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Complete Root Coverage for Miller Class I and II – Recession Type Defects: Meta-Analysis of CAF+EMD Versus CAF+FCTG

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ABSTRACT

Background: To the best of our knowledge, the equality of CAF + EMD and CAF + FCTG regarding complete root coverage in Miller class I and II recession-type defects is still uncertain.

Aim: The aim of the current paper is to compare the effect of CAF + EMD versus CAF + FCTG regarding complete root recession coverage. Thereby, equality on the longer term of both therapeutic options is hypothesized (H0- hypothesis).

Materials and methods: Three reviewers searched independently within the electronic database Pubmed/Medline. Only RCTs reporting quantitative data for the outcome variable percentage complete root coverage (%CRC) for the therapeutic options CAF + EMD or CAF + FCTG were considered. Additionally a manual search in the reference lists of all included publications was accomplished.

Results: After electronical and manual search for relevant studies, the three independent reviewers (DZ, TU, AL) screened 552 titles, resulting in 102 abstracts and 41 full-texts. Eventually, twenty-five papers could be included for meta-analysis. By comprehensively comparing data from RCTs for the outcome variable "percentage complete root coverage", statistically significant weighted mean differences in favor of CAF + FCTG were found at 6, 12 and 24 months.

Conclusion: Regarding percentage complete root coverage, CAF + EMD is not as effective as CAF + FCTG for Miller class I and II recession- type defects.

Keywords: *Miller class I and II recession-type defects, root coverage, coronally advanced flap, free connective tissue graft, enamel matrix derivative*

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Introduction

Gingival recession is defined as displacement of the gingival margin apical to the cemento-enamel junction with root surface exposure (Wennström 1996). Recession-type defects can be seen in subjects of all ages with suboptimal as well as with excellent oral hygiene (Sagnes & Gjermo 1976). Possible causes are for example periodontal disease, traumatic tooth brushing, as well as malposition of teeth or orthodontic tooth movement out of the bony envelope (Gorman 1967; Boyd 1978; Miller & Allen 1996).

Main indications for root coverage procedures are esthetic / cosmetic demands, root sensitivity as well as changing the topography of the marginal soft tissue to facilitate plaque control (Wennström, et al. 2008; Zuhr & Hürzeler 2011). Interestingly, Miller (1985) created a classification system for recession-type defects to predict treatment success. Thereby, it is presumed that for Class I and II recession–type defects (i.e. recession within the attached gingiva and recession up to the mucogingival margin, respectively) complete root coverage can be achieved.

Up to now, the so-called coronally advanced flap (CAF) combined with a free connective tissue graft (FCTG) is considered the "gold standard" for root coverage therapy (Cairo, et al. 2014; Chambrone & Tatakis 2015). Consequently, alternative techniques are generally compared to CAF + FCTG and evaluated according to their ability to reduce recession and achieve root coverage (Oates, et al. 2003, Academy-Report 2005, Chambrone, et al. 2009). During the last decades, an alternative method avoiding a second surgery for the FCTG, the „Coronally Positioned Flap" in combination with "Enamel Matrix Derivative" (CAF + EMD) gained attention (Modica et al. 2000) However, to the best of our knowledge, the equality of CAF + FCTG and CAF + EMD regarding complete root coverage in Miller class I and II recession-type defects is still uncertain. Therefore, the aim of the current paper is to compare the effect of CAF + EMD versus CAF + FCTG regarding complete root recession coverage. Thereby, equality on the longer term of both therapeutic options is hypothesized (H_0- hypothesis).

Material and Methods

Search Strategy

Three reviewers (Daniela Zitsch (DZ), Thomas Ulrich (TU), Andreas Leiner (AL)) searched independently within the electronic database PubMed/Medline, US National Library of Medicine, National Institute of Health (http://www.ncbi.nlm.nih.gov/pubmed) for relevant publications.

The typewritten search strategy for „Coronally Advanced Flap" in combination with a "free connective tissue graft" (CAF + FCTG) was: (Recession coverage OR root coverage OR plastic periodontal surgery) AND (FCTG OR free connective tissue graft OR connective tissue graft OR subepithelial graft)

Thereafter, that search strategy for CAF + FCTG was translated by the search engine of Pubmed/Medline to:
((Recession[All Fields] AND ("AHIP Cover"[Journal] OR "coverage"[All Fields])) OR (("plant roots"[MeSH Terms] OR ("plant"[All Fields] AND "roots"[All Fields]) OR "plant roots"[All Fields] OR "root"[All Fields]) AND ("AHIP Cover"[Journal] OR "coverage"[All Fields])) OR (("plastics"[MeSH Terms] OR "plastics"[All Fields] OR "plastic"[All Fields]) AND periodontal[All Fields] AND

(“surgery”[Subheading] OR “surgery”[All Fields] OR “surgical procedures, operative”[MeSH Terms] OR (“surgical”[All Fields] AND “procedures”[All Fields] AND “operative”[All Fields]) OR “operative surgical procedures”[All Fields] OR “surgery”[All Fields] OR “general surgery”[MeSH Terms] OR (“general”[All Fields] AND “surgery”[All Fields]) OR “general surgery”[All Fields]))) AND (FCTG[All Fields] OR (free[All Fields] AND (“connective tissue”[MeSH Terms] OR (“connective”[All Fields] AND “tissue”[All Fields]) OR “connective tissue”[All Fields]) AND (“transplants”[MeSH Terms] OR “transplants”[All Fields] OR “graft”[All Fields])) OR ((“connective tissue”[MeSH Terms] OR (“connective”[All Fields] AND “tissue”[All Fields]) OR “connective tissue”[All Fields]) AND (“transplants”[MeSH Terms] OR “transplants”[All Fields] OR “graft”[All Fields])) OR (subepithelial[All Fields] AND (“transplants”[MeSH Terms] OR “transplants”[All Fields] OR “graft”[All Fields])))

