Efficacy of tunnel technique in the treatment of localized and multiple gingival recessions: a systematic review and a meta-analysis

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One-sentence summary: The tunnel technique is a highly effective procedure for treating gingival recessions, especially when performed with a split-thickness flap using a microsurgical approach; its efficacy seems comparable with coronally advanced flap.

Key words: gingival recession, tooth root, surgical flaps, meta-analysis, evidence-based dentistry

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Abstract

Background: Tunnel technique (TUN) has recently gained popularity among clinicians for its promising clinical and esthetic results when treating gingival recessions (GRs) defects. However, the evidence of the efficacy of TUN in the literature is still to be determined. Therefore, the aim of the present systematic review and meta-analysis was to investigate the predictability of TUN and its comparison to coronally advanced flap (CAF) procedure.

Material and Methods: A literature search on PubMed, Cochrane libraries, EMBASE, and hand-searched journals until November 2017 was conducted to identify clinical studies investigating TUN for root coverage procedures. Only RCTs were considered for the meta-analysis comparing TUN and CAF.

Results: Twenty articles were included in the systematic review and six in the meta-analysis. The overall calculated mRC of TUN for localized and multiple GRs was 82.75 ± 19.7% and 87.87 ± 16.45%, respectively. Superior results were found in maxillary GRs and in Miller class I and II GRs. TUN outcomes may be enhanced by split thickness flap preparation and microsurgical approach. TUN and CAF had comparable mRC, CRC, KT gain and RES when varying combinations of graft material were evaluated. However, CAF showed superior outcomes to TUN when the same graft (connective tissue or acellular dermal matrix) was used in both techniques.

Conclusions: TUN is an effective procedure in treating localized and multiple GRs defects. Limited evidence is available when comparing TUN and CAF; however, CAF seemed to be associated with higher percentage CRC than TUN when the same grafts (connective tissue or acellular dermal matrix) was used in both techniques.

Introduction

Gingival recession (GR) is defined as the apical displacement of the gingival margin with concomitant exposure of a portion of the root surface [1]. The high incidence of this defect, approximately 54% in young adults and 100% in middle-elderly adults [2], can be attributed to a large variety of predisposing and precipitating factors such as plaque-induced inflammation, traumatic tooth brushing, periodontal disease and orthodontic treatment[1, 3].

GR is not limited to only posing an esthetic concern, it also results in dental hypersensitivity, root caries, plaque accumulation, and may even be associated with minimal to a lack of keratinized tissue

(KT).[1] GR becomes an indication for treatment when esthetic appearance is compromised and/or dental hypersensitivity presents [1, 4].

With the introduction of harvesting a free gingival graft (FGG) from the palate and suturing it on the exposed root [5], other treatment modalities for correcting GR have been set forward. Surgical approaches, such as Guided Tissue Regeneration (GTR) and mucogingival procedures, have both showed great results in correcting GR [6]. Among these, the coronally advanced flap (CAF) is considered the of flap design of choice, especially when combined with a connective tissue graft (CTG) and/or enamel matrix derivatives (EMD) [7, 8].

To meet the high esthetic demands of patients, surgical procedures that preserve the integrity of the papilla have been proposed when both obtaining root coverage and regenerative therapy are needed [9].

Raetze was the first to use an envelope flap technique for covering isolated gingival recessions[10]. He created a partial-thickness "envelope" that allowed for the insertion of a CTG. After covering the previously exposed root, a cyanoacrylate adhesive was used to stabilize the partially exposed CTG. Later on, Allen modified this approach by creating a partial-thickness supra-periosteal envelope in the treatment of multiple adjacent GRs[11]. In this approach, he undermined the corresponding dental papillae to allow for more coronal movement of the flap. Zabalegui et al. later coined this technique as "the tunnel" approach [12]. Interestingly, no attempt in coronal advancement of the envelope was described at that point, resulting in the coverage of a recession defect depending solely on the exposed portion of the CTG. Aside from different names suggested for this technique, further modifications of this tunnel approach have also been proposed [13-16]. Zuhr et al. introduced a microsurgical approach while designing new instruments [13]. The “Coronally advanced modified tunnel technique”, proposed by Aroca et al. [14, 17], comprises a full thickness flap elevation, while carefully separatating the entire interproximal papillae from bone, and placing suspended sutures from composite stops placed at teeth contact points to prevent flap collapsing during healing.

The tunnel technique (TUN) has slowly gained its popularity due to its associated conservative characteristics and improved esthetic outcomes [18]. Other advantages of TUN include: great blood supply and graft nutrition [14, 19], quicker healing [12, 19], and reduced post-operative morbidity owing to limited flap opening [18]. The positive esthetic outcomes are attributable to flap elevation without dissecting the papillae or performing vertical releasing incisions [14, 15, 19]. However, despite several clinical trials having tested the TUN for the correction of localized and/or multiple GRs, no study has investigated its overall predictability with regards to the influence of recession type (single/multiple, Miller class) and location (maxilla/mandible) on the outcome. Similarly, a comparison between TUN and the commonly used CAF for root coverage has not yet been performed [15, 18, 20].

Therefore, this systematic review aimed to: a) analyze the predictability of TUN in localized and multiple GR defects; b) study the impact of each procedure on different Miller’s GR classifications (class I, II and III); c) investigate factors that influence the final mean root coverage and complete root coverage; and d) compare the outcomes of TUN and CAF when used for the treatment of localized/multiple gingival recession defects.

Material and Methods

Study Registration

The review protocol was registered and allocated the identification number CRD42017081178 in the PROSPERO International Prospective Register of Systematic Reviews hosted by the National Institute for Health Research, University of York, Centre for Reviews and Dissemination.

Patient, Intervention, Comparison, Outcome (PICO) Question

This systematic review utilized the Preferred Reporting Items Systematic review and Meta-Analyses (PRISMA) statement and checklist [21], as well as the patient, intervention, comparison, outcomes (PICO) method (Fig. 1).

P: Patients with localized or multiple GR defects classified as Miller I, II or III [22] or RT1 or RT2 [23].

I: All the recessions treated with TUN without vertical incisions and without the incision of the papillae.

C: In the meta-analysis TUN was compared to CAF.

O: mRC and CRC of TUN in the maxilla versus mandible, in localized versus multiple GRs and in Miller class III versus class I & II. The secondary outcomes were to investigate the factors that may affect mRC, CRC and KT gain and to compare TUN with CAF in a meta-analysis. Root coverage Esthetic Score (RES) [24] was also investigated as tertiary outcome.

Information Sources and Screening Process

Electronic and manual literature searches, conducted by two independent reviewers (LT and AR), covered studies until November 2017 across the National Library of Medicine (MEDLINE by Pubmed), EMBASE, and the Cochrane Oral Health Group Trials Register (Figure 1; see supplementary Data S1 in online *Journal of Periodontology*).

