ACTA ODONTOLOGICA SCANDINAVICA
2021, VOL. 79, NO. 8, 562–572
https://doi.org/10.1080/00016357.2021.1908594

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REVIEW ARTICLE

Efficacy of modified coronally advanced flap in the treatment of multiple adjacent gingival recessions: a systematic review and meta-analysis

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ABSTRACT

Objective: This systematic review (SR) aims to evaluate the efficacy of modified coronally advanced flap (mCAF) on clinical and patient-reported outcomes in the treatment of multiple adjacent gingival recessions (MAGRs).

Materials and methods: Randomized controlled trials (RCTs), case-series and prospective clinical studies on treatment of Miller class I/II or RT1 MAGRs with $\geq$ 6 months follow-up were identified from the electronic databases and hand-searched journals. Complete root coverage (CRC) was the primary outcome variable. To evaluate treatment effects, meta-analysis was conducted, wherever appropriate.

Results: A total of 1395 recessions in 408 patients were evaluated in SR and meta-analysis was performed for four RCTs. Overall CRC achieved with mCAF was 70% and mean root coverage (MRC) ranged from 51.58 to 97.27%. Meta-analysis showed that combination of mCAF with connective tissue graft (CTG) or collagen matrix (CM) demonstrated significantly higher CRC% and recession reduction than mCAF alone. Limited evidence is available to support the use of platelet rich fibrin or enamel matrix derivative or acellular dermal matrix graft along with mCAF to further enhance its efficacy.

Conclusions: mCAF is an effective procedure for treating MAGRs and in terms of achieving CRC and MRC. Additional use of CTG or CM further enhances treatment outcomes.

ARTICLE HISTORY
Received 4 November 2020
Revised 22 February 2021
Accepted 19 March 2021

KEYWORDS
Coronally advanced flap; meta-analysis; multiple gingival recessions; systematic review; root coverage

Introduction

Gingival recession (GR) results in exposure of root surface due to displacement of gingival margin apical to cementoenamel junction [1]. If left untreated, buccal GRs progress to further increase in recession depth leading to worsened aesthetics, increased dentinal hypersensitivity, risk of loss of root structure (cervical root caries or abrasions) and poor plaque control [2]. Over the years, several surgical techniques and their modifications have evolved for the treatment of single and multiple recessions [3–14].

Successful complete root coverage (CRC) can be obtained following treatment of isolated GRs; however, predictable coverage of multiple GRs is often more challenging for the clinician due to the factor such as large avascular recipient bed, root prominence, shallow vestibule, unevenness in recession depths and residual keratinized tissue width of affected teeth [15,16]. Moreover, selection of surgical approach for simultaneous treatment of all the affected teeth and thereby reducing the number of surgeries should also be considered.

Among the various surgical techniques, conventional coronally advanced flap (CAF) is considered as a reliable surgical approach for treatment of GRs [17]. However, placement of vertical releasing incisions may disrupt the vascularity of the flap or negatively influence the aesthetic outcome due to keloid/scar formation. In order to overcome these disadvantages, Zucchelli and De Sanctis proposed a modification of CAF, i.e. modified CAF (mCAF) by eliminating the vertical releasing incisions [9]. This envelope type of flap with submarginal oblique incisions in papillary area anticipates the rotational movement of surgical papilla during coronal advancement. Improved clinical outcomes have been reported invariably with additional use of connective tissue graft (CTG) [18]; however, its inherent disadvantages of limited availability and donor site morbidity further warrants the exploration of other biomaterials such as acellular dermal matrix, xenogenic collagen matrices, barrier membranes, platelet rich fibrin and living tissue engineered human fibroblast derived dermal substitute as an adjunct to flap alone root coverage procedures.

Previous systematic reviews (SRs) evaluating the efficacy of periodontal plastic surgical procedures for treating multiple adjacent GRs have elucidated variability in surgical techniques and heterogeneity in data which further precluded

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Supplemental data for this article can be accessed here.

the conclusion of best technique available for treating such defects [15,19–21]. A recent Cochrane review by Chambrone et al. [21] included studies that had utilized two different types of CAF designs, thereby attenuating the effect of different flap design on treatment outcomes. Thus, there is a need to systematically review the available technique and to evaluate the treatment outcomes in order to provide evidence-based decision on its routine use.

In context to the evaluation of efficacy of a single surgical approach, tunnel procedures were found to be effective for treatment of multiple GRs in a recent SR [22]. Although the treatment of multiple adjacent GRs with mCAF has been extensively reported, no study has investigated its overall efficacy for root coverage and other treatment outcomes. Therefore, the purpose of this SR was to determine the efficacy of mCAF for the treatment of multiple adjacent GRs and to compare the outcomes of mCAF alone or in conjunction with some additives.

Materials and methods

Protocol development and study registration

A detailed protocol was developed following the guidelines of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [23,24], the Cochrane Handbook [25] and Assessment of Multiple Systematic Reviews (AMSTAR) checklist [26].

The review protocol was registered in the PROSPERO (CRD42018100362) International Prospective Register of Systematic Reviews hosted by the National Institute for Health Research, University of York, Centre for Reviews and Dissemination.

Focussed question

What is the efficacy of mCAF in terms of clinical and patient-reported outcomes for the treatment of multiple GRs?

Eligibility criteria of studies selection

Randomized controlled trials (RCTs), prospective clinical studies, case control studies and case series published in English language with at least 10 subjects and a minimum follow-up period of 6 months were included in this SR. Case reports, cross-sectional studies and retrospective studies were excluded.

Inclusion of the studies based on above mentioned criteria was done by PICO method as follows.

(P) Types of participants

Patients with a clinical diagnosis of multiple adjacent buccal recessions of $\geq$2 mm mean depth without interdental attachment loss, i.e. Miller class I (marginal tissue recession not extending up-to mucogingival junction and there is no loss of interproximal bone or soft tissue) and II (marginal tissue recession extending to or beyond mucogingival junction and there is no loss of interproximal bone or soft tissue) [27] or RT1 defects (GR with no loss of interproximal attachment) [28].

(I) Type of interventions

Root coverage procedures utilizing mCAF for the treatment of multiple recessions were considered. Irrespective of the different nomenclature used, surgical approaches utilizing envelope flap design (without vertical incisions) with oblique submarginal papillary incisions and positioned coronally to completely cover the recession defects were considered as mCAF and thus, were eligible to be included. Studies reporting mCAF with one or more vertical incisions and treatment of both single and multiple recessions were excluded.

(C) Comparison between interventions

Studies comparing mCAF with conventional CAF (with vertical incisions), other techniques (tunnel or its variants, i.e. coronally advanced tunnel, vestibular incision subperiosteal tunnel access (VISTA), pinhole technique) and its combination with additives such as CTG, acellular dermal matrix graft (ADMG), enamel matrix derivative (EMD), xenogenic collagen matrix (CM), barrier membrane or any other; were investigated. Meta-analysis was done when more than one RCT of similar surgical treatment was found.