In analogue, the typewritten search strategy for “Coronally Advanced Flap” in combination with “Enamel matrix Derivative” (CAF + EMD) was: (Recession coverage OR root coverage OR plastic periodontal surgery) AND (Emdogain OR EMD OR Amelogenin OR enamel proteins OR growth factor)

Thereafter, that search strategy for CAF + EMD was translated by the search engine of PubMed/Medline to:
((Recession[All Fields] AND (“AHIP Cover”[Journal] OR “coverage”[All Fields])) OR ((“plant roots”[MeSH Terms] OR (“plant”[All Fields] AND “roots”[All Fields]) OR “plant roots”[All Fields] OR “root”[All Fields]) AND (“AHIP Cover”[Journal] OR “coverage”[All Fields])) OR ((“plastics”[MeSH Terms] OR “plastics”[All Fields] OR “plastic”[All Fields]) AND periodontal[All Fields] AND (“surgery”[Subheading] OR “surgery”[All Fields] OR “surgical procedures, operative”[MeSH Terms] OR (“surgical”[All Fields] AND “procedures”[All Fields] AND “operative”[All Fields]) OR “operative surgical procedures”[All Fields] OR “surgery”[All Fields] OR “general surgery”[MeSH Terms] OR (“general”[All Fields] AND “surgery”[All Fields]) OR “general surgery”[All Fields]))) AND ((“enamel matrix proteins”[Supplementary Concept] OR “enamel matrix proteins”[All Fields] OR “emdogain”[All Fields]) OR EMD[All Fields] OR (“amelogenin”[MeSH Terms] OR “amelogenin”[All Fields]) OR ((“dental enamel”[MeSH Terms] OR (“dental”[All Fields] AND “enamel”[All Fields]) OR “dental enamel”[All Fields] OR “enamel”[All Fields]) AND (“proteins”[MeSH Terms] OR “proteins”[All Fields])) OR (“intercellular signaling peptides and proteins”[MeSH Terms] OR (“intercellular”[All Fields] AND “signaling”[All Fields] AND “peptides”[All Fields] AND “proteins”[All Fields]) OR “intercellular signaling peptides and proteins”[All Fields] OR (“growth”[All Fields] AND “factor”[All Fields]) OR “growth factor”[All Fields])

Screening Process

The three independent reviewers (DZ, TU, AL) searched titles and evaluated abstracts as well as fulltexts for meta-analytical inclusion. Any difference between the reviewers was resolved by discussion. Eventually, for papers selected for meta-analysis, data extraction sheets were developed, tested and operated (Table 1). Thereafter, data for meta-analysis were synopsized in an excel-sheet.

Manual Search

Additionally to the search in the electronic database PubMed/Medline, a manual search for relevant studies was performed independently by the three reviewers (DZ, TU, AL). Thereby, the references of the studies included for meta- analysis were screened according to the above detailed process (i.e. title-, abstract-, and full text-analysis).

Outcome Variable

In this paper the outcome variable percentage complete root coverage (%CRC) is meta-analyzed.

Thereby, the formula for the outcome variable was:

$$\%CRC = \frac{\text{number of teeth with complete coverage}}{\text{number of treated teeth}}$$

Inclusion- / Exclusion Criteria

To test the hypothesis of equality on the longer term of both therapeutic options only randomized controlled clinical trials (RCTs) were considered for the current systematic review / meta- analysis. Further, studies with a publishing date before the year 2000 were excluded. Moreover, only RCTs with at least 10 patients per treatment protocol were included. Thereby, only reports on Miller class I and II recession- type defects were considered. Studies with Miller Class III and IV recession– type defects were excluded. It goes without saying that only studies using either FCTG or EMD in combination with a "Coronally Advanced Flap" were included. For comparison, the included studies should present quantitative data at 6, 12, 18 and/or 24 months after surgery.

Quality Assessment

Risk of bias assessment of the included articles was accomplished. It was done according to the „Cochrane Handbook" (http://handbook.cochrane.org/chapter _ 8 / 8 _ 5the _ coch- rane_collaborations_tool_for_ assessing_risk_of_bias-htm).Thereby, five main criteria were analyzed: random sequence generation (RSG), allocation concealment (ALC), blinding of outcome assessment (BOA), incomplete outcome (ICD), selective reporting (SLR). Accordingly, by judging a paper for all five criteria as being associated with a low risk of bias, the publication was judged as being associated with a low risk of bias. Further, by judging a paper for three to four criteria as being associated with a low risk of bias, the paper itself was judged as being associated with a moderate risk of bias. Whereas, by judging a paper for less than three criteria as being associated with a low risk of bias, the publication itsef was judged as being associated with a high risk of bias (Higgins & Green 2011).

