not).[183,184] Although not significant and ranging from 65% to 67% MRC, recession recurrence was doubled when CAF was used alone.[183,184] For SCTGs, restored and non-restored cervical lesions were equally favored by soft tissue RC as expressed by a minimum MRC of 90% after 24 months, but half of the sites presenting 100% coverage at the 6-month evaluation were no longer completely covered by soft tissue.[185,186] Regarding color alterations of the restorative materials, seven of 16 (43.7%)[184] and eight of 18 (44.4%)[186] of the restorations treated with CAF and SCTG, respectively, presented a color that did not match the tooth color at the 24-month evaluation. For probing depth (PD), there was a significant increase for both restored and non-restored sites after 2 years,[186] but no significant bleeding on probing was found regardless of the follow-up period.[182-186]

Within the included RCTs, maxillary Class I recession defects with NCCLs were restored 2 weeks before[182] or during[183-186] the surgical procedures. Two RCTs[183-186] evaluated only 1- to 2-mm cervical lesions, whereas the third study[182] did not report the depth of defects. Apart from these features, there were no clinical differences between restored and non-restored cervical lesions 6 months after treatment (in terms of GR, CAL change, and esthetics), but SCTG showed a trend of better outcomes than CAF.[185] It was also verified by one of these RCTs[185] (in an additional report)[188] that cervical lesion restoration with resin-modified glass ionomer did not lead to detrimental effects on the subgingival microflora/biofilm or the inflammatory markers present at the GCF after a 6-month period.

Additionally, the authors of two of these RCTs[183-186] performed a stepwise multivariate linear regression of the 78 NCCLs included in their previous publications to assess whether the shape of the

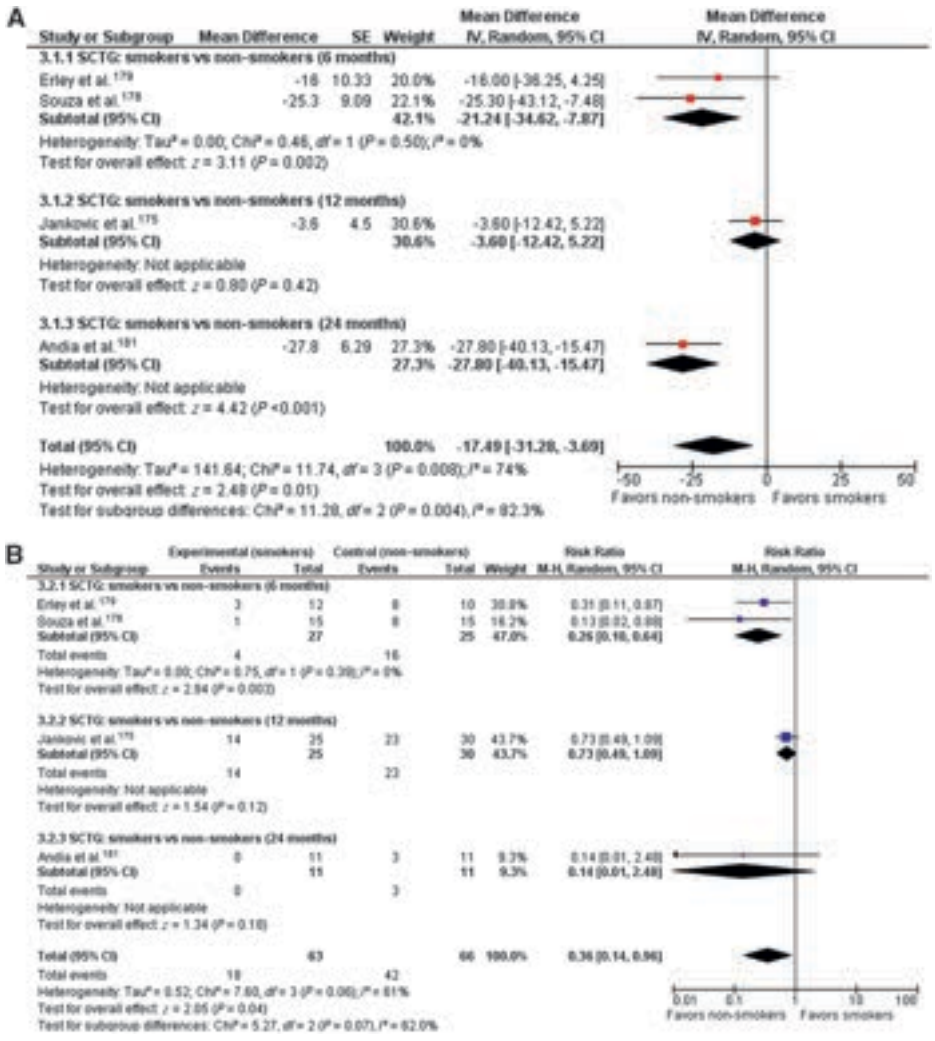

Figure 3.
Forest plot of random-effects meta-analysis comparing SCTG-based procedures in non-smokers versus smokers. IV = inverse variance; M-H = Mantel-Haenszel; τau^2 = Kendall τ test; z = z test. ***A)*** *Difference in the percentage of recession reduction.* ***B)*** *Difference in the number of sites exhibiting CRC.*

lesions (height and width), KT (width and thickness), papillae anatomy (height and width), bone level, and the post-surgical level of the gingival margin could modify GR and CAL short-term changes (i.e., 6 months after surgery).[187] It could be demonstrated that the depth of the cervical lesion may influence the amount of RC when CAF is used (i.e., the deeper the cervical lesions, the greater the coverage).[189] Also, the vertical extension (height) of the cervical lesion was found to influence GR change independently of surgical treatment, i.e., whether the defect was treated with CAF or SCTG.[189] Although larger defects lead to greater changes in baseline recession depth, it was observed that CRC of the defect might not be achieved.[189]