(O) Types of outcome measures

The primary outcome measure was the percentage of CRC. Secondary outcome variables were mean root coverage (MRC), recession reduction (RecRed: mm), clinical attachment level gain (ΔCAL: mm), gain in keratinized tissue width (ΔKTW: mm), change in gingival thickness (ΔGT: mm) and changes in probing depth (ΔPD: mm). Qualitative aesthetic (patient's aesthetic satisfaction) and patient-centred outcomes (root hypersensitivity, postoperative pain and complications) were also analysed. Studies with insufficient data and those with missing primary outcome were excluded.

Information sources and screening process

A comprehensive search was done for the identification of studies published before July 2020 by two independent reviewers (AB and VSY) using a priori customized search strategy for each database. Electronic searches were performed in MEDLINE (PubMed), Excerpta Medical Database by Elsevier (EMBASE), Cochrane Central Register of Controlled trials (CENTRAL) in the Cochrane Library using a combination of MeSH terms and free text words for each database (Supplementary data S1). Further, Grey Literature Report and OpenGrey databases were searched for unpublished data.

Manual search in relevant journals, reference list of consensus reports, position papers and previous SRs was thoroughly conducted for articles identification (Supplementary data S2).

Study selection and data extraction

Titles, abstracts and keywords of all the retrieved citations were screened by two independent calibrated authors (AB, VSY). Abstracts were excluded if the aforementioned inclusion criteria were not fulfilled. However, abstracts with unclear information or where only title was available, were subjected to full text analysis to avoid exclusion of potentially relevant studies. Full text reading of selected publications was then carried out independently for eligibility assessment by the same two authors and those fulfilling the inclusion criteria were included in present SR. Cohen's kappa (κ) test was used to evaluate the search agreement between two authors. At each stage, disagreement between the authors was resolved through discussion. If a consensus could not be reached, decision of third author (RKS) was decisive. Whenever necessary, the corresponding authors of the pertinent studies were contacted via email to obtain any missing or unpublished data.

Data extraction was done independently and in duplicate by two authors (AB and VSY) using a data extraction sheet, pilot tested in five studies. These sheets included the information regarding (A) study characteristics, (B) subjects characteristics, (C) primary and secondary outcomes variables and (D) aesthetic and patient-centred outcomes. Data thus collected was then filled into electronically generated table templates.

When articles of same study population were published at different follow-up durations, article with longest follow-up duration was selected. Similarly, when the results at different follow-up periods were provided in the same article, results of longest follow-up period were considered for data interpretation.

Methodological quality assessment and assessment of risk of bias

Methodological quality of included RCTs was evaluated according to the Cochrane Collaboration's Tool for Assessing Risk of Bias as described in the Cochrane Handbook of Systematic Reviews of Interventions [25]. Two authors (AB and NT) independently performed the quality assessment of each included trial. Interexaminer agreement was assessed using kappa coefficient.

To assess the risk of bias of case-series, Joanna Briggs Institute Critical Appraisal Checklist for Case Series [29] was used.

Statistical analysis/summary measures and synthesis of results

Dichotomous data, i.e. CRC (%) were expressed as odds ratio and 95% confidence intervals (CIs). Continuous data: MRC, RecRed, ΔKTW, ΔGT, ΔPD and ΔCAL were expressed as weighted mean difference (MD) and 95%CI. In studies, wherever the standard deviation (SD) of MD was not given, square root of sum of variance was used to calculate SD of the difference. Statistical heterogeneity in estimates of treatment effects between different studies was assessed by Chi-square test and I^2 statistic. I^2 value of 30–60% denotes moderate heterogeneity whereas 50–90% implies substantial heterogeneity. Fixed effect analysis model was used to pool the results from various studies. Random-effect analysis model was applied when notable heterogeneity was observed between the studies. Unit of statistical analysis was the recession site. Data were analysed using statistical software program (RevMan software, version 5.0, The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark). p Value less than .05 was considered as significant for analysis. Data that could not be analysed quantitatively were described descriptively.

Results

Study selection

The details of search results and screening process on the basis of PRISMA guidelines are shown in Figure 1. A total of 783 records were found from electronic and manual searches. After removal of duplicates and initial screening of titles and abstracts, a total of 71 studies were thereof selected for full text evaluation. Finally, 18 studies were included in this SR [9,30–46]. Details of included studies are provided in Supplementary data S4 (Tables 1–3). Among these, four RCTs [36–38,45] were subjected to meta-analysis. Fifty-three articles were excluded and the reasons for their exclusion are provided in Supplementary data S5.

Kappa score for inter-reviewer agreement was 0.83 for potential article inclusion (titles and abstracts) and 0.87 for selected studies (full-text articles). Details of missing information and the unpublished data were provided only by one author [39].

Study characteristics

Study design and study population

Thirteen articles were RCTs [33–45], one was prospective clinical trial [46] and four were case series [9,30–32]. Eight RCTs employed parallel groups design [33,35–38,42,44,45] whereas other five used a split-mouth study design [34,39–41,43]. Overall, 408 subjects with an age range of 18–60 years were treated in selected studies. All the studies reported data about smoking status. Nine studies included recession in maxilla only [30,33,35,37,38,41,42,44,45] whereas six articles reported recession defects in both maxilla and mandible [31,32,34,40,43,46]. Two studies did not mention about the location of recession [36,39]. Treated teeth were mainly incisors, canines and premolars (I-C-PM). Molars were treated in addition to I-C-PM in seven studies [31,32,34,35,38,45,46]. Follow-up duration varied from 6 months in eight studies [31,34,35,39–43] to 12 months in six studies [32,33,36,38,44,45], 18 months in one study [43] and 5 years in two studies [30,37]. Fourteen studies were conducted in university setting [30–32,34,35,37–44,46], one study in both university and private practice [33] and one study in private setting [45]. Sixteen trials were single centre studies and one