Additionally, a manual search of related journals was also performed (see supplementary Data S2 in online *Journal of Periodontology*). Finally, previous systematic reviews investigating root coverage procedures for gingival recession were screened for article identification (see supplementary Data S2).

Eligibility Criteria

Articles were included in this systematic review if they met the following criteria: 1) surgical treatment of GR(s) with TUN, 2) randomized clinical trial, cohort study, case-control study, case series with at least 10 patients. Contrarily, articles were to be excluded if: 1) TUN included one or more vertical incision(s) and/or incisions of the papillae, 2) the study included < 10 patients, 3) the study is a case report, 4) envelope flap was not coronally advanced. Regardless of the various nomenclature proposed for this surgical technique, only approaches which involved an envelope flap preparation, maintaining the integrity of the papillae, free of vertical incisions and performing a coronal advancement to completely cover the GR(s) were considered a TUN and thus, were included.

Data extraction

Studies were excluded by screening titles and abstracts and full-text reading by two investigators (L.T., S.B.) using a predetermined data extraction form to confirm the eligibility of each study based on the aforementioned criteria. The primary outcomes were the mRC and CRC, while the secondary outcomes were KT gain and RES. Data was independently extracted by two authors (L.T. and S.B.). Patient characteristics, treatments and clinical outcomes were registered. When clinical data was lacking, authors of the trials were contacted. At each stage, disagreement between reviewers was resolved through discussion and consensus. If a disagreement persisted, the judgment of a third reviewer (A.R.) was decisive.

Quality and Risk of Bias assessment

Two authors (LT, AR) independently evaluated the included reports using all the checklist items of the respective scales. The Cochrane Risk of Bias Tool for Randomized Controlled Trials was used to evaluate randomized controlled trials (RCTs) [25], while the Joanna Briggs Institute Scale for Case Series [26] which provided guidelines for the assessing the risk of bias of case-series (see supplementary Data S3 in online *Journal of Periodontology*).

Statistical analysis

All analyses were performed using the metafor statistical package [27] with the statistical software environment Rstudio†. In summary, the weighted mean values of mRC, CRC and KT gain were calculated according to Lipsey & Wilson [28]. Regression analyses were performed using Fixed-Effects models and the rma function to assess the roles of independent variables relative to the outcomes (mRC, CRC, KT gain).

Planned methods for meta-analysis

Six RCTs, outlining similar comparisons, outcome measures and abiding by the predetermined eligibility criteria, were selected for the meta-analysis. Changes in the following primary outcome measures were considered for comparison between CAF and TUN: mRC, CRC, KT gain and RES.

Pooled weighted mean differences (WMD) and standard deviations (SD) for mRC and KT were calculated. For CRC assessment, percentage values were transformed to the corresponding binary outcomes representing the number of recessions that achieved complete root coverage. Changes in RES scores had to be expressed as the average difference between baseline and follow-up of the treated sites mentioned in each corresponding article. Next, the contribution of each study was weighted accordingly and the random effects model was selected (the DerSimonian-Laird method), as heterogeneity between studies was previously assumed. Forest plots were produced to summarize the differences in both groups. A p value of <0.05 was determined significant. Heterogeneity among studies was assessed with Chi-square (X^2) test and the I^2 statistics test according to the Cochrane Handbook for systematic reviews [29]. In the case of detected heterogeneity, subgroup analyses of the respective studies were performed for investigating the sources. Funnel plots were used to visualize bias among selected publications. The reporting of these meta-analyses adheres to the PRISMA statement [21] (Fig. 1).

Results

Study selection

Search results based on the PRISMA guidelines are depicted in figure 1. Twenty articles reporting on 1181 recessions treated with TUN, with a mean follow-up of 11 months, were included in the present systematic review (Table 1 and 2) [14-18, 20, 30-43]. Among these, six RCTs comparing CAF versus TUN [15, 18, 20, 31, 37, 38] were considered for the meta-analysis. Excluded articles and reasons for exclusion are reported in supplementary Data S4 in the online *Journal of Periodontology*.

Study characteristics

Study design and study population

Eleven articles were RCTs [14, 15, 17, 18, 20, 30, 31, 33, 37, 38, 40], while nine were case series [16, 32, 34-36, 39, 41-43].

None of the studies included smoking patients. Five articles focused only on localized GRs [18, 36, 38-40], three treated both single and multiple GRs [15, 20, 43], whereas the remaining studies included only multiple GRs [14, 16, 17, 30-35, 37, 41, 42].

One article treated only Miller class III GRs [17], 3 studies Miller class I, II and III GRs [16, 34, 36], and the remaining articles focused only on Miller I and II GRs [14, 15, 18, 20, 30-33, 35, 37-43].

The general characteristics of the included studies are outlined in table 1.

Type of Intervention

Interventions were heterogeneous (Table 2). Two RCTs compared TUN + CTG versus CAF + CTG [18, 20], two RCTs TUN + Acellular Dermal Matrix (ADM) with CAF + ADM [37, 38], one RCT TUN + CTG with CAF + EMD [15], two TUN + CTG with TUN + Xenogeneic Collagen Matrix (XCM) [14, 33], one RCT TUN + CTG with TUN + Fascia Lata (FL) [30], one RCT TUN + CTG with TUN + CTG + EMD [17], one RCT TUN + ADM with TUN + ADM + Platelet Rich Plasma (PRP) [40] and one RCT TUN + CTG with CAF [31]. Five case series investigated the outcomes of TUN + CTG [16, 35, 36, 39, 41], three TUN combined with a CTG substitute [32, 34, 42] and one TUN + EMD [43].

Bias assessment

The results of bias risk assessment for the included RCTs, using The Cochrane Risk of Bias Tool, are summarized in supplementary Data S5 in the online *Journal of Periodontology*; four articles had a low risk of bias [14, 18, 20, 37], six were considered to have a moderate risk of bias [15, 17, 31, 33, 38, 40], and one study had a high risk of bias [30].

The results of bias risk assessment for the included case series, using The Joanna Briggs Institute Scale for Case Series, are summarized in supplementary Data S6 in the online *Journal of Periodontology*; seven studies had a moderate risk of bias [16, 32, 35, 36, 39, 41, 43], and 2 had a high risk of bias [34, 42].

Synthesis of results

To quantitatively address the review questions, data from studies was extracted and organized into tables to condense an overview of, intervention characteristics, clinical outcomes and, the quality of methods and reporting.

A total of 1181 GRs in 439 patients from 20 studies were evaluated in the present systematic review.

The overall mRC of TUN for localized GRs was 82.75 ± 19.7%, while the mRC of TUN for multiple GRs was 87.87 ± 16.45%. The CRC of TUN was lower in localized than multiple GRs (47.15% vs 57.46%, respectively). The mRC and CRC values according to the location (maxilla/mandible), Miller classification (I&II/III) and type of GRs (localized/multiple) are shown in table 3.

