Influence of tooth location on coronally advanced flap procedures for root coverage

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Abstract

Background: The efficacy of Coronally Advance Flap (CAF) has been extensively evaluated and several parameters influencing the final results, such as interproximal attachment loss, recession defect size, papilla dimension, flap thickness, have also been identified. However, the influence of tooth location has not been systematically investigated yet. Therefore, the aim of this systematic review was to evaluate the influence of tooth location on the outcomes of CAF.

Material and Methods: A literature search on PubMed, EMBASE, Cochrane libraries and hand-searched journal until September 2017 was performed to identify clinical studies reporting the outcome of CAF for localized gingival recessions (GRs) for each single tooth.

Results: Eighteen articles reporting 399 localized GRs treated with CAF were included in the present systematic review. Canines and incisors were related to a higher mRC and CRC than premolars and molars (odds ratio 1.63) ($p<0.05$), while the right side showed a higher CRC than the left side (odds ratio 1.60) ($p<0.05$). No differences were found between maxillary and mandibular dentition ($p>0.05$). The addition of a graft such as Connective Tissue Graft (CTG) with or without Enamel Matrix Derivative (EMD) was shown to enhance the outcomes compared to CAF alone ($p<0.05$). CRC was negatively affected by initial clinical attachment level ($p<0.05$), but not from the initial recession depth ($p>0.05$).

Conclusions: Tooth location plays an important role on mRC and CRC following CAF. The addition of CTG or substitutes, especially with biological agents (EMD), enhance the clinical outcomes compared to CAF alone.

Introduction

Gingival recession (GR) is defined as the apical shift of the gingival margin with the concomitant exposure of a portion of the root surface [1]. This condition affects a large part of population, regardless of the standard of oral hygiene [2, 3]. It is estimated that 54.5% of young adults and 100% of middle-elderly adults suffer from GRs, with an average prevalence of 78.6% [2]. More recently, Rios et al. reported a prevalence of 99.7% of GRs ≥ 1 mm among Brazilian population, and that gender, age, smoking and high education were risk factors for buccal GR [4]. Nieri and coworkers showed that 80% of patients had one or more buccal GRs and that their perception of GRs was greater on anterior areas, deep GRs and among young patients [5]. The high prevalence of these mucogingival defects can be attributed to a large variety of predisposing and precipitating factors that include but are not limited to: plaque-induced inflammation[1]; toothbrush trauma[6]; periodontal disease[7], malposition[2]; frenum pull; iatrogenic; improper flossing[8]; trauma associated with class II malocclusion[9]; piercing trauma[10]; and orthodontic treatment [11].

When GR affects the esthetic area and/or it is associated with dental hypersensitivity, exhibits a lack of an adequate band of keratinized tissue, or is concomitant with a carious or non-carious cervical lesion, treatment is often indicated [1, 12]. Indeed, the efficacy of surgical treatment for correction of GR defects has been extensively demonstrated [13] with long-term stable outcomes[14].

Several surgical techniques, such as guided tissue regeneration (GTR)[15]; subepithelial connective tissue graft procedure (SCTG)[16]; coronally advanced flap (CAF)[17]; lateral positioned flap[18]; double papilla technique[19]; semilunar pedicle flap[20]; oblique rotated flap[21]; tunnel technique[22]; and surgical techniques based on modifications of these protocols[23], have been proposed for the treatment of GR defects. Among these procedures, it has been demonstrated that CAF represents the most predictable technique for the correction of GR defects[13, 24]. Similarly, although several connective tissue substitutes have been tested in attempt to eliminate the drawbacks related with a secondary surgical site [25-28], however, autogenous connective tissue graft (CTG) remains to be considered the gold standard providing with the most predictable and long-term satisfactory results [1, 13, 29].

The final outcomes of the CAF procedures depend not only on the origin of the graft but also on several critical anatomical factors[30]. Indeed, several investigations have highlighted the impact of not only Miller's classification, but also the recession defect size; interdental papilla dimension; root prominence; quantity of keratinized tissue; tooth location; and the concomitant presence of non-carious cervical lesions [31-35]. Among these, tooth location should be further evaluated since it may play a key role of importance. Although it is believed that optimal results of periodontal plastic surgery may in certain areas be more challenging to obtain [30, 36-38], no studies have investigated yet the outcome of CAF depending on each specific tooth location.

The need for evaluating the predictability of CAF in the different locations in the oral cavity becomes apparent when the results of the different studies are being compared without regard to the specific teeth treated. In addition, several clinical studies have investigated only certain areas limited to maxillary canines and premolars [12]. Indeed, studies that treated recessions localized in both the maxilla and the mandible reported better outcomes for maxillary teeth [39-41]. According to McGuire and Scheyer, vascular supply and muscle pull may negatively influence the outcome of periodontal plastic surgery in the lower jaw [38]. Moreover, anatomic conditions like marginal frenula, high muscle pull and shallow vestibule that are frequently encountered in the lower incisors are considered limiting factors for periodontal plastic surgery [1]. Given the influence of tooth location on the outcomes of periodontal plastic surgery, it is of paramount importance to understand the true probability of achieving a complete root coverage following CAF in different anatomical areas. Hence, the aim of this systematic review was to evaluate the clinical outcomes of CAF in relation to the location of the GR defect.

Material and Methods

Study Registration

The review protocol was registered and allocated the identification number (CRD42017081100) 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.