A similar non-randomized study[190] assessed the predictability of treating NCCLs based on the maximum RC level (i.e., "a line [line of root coverage] that should coincide with the anatomic cementoenamel junction when it was not clinically detectable on the tooth with Miller Class I or II gingival recession"). Through the use of five different treatment procedures to attain RC within a sample of 94 patients (26 Class I, 20 Class II, 38 Class III, and 10 Class IV recessions), it could be demonstrated that the predetermination of the maximum RC level of cervical lesion associated with GR may be considered a useful tool during selection of treatment options because it can provide satisfactory esthetic outcomes and correct emergence profiles.[190] Moreover and as suggested by the authors, the selection of procedures should be based on the following types of treatment: 1) Types I and II (radicular cervical lesions plus Class I or II GR): RC alone; 2) Type III (crown–radicular cervical lesion plus Class I, II, or III GR): coronal and radicular odontoplasty + restoration + RC; 3) Type IV (radicular cervical lesion plus Class III or crown–radicular cervical lesion plus Class I or II with the deepest point of the cervical lesion localized at the level of the anatomic crown): coronal and radicular odontoplasty + restoration + RC; and 4) Type V (radicular cervical lesion plus Class III or IV GR when the cervical lesion was located "on that portion of the root surface that was not coverable with soft tissues"): restoration alone.[190]

A novel technique to identify and reconstruct the CEJ level of teeth with NCCLs using a combination restorative-periodontal approach for the treatment of localized or multiple GR was proposed in a recent prospective study.[191] Based on the contralateral homologous tooth or adjacent teeth used to identify the level of lost CEJ, the crown length, and the shape of the gingival margin at each one of the 25 teeth with Class I or II GR (15 treated with CAF and 10 with SCTG + CAF), these authors considered this a useful technique based on

the reported MRC (91%) and CRC (80%) found 24 months after therapy.[191]

Regarding the treatment of carious or restored roots requiring RC, Fourel,[192] Miller,[193] Prato et al.,[194] Corsair,[195] and Goldstein et al.[196] described their outcomes using different treatment approaches. The first author reported the 4-year results of caries lesions on two maxillary teeth (#11 and #12) treated with thorough scaling ("until all softened dentin was removed and only rock-solid dentin was present") and CAF.[192] Soft tissue coverage of 3.6 and 4.0 mm were observed 4 years after surgery comprising previously carious and non-carious exposed root surfaces of teeth #11 and #12.[192] The second treated five localized, deep GRs (range of 4 to 7 mm) based on caries removal, vigorous scaling and root planing (SRP), citric acid application, and FGG, with 100% success (i.e., CRC).[193] The third presented two cases of previously restored roots in which the treatment consisted of the following: 1) removal of restoration; 2) SRP; 3) GTR with non-RS + CAF; 4) membrane removal 30 days after surgery; and 5) additional flap advancement over the remaining exposed cervical lesion/recession.[194] The authors reported that the satisfactory clinical results achieved with therapy (i.e., CRC of 4 and 5 mm in previously restored areas) could be maintained for ≥18 months.[194] The fourth reported the removal of a composite Class V restoration at tooth #11, the subsequent use of an SCTG to cover the 4-mm GR present on the buccal surface, and the 7-year follow-up showing CRC of the defect.[195] The last study provided a direct comparison between 27 teeth with restored (n = 9) and non-restored (n = 18) carious roots and 33 intact teeth with GR (Class I or II GR ranging from 2 to 6 mm for both groups) treated with SCTG + CAF.[196] Carious dentin and restorations were removed before the surgical procedures when indicated, and all recession defects were thoroughly planed and covered without the use of RMAs or restorative treatment.[196] Eighteen (66.6%) of 27 carious roots and 26 (78.8%) of 33 intact roots achieved CRC, with MRC of 97.7% and 99.1%, respectively.[196] Given the lack of statistical differences between groups and the absence of recession/caries recurrence through the follow-up period (12 to 72 months), it was concluded that "the treatment of GR on previously carious roots using SCTG is highly effective and predictable."[196]

The influence of the type of mechanical root-surface preparation/instrumentation was reported in two RCTs.[104,129,197] The first one compared root-surface polishing at slow speed with a rubber cup for 60 seconds against SRP with curets before flap elevation at 3 months (10 GRs per group) and 14 years (nine GRs per group) after treatment (Table 2).[104,197] It was found that at neither the short- nor long-term examinations were there significant differences between groups when CAF was the procedure of choice of GR ≥2 mm, except for KT width.[104,197] Based on the initial band of KT, the authors suggested that root polishing may be more indicated than SRP when the amount of KT is >3 mm (and vice versa for KT ≤3 mm).[197] The second study compared the effect of hand and ultrasonic instrumentation on the outcomes of 22 Class I defects (11 per group) treated with CAF and similarly did not find significant differences between groups in terms of MRC (95.4% and 84.2%, respectively) or CRC (82% and 55%, respectively).[129] In addition, two recent RCTs evaluated root-surface biomodification with neodymium:yttrium-aluminum-garnet (Nd:YAG)[60] or erbium:yttrium-aluminum-garnet (Er:YAG)[61] lasers before the use of SCTG + CAF (Table 2), but none of these root-modification methods enhanced the outcomes of treatment.

Tooth Type and Location

As mentioned previously, most of the RCTs described the treatment of maxillary canines and premolars.[1-11,21-27] Specifically to other tooth types, the effect of treatment on mandibular incisors/posterior teeth and lingual defects have been studied also.