Cochrane Review Manager / Meta-analytic Approach

The so-called „Cochrane Review Manager (RevMan)" (current version 5.3.5; http:// community.cochrane.org / editorial-and-publishing-policy-resource/review-manager-revman) is a software program providing guidance to write systematic reviews and / or meta-analyses. All relevant data - the authors agreed to analyze all parameters on tooth level and not on patient level - at 6, 12, 18 and / or 24 months of all included studies were conveyed to RevMan version 5.3.5 and meta-analyzed. Thus, for comprehensive comparison at different time points, „weighted means" for the outcome variable percentage complete root coverage (%CRC) were determined by the calculator program of RevMan version 5.3.5. Further, RCTs evaluating CAF + EMD versus CAF + FCTG per protocol were compared directly. However, meta-analysis

with RevMan version 5.3.5 is only possible, if standard deviations are given. It goes without saying that for the variable %CRC no standard deviations could be retrieved from the included RCTs. Therefore, for all %CRC-data a standard deviation tending to zero and thereby not effecting the meta-analysis (i.e. 0.001) was operated. Further, for directly compared data statistical heterogeneity was tested. As a result, either fixed- or random-statistical models were operated. A significance level of 0.05 was chosen. Additionally, forest plots were generated.

Heterogeneity

Heterogeneity was defined and tested according to the „Cochrane Handbook" for systematic reviews (http://handbook. cochrane .org / chapter_9/9_5_2_ identifying _ and _ measuring_heterogeneity.htm). Thereby, RevMan version 5.3.5 is operating a chi-squared test (χ^2, or Chi^2) to determine heterogeneity and its impact on the meta-analysis is represented with I^2. The test evaluates whether observed differences in results are compatible with chance alone. A low p-value ($p < 0.1$ or a large chi-squared statistic relative to its degree of freedom) provides evidence of heterogeneity of intervention effects (i.e. variation in effect estimates beyond chance). The interpretation of I^2 can be done as follows: 0% to 40% might not be important, 30% to 60% may represent moderate heterogeneity, 50% to 90% may represent substantial heterogeneity and 75% to 100% might be seen as considerably heterogeneity (Higgins & Green 2011).

Detailed Hypotheses

As stated above, the aim of the current meta-analysis is to compare the effects of CAF + EMD and CAF + FCTG regarding root recession coverage. Thereby, equality on the longer term of both therapeutic options is hypothesized (H_0- hypothesis). More in detail, equality for the outcome variable percentage complete root coverage (%CRC) is hypothesized.

Results

Selection of the Studies

After electronical and manual search for relevant studies, the three independent reviewers (DZ, TU, AL) screened 552 titles, resulting in 102 abstracts and 41 full-texts. Eventually, twenty-five papers could be included for the meta-analysis (Fig. 1). After fulltext reading excluded papers are listed in Table 3. Reasons for exclusion are given.

Included studies

In the end the following studies could be included:

Table 2. *Included Studies*

Study	Characteristics
Abolfazli et al. 2009	Patients: 12 Recession defects: 24 Therapies: CAF + FCTG vs. CAF + EMD
Alkan & Parlar 2011	Patients: 12 Recession defects: 24 Therapies: CAF + EMD vs. CAF + FCTG
Alkan & Parlar 2013	Patients: 12 Recession defects: 56 Therapies: CAF + EMD vs. CAF + FCTG
Cairo et al. 2012recession reduction (RecRed	Patients: 29 Recession defects: 29 Therapies: CAF vs. CAF + FCTG
Cardaropoli et al. 2012	Patients: 18 Recession defects: 22 CAF + PCM vs. CAF + FCTG
Castellanos et al. 2006	Patients: 22 Recession defects: 22 Therapies: CAF vs. CAF + EMD
Cordaro et al. 2012	Patients: 12 Recession defects: 58 Therapies: CAF vs. CAF + EMD
Cortellini et al. 2009	Patients: 85 Recession defects: 85 Therapies: CAF vs. CAF + FCTG
Cueva et al. 2004controlled, clinical investigation was to evaluate the differences in clinical parameters of root coverage procedures utilizing coronally advanced flaps (CAF	Patients: 17 Recession defects: 58 Therapies: CAF vs. CAF + EMD
Hägewald et al. 2002	Patients: 36 Recession defects: 72 Therapies: CAF + Placebo vs. CAF + EMD
Jaiswal et al. 2012	Patients: 20 Recession defects: 46 Therapies: CAF vs. CAF + EMD
Kuis et al. 2013	Patients: 37 Recession defects: 114 Therapies: CAF vs. CAF + FCTG
Kumar & Murthy 2013while keratinized tissue width (KTW	Patients: 12 Recession defects: 24 Therapies: CAF + FCTG vs. CAF + PCG

McGuire & Nunn 2003 McGuire & Scheyer 2010	Patients: 20 Recession defects: 40 Therapies: CAF + EMD vs. CAF + FCTG Patients: 25 Recession defects: 50 Therapies: CAF + FCTG vs. CAF + CM
McGuire et al. 2014	Patients: 30 Recession defects: 60 Therapies: CAF + FCTG vs. CAF + HPDGF + β-TCP
Modica et al. 2000one site was randomly assigned to the test group and the contralateral site to the control group. The treatment consisted of a CAF procedure with (test	Patients: 12 Recession defects: 28 Therapies: CAF vs. CAF + EMD
Del Pizzo et al. 2005	Patients: 15 Recession defects: 30 Therapies: CAF vs. CAF + EMD
Roman et al. 2013	Patients: 42 Recession defects: 68 Therapies: CAF + FCTG vs. CAF + FCTG + EMD
Salhi et al. 2014 Sayar et al. 2013	Patients: 40 Recession defects: 40 Therapies: CAF + FCTG vs. FCTG + Pouch Technique Patients: 13 Recession defects: 40 Therapies: CAF + FCTG vs. CAF + EMD
da Silva et al. 2004	Patients: 11 Recession defects: 22 Therapies: CAF vs. CAF + FCTG
Spahr et al. 2005	Patients: 30 Recession defects: 60 Therapies: CAF + Placebo vs. CAF + EMD
Zucchelli, Marzadori, et al. 2014	Patients: 50 Recession defects: 50 Therapies: CAF + FCTG vs. CAF + FCTG + removed LST
Zucchelli, Mounssif, et al. 2014	Patients: 50 Recession defects: 149 Therapies: CAF vs. CAF + FCTG