Eligibility Criteria

Articles were included in this systematic review if they met the following criteria: 1) Patients with a clearly specified diagnosis of localized gingival recession, 2) GRs classified as Miller class I or II or RT1 [31, 42], 3) Randomized clinical trials, controlled prospective studies, Cohort, case series and retrospective studies involving human participants that reported results in terms of percentage of root coverage per tooth by using CAF technique, 4) Case series with at least 10 recessions. Accordingly, articles were to be excluded if: 1) Case report; 2) Systematic review; 3) Preclinical animal studies; 4) Articles not reporting the results of each specific tooth; 5) Articles not using CAF as surgical technique; 6) Articles using the envelope CAF design; 7) articles using CAF for treating multiple gingival recessions; 8) articles considering only Miller class III and/or IV GRs. For articles reporting both single and multiple recessions, or both Miller class I/II and III, only data regarding Miller class I/II localized GRs were included in the present systematic review.

Patient, Intervention, Comparison, Outcome (PICO) Question

This systematic review utilized the Preferred Reporting Items Systematic review and Meta-Analyses (PRISMA) statement and checklist [43], as well as the patient, intervention, comparison, outcomes (PICO) method.

Types of patients

Patient with localized GR defects classified as Miller I, II[31] or RT1 (Recession Type 1)[42]. A table reporting the specific teeth treated together with the related outcomes following CAF must be provided in order to include the article in the present review.

Types of interventions

All the recessions treated with conventional CAF[44, 45] has been considered. Only flaps with two vertical releasing incisions, de-epithelialization of the surgical papillae and a suturing positioned coronally advanced position respect to the CEJ have been included.

Types of outcomes measured

The primary outcome was to investigate the mean root coverage (mRC) and the complete root coverage (CRC) of CAF for each single tooth. The secondary outcomes were: (a) to compare the mRC and the CRC in the upper and lower jaw, (b) to evaluate the influence of autologous CTG or substitutes, c) to evaluate the influence of CTG or substitutes on keratinized tissue (KT) gain, (d) to assess the buccal probing depth reduction and the clinical attachment level (CAL) gain for each single tooth and e) to evaluate which factors affect the mRC, CRC, KT gain and CAL gain.

Types of studies

Randomized clinical studies (RCTs), controlled clinical trials, prospective cohort studies, case series were considered in this systematic review.

Only RCTs were considered when logistic regression model was performed.

Focused question

In patients presenting localized gingival recessions, what is the influence of tooth location on the outcomes of coronally advanced flap procedures?

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 (see supplementary Data S1 and S2 in online *Journal of Periodontology*). Additionally, a manual search of related journals, including a complete search of *Journal of Clinical Periodontology, Journal of Periodontal Research, Journal of Periodontology, Journal of Dental Research, International Journal of Periodontics and Restorative Dentistry*, was also performed. Finally, previous systematic reviews investigating root coverage procedures for gingival recession were screened for article identification (see supplementary Data S3 in online *Journal of Periodontology*). Several authors were contacted to obtain specific data for each tooth treated.

Data extraction

Studies were excluded by two authors through screening of titles and abstracts (LT and AR). The definitive stage of screening involved full-text reading by the same two reviewers using a predetermined data extraction form to confirm the eligibility of each study based on the aforementioned inclusion and exclusion criteria. The primary outcomes were the mRC and CRC, while the secondary outcomes were KT gain and CAL gain. Data was then independently extracted by these two review authors. Patient characteristics, treatments and clinical outcomes were systematically registered. When clinical data was lacking, authors of the trials were contacted.

Where clinical data were provided at multiple time points, the follow-up closest to 1 year was used.

At each stage, disagreement between reviewers was resolved through discussion and consensus. If a disagreement persisted, the judgment of a third reviewer (F.S.) was decisive.

Statistical analysis

All statistical analyses were performed using the Rstudio software environment ‖.

To compare the outcomes of RCTs and non-RCTs, independent sample t-tests and in case of paired data, a paired sample t-test was performed where a $p<0.05$ was deemed significant.

Logistic regression analyses were performed based on data from RCTs. For continuous data logistic regression models were created to assess the roles and influence of several variables to predictor outcome variables. For binary outcomes logistic regression models were created to similarly assess the influence of the different parameters on the outcome. Additionally, scatter plots and box plots were produced to better visualize the pattern of influence of specific factors on the outcomes.

Quality and Risk of Bias assessment

The Cochrane Risk of Bias Tool for RCTs has been used to evaluate the studies[46]. The assessment of the quality of nonrandomized studies and case series has been evaluated using the Newcastle-Ottawa scale [47] and the Johanna Briggs Institute Scale for Case Series [48], respectively (see supplementary Data S4 in online *Journal of Periodontology*).

Results

Study selection

The search results based on PRISMA guidelines are depicted in supplementary Data S1 in the online *Journal of Periodontology*. The electronic search in MEDLINE, through Pubmed, identified 2179 articles until September 2017, while the EMBASE and Cochrane Library searching provided 219 and 114 records, respectively. Thirteen articles were identified through manual searching. After eliminating duplicates, 2232 articles were selected. Among these, 191 articles met the inclusion criteria when their titles and abstracts were examined and therefore were considered eligible for the full text assessment of eligibility. After reading the full-text, 170 articles were excluded due to insufficient data on specific locations, while 7 studies were excluded because they treated only multiple GRs, only class RT2 GRs or flap design different from CAF (supplementary Data S5 in online *Journal of Periodontology*). The k value for inter-reviewer agreement for potentially relevant articles was 0.85 (titles and abstracts) and 0.89 (full-text articles), indicating a consistent agreement between the two reviewers. The supplementary data of 4 articles were provided by 4 authors after being contacted [49-52]. Hence, 18 articles reporting 399 localized GRs treated with CAF, with a mean follow-up of 9.6 months, were included in the present systematic review (Table 1).