Data of 50 consecutively treated patients presenting with one molar tooth with Class I or II GR ≥3 mm (and without furcation involvement greater than Class I) treated with SCTG + CAF (39 defects) or SCTG + double papilla flap (11 cases) support that these teeth may be effectively treated based on the significant gains in clinical parameters (i.e., MRC of 91.1%, CRC of 58%, and CAL and KT gains of 4.6 and 2.2 mm, respectively).[198] Recently, de Sanctis et al.,[199] after treating 10 patients presenting sites of multiple GR (26 Class I or II GR) in posterior mandibular teeth with SCTG + CAF, reported significant recession reduction (mean coverage of 91.2% and 50% CRC) and CAL and KT gain 12 months after surgery. Regarding results of efficacy trials, the unique RCT on the treatment of Class I or II GRs on molar teeth compared the 12-month results of a modification of the LPF (i.e., laterally moved CAF) to SCTG + CAF[131] (Table 2). Of the 25 patients/defects treated per group, 12 (48%) in SCTG + CAF and one (4%) in the LPF achieved CRC, and logistic regression analysis showed that 100% RC was significantly higher for the first group (odds ratio = 22.1; 95% CI = 2.4 to 200.6).[131] Furthermore, significantly less postoperative pain/discomfort and better masticatory ability for the modified LPF group were identified. Conversely, no significant differences in MRC (88.8% for SCTG + CAF and 74.2% for modified

LPF) or in patient/professional esthetics evaluation were identified.[131]

A couple of case series tested the role of RC procedures on mandibular incisors. Within the 100 defects treated by Miller in 1985 (already mentioned under "Effect of treatment of Miller[17] Class III GRs"), 77 were incisors (76 located in the mandible).[132] All the 10 Class I defects reached 100% RC, whereas among the 51 Class II defects (recession depth ranging from 3 to 7 mm), CRC was achieved in 47 (92.1% CRC and 95.7% MRC).[132] For the 15 Class III defects, 14 reached 100% CRC, and one reached 80% CRC (98.6% MRC and 93.3% CRC; recession depth range of 4 to 8 mm).[132] When SCTG-based procedures were used, overall MRC of 88.8% (80.2% SCTG + CAF, 90.5% SCTG + tunnel + laterally positioned pedicle, and 95.9% SCTG + double papilla flap; $P = 0.009$) and CRC of 62.7% (20 of 41 defects for SCTG + CAF, 24 of 38 for SCTG + tunnel + laterally positioned pedicle, and 30 of 39 for SCTG + double papilla flap) were found.[200]

When maxillary and mandibular sites were considered, it was reported that significantly greater improvements of recession depth and width of KT were observed for maxillary multiple recession defects treated with SCTG + CAF compared with alike mandibular defects.[201] For single defects treated with LPF, only KT change was significantly greater for maxillary teeth.[202]

With respect to the treatment of palatal/lingual defects, the case reports by Harris[203] (a 6.5-mm palatal recession on a molar teeth), Wilcko et al.[204] (two Class II, one Class II, and two Class III lingual GRs), and Soileau[205] (one Class II GR at the mandibular incisal area) suggested promising results of treatment linked to the use of SCTG (i.e., 84.6%, 100%, 100%, and 70.8%, respectively).

Long-Term Effectiveness Outcomes and Unusual Conditions That May Be Reported During Conventional Daily Practice

The outcomes of 17 practice-based and/or non-randomized studies with a minimum follow-up period of 24 months have been described in 19 papers,[206-223] comprising a total of 563 patients (one study did not report the number of patients treated[219]) and 904 defects (Table 3). Within these studies, a minimum mean GR reduction of 70% was recorded, and CRC ranged from 25% to 92.5%.[206-223] Of these studies, Pini Prato et al.[215] found that "a coronal displacement of the gingival margin was observed in the SCTG + CAF treated sites, while an apical relapse of the gingival margin was noted in the CAF-treated sites between the 6-month and 5-year follow-ups."

With regard to the recent RCTs (Table 2), three recent publications that described very long results (≥10 years) deserve special attention as well. The data regarding a 14-year RCT on CAF showed that KT width and CRC were quite stable during this period.[104] Of the nine GRs available for analysis in each of the root preparation procedures tested, five in the polishing group and three in the SRP group showed CRC.[104] Creeping attachment was observed in two GRs (one per group) that were not completely covered 3 months after surgery, and one GR (SRP) 100% covered at 3 months developed a new recession at the final examination (overall, recession relapse was found in 39% of the 18 GRs treated).[104] Nickles et al.[96] described significant loss of RC for teeth treated with GTR or SCTG at the 10-year examination; however, sites treated with GTR lost significantly more soft tissue than those receiving SCTG ($P = 0.002$). McGuire et al.[91] reported that, within the remaining sample of nine individuals (of the 19 examined at 12 months) reexamined 10 years after treatment, there was some loss of RC, but at both 12 and 120 months, MRC and CRC were similar for teeth treated with EMD + CAF or SCTG + CAF.

Additionally, other unusual outcomes that have not been explored by the included SRs were evaluated. For instance, there have been reports on the development of cyst-like areas,[224,225] root resorption,[226,227] bone exostosis,[228] or epithelial cell discharge[229] secondarily to the use of SCTG-based procedures, described 4[229] to 24[227] months after the procedure. Likewise, foreign body reaction was reported when combined with a bioabsorbable GTR device.[230]

Similar to the data by Pini Prato et al.,[215] certain clinical trials and case reports have explored the potentially relevant factors associated with the occurrence of postoperative migration of the gingival margin in a coronal direction, covering areas of previously partially or totally denuded root surfaces (i.e., creeping attachment).[231] The amount of creeping attachment within each publication related to the type of RC procedure, percentage and amount of RC, and follow-up years are described in supplementary Table 1 in online *Journal of Periodontology*. Overall, long-term data showed that 0.3 to 9 mm of creeping attachment may occur.[146,202,212,232-240]

PATIENTS' PREFERENCES (PATIENT-CENTERED OUTCOMES)

Within the included SRs, the use of CAF alone or combined with biomaterials was described as being less painful and more comfortable, whereas use of SCTG and non-RS has been associated with

increased morbidity (i.e., postoperative pain, bleeding, and swelling during the early phase of healing) and some complications (i.e., membrane exposure/contamination), respectively.[1,4,5,7,10,11] Conversely, because of the lack of information on esthetics change reported by the patient, decrease in root hypersensitivity, and postoperative pain, the key patient-centered outcomes could not be adequately assessed by the body of SRs. For instance, findings from one SR on cervical dentin hypersensitivity[29] showed that there is not enough evidence to support or refute the assumption that RC may decrease hypersensitivity. Overall, the base of SRs suggests that patients were satisfied with the final esthetics achieved, despite the potential postoperative discomfort and complications during the early phase of healing related to autogenous graft procedures.