Risk of Bias

In the present systematic review / meta-analysis of the current literature, three included studies were judged as being associated with a low risk of bias (Cortellini et al. 2009, McGuire & Nunn 2003 and Roman et al. 2013), whereas twenty studies were judged as being associated with a moderate risk of bias (Abolfazli et al. 2009, Alkan & Parlar 2011, Alkan & Parlar 2013, Cairo et al. 2012recession reduction (RecRed, Cardaropoli et al. 2012, Cordaro et al. 2012, da Silva et al. 2004, del Pizzo et al. 2005, Hägewald et al. 2002, Jaiswal et al. 2012, Kuis et al. 2013, Kumar & Murthy 2013while keratinized tissue width (KTW, McGuire & Scheyer 2010, McGuire et al. 2014, Modica et al. 2000one site was randomly assigned to the test group and the contralateral site to the control group. The treatment consisted of a CAF procedure with (test, Salhi et al. 2014, Sayar et al. 2013, Spahr et al. 2005, Zucchelli Mounssif, et al. 2014 and Zucchelli, Marzadori, et al. 2014), and two studies were judged as being associated with a high risk of bias (Castellanos et al. 2006 and Cueva et al. 2004)(Tab. 4).

Percentage Complete Root Coverage (%CRC)

RCTs comprehensively compared at six months

For meta- analysis of percentage complete root coverage (%CRC) at six months the studies of Cordaro et al. (2012); Cueva et al. (2004); Modica et al. (2000with the adjunct of EMD for test sites, was performed. Clinical measurements (recession length, keratinized tissue, probing depth, and clinical attachment level) for CAF + EMD and the studies of Cairo et al. (2012); Cortellini et al. (2009); Kuis et al. (2013); McGuire et al. (2014); Roman et al. (2013); Salhi et al. (2014); da Silva et al. (2004); Zucchelli, Mounssif, et al. (2014recession reduction (RecRed) for CAF + FCTG could be included.

At six months after root coverage surgery a weighted mean percentage complete root coverage of 54.1% (SD: 19.3%) for CAF + EMD was calculated. For CAF + FCTG a weighted mean percentage complete root coverage of 78.8% (SD: 18.2%) was found. Thereby, the calculated weighted mean difference of 24.7% (95% CI [19.8%, 29.7%]) in favor of CAF + FCTG was statistically significant (Fig. 3).

However, it should be kept in mind that only two of the included studies were judged as being associated with a low risk of bias (Cortellini et al. 2009; Roman et al. 2013), eight studies were judged as being associated with a moderate risk of bias (Cairo et al. 2012; Cordaro et al. 2012; Kuis et al. 2013; McGuire et al. 2014; Modica et al. 2000; Salhi et al. 2014; da Silva et al. 2004; Zucchelli, Mounssif, et al. 2014)recession reduction (RecRed and one study as being associated with a high risk of bias (Cueva et al. 2004)controlled, clinical investigation was to evaluate the differences in clinical parameters of root coverage procedures utilizing coronally advanced flaps (CAF.

RCTs directly compared at six months

At six months, no publication reported the effect difference for the outcome variable %CRC directly.

RCTs comprehensively compared at twelve months

For meta- analysis at twelve months the studies of Abolfazli et al. (2009); Alkan & Parlar (2011); Castellanos et al. (2006); McGuire & Nunn (2003) for CAF + EMD and the studies