Study characteristics

Study design and study population

Twelve articles were RCTs [25, 49-59], 2 case-control [60, 61] and 4 were case series [62-65]. The general characteristics of the included articles are depicted in Table 1.

Type of Intervention

CAF alone was investigated in nine study [25, 54, 56, 58-60, 63-65] while 5 articles evaluated CAF + CTG [50, 51, 55, [60, 61], 2 CAF + Xenogeneic Collagen Matrix (XCM) [49, 61], 1 CAF + Acellular Dermal Matrix (ADM) [57], 4 CAF + Enamel Matrix Derivative (EMD) [52-54, 56], 1 CAF + Free Rotated Papilla Autograft (FRPA) [62], 1 CAF + Platelet-Rich Plasma (PRP) [25], and 1 CAF + Periosteal Pedicle Graft (PPG) [55]. The general characteristics of the intervention and results are depicted in Table 2.

Bias assessment

The results of bias risk assessment for the included RCTs, using The Cochrane Risk of Bias Tool, are summarized in supplementary Data S6 in the online *Journal of Periodontology*; 6 articles were considered to have a low risk of bias [25, 50, 51, 54-56], 4 studies were considered to have a moderate risk of bias [52, 53, 57, 58], and 2 studies a high risk of bias [49, 59].

The results of bias risk assessment for the included case-control using the Newcastle-Ottawa scale, are summarized in supplementary Data S7 in the online *Journal of Periodontology*; The scores obtained were 7 [60] and 6 [61], showing an acceptable (low-medium risk of bias) methodologic level of evidence. 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 S8 in online *Journal of Periodontology*; low risk of bias was determined for 2 studies [64, 65], while the remaining 2 were considered to have a moderate risk of bias [62, 63].

Synthesis of results

To quantitatively address the review questions, data from all the selected studies was extracted and organized into tables to condense an overview of the included investigations, characteristics of the interventions and reported clinical outcome parameters (mRC, CRC, KT gain). mRC, CRC, KT gain, PD red and CAL gain were calculated where not already specified by the authors.

A total of 399 GRs from 18 studies were evaluated in the present systematic review. Among them, 269 GRs were provided by RCTs. Independent sample t-test comparing mRC and CRC for each site showed that there is no difference between the outcomes reported by RCTs and non-RCTs (p>0.05). The average mRC and CRC for each tooth location was heterogeneous (Fig. 1). Maxillary canines were the most treated teeth (34.3%), while maxillary first premolars and mandibular central incisors were the second and the third most selected teeth for root coverage (19.0 and 10.8 % respectively). On the other hand, right maxillary lateral incisor and right mandibular second premolar were the least treated teeth and no information was available for second molars. Table 3 depicts the frequency with which each tooth has been included in the selected studies.

Regression analysis

Logistic regression model was performed only considering data from RCTs. No significant differences were observed when the effect of different operators on the outcomes of mRC, CRC, KT gain, PD red, CAL gain were explored for each tooth site (p>0.05). Anterior teeth (incisors and canines) were related to significant higher mRC (p<0.05), CRC (p<0.01), KT gain (p<0.05), PD red (p<0.01) and CAL gain (p<0.01) than posterior teeth (premolars and first molars) (Fig. 2A). The odds for achieving CRC for anterior teeth was 1.63 compared to posterior teeth. Maxillary and mandibular teeth showed similar mRC and CRC (p>0.05), while KT gain, PD red and CAL gain were found significantly superior in the lower arch (p<0.001) (Fig. 2B,2C) Teeth present on the right arches were associated with significantly higher CRC than teeth on left arches ($p<0.05$). The odds of obtaining CRC for right side was 1.6 compared to left side. Although smoking patients showed lower mRC and CRC than non-smoking patients, this difference was not statistically significant ($p>0.05$) (Fig. 2D).

When comparing different grafting material, the addition of CTG, CTG + EMD, or ADM showed superior mRC and CRC than CAF alone ($p<0.05$). Similarly, CAF + CTG showed comparable results, in terms of mRC and CRC with CAF + ADM, CAF + CTG + EMD, CAF + EMD, CAF + PPG and CAF + PRP ($p>0.05$), while lower results were achieved in CAF + XCM and CAF alone ($p<0.05$). Significant superior KT gain than CAF alone was found for CAF + CTG + EMD ($p<0.01$), CAF + CTG ($p<0.05$), CAF + ADM ($p<0.05$) and CAF + PPG ($p<0.05$). CAF + CTG was associated with higher KT gain than CTG substitutes ($p<0.05$). Indeed, KT gain was positively influenced by the initial KT width ($p<0.001$) and by CAF + CTG ($p<0.001$). CRC was positively related to initial CAL ($p<0.05$) but not associated with initial recession depth ($p>0.05$); mRC was not affected by initial recession depth and initial CAL ($p>0.05$). CAL gain was significant affected by initial CAL ($p<0.001$), while PD red was positively influenced by initial PD ($p<0.001$) and the use of CAF + CTG ($p<0.01$) or CAF + EMD (($p<0.001$). Table 4 compares mRC, CRC, KT gain, PD red and CAL gain based on tooth location.

Discussion

CAF may represent the most investigated flap approach for GR coverage [66]. As such, multiple parameters that can influence the results of this procedure have been investigated including interproximal attachment loss, amount of keratinized tissue, recession defect depth, height of papilla, etc.[30, 67]. However, among them, the influence of tooth location on the outcome of CAF has not been extensively investigated yet.