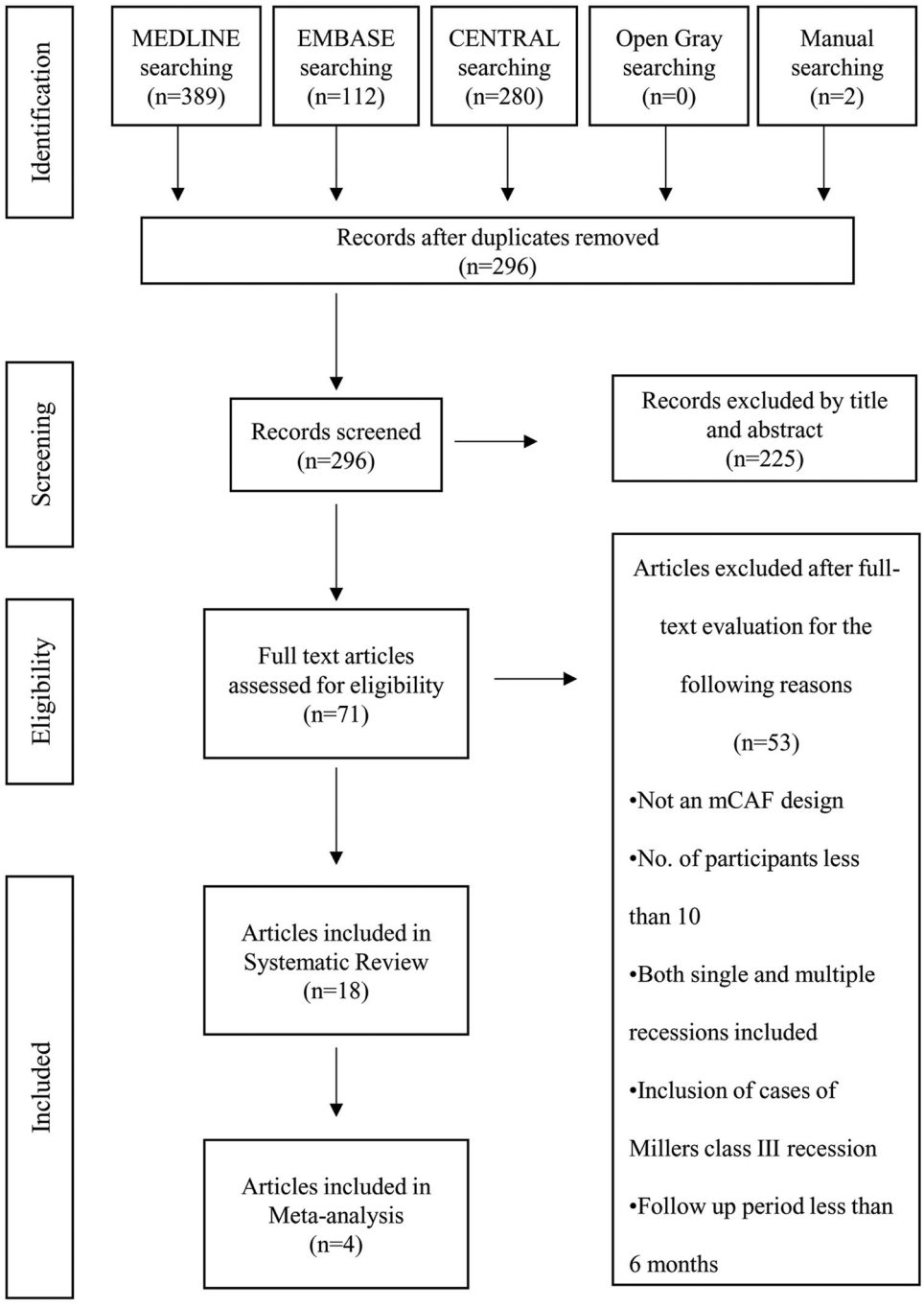

Figure 1. PRISMA flowchart for selection process.

reported as multicentre trial. Five studies were reported as self-supported [35,37,38,44,46] and one had an institutional grant [32] and one was partially funded by a private industry [45] whereas rest of the studies did not report about any financial support. General characteristics of the included studies are shown in Table 1 (Supplementary data S4).

Types of interventions

A multitude of interventions were performed in various studies. These comprised of mCAF versus CAF; versus tunnel technique + CTG; versus a combination of mCAF with CTG, CM, PRF; versus variation of suspended sutures using buttons application. Also, in some trials, mCAF + CTG were compared with mCAF + EMD or ADMG.

Risk of bias assessment

Results of the risk of bias for the included RCTs are shown in supplementary data S3. Five trials [33,35,37,38,45] had a low risk of bias, five [36,41–44] were considered to have moderate risk of bias and three trials [34,39,40] were judged to be at high risk of bias.

Bias risk assessment for case series yielded two studies [31,32] with low risk of bias and two studies [9,30] with moderate risk of bias (Supplementary Data file S3).

Effects of intervention

A total of 1395 recession defects (1149 in RCTs and 201 in case series and 45 in prospective study) in 408 participants from 17 studies were included in this SR. Zucchelli and De Sanctis [30] presented long-term outcomes of its previous study [9] thus, numbers of recessions were considered from the study with long-term follow-up. Overall CRC achieved with mCAF for multiple recession defects was 70% (range: 47–89.3%). MRC obtained with mCAF ranged from 51.58 to 97.27%. mCAF along with CTG yielded CRC in the range of 55.6–93.10%. Also, MRC for mCAF + CTG was reported to be higher, i.e. in the range of 79.7–97.14%.

mCAF versus CAF

When considering mCAF and CAF, both the interventions resulted in comparable CRC%, RecRed and gain in CAL; however, mCAF group showed better post-operative course as well as aesthetic outcome [33]. Also, gain in KTW was found to be greater in mCAF group. Results obtained in Ahmedbeyli et al.'s study [44] yielded greater CRC, MRC, RecRed and gain in KTW in mCAF + ADMG group as compared to CAF + ADMG group. Patient satisfaction and aesthetic score were also higher in mCAF group in this study. This is in contrast to the results obtained in Skurska et al.'s study [32] where there was no difference in outcomes between CAF + CTG and mCAF + CTG groups.

mCAF versus mCAF + CTG

Two studies [37,38] were included in this meta-analysis. Overall meta-analysis showed that mCAF + CTG had significantly higher percentage of CRC (odds ratio: 3.75; 95%CI: 1.84, 7.65; p=.0003) (Figure 2(a)) and mean recession reduction (MD: 0.42; 95%CI: 0.14, 0.69; p=.003) (Figure 2(c)).

For gain in KTW and ΔCAL, there was insignificant difference between two groups (MD: 0.87; 95%CI: −0.12, 1.86; p=.08 and MD: −0.15; 95%CI: −0.62, 0.32; p=.53) (Figure 2(b,e)). Only one study [37] was included for reduction in PD, where mCAF group revealed better PD reduction (MD: −0.09; 95%CI: 0.15, −0.03; p=.006) (Figure 2(d)).

Significant heterogeneity was detected for recession reduction (χ^2=2.68, df = 1, p=.10 and I^2=63%) (Figure 2(c)), changes in width of keratinized tissue (χ^2=18.57, df = 1, p=.0001 and I^2=95%) (Figure 2(b)) and reduction in CAL (χ^2=12.20, df = 1, p=.0005 and I^2=92%) (Figure 2(e)).

Due to heterogeneity of criteria and methods used to evaluate post-operative discomfort and morbidity as well as patient's aesthetic satisfaction, formal pooling of the data for meta-analysis was not carried out for these two parameters.

Postoperative morbidity for both the groups in Zucchelli et al.'s study [37] was limited and statistically significant better post-operative course was seen in mCAF group as evaluated by visual analogue scale (VAS) score. Likewise, Cairo et al. [38] showed that patients allocated to mCAF + CTG group had experienced significantly higher post-operative discomfort (VAS score 44.0 ± 9.3 in mCAF + CTG group versus 28.9 ± 7.0 in mCAF group, p<.0001).