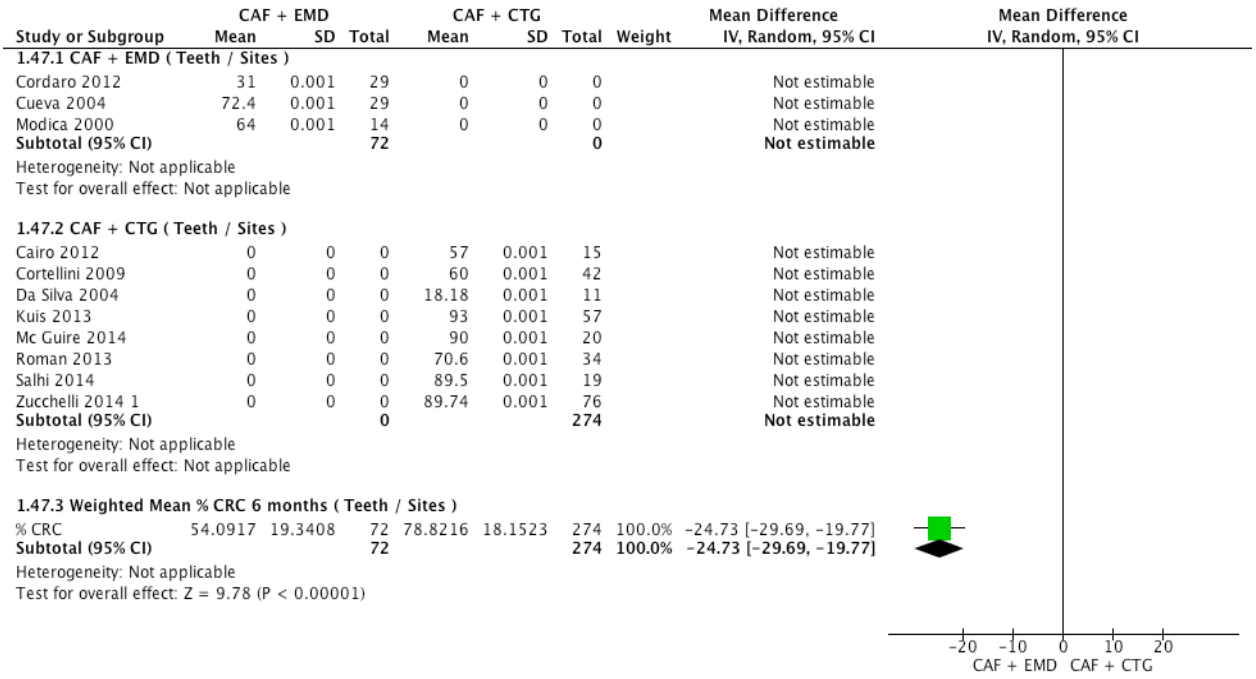

Fig. 2. *Percentage complete root coverage at six months*

of Abolfazli et al. (2009); Alkan & Parlar (2011); Cardaropoli et al. (2012); Kuis et al. (2013); McGuire & Nunn (2003); Roman et al. (2013); Zucchelli, Marzadori, et al. (2014); Zucchelli, Mounssif, et al. (2014) for CAF + FCTG could be included.

At twelve months after root coverage surgery a weighted mean percentage complete root coverage of 67.0 % (SD: 16.2%) for CAF + EMD was calculated. For CAF + FCTG a weighted mean percentage complete root coverage of 78.4% (SD: 14.7%) was found. Thereby, the calculated weighted mean difference of 11.5% (95% CI [7.1%, 15.9%]) in favor of CAF + FCTG was statistically significant (Fig.3).

However, it should be understood that only two studies were judged as being associated with a low risk of bias (McGuire & Nunn 2003; Roman et al. 2013), six studies were judged as being associated with a moderate risk of bias (Abolfazli et al. 2009; Alkan & Parlar 2011; Cardaropoli et al. 2012; Kuis et al. 2013; Zucchelli, Marzadori, et al. 2014; Zucchelli, Mounssif, et al. 2014) and one study as being associated with a high risk of bias (Castellanos et al. 2006).

RCTs directly compared at twelve months

At twelve months after plastic periodontal surgery three papers comparing percentage complete root coverage for CAF + EMD versus CAF + FCTG per protocol, i.e. directly, were eventually included in the current meta-analysis (Abolfazli et al. 2009; Alkan & Parlar 2011; McGuire & Nunn 2003) (Fig.4). Thereby, Abolfazli et al. (2009) found a percentage of complete root coverage of 50% for CAF + EMD and 58.3% for CAF + FCTG. The mean difference was 8.0% in favor of CAF + FCTG. This difference was statistically significant (Fig. 4). In contrast, McGuire & Nunn (2003) found a percentage of complete root coverage of 89.5% for CAF + EMD and 79% for CAF