A review addressing the most critical elements for root coverage by De Sanctis and Clementini mentioned the location as a factor that may affect the success, primarily based on mRC and CRC, of the surgical procedure [30]. Our results confirmed that tooth location is an important parameter that can affect the outcome of CAF, in particular when anterior and posterior teeth were compared. Result from our regression analysis showed a higher mRC and CRC in the anterior teeth than in the posterior teeth, with an odds ratio of 1.6 for achieving CRC in canines and incisors compared to premolars and molars. In agreement with our findings, Aroca et al. found that posterior teeth were related to lower outcomes [68]. In this sense, it has been suggested that the amount of KT apically and laterally to the GR may have an impact on CRC [30]; thus, it can be assumed that the reduced width of attached gingiva that usually characterizes premolars compared to anterior teeth [69] may have contributed to the lower mRC and CRC of the posterior teeth. Therefore it should be considered that it is not tooth location per se but several other factors in combination, such as the amount of KT or the gingival thickness, that are likely to be higher in certain areas of the mouth and thus affecting the outcomes of CAF procedures.

Huang et al. concluded that achieving CRC in maxillary teeth is more predictable than in mandibular teeth, although this trend was not statistically significant [36]. However, our results failed to identify a significant difference in terms of mRC and CRC when comparing upper and lower arch. This may be due to the limited sample size and the heterogeneity of the teeth included (19 maxillary vs. 4 mandibular teeth, mostly of them canines) in the study of Huang et al. [36]. On the other hand, logistic regression analysis showed greater KT gain, PD red and CAL gain in the mandible compared to the maxilla. Nevertheless, these results should be interpreted cautiously given the non-uniform distribution of the treated teeth between upper and lower jaw, together with the different grafts used.

Interestingly, teeth in the right side were related to greater CRC than corresponding ones in the left side (odds ratio 1.60). This fact could be explained by the role of tooth brushing technique in the maintenance of the gingival margin over time [30, 70]. It could also be speculated that for most of the right-handed patients, the left side is often more traumatized [71] due to the application of higher pressure during brushing and thus potentially jeopardizing the outcome of the surgery, both in short and long-term.

The present review included 399 teeth, mainly maxillary teeth, being more than one third (34.34%) maxillary canines, followed by maxillary first premolar (19.04%). As highlighted by Chevalier et al. 2017, most of the studies available in the literature report on anterior maxillary teeth only [61]. Therefore, it can be speculated that the available information for mRC and CRC of CAF reflects to a greater extent the expected results on the maxillary teeth, especially canines and first premolars. In a meta-analysis evaluating complete root coverage following different procedures, Clauser et al. observed that non-RCTs were related to higher CRC than RCTs. However, our results based only on CAF for single GRs showed that RCT and non-RCTs achieved comparable results.

Coronally advanced flap alone is often performed together with CTG or other graft substitutes in an attempt to not only increase root coverage but also increase tissue thickness, augment KT width and enhance the esthetic outcomes [72]. Because of the nature of the technique, with or without graft, CAF alone is generally considered a different procedure from CAF + CTG or CAF + CTG substitutes. As it has been clearly demonstrated in the literature, higher clinical outcomes can be obtained whenever a graft is combined with CAF [13, 28, 73]. Overall, the addition of a grafting material to CAF (ADM, CTG, CTG + EMD) enhanced the mRC, CRC and KT compared to CAF alone. Despite numerous beneficial effects of CTG when compared to different soft tissue grafting substitutes[12, 13], the main advantage of a graft beneath the flap may be the "scaffold effect" that promotes wound healing with favorable thickening of the gingiva [73, 74]. It has been showed that increased marginal soft tissue thickness, which is typically observed when a graft is positioned below the flap, is positively related to higher mRC [74] and to a tendency of the gingival margin to coronally migrate over time [14, 75, 76]. In agreement with Cairo et al., the present study confirm the efficacy of CAF, especially when a CTG with or without EMD is added [13, 24]. However, care should be taken when interpreting the results due to the small number of patients in certain included groups (such as CTG + EMD) and the lack of information regarding the patient phenotype or gingiva thickness at the baseline. Indeed, it has been demonstrated that the gingival thickness not only dictate the need of a CTG or a CTG substitute [72] but it is also one of the main decisive factors that affect the accomplishment of complete root coverage [36, 77].

Logistic regression model showed that initial clinical attachment loss is negatively related to CRC, while the initial recession depth does not affect CRC. The importance of clinical attachment loss has always been considered a key factor for final root coverage [30], as it is the basis of the two main GR classifications [31, 42]. On the other hand, whether the baseline depth of the GR affects CRC is controversial in the literature. Several authors reported better results in presence of shallow GRs [78,

[79], while others found higher CRC when the initial GR was deeper [80, 81]. However, our results showed that initial recession does not have an effect on CRC.

Although the limited sample probably prevented a statistically significant difference, smoking habit seemed to be associated with lower mRC and CRC. The detrimental effect of tobacco in root coverage procedures in patients smoking more than 10 cigarettes per day has been demonstrated [82]. Therefore, it can be assumed that is the frequency of smoking rather than the habit per se that can cause detrimental results of root coverage procedures. However, out of the 7 articles that included smokers, only 4 reported the cut-off value of 10 cigarettes per day for consider a patient "smoker", while other articles did not report a clear cut-off definition of smoking.