Despite not being considered eligible for inclusion in the included SRs, two large sample case series reporting data on 728 patients were retrieved for analysis.[241,242] In one prospective study, the frequency of occurrence of three postoperative complications (i.e., pain, swelling, and bleeding) and the potential predictors related to these adverse effects were assessed within a sample of 228 patients submitted to the 331 surgical procedures performed to treat Class I or II GRs using FGG, SCTG + double papilla flap, or ADMG.[241] FGGs were used in 70 cases, SCTG + double papilla flap in 172, and ADMGs in 89 (84 ADMG + double papilla flap and five ADMG as FGGs), and within them, moderate to severe pain (27% to 40%) and swelling (19% to 60%) were the most significant adverse events (<6% of the sample experienced moderate or severe bleeding, but all of them were associated with the use of autogenous grafts).[241] The use of a double papilla flap was less associated with pain than FGG (27% versus 38.7%), whereas FGG presented less swelling (21.3% versus 31.6%), and SCTG was the unique procedure in which moderate or severe discomfort 1 week after surgery was reported (7.6%).[243] These authors demonstrated that long surgical procedures (P = 0.001) and smoking status (P = 0.01) were directly linked to pain and/or swelling post-surgically, that procedures involving FGG increased pain (P = 0.002) or bleeding (P = 0.03; compared with SCTG), and that the use of ADMGs significantly reduced swelling (P = 0.02) or bleeding (P = 0.001).[243]

In a practice-based evaluation of 500 consecutively treated patients treated with SCTGs (479 involving RC and 21 augmentation procedures), the incidence of infection (0.8%), bleeding (3.0%), swelling (5.4%), and pain (18.6%) was considered very low, and none of the potential predictor factors included in the statistical model (i.e., age, sex, smoking, purpose of the graft, recipient site size, or defect location) were directly associated with such complications.[244]

In one RCT reporting outcomes on SCTGs and growth factor–based procedures, patients "rated mild or no discomfort due to bleeding, swelling, sensitivity, clinical rating of color/texture of the tissues" as similar for sites treated with SCTGs or growth factor–based procedures.[93] Also, 25 (78.1%) patients experienced mild or moderate adverse events, such as mild contusion, followed by face swelling.[93]

Regarding the effect of RC on cervical dentin hypersensitivity and quality of life of patients, a recent paper describing the outcomes of 25 Class I GRs (in 22 patients) treated with SCTG + CAF showed that cervical dentin hypersensitivity (by thermal [cold] and evaporative [air blast] stimuli) was significantly reduced (P <0.001) 3 months after surgery.[243] Also, it was concluded by the authors that RC procedures positively influenced patients' oral health–related quality of life independently of the amount of RC achieved.[243] Another long-term study evaluating CAF-treated sites (and already presented in Table 3) showed that, at baseline, 33 (55%) of 60 patients presented cervical dentin hypersensitivity, whereas after 8 years of follow-up, 10 (18%) of 57 did not.[216] For GTR-based procedures, no significant changes in cervical dentin hypersensitivity were seen 12 months after treatment.[82]

Recent data provided additional information on patients' perceptions on the presence of GR, requests for treatment, and post-surgical satisfaction.[218,244] For instance, cross-checking data of questionnaires and clinical examination of 120 consecutively treated patients indicated that perception of buccal defects by patients should be taken into consideration during decision-making (i.e., their individual and spontaneous requests for treatment), because only a small percentage of GRs were perceived by them (218 of 783 [28%]), and most of them were asymptomatic in nature or considered of no esthetic or functional importance (73%).[244] Rossberg et al.[217] described that 80% of a group of patients followed for a period of 11.4 years had requested surgical correction of the defects for esthetics and 20% for cervical dentin hypersensitivity, but all of them were satisfied with the improvements achieved.

Among patients submitted to treatment, the results of VASs have been described for ADMG, CAF, laterally moved CAF, GTR, SCTG, and CM. McGuire et al. did not find statistically significant differences in "the clinical rating of color/texture of the tissues" between the SCTG + CAF and bone

substitutes + growth factors + CAF,[93] nor between CM + CAF and SCTG + CAF.[92] Wessel and Tatakis,[245] after treating 12 individuals with SCTGs and 11 with FGGs found that, 3 days after surgery, 91.6% of the individuals submitted to SCTG and all submitted to FGG complained of some postoperative pain since the surgery, with VAS scores of 3.5 and 4.8, respectively. Despite the lack of significant difference between procedures, the proportion of patients reporting pain in the palate was significantly greater for FGGs ($P = 0.045$). Eighteen days later, approximately half of the patients treated with SCTGs or FGGs were still experiencing pain but with lesser VAS values than those recorded earlier and without significant differences between groups (1.6 and 1.4, respectively).[245] Overall, within-group comparisons for the FGG group showed a significant reduction of the VAS pain score between 3 and 21 days ($P = 0.005$) and no changes for the SCTG group ($P = 0.07$).[245]

Information on 15 Class I or II GRs treated with ADMG indicates high and better scores related to patient opinion (8.1 of 10) than those recorded by an independent periodontist (6.7 of 10) at 12-month follow-up.[246] Zucchelli et al.[131] showed the following: 1) RC involving only pedicle grafts (laterally moved CAF) presented better postoperative course and chewing ability ($P < 0.01$) than SCTG + CAF; 2) the use of autogenous graft led to significantly ($P < 0.01$) better postoperative sensitivity; and 3) the lack of significant differences between groups in terms of esthetics ($P > 0.05$).[131]

For CAF-based procedures in multiple GRs, similar outcomes concerning 6-month esthetics and 1-week postoperative pain were reported when vertical releasing incisions were performed.[98] When CAF with and without vertical incisions were compared in such defects (multiple GRs), similar patient satisfaction outcomes (overall satisfaction, color match, RC) were reported, but flaps without vertical incisions provided significantly better ($F = 8.9$; $P < 0.01$) postoperative course during the first week of healing.[128]