Patient's aesthetic satisfaction in Zucchelli et al.'s study [37] revealed that both the groups showed high aesthetic satisfaction based on VAS. Better colour match scores (both 1 year and 5 years) were obtained in mCAF group. Contour assessment score at 5 year evaluation was better for mCAF + CTG group. However, greater keloids formation was seen in mCAF + CTG group.

Cairo et al. [38] showed that mCAF group is associated with better aesthetics as evaluated by root coverage esthetic score (RES) score at sites with thick periodontal biotype.

mCAF versus mCAF + CM

Out of three studies, two trials [36,45] were included for this meta-analysis. mCAF + CM group showed greater CRC (odds ratio: 2.22; 95%CI: 1.19, 4.12; p=.01) (Figure 3(a)) and MRC (MD: 11.81; 95%CI: 5.86, 17.77; p=.0001) (Figure 3(b)), and ΔGT (MD: 0.71; 95%CI: 0.35, 1.07; p=.0001) (Figure 3(d)). However, recession reduction, gain in KTW and reduction in PD and CAL did not show any significant difference between two groups (Figure 3(c,e,f,g)). Substantial heterogeneity was seen among various parameters (RecRed, ΔGT, ΔKTW, ΔPD and ΔCAL).

Post-operative morbidity/discomfort and patient's aesthetic satisfaction was mentioned by only one study by Rotundo et al. [45] where no significant difference was seen between two groups. Gupta and Gupta [39] used collagen membrane as an adjunct to mCAF and found that mCAF + collagen membrane was more effective than mCAF alone in RecRed, gain in KTW and CAL gain.

mCAF versus mCAF + PRF and mCAF + CTG versus mCAF + PRF

Only one trial [34] reported this comparison and showed higher CRC % and MRC in mCAF group. No significant difference could be detected between mCAF versus mCAF + PRF group in terms of changes in KTW, PD and CAL. In another study where mCAF + CTG versus mCAF + PRF were compared, better results with mCAF + CTG have been reported in terms of all the above parameters [40]. However, in both the studies mCAF + PRF group displayed greater increase in GT.

mCAF + CTG versus mCAF + EMD

Study by Alexiou et al. [41] did not report any significant difference between two groups in terms of any parameter except KTW which was higher in mCAF + EMD group.

mCAF + CTG versus mCAF + ADMG

For mCAF + CTG, original data [43] showed greater CRC of 87.8% as compared to mCAF + ADMG (CRC: 70.7%). Similarly, MRC was higher in mCAF + CTG group, i.e. 95.38% versus 88.14% in ADMG.

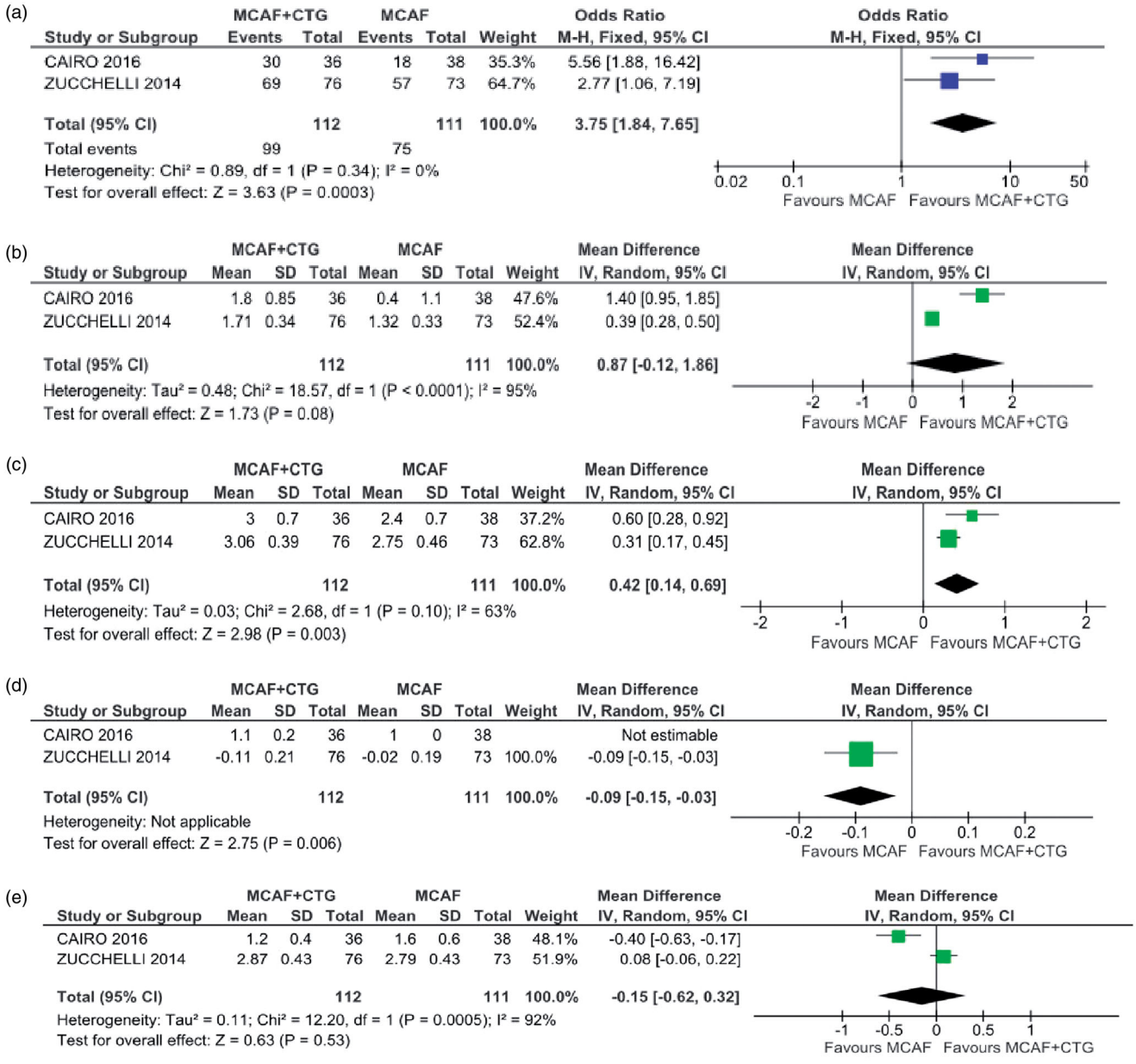

Figure 2. Forest plot comparing mCAF versus mCAF + CTG in terms of: (a) CRC; (b) ΔKTW; (c) Rec Red; (d) ΔPD; (e) ΔCAL.

Discussion

Although some SRs [15,19–21] have addressed the efficacy and predictability of periodontal plastic surgery procedures in the treatment of multiple adjacent GRs, evidence assessing the overall efficacy of mCAF technique remains elusive. The reason for this may be ascribed to either due to dearth of sufficient number of RCTs with mCAF to be included in previous SRs or to the lack of availability of one standard reference technique for the treatment of multiple GRs against which comparison can be drawn. Thus, present SR was conducted with an aim to assess the efficacy of mCAF in the treatment of Miller's class I and II or Cairo's RT1 multiple GRs and to address the ambiguity of overall predictability of mCAF. In order to increase the reliability of results, a priori protocol was designed as per the best practices of evidence based dentistry.