Within the limitations of the present study, several factors can be described. Firstly, the larger part of the studies in the literature did not report the outcome of root coverage procedure for each specific tooth location; secondly, the major part of data was obtained from maxillary teeth, especially canines and first premolars, and thus the mRC and CRC of teeth with small sample may not be as representative and generalizable due to possible selection bias. Third, the included studies mainly used CAF alone or CAF + CTG. Moreover, a clear definition of smoking was lacking in some studies. In addition, the heterogeneity of the studies should also be taken into consideration, given the different follow-up, study design, setting and teeth treated. Finally, important parameters that can affect the CRC and mRC of CAF, such as the gingival biotype/phenotype and the gingival thickness, could not be evaluated.

Conclusions

Taking into consideration the limitations of the present study, it can be concluded that tooth location plays an important role on mean root coverage and complete root coverage following coronally advanced flap procedure. Higher outcomes are expected in anterior and right sides compared to posterior and left sides. Clinical attachment loss negatively affects complete root coverage. The addition of connective tissue grafts or substitutes, especially with biological agents, can enhance the clinical outcomes when compared to coronally advanced flap alone.

Indication for further research

- RCTs based on the CONSORT guidelines
- Increase the number of RCTs that report the mRC, CRC, PD red, KT gain, CAL gain for each specific tooth location
- Further RCT whose results are equally based on maxillary and mandibular recessions, as well as on anterior and posterior teeth
- Studies that include smokers should always report the definition of smokers, specifying also the mean cigarettes/day of the test and control groups

Implications for clinicians

Clinicians should be aware that CAF, especially when combined to a CTG or substitutes, is a highly effective periodontal plastic procedure for the treatment of single GRs. However, the results presented in the literature mainly describe maxillary canines and premolars and may not be generalizable for other sites. Indeed, the present study revealed that tooth location (whether anterior/posterior or right/left) can affect the outcome of CAF. Clinician should be aware that lower clinical outcomes may be expected when posterior GRs, especially if located in the left side, are treated. In addition, while the initial recession depth seems not related to mRC or CRC, the initial CAL may limit the CRC.

Footnotes

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

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Figures and Tables

Figure 1. Mean Root Coverage (mRC) and Complete Root Coverage (CRC) according to the tooth location

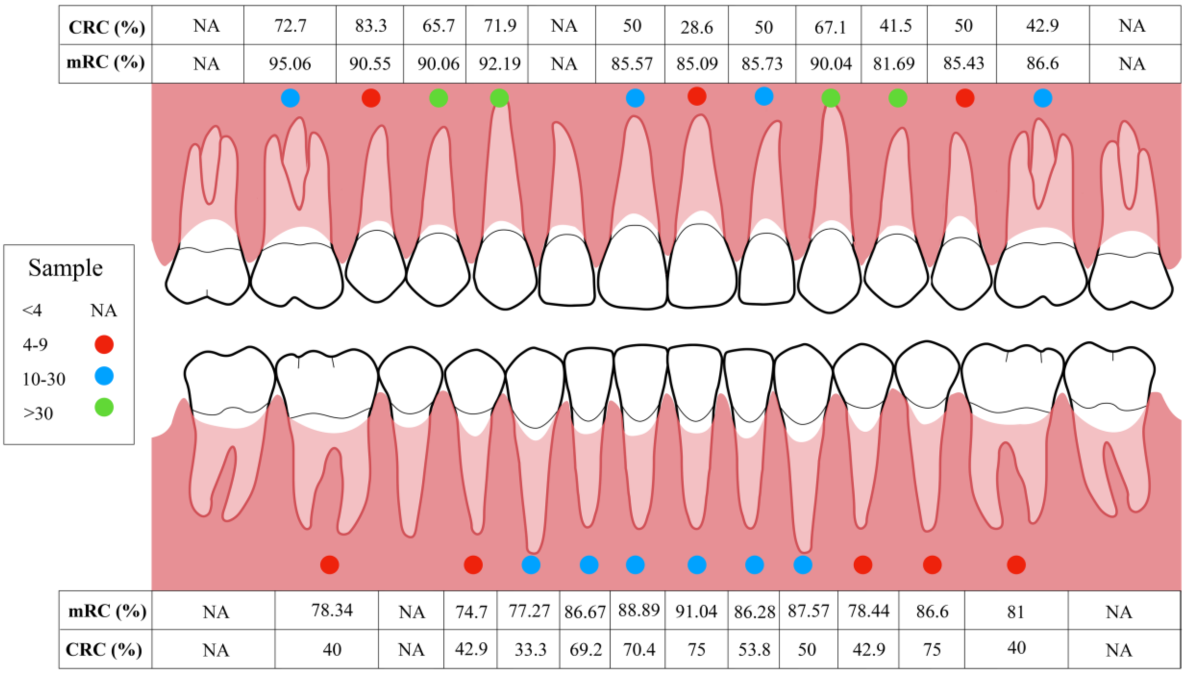

Figure 2. Logistic regression model showing: A) mRC between anterior and posterior teeth, B) KT gain in maxillary and mandibular teeth, C) CAL gain in maxillary and mandibular teeth, D) mRC in smoking and non-smoking patients.