In addition, of the nine patients re-examined by McGuire et al.[91] 10 years after treatment, 66.6 (n = 6) favored EMD + CAF instead of SCTG + CAF, one favored SCTG, and two had no preference. In terms of esthetic satisfaction, six patients had no preference for a particular type of treatment, two favored esthetic results with the EMD, and one favored results with SCTG.[91]

DISCUSSION

As reported within the base of SRs included in this review, the treatment of GR with RC procedures plays an important role in contemporary periodontology. Since the first SR published in 2002,[9] there has been a continuously increasing interest in the systematic evaluation of clinically relevant scientific evidence regarding the esthetic and functional effects of treatment gingival defects. The interest is not only focused on the clinician's knowledge but includes patient-centered outcomes (e.g., esthetic assessment, functional limitations, discomfort, root sensitivity, and preferences) as well.[6,7]

With respect to the effect of treatment of Class I and II recession defects, an accurate review of SRs showed that SCTG-based procedures led to the most significant gains in defect coverage and KT width, increases in the number of sites with CRC, and greater long-term stability of outcomes. These results could be confirmed by some of the meta-analyses presented in part II (Figs. 1 and 2), as well as by the outcomes of the 94 RCTs presented in Table 2. It could also be confirmed that the combination of CAF with soft tissue graft substitutes, such as CM and EMD, led to more positive outcomes compared with CAF alone; these combined treatments could be viable alternatives to SCTGs (with clinical outcomes close to those reported for SCTGs). Overall, all the soft tissue RC procedures described in the literature for localized and MRTDs can significantly improve RD and CAL in the short term (i.e., 6 months after treatment).

The outcomes of the 12 sets of meta-analysis, combining data of pairwise comparisons in non-smoking individuals, on the mean percentage RC showed the following: 1) ADMG + CAF provided 15.6% more RC than CAF alone; 2) EMD + CAF led to 12% to 15% additional improvements when compared with CAF alone when follow-ups >6 months were included in the pooled estimates; 3) SCTG-based procedures performed 5% to 8% better than CAF, 8.9% better than CM + CAF, 9.3% better than GTR + CAF, and 32.5% better than FGG, and SCTG provided slightly (5.3%) but significantly superior outcomes than EMD + CAF when the longer-term outcomes were used in the analysis; and 4) SCTG-based microsurgical procedures improved outcomes by 9.0% when compared with macrosurgical (conventional) techniques. Regarding the number of sites exhibiting CRC after therapy, SCTG-based procedures were superior to CAF, FGG, and GTR, whereas EMD was superior to CAF alone. Additionally, SCTG-based microsurgical approaches increase the number of sites exhibiting CRC. Based on these significant differences in terms of CRC, the NNT was calculated to determine how many defects would need to be treated with a respective procedure to result in one more defect achieving CRC than would have occurred using another RC procedure. As a result, three defects with FGGs, five to seven with CAF, and six with

Table 3.

Characteristics and Outcomes of Long-Term (≥24 Months) Practice-Based and/or Non-Randomized Studies

Study	Participants (n)/ Age (y)	Interventions (GR)	Follow-Up	ΔGR (mm)	ΔCAL (mm)	ΔKTW (mm)	SCRC (%)	MRC (%)	RMA
Caffesse and Guinard[206] and Guinard and Caffesse[207]	21/19 to 68	LPF	36 mo	3.2	3.7	3.1	NR/14	82.3	No
		FGG and CAF		3.0	3.3	3.5	NR/12	71.4	No
Chambrone and Chambrone[202]	32 (NS)/18 to 55 Class I or Class II GR	LPF (max GR)	24 mo	4.3	4.8	3.7	6/16 (62.5)	94.5	Yes
		LPF (mand GR)		4.5	5.4	3.2	5/16 (68.7)	93.2	Yes
de Sanctis and Zucchelli[208]	40/20 to 38 Eight smokers Class I or II GR	CAF	36 mo	3.6	3.6	1.8	34/40 (85)	96.7	No
Griffin and Cheung[209]	06/18 to 60 One smoker Class I or II GR	PCG + CAF	36 mo	2.4	3.8	0.9	21/37 (56.7)	85.8	No
Gunay et al.[210]	20 (NS)/16 to 58 Class I or Class II GR	SCTG + EMD + CAF	24 mo	4.0	4.6	2.6	25/36 (69.4)	92.1	Yes
		EMD + CAF		3.0	3.8	2.2	31/37 (83.7)	94.3	Yes
Harris[211]	100/18 to 70 Seven smokers Class I or II GR	SCTG	27.5 mo	3.7	4.4	3.0	135/146 (92.5)	98.4	Yes
Lee et al.[212]	15 (NS)/22 to 44 20 GR Class I or Class II and One Class III	SCTG + CAF	36 mo	3.3	3.1	1.9	11/21 (52.4)	91.3	No
Moses et al.[213]	65/17 to 59 Class I or II GR	SCTG + DPF	24 mo	4.5	3.8	2.4	NR/37	84.3	No
		EMD + CAF		3.3	3.6	1.2	NR/28	76.9	Yes
Pini Prato et al.[214]	50/15 to 40	GTR with non-RS + CAF	48 mo	4.2	5.0	1.8	NR/25	73.1	No
		FGG and CAF		3.8	3.1	5.1	NR/25	72.3	No

Table 3. (continued)

Characteristics and Outcomes of Long-Term (≥24 Months) Practice-Based and/or Non-Randomized Studies