Regression analysis

Linear regression analyses showed that CTG or substitutes (ADM, FL, XCM, PADM), RecDepth0, papillae elevation and suture techniques do not influence the mRC. Contrarily, maxillary GRs, split thickness flaps and a suture diameter ≥ 6-0 were significantly associated with a greater mRC ($p<0.001$).

CRC was significantly influenced by: RecDepth0 ≤ 2.5 mm ($p<0.05$), a split thickness flap ($p<0.001$), and a suture diameter ≥ 6-0 ($p<0.05$).

KT gain was not affected by CTG or substitutes, RecDepth0, flap thickness, papillae elevation, suture diameter, suture technique or recession area ($p>0.05$).

Meta-analysis

The characteristics of the six trials comparing TUN and CAF [15, 18, 20, 31, 37, 38] are depicted in table 4. All the articles reported data on mRC, CRC and KT gain, however, only four assessed RES [15, 18, 20, 37]. Data for the studied outcomes and analyses' results are detailed below.

Mean Root Coverage

The analysis of all six studies did not show a statistically significant difference between the CAF and the TUN groups for mRC. The WMD between the TUN and the CAF group was 4.38 (95% CI [-9.06, 17.83]) (p=0.52). Comparison between the articles presented considerable heterogeneity as represented in the funnel plot (see supplementary Data S7 in online *Journal of Periodontology*), I^2=93.37% ($p<0.001$) (Fig. 2a). Hence, a random effects model was used for data interpolation. A subgroup analysis, performed for studies utilizing only a CTG [18, 20] (see supplementary Data S8 in online *Journal of Periodontology*), led to an insignificant WMD value of 0.44 (p=0.44) with low heterogeneity (I^2=23.7%, p=0.25). However, when a similar subgroup analysis was performed for articles utilizing ADM as the choice of graft [37, 38], a statistically significant difference in mRC, favoring

CAF (17.99 (95% CI [12.79, 23.19]) with low heterogeneity among the results (I^2=0%, p=0.9), was observed (Fig. 2f).

Complete Root Coverage

Initially, the analysis of CRC for all studies did not statistically favor either group (p=0.3) with considerable heterogeneity among articles (I^2=82.25%, p<0.001) (Fig. 2b). A Subgroup analysis of trials utilizing only CTG [18, 20] or ADM [37, 38] revealed a significant p value of 0.003 and 0.0007, respectively, both in favor of CAF. This indicates the significantly higher number of GRs that achieved a CRC when treated with CAF+CTG or CAF+ADM versus TUN+CTG and TUN+ADM (Fig. 2e, 2g). Low heterogeneity was observed, with values of I^2=0% (p=0.7) and I^2=2% (p=0.3), for subgroup analyses in the CTG and ADM groups.

Keratinized Tissue Gain

There was no significant difference in changes of KT when comparing the TUN and CAF. The WMD between the two groups was -0.09 (95% CI [-0.50, 0.32]) (p=0.6) when all articles were analyzed and -0.16 (95% CI [-0.42, 0.10], p=0.2) when only the 2 trials using a CTG were assessed [18, 20] (see supplementary Data S8 in online *Journal of Periodontology*). The former comparison yielded a considerable heterogeneity (I^2=89%, p<0.001), while the latter presented low heterogeneity (I^2=0%, p=0.4). When a subgroup analysis was performed for studies only with ADM grafting material [37, 38], a significant difference in KT was observed in favor of CAF (0.36 (95% CI [0.20, 0.52], p<0.001]) with low heterogeneity (I^2=0%, p=0.4) (Fig. 2h).

Root coverage Esthetic Score (RES)

Only 4 studies compared changes in the RES [15, 18, 20, 37]. Analyses demonstrated no significant differences among studies comparing TUN and CAF (*p*=0.9) (Fig. 2d). However, considerable heterogeneity was noted among the 4 included studies (I^2 =91.32%, *p* <0.001). When a subgroup analysis for the articles with only CTG was performed [18, 20], no statistically significant difference, with regards to RES, was observed (*p*=0.4), with low heterogeneity (see supplementary S8 in online *Journal of Periodontology*).

Meta-regression analyses demonstrated that single versus multiple recession treatment, the location of the treated GR (maxilla/mandible), the study setting (private practice/university setting) and the follow-up period (4, 6 or 12 months) had no significant effect (p>0.05) on the demonstrated results of the performed meta-analysis.

Discussion

Although several systematic reviews have already assessed the predictability of root coverage procedures [8, 44], evidence addressing the efficacy of the TUN remains scarce. One reason may have been the limited number of RCTs available to be included in previous periodontal plastic surgery reviews [44-46], another plausible reason might have been the exclusion of this technique from the meta-analysis [44, 46]. Therefore, the effectiveness of TUN, as well as its comparison with other traditional procedures, is yet to be determined [4].

Recently, new trials have explored TUN for root coverage procedures [18, 20, 33], some of which primarily focused on comparing TUN with CAF [18, 20].

The present systematic review considered both randomized and non-randomized trials in the evaluation of TUN's overall predictability; however, only RCTs were included in the meta-analyses that have investigated whether or not TUN can be considered superior to CAF.

TUN was found to be a highly effective procedure in treating GRs, exhibiting an overall mRC of 82.8% for single and 87.9% for multiple GRs, in addition to a CRC of 47.2% and 57.5%, respectively. Despite few studies compared TUN in single and multiple GRs [15, 20], a possible explanation for the higher values in multiple GRs may be due to the less challenging nature of gaining flap mobility with larger flaps, as is the case with treating multiple versus single GR. This is no surprise, as it has been one of the main challenges of TUN [15]. The greater extension of the flap in multiple GRs facilitates its passive displacement and suturing at a coronal position. Contrarily, as in single GRs, minimal flap extension may limit flap mobility, reducing the chances of achieving CRC [18]. For this reason, when treating single GRs, Zuhr et al. suggested leaving a small portion of the CTG exposed, discouraging the use of TUN for single recession defects deeper than 5 mm.[15] This is in agreement with our findings, showing a positive correlation between shallow GRs and a greater incidence of CRC.

In terms of mRC and CRC, our results also demonstrated that TUN is more effective in treating maxillary and Miller class I and II GRs. Positive clinical outcomes for treating maxillary GRs with a CAF have previously been reported [47, 48]. Similar to the findings of this review, De Sanctis and Clementini had also referred to tooth location being a critical factor of success, particularly pertaining to mRC and CRC [49]. It can be speculated that high muscle pull together with a shallow vestibule (a typical characteristic of mandibular teeth) may play a key role in preventing complete resolution of GRs [1, 50]. Similarly, interproximal attachment loss has always been considered a key factor for final root coverage [49], as is the basis of the two main GR classifications [22, 23].