Primary and secondary outcomes

CRC was considered as the primary outcome variable as it is of particular relevance from both aesthetic (patient's aesthetic satisfaction) and functional (resolution of dentinal hypersensitivity) aspects [47]. Findings from this SR suggested that mCAF exhibits moderate to high level of efficacy for root coverage in Miller class I/II recessions, though a high degree of variability in terms of proportion of CRC was noted among the different studies. This can be attributed to an array of factors such as defect and patient characteristics, anatomical variations at recipient sites, 'centre effect' and operator's experience [48].

Overall CRC observed with mCAF was 70% while MRC was found in the range of 51.58–97.2%. In a recent SR, Tavelli et al. [22] reported CRC of 61.88% and MRC of 89.16 ± 12.38% with tunnel technique in multiple Miller class

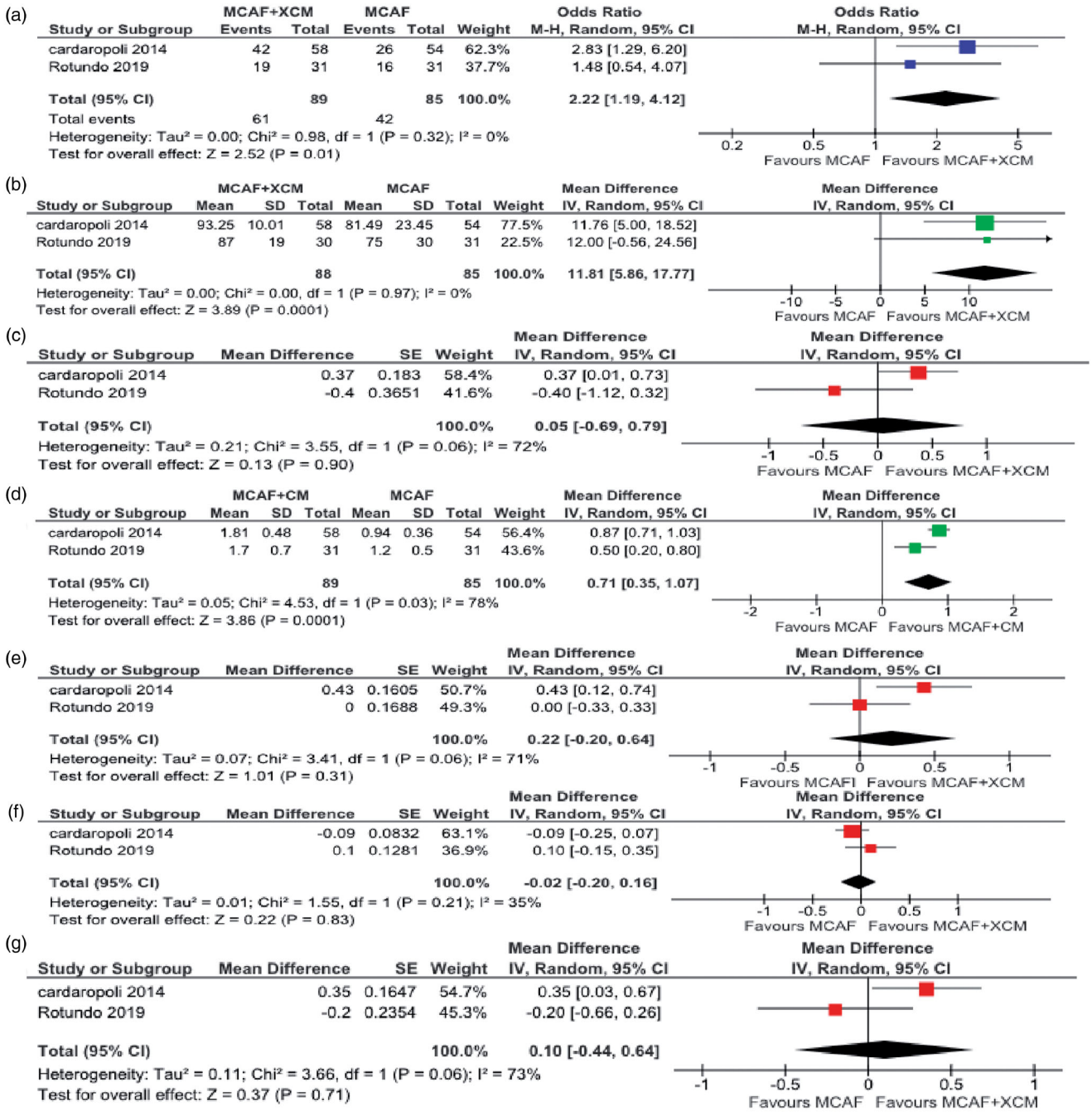

Figure 3. Forest plot comparing mCAF versus mCAF + CM in terms of: (a) CRC; (b) MRC; (c) Rec Red; (d) ΔGT; (e) ΔKTW; (f) ΔPD; (g) ΔCAL.

I and II recessions. Possible explanation for higher values achieved with mCAF may be improved access for partial thickness dissection to achieve passive coronal advancement and preservation of entire thickness of marginal tissue due to split-full-split flap design [30]. Surprisingly, there is only one study which compared mCAF with tunnel technique and had moderate risk of bias [42]. There were no studies reported in the literature about comparison of mCAF with VISTA or pin-hole technique. Future research is therefore highly warranted to fill these lacunae.

Although similar clinical outcomes in terms of recession reduction were reported between CAF (with vertical incisions) and mCAF, with or without additives [33,44], vertical releasing incisions in standard CAF might compromise the vascularity and aesthetics. Another potential advantage of mCAF in comparison to the previously reported envelope flaps [8,49] is derived from the incision design in papillary area. Sub-marginal oblique papillary incisions in mCAF allow precise adaptation of surgical papilla over de-epithelialized anatomical papilla; however, horizontal incisions in the papilla at or coronal to cementoenamel junction jeopardize the marginal tissues and adaptation of CTG.

There is robust evidence that sub-epithelial CTG procedures should be treated as gold standard for the treatment of recession coverage due to their enhanced predictability in achieving CRC, stability over time as well as concomitant

increase in width and thickness of keratinized tissue [37,50]. Results of our SR corroborated well with this observation and those from previous reviews [19,21,47]. Further, meta-analysis showed a higher percentage of CRC (odds ratio: 3.57) and greater recession depth reduction (MD: 0.42) when mCAF was combined with CTG. The potential benefits of grafting as biological filler under the flap enhance the stability of flap margin due to its 'scaffold effect', thereby minimizing the apical contraction of the flap during initial stages of healing [51,52]. Additionally, an increase in the thickness of gingival margin favours the root coverage and long-term stability of the results achieved [50].