Study	Participants (n)/ Age (y)	Interventions (GR)	Follow-Up	ΔGR (mm)	ΔCAL (mm)	ΔKTW (mm)	SCRC (%)	MRC (%)	RMA
Pini Prato et al.[215]	13/24 to 51 Three smokers 79 GR Class I or Class II and 14 Class III	SCTG + CAF CAF	60 mo	3.2 2.2	NR	NR	23/44 (52.3) 17/49 (34.7)	88.8 75.9	No No
Pini Prato et al.[216]	57/29.7 (mean) 11 smokers	CAF	96 mo	2.3	2.6	–0.5	20/57 (35.1)	71.8	No
Rossberg et al.[217]	20/22 to 57 36 GR Class I or Class II and three Class III or IV	SCTG (envelope)	11.4 y (6 to 22 y)	2.7	NR	4.7	32/39 (82.0)	89.7	No
Scabbia and Trombelli[218] andTrombelli et al.[219]	20/23 to 35	GTR with non-RS + CAF	48 mo	3.5	3.9	1.2	5/20 (25.0)	77.7	No
	Nine smokers Class I or II		10 y	3.2	3.3	1.2		72.7	
Tözüm[220]	NR/NR Class II GR	SCTG (tunnel)	36 mo	3.1	3.8	NR	NR/14	92.2	No
Wennström and Zucchelli[221]	67/19 to 38	SCTG + CAF	24 mo	3.9	3.7	2.8	51/58 (87.9)	98.9	No
	Class I GR	CAF		3.9	3.6	1.1	36/45 (80.0)	97.1	
Zahedi et al.[222]	15 (NS)/25 to 60 Class I GR	GTR with RS + CAF	24 mo	2.9	3.5	0.4	9/15 (60.0)	82.2	No
Zucchelli and De Sanctis[223]	22/18 to 34 Five smokers Class I or II GR	CAF	60 mo	2.5	2.5	1.4	62/73 (85.0)	94	No

DPF = double papilla flap; KTW = KT width; mand = mandibular; max = maxillary; NR = not reported; NS = non-smoking; PCG = platelet concentrate graft; SCRC = sites with CRC; Δ = mean change from baseline.

GTR need to be treated so that one can reach this benefit over defects treated with SCTG. For CAF, four defects need to be treated to accomplish CRC over sites treated with EMD + CAF, and four defects should be treated with SCTG-based macrosurgical approaches to obtain one more site exhibiting CRC than SCTG-based microsurgical approaches.

Despite the strong evidence on RC outcomes and the strong relationship between root-surface exposure and cervical dentin hypersensitivity, one of the included SRs suggested that there is not enough evidence to support or refute the use of RC procedures for treating such types of hypersensitivity.[29] This result is certainly associated with the lack of adequate assessments within RCTs given that cervical dentin hypersensitivity usually has not been considered among RCT outcomes. The lack of strong supportive evidence does not mean that there is no evidence; it seems reasonable to consider that successful coverage of recessions on teeth presenting with cervical dentin hypersensitivity can (from a clinical point of view) also decrease hypersensitivity. In fact, among the restricted group of studies that investigated cervical dentin hypersensitivity,[216,243] it was demonstrated clearly that CAF[216] alone or SCTG[243] provided significant improvements in thermal and evaporative hypersensitivity. Nevertheless, cervical dentin hypersensitivity outcomes merit additional investigation and should be part of future research studies on RC.

Considering the use of RMA, there is clear support from the literature on the lack of additional benefits provided by the use of chemical agents (i.e., citric acid, EDTA, or tetracycline hydrochloride solution)[4-7,9,28] or biomodification therapies (i.e., Er:YAG[61] or Nd:YAG lasers[60]). In general terms, such agents and therapies did not lead to any detrimental effect on the expected final clinical outcomes, and they were not able to improve the results of treatment. In addition, the type of mechanical method used for root debridement (i.e., rubber cup, manual curets, or ultrasonic devices) does not appear to modify RC outcomes.[104,129,198]

With respect to the assumptions explored in parts II and III, the lack of information on Class III and mainly Class IV recession defects was evident. For Class III defects, the use of RC procedures provided rates of MRC that ranged from 54.8%[140] to 85.0%[141] within the included RCTs specially designed to evaluate these defects. Within other studies that included Class I or II GR defects as well, an MRC ranging from 51.5%[135] to 98.1%[132] was found for Class III defects. For both groups of studies, SCTGs provided the best results. CRC varied between 42.8%[136,138] and 90.5%[132] for Class III defects within studies that also included Class I and/or II defects and between 57% (SCTG + CAF)[141] and 64% (CAF)[141] for trials evaluating exclusively Class III recessions. These results indicated that Class III defects treated with RC may achieve good and predictable clinical results. Concerning Class IV recessions, there were only a few case reports published, and some degree of RC could be achieved, whereas the final esthetic results could be improved by combined restorative approaches performed subsequent to the healing period.[144-146] However, such limited information does not allow at this point definitive conclusions or the establishment of some degree of predictability for these defects.

Regarding the histologic attachment formed during the RC wound-healing process, ADMG, CAF, CM, FGG, LPF, and SCTG led mainly to the development of long junctional epithelium and CT attachment with collagen fibers running parallel to the root surface,[148,149,152-154,157-160,163,165] whereas procedures involving GTR, EMD, and growth factors led to partial regeneration of the lost tissues.[51,93,151,154-156,158,162] Moreover, it was described that SCTGs are mostly formed by components of the lamina propria;[173] regardless of whether trimmed from FGG or harvested directly from the palate, SCTGs result in the same graft dimensions and postoperative pain/bleeding,[130] and the palatal vault provides suitable dimensions to allow harmless graft removal[174] even when harvesting more than once from the same location.[175]

Some recipient- and donor-site anatomic characteristics that were evaluated by the included studies indicated that reduced flap thickness,[166-168] deep baseline recession depth,[7,167,171,172] and flaps positioned and sutured apical to the CEJ (i.e., the more apical the gingival margin after surgery)[171] may negatively influence achievement of CRC. Moreover, it should be noted that some trials included in this study[34,84,96,224] focused their interest in improvements to the flap design (i.e., procedures not involving the use of vertical releasing incisions). However, at this point in time, there are not enough outcomes to support or refute the superiority of these procedures (i.e., the outcomes of these studies did not provide superior outcomes to those achieved by "conventional" procedures, and there is a lack of short- and long-term data on SCTG + tunnel approaches/flap without vertical incisions versus conventional CAF technique + SCTG). Consequently, it seems a little premature to conclude, based on the available base of RCTs, any significant clinical difference between flaps advocating or not the use of vertical releasing incisions.