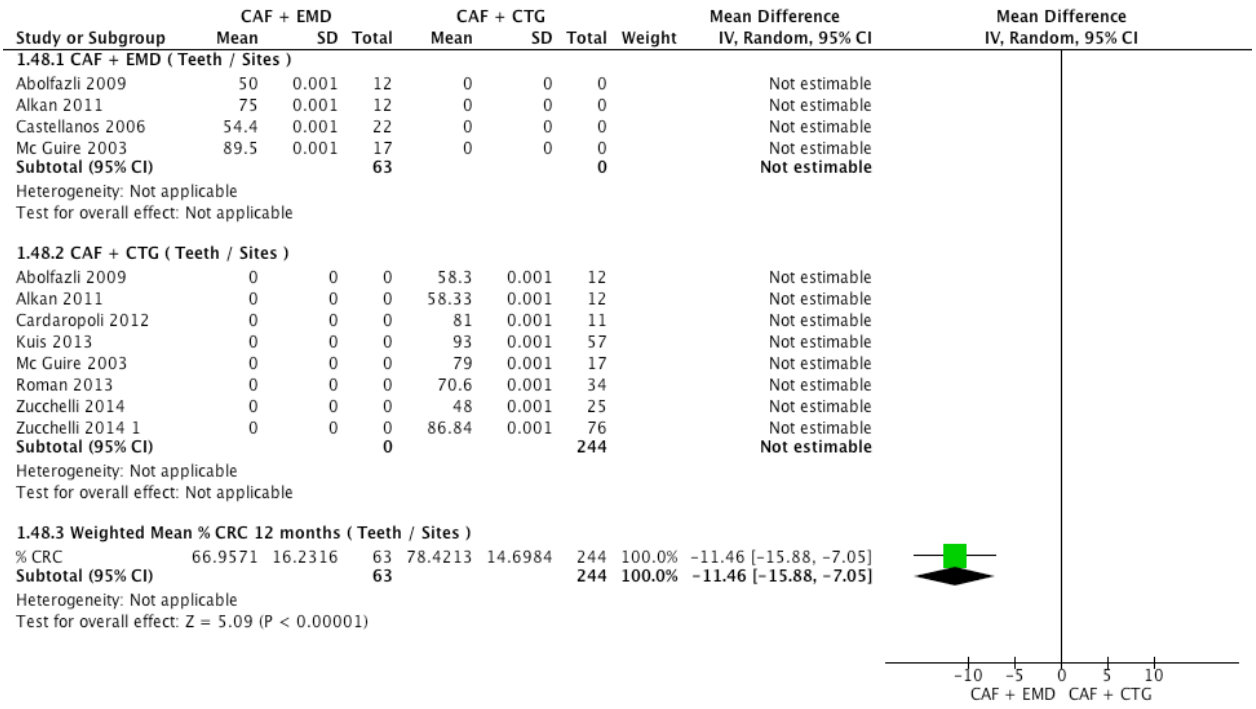

Fig. 3. *Percentage complete root coverage at twelve months*

+ FCTG. The mean difference was 10.5% in favor of CAF + EMD. Again, this difference was statistically significant (Fig. 4). Further, Alkan & Parlar (2011) reported a percentage of complete root coverage of 75% for CAF + EMD and 58.3% for CAF + FCTG. The mean difference was 16.7% in favor of CAF + EMD. This difference was statistically significant (Fig. 4). In total, the weighted mean difference between CAF + EMD and CAF + FCTG of all three studies together was 6.3% (95% CI [-7.7%, 20.3%]). This difference was not statistically significant (Fig. 4).

Additionally, it should be mentioned that statistical heterogeneity across the studies could be found (Heterogeneity: Chi^2 = 2068926160.98, df = 2 ($P < 0.00001$); I^2 = 100%). Moreover, it should be kept in mind that only one study was judged as being associated with a low risk of bias (McGuire & Nunn 2003), whereas two studies were judged as being associated with a moderate risk of bias (Abolfazli et al. 2009; Alkan & Parlar 2011).

Comparing comprehensively versus directly at twelve months

The weighted mean difference of comprehensively compared data was statistically significant in favor of CAF + FCTG (11.6%; 95% CI [7.1%, 15.9%]), whereas the weighted mean difference of directly compared data (6.3% in favor of CAF + EMD; 95% CI [-7.7%, 20.3%]) was not statistically significant.

RCTs comprehensively compared at 24 months

For meta- analysis at twenty-four months the studies of Abolfazli et al. (2009); Cordaro et al. (2012); Del Pizzo et al. (2005); Spahr et al. (2005) for CAF + EMD and the studies of Abolfazli et al. (2009); Kuis et al. (2013) for CAF + FCTG could be included.

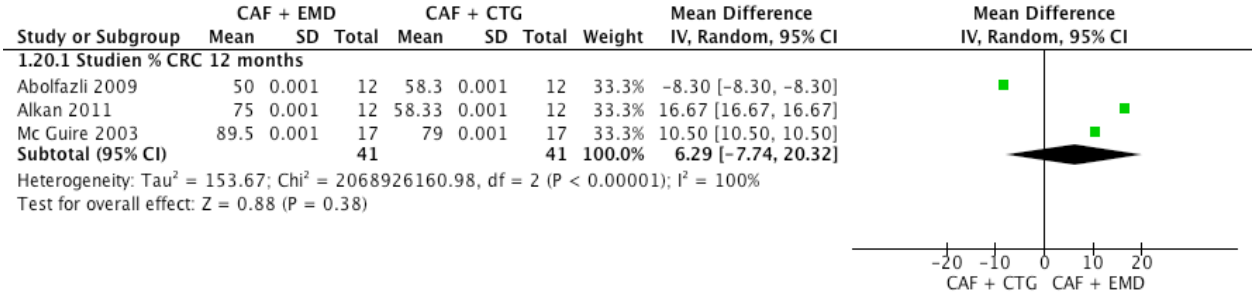

Fig. 4. *Percentage complete root coverage at twelve months (directly compared)*

At twenty-four months after root coverage surgery a weighted mean percentage complete root coverage of 40.5% (SD: 21.6%) for CAF + EMD was calculated. For CAF + FCTG a weighted mean percentage complete root coverage of 85.5% (SD: 8.7%) was found. Thereby, the calculated weighted mean difference of 45.0% (95% CI [40.0%, 50.0%]) in favor of CAF + FCTG was statistically significant (Fig. 5).

Further, all five studies were judged as being associated with a moderate risk of bias (Abolfazli et al. 2009; Cordaro et al. 2012; Kuis et al. 2013; Del Pizzo et al. 2005; Spahr et al. 2005).

RCTs directly compared at twenty-four months

At twenty-four months only one study comparing CAF + FCTG versus CAF + EMD per protocol, i.e. directly, was eventually included in the current paper (Abolfazli et al. 2009). For CAF + EMD 25% complete root coverage and for CAF + FCTG 66.6% complete root coverage was found. This difference was statistically significant in favor of CAF + FCTG.

Discussion

Briefly, the current meta-analysis aimed to compare the effects of CAF + EMD versus CAF + FCTG regarding root recession coverage. Thereby, it was hypothesized (H_0-hypothesis) that for the outcome variable "percentage complete root coverage" the results achieved by CAF + EMD do not differ statistically significant from CAF + FCTG on the longer term.