Similarly, high level of efficacy in terms of CRC was also observed with mCAF + CM (odds ratio: 2.22) in meta-analysis as compared to mCAF. Thus, this finding lends support to the results from previous clinical [53,54], and human histological studies [55] that have confirmed the formation of long junctional epithelial attachment and connective tissue adhesions below CM and thus, might be a reason for its favourable results in recession treatment.

It is interesting to speculate better clinical outcomes with addition of wound healing enhancers (PRF or EMD) to procedures using flap alone in multiple recession defects. However, despite of limited evidence, findings of present review do not support the adjunctive benefits of PRF compared to mCAF alone [34] or as an effective substitute for CTG [40]. Similarly, with EMD, no significant differences between mCAF + CTG and mCAF + EMD for MRC and CRC were observed [41].

In terms of KTW, a significant gain compared to baseline was observed in all the included studies. This could be explained by the cascades of events occurring during wound healing and maturation. These events may be related to the tendency of mucogingival junction to shift apically in its genetically determined position following coronal advancement [56], granulation tissue derived from periodontal ligament and potential of underlying connective tissue to induce the formation of keratinized gingiva [57,58]. Comparing mCAF and CAF, it was shown that mCAF resulted in a greater increase in KTW than conventional CAF [33]. It may be speculated that disruption of mucogingival junction by vertical releasing incisions in CAF may delay its realignment resulting in a relatively less increase in KTW. However, long-term observations should validate this hypothesis. Furthermore, adjunctive use of CTG with mCAF showed an additional gain in KTW at the end of study period [31,32,37,38,46]. However, the meta-analysis of studies comparing mCAF with mCAF + CTG [37,38] did not yield any statistically significant difference for KTW gain (p=.08), though there was a tendency for favouring CTG group as seen in forest plot. Also, it is apparent from meta-analysis that these studies showed higher heterogeneity for gain in KTW indicating the possible influence of patient's and defect related factors.

Use of CM with mCAF demonstrated a higher gain in GT as compared to mCAF (p=.0001). However, characteristics of the collagen membrane or matrix used in different studies may influence the recession treatment outcomes and therefore the findings cannot be generalized to gather evidence. Addition of PRF did not yield superior outcomes; in fact inferior results were reported. Similarly, gain in KTW with addition of EMD to mCAF was significantly less than mCAF + CTG.

Patient reported outcomes

There is paucity of data on patient reported outcomes. Postoperative morbidity and complications were reported only in few studies [33,35,37,38,44,45]. CTG harvesting added additional postoperative pain as reflected by low VAS values [37]. Although sufficient data are not available from the included studies, it could be easily understood that use of autologous substitutes minimizes the patient's morbidity [36,44]. Future studies are encouraged to provide outcomes in terms of patient morbidity also.

As patient's perception about aesthetics has dramatically changed in past few years, merely achieving CRC does not by itself guarantees successful treatment outcome. Colour match/textural integration with the adjacent tissue, gingival contour, absence of keloids/scars and alignment of mucogingival junction should also be taken into consideration. Unfortunately, patient's satisfaction and professional evaluation for aesthetics following root coverage procedures was seldom reported in the included trials. Results were more favourable for mCAF in terms of aesthetics and postoperative morbidity in comparison to CAF with vertical incisions [33]. Further, a clinical trial by Cairo et al. [38] reported that similar clinical outcomes and better aesthetics were achieved with mCAF alone when keratinized tissue thickness was $>$0.8 mm and the use of CTG should be restricted to sites with thin gingiva ($<$0.8 mm). In accordance to these observations, Stefanini et al. proposed a decision-making strategy of site-specific application of CTG to achieve similar clinical and aesthetic results [59]. Nonetheless, data presentation for aesthetic evaluation was rather non-standardized and heterogeneous as some described it in anecdotal form or VAS and others mentioned scoring system, i.e. RES. It is important that future RCTs must report data on patient's aesthetic satisfaction using a standardized questionnaire as this constitutes one of the prime reasons for undergoing mucogingival surgical procedure.

Quality of evidence

Overall quality of evidence was moderate as most trials were at a low or medium risk of bias. Allocation concealment and masking of participant and clinician were the two categories that were not reported in few trials; however, blinding of participants and clinician may not be fully possible with study designs which used an additional graft material.

Potential biases and limitations

We have tried to limit the selection bias in this SR by collecting the data from different databases in duplication. Potential source of bias in this review may arise from the

defect related factors like defect severity, location of recession defects (anterior versus posterior), post-surgical antibiotic usage and cigarette smoking. Defects severity and local anatomical challenges may definitely incur heterogeneity; however, it is difficult to control these factors when considering the inclusion of multiple recessions. Smoking is also known to influence the short as well as long-term outcomes of recession coverage. Most of the studies in this review mentioned about the smoking status of participants; however, this parameter has neither been categorized in detail at the time of inclusion (former/current/non-smoker) nor been separately analysed while framing results in the included studies. Small number of included studies and different duration of follow-up of included studies were some of the other reasons of creating heterogeneity in the results of this review.

Additionally, pair-wise comparison of meta-analysis approach has been applied in this review that limits the comparison of different treatment arms and the power of the statistical analysis. A network meta-analysis model [60,61] integrating both direct and indirect effects from the available evidence may further shed light upon the efficacy of mCAF procedure for root coverage.

Further, inclusion of case-series and prospective studies might have limited reliability and caused higher bias. Studies reporting mCAF procedure only in multiple Miller class I and II recessions or RT1 defects were included, further limiting the assessment of its efficacy in Miller class III recession or RT2 defects. Meta-analysis was conducted on limited number of included articles and showed high heterogeneity in some outcomes. Unfortunately, lack of availability of standardized questionnaire to quantitatively evaluate the patient's aesthetic satisfaction made it difficult to compare this parameter and thus could not be analysed through meta-analysis.

Conclusions

Within the limitations of this SR and meta-analysis, it can be concluded that mCAF is an effective surgical approach to treat multiple adjacent recession defects. Additional use of CTG or CM potentiates the benefits of surgical therapy; however, a decision is made on primary indication of root coverage as per patient's demand while considering the defect characteristics. Insufficient evidence is available to indicate the use of potential biological agents such as PRF or EMD with mCAF.

Implications for future research

- Availability of high quality primary studies in the form of RCTs for the comparison of CTG with other substitutes as an adjunct to mCAF procedure for multiple recessions must be ensured.
- Patient reported outcomes in terms of postoperative morbidity and aesthetic evaluation using a standardized approach.
- RCTs for evaluating the efficacy of mCAF with other surgical techniques such as CAF and tunnel or its variants with and without grafts or biologics.
- RCTs for comparison of mCAF alone or with a soft tissue graft.
- Studies evaluating the efficacy of mCAF in Miller class III or RT2 recessions are limited and highly warranted.
- Studies with long-term follow up and large sample size.