Another important issue linked to the prognosis of soft tissue RC is tobacco smoking.[2] Evidence is clear that smokers may benefit from soft tissue

RC; however, the use of an SCTG does not provide the same effect of treatment as that achieved in non-smokers.[2] By updating the meta-analysis by Chambrone et al.[2] and reporting the difference in mean percentage RC, it could be demonstrated that non-smokers may obtain 17.5% additional RC than smokers when patients were treated with an SCTG. Likewise, non-smokers had greater benefit regarding the number of sites with CRC, indicating that at least three defects in smokers need to be treated with an SCTG to result in one more defect reaching CRC than in the non-smokers. These outcomes may be explained by the characteristics of the donor (i.e., less vascularized palatal vault[177]) and recipient (i.e., less vascularized flap)[2] sites of smokers, characteristics that might influence revascularization and incorporation of the SCTG and overall wound healing.[2] Conversely, when CAF was used alone, significant differences could not be noted; however, limited evidence is available for analysis, and, independently of the surgical procedure tested, it should be noted that smoking status was confirmed biochemically in only two trials.[176,179] For the remaining trials,[170,175,177,178,180,181] the investigators used the number of cigarettes smoked per day as the threshold for the patient inclusion.

It has been argued that root-surface conditions may influence final RC procedure outcomes. Some RCTs[182-185] assessed the use of combined restorative/surgical approaches when treating GRs. The combined use of restorative materials (i.e., resin-modified glass ionomer or microfilled resin composite) did not lead to negative effects on bleeding scores[182-185] or subgingival microflora.[188] However, these studies showed no significant differences in MRC between restored and non-restored groups, although it was noted that almost 45% of the cervical restorations presented a color that did not match the tooth color 24 months after treatment. Furthermore, because the color of the restorations may change over time, it should be evaluated how these can be removed. It may be suggested that teeth with NCCLs could be first treated, for instance, by SCTG + CAF and then, after healing, receive a supplementary restorative procedure. For carious root surfaces, the outcomes of the few studies available indicate that, when the carious dentin and existing root restorations are properly removed before the surgical procedures and the root surfaces are thoroughly planed, RC procedures may be greatly effective and predictable.[193-197]

As reported previously,[1-7,9] the majority of defects treated in most studies were located in the maxilla (canines and premolars). For other groups of teeth, such as incisors and molars specifically, similar high rates of success might be achieved as well.[131,132,199-201] Two practice-based case series studies suggested that procedures involving CAF procedures may perform better in the maxilla than in the mandible.[206,207] Additionally, data from the few case reports on the treatment of lingual/palatal defects suggest that these type of defects may be safely and successfully treated.[204-206]

With respect to the long-term outcomes that may be expected in private practice, it seems possible to anticipate a mean 70% RC ≥2 years after treatment.[207-225] There is a marked variation on the amount of RC achieved in different studies (25% to 92.5%), but SCTG-based procedures provided the best and more stable outcomes, whereas CAF alone may be associated with the greatest amount of apical relapse of gingival margin position over time (Table 3).[207-225] This is in line with the data from the three RCTs included in this study.[91,96,104] It is also important to highlight that, despite the possible occurrence of some adverse events related to the treatment with SCTGs (i.e., development of cyst-like areas,[226,227] root resorption,[228,229] or bone exostosis[230]), these were restricted to a very limited number of cases and cannot per se undermine the safety/success of autogenous grafts. Overall, all RC procedures can be considered safe. Likewise, the results of some graft procedures (i.e., FGGs and SCTGs) may be improved over time by the coronal displacement of the gingival margin (creeping attachment). However, neither the "favorable" (creeping attachment) nor the "unfavorable" (adverse events) outcomes can be anticipated.

In addition to the data presented by the included SRs,[1-10,21-27] information on diverse patient-centered outcomes could be obtained by two large studies, one university based[241] and another practice based.[242] It could be verified that some patients may experience some degree of pain and swelling during the early phases of healing, but only a very few of them experience bleeding.[241,242] In fact, these early postoperative adverse effects may not interfere with the final result or even amount to contraindications for treatment.

It is clear that less traumatic procedures, with less chair time and involving only one surgical site, are preferred by most patients.[1-10,21-27] Independent of such preferences, most of the treated patients considered esthetics as their main concern, and in the great majority, the final outcomes of the performed surgical procedure (irrespective of inclusion of one or more surgical sites) fulfilled their personal expectations.[1-10,21-27,30-246] However, differences among studies in terms of procedures, analysis (i.e., patient based or site based), sample size, follow-up period, experience of operators, lack of baseline, and final recession characteristics prevent additional conclusions on this topic.

In addition, it should be clear that effectiveness is a very significant question, which has not been explored to the same extent that efficacy has. In this study, publications from private offices are regarded as evidence of effectiveness (for instance, the publication from Pini Prato et al.[104]). Publications like this one may not be considered as examples of the average private practice setting. The idea of effectiveness is based on outcome of therapy by average clinicians in the community and not by "experts." Conversely, it should be noted most clinicians are not used to design research protocols or conducting/running clinical studies, and in the great majority may sometime present the results of their work as case reports. These issues are important and deserve distinction, because often there is a gap between protocols investigated by experts and those implemented in clinical practice.

CONCLUDING REMARKS

A comprehensive assessment of the relevant literature, performed as part of the 2014 American Academy of Periodontology *Workshop on Periodontal Regeneration and Tissue Engineering*, revealed a sizable volume of publications for most RC procedures. This comprehensive assessment of the RC literature, the "decision tree" generated from it (Fig. 4), and the ensuing consensus report should help clinicians in their daily practice as they try to make the best possible choice of treatment modality to satisfy their patients' needs. Regarding the focused questions addressed in this review, the following can be concluded.