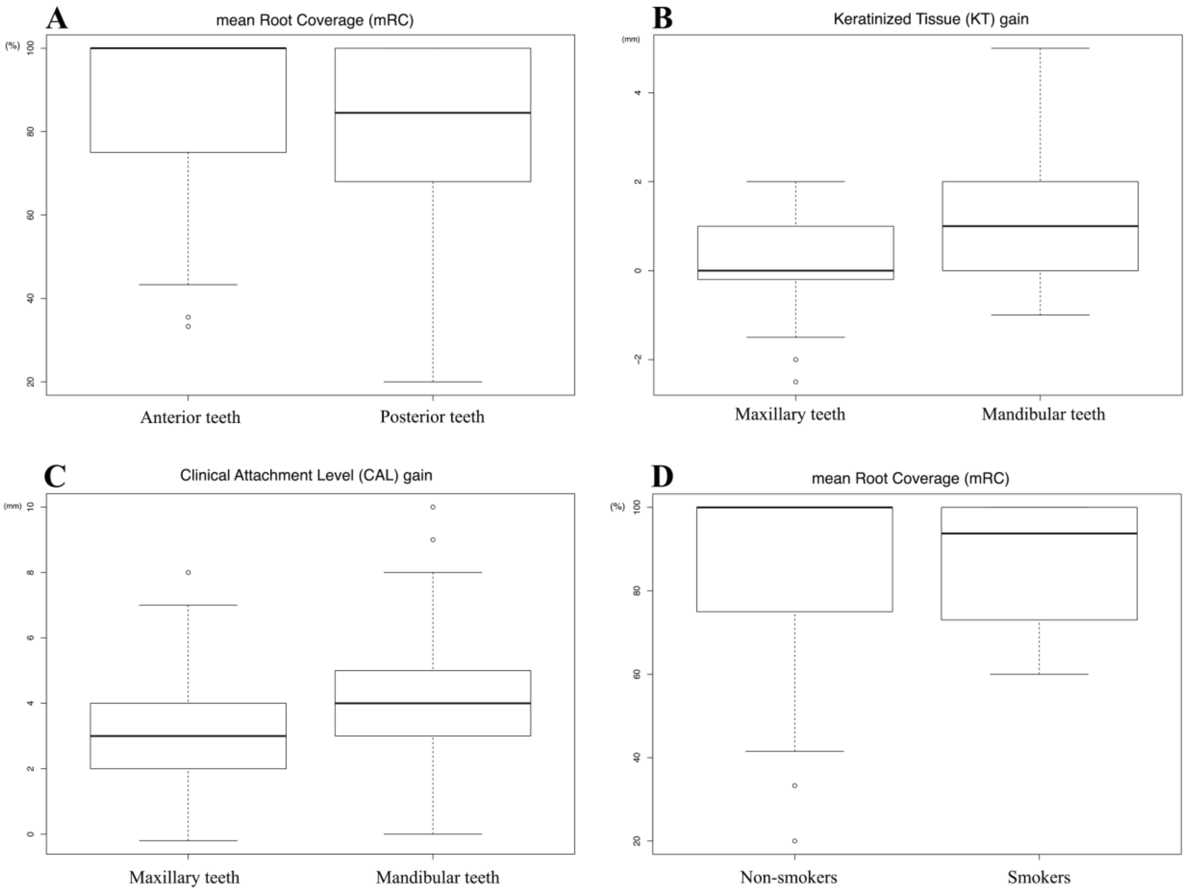

Table 1. Baseline characteristics of the included studies

Table 2. General characteristics of the intervention and results

Table 3. Frequency of treated teeth according to their location

Table 4. Comparison of mean Root Coverage (mRC), Complete Root Coverage (CRC), Keratinized Tissue Gain (KT gain), Probing Depth reduction (PD red) and Clinical Attachment Level gain (CAL gain) based on tooth location

Supplementary data

Data S1. PRISMA flowchart

Data S2. Electronic search strategy

Data S3. References of the previous systematic reviews screened for articles identification

Data S4. Bias assessment scales and related parameters for the evaluation of risk of bias

Data S5. Characteristics and references of the excluded articles

Data S6. The results of the bias risk assessment for the included RCTs using The Cochrane Risk of Bias Tool for Randomized Controlled Trials

Data S7. The results of the bias risk assessment for the included non-randomized trials studies using the Newcastle-Ottawa quality assessment scale

Data S8. The results of the bias risk assessment for the included case series using The Joanna Briggs Institute Scale for Case Series

Table 1. General overview of the included studies

Study	Study design, follow-up	Mean Age (years), Patients (N) and Recessions (N)	Smoking habits	Recession type	Location	Site, setting and funding
Bellver-Fernandez et al. 2016 [60]	Retrospective Case-control	Mean age: 39.6 ± 9.3 Recruited patients: 17 Drop-out	4 Patients were smokers (> 10 cig/day)	Miller I, II, III Localized GRs Rec 0 NR	Maxillary and mandibular teeth	Spain, Private practice, NR

		patient: 0 GRs: 22				
Berlucchi et al. 2002 [53]	RCT	Mean age: 30.6 Recruited patients: 14 Drop-out patients: 0 GRs: 26	Non-smoking patients	Miller I, II Localized and multiple GRs Rec 0 NR	Maxillary and mandibular teeth	Italy, NR, NR
Chevalier et al. 2017 [61]	Case-control	Mean age: 38.75 Recruited patients: 4 Drop-out patients: 0 GRs: 17	Non-smoking patients	Miller I Localized and multiple GRs Rec 0 NR	Maxillary and mandibular teeth	France, University, NR
Del Pizzo et al. 2005 [54]	RCT	Mean age: 39.46 ± 10.7 Recruited patients: 15 Drop-out patients: 0 GRs: 30	Non-smoking patients	Miller I, II Localized GRs Rec 0 ≥ 3 mm	Maxillary and mandibular canines and first premolars	Italy, University, NR
Francetti et al. 2004 [62]	Case series	Mean age: 30.3 ± 6.3 Recruited patients: 16 Drop-out patients: 0 GRs: 16	NR	Miller I, II Localized GRs Rec 0 ≥ 2.5 mm	Maxillary and mandibular teeth. Molars were not included	Italy, NR, NR