Implications for clinicians

Clinicians should be aware of the predictability of mCAF procedure for root coverage in multiple recessions. Treatment outcomes benefit from split-full-split flap design and absence of vertical releasing incisions. Although evidence is limited, use of soft tissue grafts can be recommended when the primary goal is to achieve CRC for improved aesthetics and resolution of dentinal hypersensitivity. But it should be understood that clinician's decision for adjunctive use of soft tissue graft is based on the baseline gingival thickness and KTW apical to recession defect to achieve ideal aesthetic outcomes and limit patient's morbidity or treatment cost. Finally, studies are not sufficient to guide the clinician about the selection of mCAF over tunnel technique for multiple recessions; therefore, operator's expertise may be a decisive factor to choose among the two approaches.

Disclosure statement

This study has been self-funded by the authors. The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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References

[1] Wennström JL. Mucogingival therapy. Ann Periodontol. 1996;1(1):671–701.
[2] Chambrone L, Tatakis DN. Long-term outcomes of untreated buccal gingival recessions: a systematic review and meta-analysis. J Periodontol. 2016;87(7):796–808.
[3] Langer B, Langer L. Subepithelial connective tissue graft technique for root coverage. J Periodontol. 1985;56(12):715–720.
[4] Allen EP, Miller PD Jr. Coronal positioning of existing gingiva: short term results in the treatment of shallow marginal tissue recession. J Periodontol. 1989;60(6):316–319.
[5] de Sanctis M, Zucchelli G. Coronally advanced flap: a modified surgical approach for isolated recession-type defects: three-year results. J Clin Periodontol. 2007;34(3):262–268.
[6] Harris RJ. The connective tissue and partial thickness double pedicle graft: a predictable method of obtaining root coverage. J Periodontol. 1992;63(5):477–486.
[7] Zucchelli G, Cesari C, Amore C, et al. Laterally moved, coronally advanced flap: a modified surgical approach for isolated recession-type defects. J Periodontol. 2004;75(12):1734–1741.
[8] Bruno JF. Connective tissue graft technique assuring wide root coverage. Int J Periodontics Restorative Dent. 1994;14(2):126–137.

[9] Zucchelli G, De Sanctis M. Treatment of multiple recession-type defects in patients with esthetic demands. J Periodontol. 2000; 71(9):1506–1514.
[10] Zabalegui I, Sicilia A, Cambra J, et al. Treatment of multiple adjacent gingival recessions with the tunnel subepithelial connective tissue graft: a clinical report. Int J Periodontics Restorative Dent. 1999;19(2):199–206.
[11] Zuhr O, Fickl S, Wachtel H, et al. Covering of gingival recessions with a modified microsurgical tunnel technique: case report. Int J Periodontics Restorative Dent. 2007;27(5):457–463.
[12] Aroca S, Keglevich T, Nikolidakis D, et al. Treatment of class III multiple gingival recessions: a randomized-clinical trial. J Clin Periodontol. 2010;37(1):88–97.
[13] Zadeh HH. Minimally invasive treatment of maxillary anterior gingival recession defects by vestibular incision subperiosteal tunnel access and platelet-derived growth factor BB. Int J Periodontics Restorative Dent. 2011;31(6):653–660.
[14] Chao JC. A novel approach to root coverage: the pinhole surgical technique. Int J Periodontics Restorative Dent. 2012;32(5): 521–531.
[15] Hofmänner P, Alessandri R, Laugisch O, et al. Predictability of surgical techniques used for coverage of multiple adjacent gingival recessions – a systematic review. Quintessence Int. 2012;43(7): 545–554.
[16] Tonetti MS, Jepsen S, Working Group 2 of the European Workshop on Periodontology. Clinical efficacy of periodontal plastic surgery procedures: consensus report of Group 2 of the 10th European Workshop on Periodontology. J Clin Periodontol. 2014;41:S36–S43.
[17] Cairo F, Pagliaro U, Nieri M. Treatment of gingival recession with coronally advanced flap procedures: a systematic review. J Clin Periodontol. 2008;35(8 Suppl.):136–162.
[18] Chambrone L, Chambrone D, Pustiglioni FE, et al. Can subepithelial connective tissue grafts be considered the gold standard procedure in the treatment of Miller class I and II recession-type defects? J Dent. 2008;36(9):659–671.
[19] Graziani F, Gennai S, Roldán S, et al. Efficacy of periodontal plastic procedures in the treatment of multiple gingival recessions. J Clin Periodontol. 2014;41(Suppl. 15):S63–S76.
[20] Chambrone L, Lima LA, Pustiglioni FE, et al. Systematic review of periodontal plastic surgery in the treatment of multiple recession-type defects. J Can Dent Assoc. 2009;75(3):203a–203f.
[21] Chambrone L, Salinas Ortega MA, Sukekava F, et al. Root coverage procedures for treating localised and multiple recession-type defects. Cochrane Database Syst Rev. 2018;10:CD007161.
[22] Tavelli L, Barootchi S, Nguyen TVN, et al. Efficacy of tunnel technique in the treatment of localized and multiple gingival recessions: a systematic review and meta-analysis. J Periodontol. 2018; 89(9):1075–1090.
[23] Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. J Clin Epidemiol. 2009;62(10):e1–e34.
[24] Moher D, Liberati A, Tetzlaff J, et al. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: the PRISMA statement. PLoS Med. 2009;6(7):e1000097.
[25] Higgins JPT, Altman DG, Gøtzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011;343:d5928.
[26] Shea BJ, Reeves BC, Wells G, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ. 2017; 358:j4008.
[27] Miller PD. A classification of marginal tissue recession. Int J Periodontics Restorative Dent. 1985;5(2):8–13.
[28] Cairo F, Nieri M, Cincinelli S, et al. The interproximal clinical attachment level to classify gingival recessions and predict root coverage outcomes: an explorative and reliability study. J Clin Periodontol. 2011;38(7):661–666.
[29] Moola S, Munn Z, Tufaranu C, et al. Systematic reviews of etiology and risk. In: Aromataris E, Munn Z, editors. Joanna Briggs institute reviewer's manual. Adelaide: The Joanna Briggs Institute; 2017.
[30] Zucchelli G, De Sanctis M. Long-term outcome following treatment of multiple Miller class I and II recession defects in esthetic areas of the mouth. J Periodontol. 2005;76(12):2286–2292.
[31] Carvalho PFM, da Silva RC, Cury PR, et al. Modified coronally advanced flap associated with a subepithelial connective tissue graft for the treatment of adjacent multiple gingival recessions. J Periodontol. 2006;77(11):1901–1906.
[32] Skurska A, Dolińska E, Sulewska M, et al. The assessment of the influence of vertical incisions on the aesthetic outcome of the Miller class I and II recession treatment: a split-mouth study. J Clin Periodontol. 2015;42(8):756–763.
[33] Zucchelli G, Mele M, Mazzotti C, et al. Coronally advanced flap with and without vertical releasing incisions for the treatment of multiple gingival recessions: a comparative controlled randomized clinical trial. J Periodontol. 2009;80(7):1083–1094.
[34] Aroca S, Keglevich T, Barbieri B, et al. Clinical evaluation of a modified coronally advanced flap alone or in combination with a platelet-rich fibrin membrane for the treatment of adjacent multiple gingival recessions: a 6-month study. J Periodontol. 2009; 80(2):244–252.
[35] Ozcelik O, Haytac MC, Seydaoglu G. Treatment of multiple gingival recessions using a coronally advanced flap procedure combined with button application. J Clin Periodontol. 2011;38(6): 572–580.
[36] Cardaropoli D, Tamagnone L, Roffredo A, et al. Coronally advanced flap with and without a xenogenic collagen matrix in the treatment of multiple recessions: a randomized controlled clinical study. Int J Periodontics Restorative Dent. 2014;34(Suppl. 3):s97–s102.
[37] Zucchelli G, Mounssif I, Mazzotti C, et al. Coronally advanced flap with and without connective tissue graft for the treatment of multiple gingival recessions: a comparative short- and long-term controlled randomized clinical trial. J Clin Periodontol. 2014;41(4): 396–403.
[38] Cairo F, Cortellini P, Pilloni A, et al. Clinical efficacy of coronally advanced flap with or without connective tissue graft for the treatment of multiple adjacent gingival recessions in the aesthetic area: a randomized controlled clinical trial. J Clin Periodontol. 2016;43(10):849–856.
[39] Gupta P, Gupta H. Comparative evaluation of envelope type of advanced flap with and without type I collagen membrane (NEOMEM^{TM}) in the treatment of multiple buccal gingival recession defects: a clinical study. Indian J Dent. 2014;5(4):190–198.
[40] Öncü E. The use of platelet-rich fibrin versus subepithelial connective tissue graft in treatment of multiple gingival recessions: a randomized clinical trial. Int J Periodontics Restorative Dent. 2017;37(2):265–271.
[41] Alexiou A, Vouros I, Menexes G, et al. Comparison of enamel matrix derivative (Emdogain) and subepithelial connective tissue graft for root coverage in patients with multiple gingival recession defects: a randomized controlled clinical study. Quintessence Int. 2017;48(5):381–389.
[42] Bherwani C, Kulloli A, Kathariya R, et al. Zucchelli's technique or tunnel technique with subepithelial connective tissue graft for treatment of multiple gingival recessions. J Int Acad Periodontol. 2014;16(2):34–42.
[43] Gürlek Ö, Gümüş P, Nizam N, et al. Coronally advanced flap with connective tissue graft or xenogeneic acellular dermal matrix in the treatment of multiple gingival recessions: a split-mouth randomized clinical trial. J Esthet Restor Dent. 2020;32(4): 380–388.
[44] Ahmedbeyli C, Dirikan Ipçi S, Cakar G, et al. Coronally advanced flap and envelope type of flap plus acellular dermal matrix graft for the treatment of thin phenotype multiple recession defects. A randomized clinical trial. J Clin Periodontol. 2019;46(10): 1024–1029.