What Is the Efficacy/Effectiveness of RC Procedures by the Degree of Recession?

The vast majority of the published RC studies consist of RCTs and SRs on Miller Class I and II single recession defects. Because of the lack of data from "efficacy trials" on other important conditions of interest, such as treatment of Miller Class III and IV defects or treatment of palatal/lingual defects, controlled clinical trials, case series, and case reports were included in the assessment of the literature in an effort to provide fundamental outcome information for such other conditions.

Miller[17] Class I and II GR. All RC procedures can provide significant reduction in recession depth and CAL gain without alteration of PD for Miller Class I and II localized recession-type defects, but MRTDs seems to be benefit as well despite the reduced quantity of information available. SCTG-based procedures provided the best outcomes for clinical practice because of their superior percentages of MRC and CRC and the significant increase of KT when compared with most of the other procedures. The use of CAF with ADMG, EMD, and CM also provided gains, many of them similar to SCTG-based procedures, and thus these may be considered as adequate substitute treatment approaches. Defects treated at the mandible and at posterior sites (i.e., molars) can be safely and satisfactorily treated as well. The final outcomes achieved seem to benefit from the use of magnification during the surgical procedures, but little evidence was available for analysis. Conversely, smoking may decrease the expected results of SCTG.

Miller Class III and IV GR. Class III defects may significantly benefit from the use of RC procedures (in the short term) when SCTG-based procedures are used. Alternatively, EMD + CAF, ADMG + CAF, and GTR + CAF can be used as graft substitutes. Overall, the marginal level of the gingival tissue of teeth adjacent to the GR seems to be the clinical reference point when planning and predicting the expected results of Class III defects. Concerning Class IV recessions, the data from the limited number of case reports suggest that these defects may be improved after treatment, but the amount of RC cannot be anticipated, and restorative procedures may be necessary to reach the final expected esthetic outcomes.

Which Factors May Influence the Outcomes (i.e., Smoking Status and Root Surface Conditions)?

For instance, is it possible to accomplish RC for teeth with NCCLs, root caries, or cervical root resorption? It was clearly demonstrated that smoking may significantly decrease the effect of therapy, especially when SCTG-based procedures had been used. With respect to the surface conditions and from the limited number of studies available, it could be seen that NCCLs, whether restored with composites/ionomer materials or not, may be safely treated by SCTG + CAF and CAF. Moreover, there is no evidence on the optimal timing for NCCL restoration (before/during RC procedure or after wound healing). For teeth restored previously or presenting caries, there is some evidence indicating the positive effects of treatment of these areas by RC procedures, but for both conditions, there is a need for removal of old restorations/caries before the surgical therapy (i.e., the need for a "clean/disease-free root surface").

What Is the Anticipated Success and Attachment Apparatus of RC Enhancements With Autogenous Grafts Compared With Alternative Methods and Materials?

As mentioned previously, SCTG-based procedures seem to be the best option in terms of clinical outcomes and cost-to-benefit ratio. Conversely, the use of matrix grafts (ADMG and CM) and EMD may be used as safe substitutes for autogenous grafts in patients with great demand for donor tissue (e.g., patients with MRTDs) or patients who do not

Figure 4.
Decision tree for the treatment of Miller[17] recession-type defects (the thicker the "branch," the stronger the base of evidence). Wound healing consisting of long junctional epithelium and CT attachment (with fibers parallel to the root surface) is expected, but some degree of tissue regeneration may occur (mainly for EMD- and GTR-based procedures). Because the majority of the publications included in the study evaluated single-tooth recession sites, the decision tree seems better designed for determining appropriate treatment for single-tooth sites, but it may guide the treatment of MRTDs as well. The use of RMAs does not promote positive or negative clinical modifications. XCM = xenogenic CM.

want to be submitted to a secondary surgical procedure at the palatal vault. Histologically, most of the techniques may result in the formation of a long junctional epithelium (over the previously exposed root surface) and CT attachment with fibers parallel to the root surface. GTR and EMD procedures can lead to partial periodontal regeneration (i.e., formation of new cementum, alveolar bone, and PDL inserted in the newly formed cementum).

What Are the Long-Term and Short-Term Advantages of Root-Surface Biomodification?

The long-term outcomes (≥24 months) presented in the literature indicate that SCTG-based procedures and EMD + CAF may provide superior outcomes than CAF and more stable results. Overall, a large part of the RC achieved in the short term may be maintained long term. The use of RMAs or other surface biomodification procedures did not provide superior gains in clinical outcomes, either short or long term, than those expected for procedures performed without such agents.

What Are the Relative Risks From a Patient's Viewpoint With the Different Approaches to RC Procedures?

Regarding patient-centered outcomes, all RC procedures were considered safe and effective for attaining RC and satisfactory esthetics. Data on root hypersensitivity is still scant, but recent data suggest the positive influence of RC treatment on such an outcome. Moreover, a small percentage of patients may experience postoperative bleeding, swelling, and pain. It could be considered that patients seem to prefer procedures that involve only one surgical site when considering these early postoperative adverse effects, but these were not associated with the final esthetic/functional outcomes.

Should CT Grafts Contain Epithelium and/or Periosteum?

The use of SCTGs containing epithelium and/or periosteum does not provide additional gains than SCTG without epithelium or periosteum, but the existing evidence is very limited.

Is There Evidence for Innovation When Treating Thin and Thick Biotypes With Existing Treatment Modalities?

SCTG, ADMG, and CM can positively change thin periodontal biotypes of recession sites to thick periodontal biotypes. As reported within long-term studies, patients treated with graft procedures (and their consequent biotype improvement) benefited from more stable outcomes and less recession recurrence. Also,

the topic of biotype (thin versus thick) is covered more specifically in the review by Kim and Neiva[247] included in this supplement. Overall, it seems reasonable to suggest that biotype modification (i.e., thin to thick biotypes) should be considered when planning and treating recession-type defects because of the positive, more stable long-term outcomes reported.

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