Ever since the introduction of TUN, several modifications have been proposed to improve this technique. These modifications have altered factors such as full or split thickness flap preparations, papillae elevation, suturing technique and the use of microsurgical approaches [13, 17, 39]. However, the extent to which the outcomes of the TUN may be improved remains unclear.

Flap preparation, whether full or split thickness, is controversial in the literature [15]. Although TUN was initially proposed as a split-thickness approach to facilitate flap mobility and sufficient advancement [12, 19], the risk of flap tearing and the documented correlation between a thicker flap and a higher probability of CRC [47, 51] has led some authors to perform a full-thickness TUN [14, 37, 39]. In contrast, Zuhr et al. claimed that a split thickness TUN may induce beneficial effects on CTG survival, ensuring enhanced blood supply [15]. Regression analysis showed significantly greater mRC and CRC values when a split thickness TUN was performed. Rebele et al. (2014) demonstrated that post-operative marginal gingival thickness can be a relevant prognostic factor of root coverage procedures and that the use of a CTG is a predictable approach in increasing this aspect [52]. Hence, it may be deduced that a split thickness TUN with adequate blood supply to the CTG[13, 15], could lead to an increased marginal soft tissue thickness and progressive coronal improvement of the gingival margin level over time.[53]

Other modifications to TUN, such as papillae detachment and elevation[14, 33] or the addition of composite stops between contact points preventing the collapse of suspended sutures[14, 41], were not associated with improved outcomes. Meanwhile, a positive correlation between 6-0 and 7-0 (smaller diameters than 5-0) suture diameters to mRC and CRC was observed. It is reasonable to assume that smaller diameter sutures (6-0 and 7-0) were used in microsurgical surgeries. Performing surgeries under optical magnification, allowing for more careful soft tissue manipulation and better wound closure, has been identified by several authors as one of the main reasons for their pleasing results [15, 20].

Due to limited data, the possible influence of a covered or partially uncovered graft could not be investigated. However, it has been suggested that minimal exposure of a CTG may aid in not only achieving CRC, but also a harmonious gingival margin [15]. The survival of the exposed portion of a CTG, however, is only possible if a minimum ratio of 11:1, between the covered and uncovered area, is performed [54]. When using XCM or ADM, instead of a CTG, it was suggested that the graft be completely covered [14, 37]. However, when investigating the effect of a grafted material on the mRC, CRC and KT gain, linear regression showed no differences among CTGs or CTG substitutes. Despite numerous beneficial effects of a CTG, such as inducing differentiation of the overlying epithelial layers[55] and providing greater mRC and CRC as compared to a flap alone [4, 8], the main advantage of a graft beneath the flap may be the "scaffold effect" that promotes wound healing with favorable thickening of the gingiva [44, 52]. It is worthy to mention that some authors who investigated the efficacy of CTG substitutes, found comparable results with the gold standard, CTG, itself [56].

To the best of our knowledge, no meta-analysis has yet compared TUN to CAF. In light of this, the results of the present review will contribute to the literature.

The meta-analysis showed comparable results between TUN and CAF, in terms of mRC, CRC, KT gain and RES, when all articles with varying grafting materials were analyzed. Five articles included in the meta-analysis reported better mRC and CRC outcomes for CAF [18, 20, 31, 37, 38], while Zuhr et al. reported results in the opposite direction, favoring TUN [15]. The "center effect" [57] and the operator expertise in sensitive procedures such as mucogingival surgeries [15] may explain the visible heterogeneity in the results among different clinicians. Moreover, as demonstrated by our own results, a microsurgical approach and a split thickness flap preparation may have contributed to the superior outcomes of TUN reported by Zuhr and coworkers.[15]

On the other hand, subgroup analyses revealed that when a CTG was used in combination with TUN or CAF, a significantly higher CRC in favor of CAF was noted. Comparably, a CAF + ADM was related to superior mRC, CRC and KT gain as compared with the TUN + ADM. The superior outcomes of a CAF can be attributed to its main advantages that include (1) the use of vertical releasing incisions, (2) increased access that facilitates periosteal dissection, and (3) the possibility of performing a split-full-split thickness flap preparation [18]. In addition, a modified CAF design, with oblique incisions at the papillae while avoiding vertical releasing incisions has also been proposed by Zucchelli et al. for the treatment of multiple GRs [58]. However, keloid formation and papillae scarring are common findings with CAF; whether for the correction of single or multiple GRs [1, 58]. It has been reported that by avoiding vertical incisions and maintaining the papillae intact, TUN can prevent keloid formation [33]. Nevertheless, despite esthetics having been considered one of the main advantages of TUN [14, 15, 18], this meta-analysis failed to confirm a superior RES for TUN over CAF. This lack of difference can be attributed to the fact that 60% of the RES value is affected by CRC (found to be higher in the CAF group), while the remaining 40% is a result of other factors such as marginal contour, the presence of keloid formation, the position of the mucogingival junction and the soft tissue contour [24]. However, several studies have reported the superiority of TUN for gingival contour, the absence of keloid formation and tissue texture [18, 37]. All these factors can play an integral role owing to CRC alone no longer being the mere goal of therapy, but added factors like gingival margin contour, the chromatic and texture integration of soft tissue and the lack of scar tissue formation possessing equal importance when root coverage procedures are discussed [15, 57].

The authors are aware of the limitations of the present systematic review. The center effect and the limited reliability of case series are two limitations worthy of mentioning, as demonstrated by Clauser et al. where CRC was more frequently obtained in non-RCTs than in RCTs. The authors speculate that the main reason may be the progressive learning curve of the operator in case series [59]. This meta-analysis comparing TUN to CAF is based on a limited number of articles and high rates of heterogeneity among their results, preventing definitive conclusion; nevertheless, CAF seemed to be associated with a superior CRC than TUN.

Conclusions

Considering the limitations of the present review, it can be concluded that TUN is highly effective in treating localized/multiple gingival recessions. However, CAF seemed to be associated with higher percentage CRC than TUN when the same grafts (connective tissue or acellular dermal matrix) was used in both techniques. Technique modifications, such as split thickness flap preparation and a microsurgical approach, may enhance the final outcomes.

Indication for further research

- Increase the number of RCTs based on the CONSORT guidelines
- New RCTs that compare TUN and CAF with at least a 1 year follow-up period
- New multicenter RCTs that compare TUN and CAF to assess the influence of the center effect
- New RCT comparing TUN and CAF without graft material or biologic agents
- Increase in the number of RCTs that evaluate RES, post-operative pain, patient satisfaction, interference with daily activity and social life

- RCT reporting the number of patients, the drop-out and the GRs treated, as well as the SD for each result provided

Implications for clinicians

Clinicians should be aware that TUN is a highly effective periodontal plastic procedure for the treatment of single and multiple GRs. Its limitations are mainly related to surgical indications in the lower arch, areas with interproximal attachment loss (Miller's Class III or RT2), localized GR defects and operator expertise.