By comprehensively comparing data from RCTs for the outcome variable "percentage

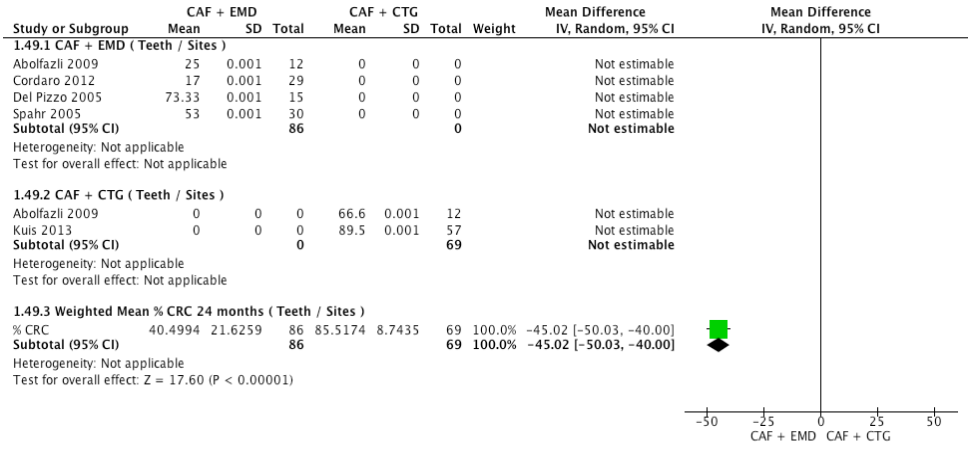

Fig. 5. *Percentage complete root coverage at twenty-four months*

complete root coverage", statistically significant weighted mean differences of 24.7% (95% CI [29.7%, 19.8%]), 11.5% (95% CI [7.1%, 15.9%]) and 45.0% (95% CI [40.0%, 50.0%]) in favor of CAF + FCTG were found at 6, 12 and 24 months, respectively. At 6 months there were no studies reporting mean differences between CAF + EMD and CAF + FCTG directly. In contrast to comprehensively compared data from RCTs, for RCTs directly comparing CAF + EMD versus CAF + FCTG, no statistically significant difference was found at twelve months. However, at 24 months a statistically significant difference in favor of CAF + FCTG was found. Thereby, it should be kept in mind that most of the studies were not judged as having a low risk of bias and statistical heterogeneity was found.
Therefore, we tend to reject the H_0 – hypothesis of no difference and we have the tendency to accept a superiority of CAF + FCTG regarding the outcome variable percentage complete root coverage on the longer term. It should be kept in mind that comprehensively comparing RCTs resulted in weighted mean percentages of complete root coverage of 78.8% (SD: 18.2%), 78.4% (SD: 14.7%), and 85.5% (SD: 8.7%) for CAF + FCTG in Miller class I and II recession-type defects at six, twelve, and twenty-four months after plastic periodontal surgery, respectively. Thus, as presumed by Miller (1985) in general complete root coverage can be achieved in Class I and II recession–type defects and obviously the mean percentages of complete root coverage increase over time. However, it should be understood that even with the so-called "gold standard" prediction of complete root coverage is not possible.

Somehow in contrast, comprehensively comparing RCTs resulted in weighted mean percentages of complete root coverage of only 54.1% (SD: 19.3%), 67.0 % (SD: 16.2%), and 40.5% (SD: 21.6%) for CAF + EMD in Miller class I and II recession-type defects at six, twelve, and twenty-four months after plastic periodontal surgery, respectively. It goes without saying that with this method the clinician cannot predict complete root coverage at all.

Moreover, conclusions of earlier reports that CAF + EMD resulted in root coverage similar to CAF + FCTG but without the morbidity and potential clinical difficulties associated with the donor site surgery (McGuire and Nunn 2003; Alkan and Parlar 2011, 2013; Sayer et al. 2013) must be - at least regarding percentage of complete root coverage - interpreted with caution.

Conclusion

Within the limits of the current meta-analysis of the literature regarding plastic periodontal surgery of Miller class I and II recession- type defects it is concluded that CAF + EMD is not as effective as CAF + FCTG as regards percentage complete root coverage.

Appendix

Table 1. *Data extraction sheet*

Publication (authors, title, journal, date)		
Abstract		
Earlier reports of same study		
Study design	Study design	
	Treatment test group	
	Treatment control group	
	Split mouth	
	Study duration	
	Funding	
Methodological quality	Allocation concealment	
	Surgeon blinding	
	Examiner blinding	
	Sequence generation	
	Sample size calculation	
	Dropouts	
Intervention	Type surgery	
	FCTG from tuberosity / palate	
	Pre-surgical treatment of site (scaling/ rootplaning, reducing root convexity, AB)	
	Healing / complications	
	Treatment of complications	
	Supportive Periodontal Therapy	

Inclusion criteria patients / sites	Number of patients (M/F/Age)	
	Other inclusion criteria patients	
	Number of sites (= teeth)	
	Miller class	
	Other inclusion criteria sites	
	Smokers	
	Single / multiple recessions	
	Upper / lower jaw	
	Type of teeth	
Outcome variable **Frequency of complete root-coverage (%CRC)** 6 / 12/ 24 months		
Control variable for oral hygiene API [%] PBI [%]		