Harris & Harris 1994 [63]	Case series	Mean age: 31.1 Recruited patients: 18 Drop-out patients: 0 GRs: 20	6 patients were smokers (cig/day NR)	Miller I Localized GRs Rec 0 NR	Maxillary and mandibular teeth. Molars were not included	USA, Private practice, NR
Huang & Wang 2007 [64]	Case series	Mean age: 42 ± 19.7 Recruited patients: 10 Drop-out patients: 0 GRs: 10	Non-smoking patients	Miller I Localized GRs Rec 0 ≥ 2.5 mm	Maxillary and mandibular teeth. Molars were not included	USA, University, Partially supported
Huang et al. 2005 [25]	RCT	Mean age: 43.8 ± 11.9 Recruited patients: 24 Drop-out patients: 1 GRs: 23	Non-smoking patients	Miller I Localized GRs Rec 0 ≥ 2 mm	Maxillary and mandibular teeth. Molars were not included	USA, University, Supported
Mahajan et al. 2012 [55]	RCT	Mean age: 25.2 Recruited patients: 20 Drop-out patients: 0 GRs: 20	Non-smoking patients	Miller I Localized GRs Rec 0 ≥ 3 mm	Maxillary and mandibular incisors and canines	India, University, NR
Modica et al. 2000 [56]	Split-mouth RCT	Mean age: 25.2 Recruited patients: 12 Drop-out	Non-smoking patients	Miller I Localized GRs Rec 0 NR	Maxillary and mandibular teeth	Italy, University, NR

		patients: 0 GRs: 24				
Papageorgakopoulos et al. 2008 [57]	RCT	Mean age: 41 ± 13 Recruited patients: 24 Drop-out patients: 2 GRs: 24	Non-smoking patients	Miller I, II Localized GRs Rec 0 ≥ 3 mm	Maxillary and mandibular teeth. Molars were not included	USA, University, Partially supported
Pini Prato et al. 1999 [59]	Split-mouth RCT	Mean age: 33.6 ± 9.9 Recruited patients: 10 Drop-out patients: 0 GRs: 20	2 Patients were smokers (cig/day NR)	Miller I, II Localized GRs Rec 0 ≥ 2 mm	Maxillary incisors, canines and premolars	Italy, University, NR
Pini Prato et al. 2000 [58]	Split-mouth RCT	Mean age: 32.3 ± 6.3 Recruited patients: 11 Drop-out patients: 0 GRs: 22	3 patients were smokers (cig/day NR)	Miller I Localized GRs Rec 0 ≥ 2 mm	Maxillary and mandibular teeth. Molars were not included	Italy, Private practice, NR
Pini Prato et al. 2005 [65]	Case-series	Mean age: 29.70 ± 6.04 Recruited patients: 60 Drop-out patients: 0 GRs: 60	11 patients were smokers (> 10 cig/day)	Miller I Localized GRs Rec 0 ≥ 2 mm	Maxillary teeth. Molars were not included	Italy, Private practice, NR

Reino et al. 2015 [49]	Split-mouth RCT	Mean age: 42 ± 7.42 Recruited patients: 20 Drop-out patients: 0 GRs: 40	NR	Miller I, II Localized GRs Rec 0 ≥ 3 mm	Maxillary teeth. Molars were not included	Brazil, University, Supported
Zucchelli et al. 2012 [50]	RCT	Mean age: 33.6±5.8 Recruited patients: 50 Drop-out patients: 0 GRs: 50	5 patients were smokers (< 10 cig/day)	Miller I, II Localized GRs Rec 0 > 2 mm	Maxillary and mandibular molars	Italy, University, self-supported
Zucchelli et al. 2014 [51]	RCT	Mean age: NR Recruited patients: 50 Drop-out patients: 0 GRs: 50	6 patients were smokers (< 10 cig/day)	Miller I, II Rec 0 ≥ 3 mm	Mandibular incisors	Italy, University, self-supported
Zuhr et al. 2014 [52]	RCT	Mean age: 37.9 ± 9.8 Recruited patients: 60 Drop-out patients: 45 GRs: 60	Non-smoking patients	Miller I, II Localized and multiple GRs Rec 0 ≤ 5 mm	Maxillary teeth. Molars were not included	Germany, Private practice, self-supported

Note. RCT: Randomized Controlled Trial. N: number. GRs: Gingival Recessions. NR: not reported. Cig/day: cigarettes a day. Rec 0: baseline recession depth.

Table 2. General characteristics of the intervention and results

Study	Preoperative preparation	Treatment (control group)	Treatment (test group)	Post-surgical treatment	Follow-up (months)	mRC ± SD (%)	Authors conclusion
Bellver-Fernandez et al. 2016 [60]	NR	CAF	CAF + CTG	0.2% CHX NSAIDs Antibiotic for 7 days Sutures removal at 15 days	18	Control: 84.6±19.6 Test: 81.7±17.8	Both techniques were effective in reducing GRs
Berlucchi et al. 2002 [53]	OHI	CAF + EMD	CAF + CTG + EMD	0.12% CHX NSAIDs Sutures removal at 14 days	6	Control: 93.97 Test: 93.59	Both techniques were highly effective in the treatment of GRs
Chevalier et al. 2017 [61]	Two sessions of professional cleaning and OHI	CAF + CTG	CAF + XCM	0.2% CHX NSAIDs Sutures removal NR	12	Control: 94.44 Test: 87.50	No significant differences between the two groups
Del Pizzo et al. 2005 [54]	OHI and root planing of the GR	CAF	CAF + EMD	0.12% CHX NSAIDs Antibiotic for 3 days Sutures removal at 14 days	24	Control: 86.67 Test: 90.67	Root coverage outcomes was similar in both groups
Francetti et al. 2004 [62]	OHI and SRP (if indicated)	CAF + FRPA	/	0.12% CHX Sutures	12	96.15	Excellent gain in root