TUN's outcomes may benefit from a split thickness flap preparation and a microsurgical approach. Nevertheless, limited evidence is available regarding the best grafting material to combine with TUN; however, the addition of a graft material is recommended.

Although operator expertise plays a key role in the final results, CAF seems to provide greater mRC and CRC than TUN.

Footnotes

† Rstudio Version 1.1.383, RStudio, Inc., Massachusetts, USA

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Figures and tables

Figure 1. PRISMA flowchart

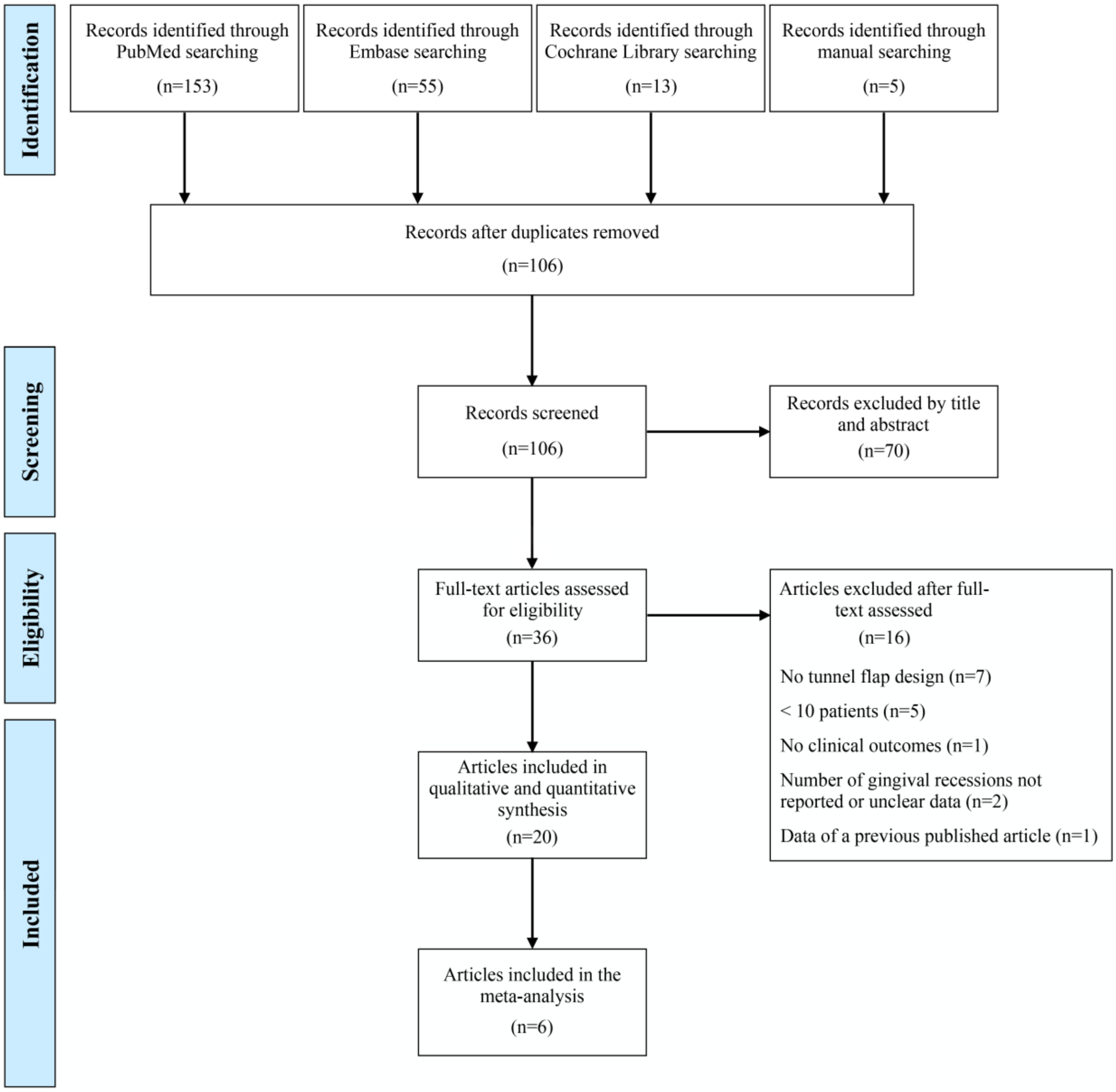

Figure 2. Meta-analysis comparing TUN and CAF in terms of: A) mRC, B) CRC, C) KT gain and D) RES; E) Sub-analysis comparing CRC of TUN + CTG and CAF + CTG; F) Sub-analysis comparing mRC of TUN + ADM and CAF + ADM; G) Sub-analysis comparing CRC of TUN + ADM and CAF + ADM; H) Sub-analysis comparing KT gain of TUN + ADM and CAF + ADM