[45] Rotundo R, Genzano L, Patel D, et al. Adjunctive benefit of a xenogenic collagen matrix associated with coronally advanced flap for the treatment of multiple gingival recessions: a superiority, assessor-blind, randomized clinical trial. J Clin Periodontol. 2019;46(10):1013–1023.

[46] Garces-McIntyre T, Carbonell JM, Vallcorba L, et al. Coronal advanced flap in combination with a connective tissue graft. Is the thickness of the flap a predictor for root coverage? A prospective clinical study. J Clin Periodontol. 2017;44(9):933–940.

[47] Cairo F, Nieri M, Pagliaro U. Efficacy of periodontal plastic surgery procedures in the treatment of localized facial gingival recessions. A systematic review. J Clin Periodontol. 2014;41(Suppl. 15): S44–S62.

[48] Cortellini P, Pini Prato G. Coronally advanced flap and combination therapy for root coverage. Clinical strategies based on scientific evidence and clinical experience. Periodontol 2000. 2012; 59(1):158–184.

[49] Barrella GE, Kolbe MF, Ribeiro FV, et al. Coronally advanced flap with two different techniques for the treatment of multiple gingival recessions: a pilot prospective comparative case series. Quintessence Int. 2016;47(1):39–50.

[50] Pini-Prato GP, Cairo F, Nieri M, et al. Coronally advanced flap versus connective tissue graft in the treatment of multiple gingival recessions: a split-mouth study with a 5-year follow-up. J Clin Periodontol. 2010;37(7):644–650.

[51] Baldi C, Pini-Prato G, Pagliaro U, et al. Coronally advanced flap procedure for root coverage. Is flap thickness a relevant predictor to achieve root coverage? A 19-case series. J Periodontol. 1999; 70(9):1077–1084.

[52] Cortellini P, Tonetti M, Baldi C, et al. Does placement of a connective tissue graft improve the outcomes of coronally advanced flap for coverage of single gingival recessions in upper anterior teeth? A multi-centre, randomized, double-blind, clinical trial. J Clin Periodontol. 2009;36(1):68–79.

[53] Cardaropoli D, Tamagnone L, Roffredo A, et al. Treatment of gingival recession defects using coronally advanced flap with a porcine collagen matrix compared to coronally advanced flap with connective tissue graft: a randomized controlled clinical trial. J Periodontol. 2012;83(3):321–328.

[54] Jepsen K, Jepsen S, Zucchelli G, et al. Treatment of gingival recession defects with a coronally advanced flap and a xenogeneic collagen matrix: a multicenter randomized clinical trial. J Clin Periodontol. 2013;40(1):82–89.

[55] Rocchietta I, Schupbach P, Ghezzi C, et al. Soft tissue integration of a porcine collagen membrane: an experimental study in pigs. Int J Periodontics Restorative Dent. 2012;32(1):e34–e40.

[56] Ainamo A, Bergenholtz A, Hugoson A, et al. Location of the mucogingival junction 18 years after apically repositioned flap surgery. J Clin Periodontol. 1992;19(1):49–52.

[57] Pasquinelli KL. The histology of new attachment utilizing a thick autogenous soft tissue graft in an area of deep recession: a case report. Int J Periodontics Restorative Dent. 1995;15(3):248–257.

[58] Karring T, Ostergaard E, Löe H. Conservation of tissue specificity after heterotopic transplantation of gingiva and alveolar mucosa. J Periodontal Res. 1971;6(4):282–293.

[59] Stefanini M, Zucchelli G, Marzadori M, et al. Coronally advanced flap with site-specific application of connective tissue graft for the treatment of multiple adjacent gingival recessions: a 3-year follow-up case series. Int J Periodontics Restorative Dent. 2018; 38(1):25–33.

[60] Tavelli L, Barootchi S, Cairo F, et al. The effect of time on root coverage outcomes: a network meta-analysis. J Dent Res. 2019; 98(11):1195–1203.

[61] Barootchi S, Tavelli L, Zucchelli G, et al. Gingival phenotype modification therapies on natural teeth: a network meta-analysis. J Periodontol. 2020;91(11):1386–1399.