				removal at 14 days			coverage
Harris & Harris 1994 [63]	OHI and SRP (if indicated)	CAF	/	0.12% CHX Periodontal dressing for 1 week Sutures removal NR	5	98.8	Simple and predictable technique for root coverage
Huang & Wang 2007 [64]	OHI and dental prophylaxis	CAF	/	0.12% CHX NSAIDs Sutures removal at 10-14 days	12	93.0±14.8	The proposed suturing technique may enhance the outcomes of CAF
Huang et al. 2005 [25]	OHI SRP and occlusal adjustment if needed	CAF	CAF + PRP	0.12% CHX NSAIDs Sutures removal at 10-14 days	6	Control: 83.5±21.8 Test: 81.0±28.7	No differences within the two groups
Mahajan et al. 2012 [55]	OHI and SRP	CAF + CTG	CAF + PPG	0.2% CHX NSAIDs Periodontal dressing for 1 week Sutures removal at 7 days	12	Control: 88.5 Test: 92.6	Comparable results within the two groups. CAF + PPG was superior in terms of patient-centred outcomes
Modica et al. 2000 [56]	OHI and SRP if needed	CAF	CAF + EMD	0.12 CHX Antibiotic for 3 days	6	Control: 80.9 Test:	EMD does not seem to significantl

				Sutures removal at 14 days		91.2	y improve the outcomes of CAF
Papageorgakopoulos et al. 2008 [57]	OHI and prophylaxis	CAF + ADM	CPT + ADM	012% CHX NSAIDs Antibiotic for 2 weeks Sutures removal at 3-4 weeks	4	Control: 99±3 Test: 95±7	Better outcomes for CAF than CPT
Pini Prato et al. 1999 [59]	OHI	CAF (root planed)	CAF (root polished)	0.12% CHX NSAIDs Sutures removal at 10 days	3	Control: 83±16 Test: 89±14	No significant differences between the two groups
Pini Prato et al. 2000 [58]	OHI	CAF (without tension)	CAF (with tension)	0.12% CHX NSAIDs Sutures removal at 10 days	3	Control: 87±13 Test: 78±15	Minimal flap tension does not influence recession reduction
Pini Prato et al. 2005 [65]	OHI	CAF	/	0.12% CHX NSAIDs Sutures removal at 10 days	6	89.94	The position of the gingival margin relative to the CEJ affects CRC
Reino et al. 2015 [49]	OHI and SRP	CAF + XCM	EFT + XCM	0.12% CHX NSAIDs Sutures removal NR	6	Control: 62.80 Test: 81.89	EFT was superior than CAF when combined with XCM

Zucchelli et al. 2012 [50]	OHI, scaling and professional tooth cleaning	CAF + CTG	LMCAF	0.12% CHX NSAIDs Sutures removal at 14 days	12	Control: 88.8±11.2 Test: 74.2±8.2	Both techniques were successful in treatment GRs at molar sites
Zucchelli et al. 2014 [51]	OHI and prophylaxis	CAF	CAF + LST removal	0.12% CHX NSAIDs Sutures removal at 14 days	12	Control: 97.87 Test: 82.8	CAF + LST removal was more effective than CAF alone in the treatment of GRs affecting lower incisors
Zuhr et al. 2014 [52]	OHI and prophylaxis	CAF + EMD	TUN + CTG	CHX NSAIDs Sutures removal at 7 days	12	Control: 71.8±20.3 Test: 98.4±3.6	TUN showed better clinical outcomes than CAF

Note. NR: Not Reported. OHI: Oral hygiene instruction. SRP: Scaling and root planing. CPT: Coronally positioned tunnel. EFT: Extended flap technique. LMCAF: Laterally moved, coronally advanced flap. LST: Labial submucosal tissue. TUN: tunnel technique. CHX: Chlorhexidine. NSAID: Non-Steroidal Anti-Inflammatory Drugs.

Table 3. Frequency of treated teeth according to their location

Arch	Tooth	Number (N)	Percentage (%)
Maxillary	Central	17	4.26
	Lateral	13	3.26
	Canine	137	34.34
	First premolar	76	19.04
	Second premolar	10	2.51
	First molar	25	6.27
Mandibular	Central	43	10.78
	Lateral	26	6.52
	Canine	22	5.51
	First premolar	14	3.51
	Second premolar	6	1.50
	First molar	10	2.51

Table 4. Comparison of mean Root Coverage (mRC), Complete Root Coverage (CRC), Keratinized Tissue Gain (KT gain), Probing Depth reduction (PD red) and Clinical Attachment Level gain (CAL gain) based on tooth location

Comparison	mRC	CRC	Odds ratio CRC	KT gain	PD red	CAL gain
Anterior / Posterior teeth	p=0.02*	p=0.01*	1.63*	p=0.04*	p<0.01*	p=0.002*
Maxillary – Mandibular teeth	p=0.45	p=0.95	1.27	p<0.001†	p<0.001†	p<0.001†
Right – Left teeth	p=0.12	p=0.38‡	1.60‡	p=0.74	p=0.86	p=0.76

Note. * statistically significant p-value favoring anterior teeth compared to posterior teeth; † statistically significant p-value favoring mandibular teeth compared to maxillary teeth; ‡ statistically significant p-value favoring right teeth compared to maxillary teeth