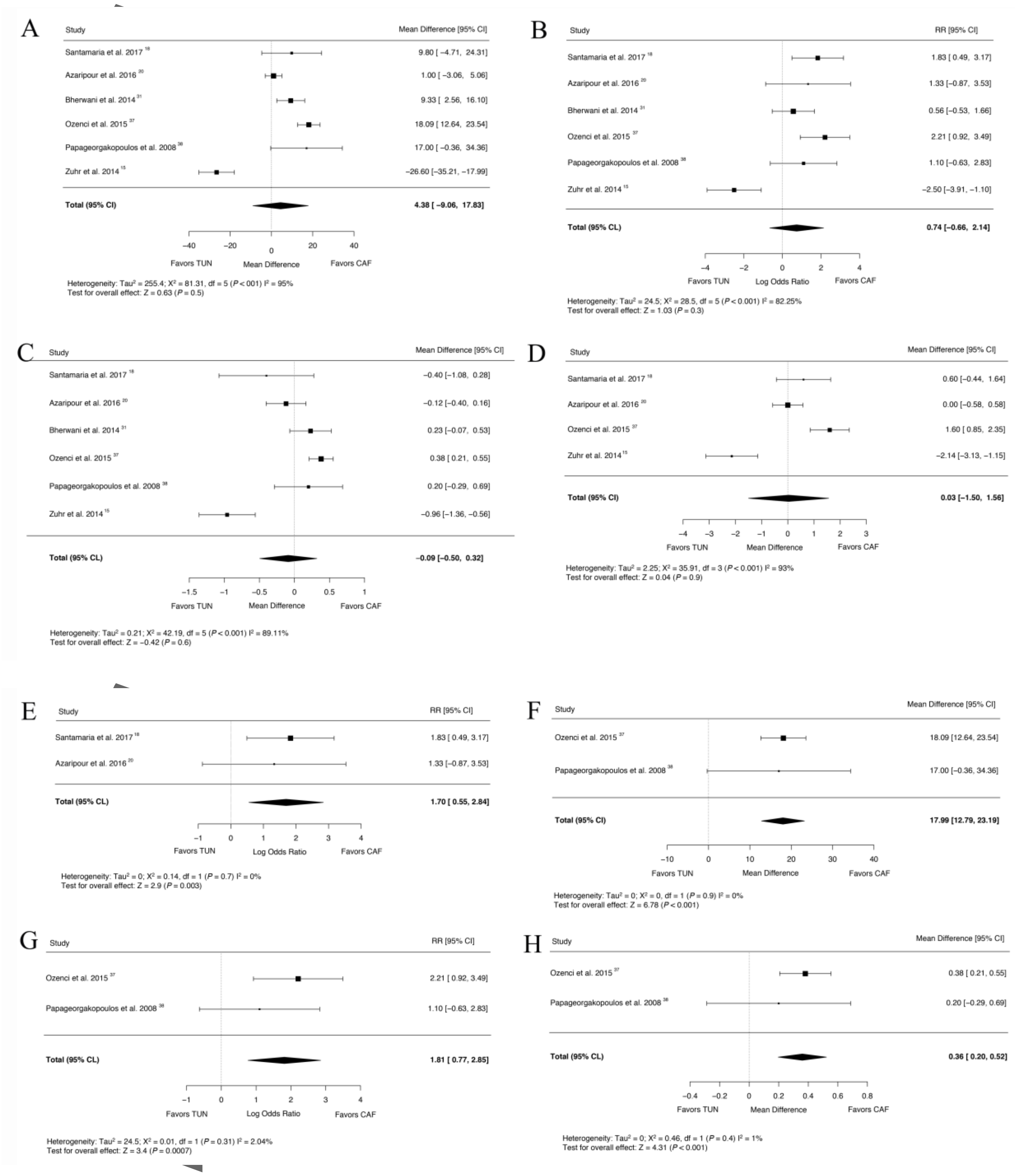

Table 1. General overview of the included studies

Table 2. General characteristics of the intervention and results

Table 3. Mean root coverage and complete root coverage according to the type, location and Miller class of gingival recession.

Table 4. General characteristics and outcomes of the studies included in the meta-analysis

Supporting data

Data S1. Electronic search strategy

Data S2. Hand-searched journals and references of the previous systematic reviews screened for articles identification

Data S3. Bias assessment scales and related parameters for the evaluation of risk of bias

Data S4. Characteristics and references of the excluded articles

Data S5. Bias risk assessment for the included RCTs using The Cochrane Risk of Bias Tool for Randomized Controlled Trials

Data S6. Bias risk assessment for the included case series using The Joanna Briggs Institute Scale for Case Series

Data S7. Funnel plots assessing the potential publication bias among the included studies in terms of: A) mRC, B) CRC, C) KT gain and D) RES

Data S8. Sub-analyses comparing TUN + CTG and CAF + CTG in terms of mRC (A), KT gain (B), RES (C)

Table 1. General overview of the included studies

Study	Study design, follow-up	Mean Age, Patients and Recessions (N)	Periodontal status and smoking habits	Recession type	Location	Site, setting and funding
Dembowska & Drozdzik 2007 [35]	Case series, 12 months	Patients n = 18 Recessions n = 48	Healthy, non-smoking patients	Multiple GRs Miller Class I and II	NR	Poland, University, NR
Papageorgakopoulos et al., 2008 [38]	RCT, 4 months	Patients n = 24 Recessions n = 24	Healthy, non-smoking patients FMPS < 20%	Single GRs Miller Class I and II Recession ≥ 3mm	Maxilla & Mandible (incisor, canine, premolar)	United States, University, partially supported by a company
Shepherd et al., 2009 [40]	RCT, 4 months	Patients n = 18 Recessions n = 18	Healthy, non-smoking patients FMPS < 20%	Single GRs Miller Class I or II Recession ≥ 3mm	Maxilla & Mandible (incisor, canine, premolar)	United States, University, partially supported by a company

Aroca et al., 2010 [17]	RCT, split-mouth, 12 months	Patients n = 20 Recession: n = 139	Healthy, non-smoking patients FMPS < 20%	Multiple GRs Miller Class III Recession ≥ 3mm	Maxilla & Mandible (incisor, canine, premolar, molar)	Hungary, University, self-supported
Aroca et al., 2013 [14]	RCT, split-mouth, 12 months	Patients n = 22 Recessions n = 156	Healthy or treated, non-smoking patients FMPS < 25%	Multiple GRs (Miller Class I and II)	Maxilla & Mandible (incisor, canine, premolar, molar)	Hungary, University, partially supported by a company
Bherwani et al., 2014 [31]	RCT, 6 months	Patients n = 20 Recessions n = 75	Healthy, non-smoking patients	Multiple GRs Miller Class I and II	Maxilla	India, University, NR
Sculean et al., 2014 [39]	Case series, 12 months	Patients n = 16 Recessions n = 16	Healthy, non-smoking patients FMPS < 25% FMBS < 25%	Single mandibular GRs Miller Class I and II Recession ≥ 3mm	Mandible (incisor, canine)	Switzerland, NR

Zuhr et al., 2014 [15]	RCT, 12 months	Patients n = 23 Recessions n = 45	Healthy, non-smoking patients FMPS < 25% FMBS < 25%	Single and multiple GRs Miller Class I and II Recession < 5 mm	Maxilla (incisor, canine, premolar)	Germany, Private practice, self-supported
Chaparro et al., 2015 [32]	Case series, 12 months	Patients n = 24 Recessions N = 93	Healthy, non-smoking patients FMPS < 20%	Multiple GRs Miller Class I and II Recession ≥ 3mm	Maxilla & Mandible (incisor, canine, premolar)	Chile, Private practice, NR
Ozenci et al., 2015 [37]	RCT, 12 months	Patients n = 20 Recessions n = 58	Healthy, non-smoking patients	Multiple GRs Miller Class I Recession ≥ 3mm	Maxilla & Mandible (incisor, canine, premolar)	Turkey, University, self-supported
Vincent-Bugnas et al., 2015 [43]	Case Series, 24 months	Patients n = 14 Recessions n = 26	Healthy, non-smoking patients	Single and multiple GRs Miller Class I	Maxilla & Mandible (incisor, canine, premolar)	France, University, self-supported
Azaripour et al., 2016 [20]	RCT, split-mouth, 12 months	Patients n = 40 Recessions n = 71	Healthy or treated, non-smoking patients FMPS < 15% FMBS < 15%	Single and Multiple GRs Miller Class I and II Recession ≥ 1 mm and < 6 mm	Maxilla & Mandible (incisor, canine, premolar, molar)	Germany, University, self-supported

Bednarz et al., 2016 [60]	RCT, 6 months	Patients n = 30 Recessions n = 97	Healthy, non-smoking patients	Multiple GRs Miller Class I and II Recession ≥ 2 mm	Maxilla & Mandible (incisor, canine, premolar, molar)	Poland, University, self-supported
Cieslik-Wegemund et al., 2016 [33]	RCT, 6 months	Patients n = 28 Recession n = 106	Healthy or treated, non-smoking patients	Multiple GRs Miller Class I and II	Maxilla & Mandible (incisor, canine, premolar, molar)	Poland, University, self-supported
Cosgarea et al., 2016 [34]	Case series, 12 months	Patients n = 12 Recessions n = 54	Healthy, non-smoking patients FMPS < 25%	Multiple GRs Miller Class I, II and III Recession ≥ 2 mm	Maxilla & Mandible (incisor, canine, premolar)	Romania, University, partially supported by a company
Nart and Valles, 2016 [36]	Case series, Mean of 20.53 months of follow-up	Patients n = 15 Recessions n = 15	Healthy or treated, non-smoking patients	Single GRs Miller Class II and III Recession ≥ 2 mm	Mandible (incisor)	Spain, Private practice, self-supported
Sculean et al., 2016 [16]	Case series, 12 months	Patients n = 12 Recessions n = 54	Healthy, non-smoking patients FMPS < 25% FMBS < 25%	Multiple maxillary GRs Miller Class I, II and III Recession ≥ 3mm	Maxilla (incisor, canine, premolar)	Switzerland, NR

Thalmair et al., 2016 [41]	Case series, 6 months	Patients n = 20 Recessions n = 63	Healthy, non-smoking patients FMPS < 25% FMBS < 25%	Multiple mandible GRs Miller Class I and II Recession ≥ 2 mm	Mandible (incisor, canine, premolar)	Germany, Private practice, self-supported
Santamaria et al., 2017 [18]	RCT, Parallel arm, 6 months	Patients n = 42 Recessions n = 42	Healthy, non-smoking patients FMPS < 20% FMBS < 20%	Single GRs Miller Class I and II	Maxilla (canine, premolar)	Brazil, University, supported by the government
Vincent-Bugnas et al., 2017 [42]	Case Series, 12 months	Patients n = 12 Recessions n = 100	Healthy, non-smoking patients	Multiple maxillary GRs Miller Class I and II Recession ≥ 2 mm	Maxilla (incisor, canine, premolar, molar)	France, NR

Note. FMPS: Full Mouth Plaque Score. FMBS: Full Mouth Bleeding Score. NR: not reported.

Table 2. General characteristics of the intervention and results

Study	Preoperative preparation	Treatment in the control group	Treatment in the test group	Post-surgical treatment	Suture removal	Follow-up (months)	mRC ± SD (%)	Authors conclusion
Dembowska & Drozdzik 2007 [35]	OH assessment	TUN + CTG	/	No brushing for 2 weeks, 0.12% CHX	After 1 week	12	99.1 ± NA (Miller I) 98.9 ± NA (Miller II)	TUN + CTG significant root coverage and KT gain
Papageorgakopoulos et al., 2008 [38]	OHI and prophylaxis	CPF + ADM	CPT + ADM	Atb, NSAIDs (or in alternative other painkillers), 012% CHX	After 3 or 4 weeks	4	99 ± 3 (control) 95 ± 7 (test)	Better outcomes for CPF than CPT
Shepherd et al., 2009 [40]	OHI and prophylaxis	CPT + ADM	CPT + PRP +ADM	Atb, NSAIDs (or in alternative other painkillers), 012% CHX	After 2 or 3 weeks	4	92 ± 7 (control) 97 ± 5 (test)	Better outcomes for CPT + ADM + PRP than CPT + ADM
Aroca et al., 2010 [17]	OHI + full mouth supragingival scaling and polishing 1 month before surgery	mTUN + CTG	mTUN + CTG + EMD	Atb and NSAIDs, no brushing for 2 weeks, 0.12% CHX. Follow-up and prophylaxis at 28 days, 3, 6 and 12 months	After 2 weeks	12	83 ± 26 (control) 82 ± 25 (test)	mTUN is effective for Miller class III GRs. EMD does not enhance the outcomes

Aroca et al., 2013 [14]	OHI + full mouth supragingival scaling and polishing 1 month before surgery	MCAT + CTG	MCAT + XCM	Atb and NSAIDs, no brushing for 2 weeks, 0.12% CHX. Follow-up and prophylaxis at 28 days, 3, 6 and 12 months	After 2 weeks	12	90 ± 18 (control) 71 ± 21 (test)	XCM may be considered an alternative to CTG, however MCAT + CTG was better than MCAT + XCM
Bherwani et al., 2014 [31]	OHI and prophylaxis	TUN + CTG	CAF + CTG	Atb and analgesics. 0.2 % CHX. Follow-up and prophylaxis at 1, 3, 5 weeks after suture removal and every 3 months	After 2 weeks	6	80 ± 15.39 (control) 89.33 ± 14.47 (test)	CAF more effective than TUN
Sculean et al., 2014 [39]	OHI and prophylaxis	MCAT + CTG + EMD	/	Atb for 7 days and NSAID for 2/3 days, no brushing for 2 weeks. 0.1% CHX for 3 weeks. Follow-up and prophylaxis after suture removal at 1, 3 6, and 12 months post-operatively	After 2 or 3 weeks	12	96.25 ± NA	MCAT is a predictable approach for localized GRs

Zuhr et al., 2014 [15]	OHI and prophylaxis	CAF + EMD	TUN + CTG	NSAID, no brushing for 2 weeks, CHX for 2 weeks. Follow-up and prophylaxis at 1, 3, 6 and 12 months post-operatively.	After 7 days	12	71.8 ± 20.3 (control) 98.4 ± 3.6 (test)	TUN better clinical outcomes than CAF
Chaparro et al., 2015 [32]	NR	TUN + ADM	/	No brushing for 8 weeks, 0.12 % CHX for 8 weeks	After 6 weeks	12	91.8 ± NA (maxilla) 89.1 ± NA (mandible)	No significant differences between mandible and maxilla; better CRC for Miller class I than Miller class II
Ozenci et al., 2015 [37]	OHI and prophylaxis. Re-evaluation at 8 weeks	CAF + ADM	TUN + ADM	Atb, NSAIDs, No brushing for 2 weeks, 0.2% CHX. Follow-up and prophylaxis once in a month until the 12-months evaluation.	After 2 weeks	12	93.8 ± 13 (control) 75.7 ± 6.5 (test)	Both the two techniques are effective. Better results for CAF + ADM than
Vincent-Bugnas et al., 2015 [43]	OH assessment	mTUN + EMD	/	NSAIDs, no brushing for 2 weeks, 0.12% CHX. Follow-up and prophylaxis at 3, 6, 12 and 24 months post-operatively	After 2 weeks	24	91.59 ± 11.17 (maxilla) 85.71 ± 16.5 (mandible)	mTUN + EMD is an effective technique for root coverage

Azaripour et al., 2016 [20]	OHI and prophylaxis	CAF + CTG	MMTT + CTG	NSAIS, 0.12% CHX, no brushing for 4 weeks. Follow-up and prophylaxis at 3, 6, and 12 months post-operatively	After 2 weeks	6	98.3 ± 9.2 (control) 97.3 ± 7.6 (test)	CAF and MMTT are equally successful in root coverage
Bednarz et al., 2016 [60]	NR	MCAT + CTG	MCAT + FL	Atb and analgesics	After 2 weeks	6	95.77 ± 0.11 (control) 94.21 ± 0.2 (test)	FL allograft is a viable alternative to CTG for root coverage procedure based on TUN
Cieslik-Wegemund et al., 2016 [33]	OHI and prophylaxis	TUN + CTG	TUN + XCM	Atb (only in the test group), 0.12% CHX, no brushing for 2 weeks	After 2 weeks	6	95 ± 11 (control) 91 ± 13 (test)	TUN + XCM achieved satisfactory results but lower than TUN + CTG
Cosgarea et al., 2016 [34]	OHI and prophylaxis	MCAT + XCM	/	Atb, NSAIDs, no brushing for 2 weeks, 0.2% CHX	After 3 weeks	12	73.2 ± 27.71	MCAT + XCM is a successful technique for Miller I, II and III GRs
Nart and Valles, 2016 [36]	OHI and prophylaxis	TUN + CTG	/	Atb, NSAISs, corticosteroids, 0.12% CHX, no brushing for 15 days, no flossing for 3 weeks	After 15 days	20.53 ± 8.89	90.92 ± 13.53 (Miller II) 74.49 ± 11.86 (Miller III)	TUN + CTG is an effective technique for mandibular incisors with Miller class II and III GRs

Sculean et al., 2016 [16]	OHI and prophylaxis	MCAT + CTG + EMD	/	Atb, NSAIDs, no brushing for 2 weeks, 0.1% CHX Follow-up and prophylaxis after suture removal at 1, 3 6, and 12 months post-operatively	After 14-21 days	12	96 ± NA	MCAT + CTG + EMD is a predictable treatment for treatment Miller class I, II and III GRs
Thalmair et al., 2016 [41]	NR	MMTT + CTG	/	NSAIDs, 0.2% CHX, no brushing for 2 weeks	After 1 week	6	93.87 ± NA	MMTT + CTG is effective in root coverage and in KT gain
Santamaria et al., 2017 [18]	OHI and prophylaxis	CAF + CTG	TUN + CTG	NSAIDs, 0.12% CHX, no brushing for 2 weeks. Follow-up and prophylaxis every 3 months	After 1 week	6	87.2 ± 27.1 (control) 77.4 ± 20.4 (test)	CAF + CTG was more effective than TUN + CTG
Vincent-Bugnas et al., 2017 [42]	OHI and prophylaxis	MCAT + XCM	/	Atb, analgesics, 0.2% CHX, no brushing for 2 weeks	After 2 weeks	12	84.35 ± 7.53	MCAT + XCM is a viable treatment for Miller class I and II GRs

__Note.__ NR: Not Reported. OHI: Oral Hygiene Instruction. OH: Oral Hygiene. mTUN: modified Tunnel technique. CPF: Coronally Positioned Flap. CPT: Coronally Positioned Tunnel. MCAT: Modified Coronally Advanced Tunnel. MMTT: Modified Microsurgical Tunnel Technique. NSAID: Non-Steroidal Anti-Inflammatory Drugs. Atb: Antibiotic. CHX: Chlorhexidine. SD: Standard Deviation.

Table 3. Mean root coverage and complete root coverage according to the type, location and Miller class of gingival recession.

	mRC ± SD (%)	CRC (%)
Localized GRs*	82.75 ± 19.7	47.15
Multiple GRs*	87.87 ± 16.45	57.46
Localized maxillary GRs*	83.08 ± 17.94	43.78
Multiple maxillary GRs*	88.63 ± 7.08	56.7
Multiple maxillary GRs (Miller I and II)	87.48 ± 8.57	58.24
Localized mandibular GRs*	82.54 ± 21.22	50
Localized mandibular GRs (Miller I and II)	84.58 ± 19.11	55.81
Multiple mandibular GRs*	85.88 ± 27.77	61.35
Multiple mandibular GRs (Miller I and II)	88.85 ± 12.38	66.36
Miller I & II localized GRs	84.58 ± 19.11	50.8
Miller I & II multiple GRs	89.16 ± 12.38	61.88
Miller III GRs	82.11 ± 25.02	37.84

Note. SD: Standard Deviation

* Miller class I, II and III are considered

Table 4. General characteristics and outcomes of the studies included in the meta-analysis.

Article	Group	CTG or substitutes	Patients (N)	Number of Recessions	Follow-up (months)	mRC ± SD (%)	CRC (%)	KT gain ± SD (mm)	RES score
Azaripour et al. 2016 [20]	CAF	CTG	20	29	12	98.3 ± 9.2	96.6	0.36 ± 0.6	9.3 ± 1.3
Bherwani et al. 2014 [31]	CAF	/	10	39	6	89.3 ±14.5	82.5	0.57 ± 0.5	NR
Ozenci et al. 2015 [37]	CAF	ADM	10	27	12	93.8 ± 13.1	85	1.25 ± 0.24	8.9 ± 1.6
Papageorgakopoulos et al. 2008 [38]	CAF	ADM	12	12	4	95 ± 10	75	0.8 ± 0.7	NR
Santamaria et al. 2017 [18]	CAF	CTG	21	21	6	87.2 ± 27.1	71.4	1 ± 0.9	8.4 ± 1.5
Zuhr et al. 2014 [15]	CAF	EMD	14	22	12	71.8 ± 20.3	21.4	-0.34 ± 0.51	6.92 ± 2.32
Azaripour et al. 2016 [20]	TUN	CTG	20	42	12	97.3 ± 7.6	88.1	0.48 ± 0.6	9.3 ± 1.1
Bherwani et al. 2014 [31]	TUN	CTG	10	36	6	80 ± 15.4	71.4	0.34 ± 0.77	NR
Ozenci et al. 2015 [37]	TUN	ADM	10	31	12	75.7 ± 6.5	37.4	0.87 ± 0.42	7.3 ± 1.25
Papageorgakopoul	TUN	ADM	12	12	4	78 ±	50	0.6 ±	NR

os et al. 2008 [38]						29		0.5	
Santamaria et al. 2017 [18]	TUN	CTG	21	21	6	77.4 ± 20.4	28.6	1.4 ± 1.3	7.8 ± 1.9
Zuhr et al. 2014 [15]	TUN	CTG	14	23	12	98.4 ± 3.6	78.6	0.62 ± 0.83	9.06 ± 0.83

<u>Note.</u> SD: Standard Deviation. NR: Not Reported.