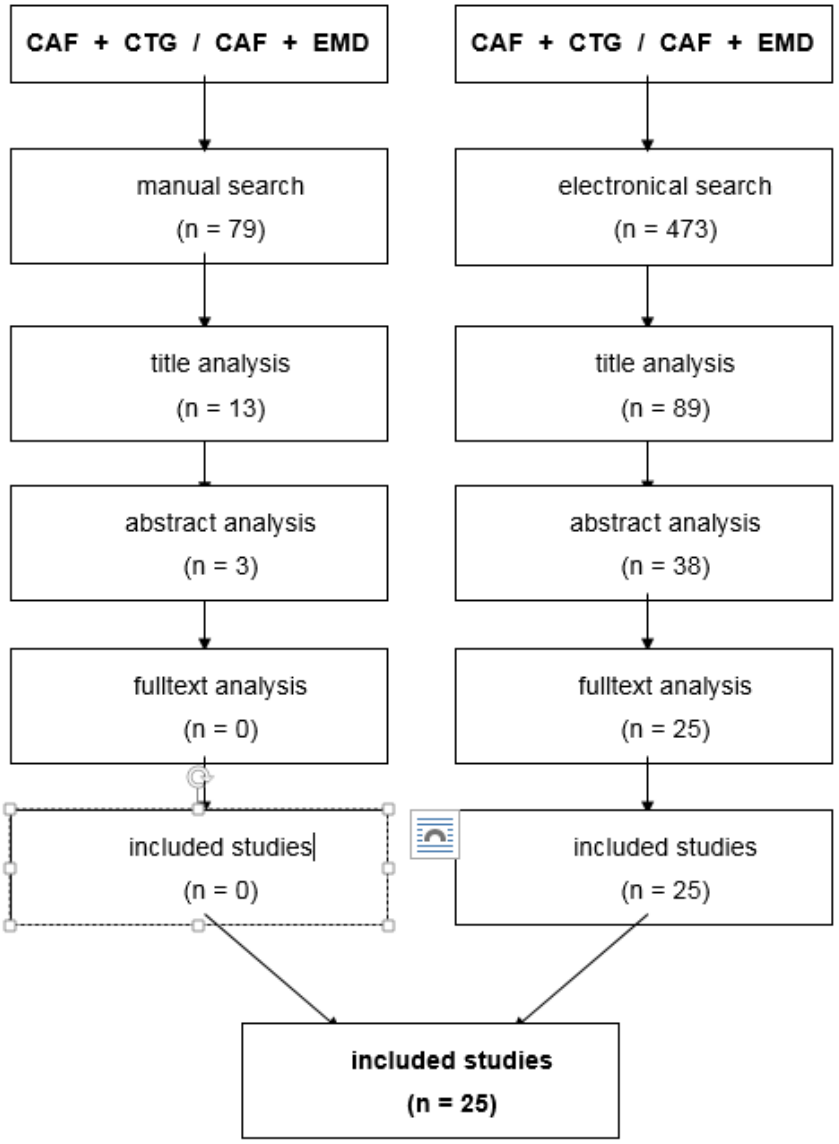

Fig. 1. *Study selection*

Table 3. *Excluded studies (RCTs) after fulltext analysis with reason*

Publication ***electronical search***	**Intervention**	**Test group**	**Control group**	**Reason(s) for exclusion**
Berlucchi et al. 2002	Recession coverage Miller Class I and II	CAF + EMD	CAF + FCTG + EMD	no RCT
Berlucchi et al. 2005	Recession coverage Miller Class I and II	CAF + EMD	no	no RCT
Cheng et al. 2007	Recession coverage Miller Class I and II	CAF + EMD	CAF or CAF + CRSC	no RCT
Cheng et al. 2014	Recession coverage Miller Class I, II and III	CAF + EMD or CAF + FCTG + EMD	CAF or CAF + FCTG	no RCT and Miller Class III recessions
Lafzi et al. 2007	Recession coverage Miller Class I and II	CAF + FCTG (P-flap)	CAF + FCTG (P-teeth)	only 8 patients
Martorelli de Lima et al. 2006	Recession coverage Miller Class I and II	CAF + FCTG	no	no RCT (no control group)
Mc Guire et al. 2012	Recession coverage Miller Class I and II	CAF + EMD	CAF + FCTG	only 9 patients
Nart et al. 2012	Recession coverage Miller Class II and III	CAF + FCTG	no	no RCT and Miller Class III recessions
Nemcovsky et al. 2004	Recession coverage Miller Class I and II	CAF + EMD	CAF + FCTG	no RCT
Pilloni et al. 2006	Recession coverage Miller Class I and II	CAF + EMD	no	single study with outcomes only at 18 months, outcomes are not comparable
Pini- Prato et al. 2010	Recession coverage Miller Class I, II and III	CAF + FCTG	CAF	Miller Class III recession
Tatakis et al. 2015	Recession coverage Miller Class I and II	CAF + EMD or CAF + ADMG	CAF + FCTG	no RCT
Tonetti et al. 2014	Recession coverage Miller Class I, II and III	CAF + EMD or CAF + GTR	CAF + FCTG	no RCT
Publication ***manual search***	**Intervention**	**Test group**	**Control group**	**Reason(s) for exclusion**
Buti et al. 2013	Recession coverage Miller Class I and II	CAF + EMD or CAF + CM	CAF + FCTG	no RCT
Montebugnoli et al. 2012	Recession coverage Miller Class I and II	BT	LMCAF	other surgical therapies
Zucchelli et al. 2005	Recession coverage Miller Class I and II	CAF	no	other surgical therapy

Table 4. *Quality assessment (risk of bias)*

Studies	*RSG*	*ALC*	*BOA*	*ICD*	*SLR*	*Risk of bias*
Abolfazli et al. (2009)	un	un	Y	N	N	Moderate
Alkan & Parlar (2011)	ad	un	un	N	N	Moderate
Cairo et al. (2012)	un	un	Y	N	N	Moderate
Cardaropoli et al. (2012)	ad	un	Y	N	N	Moderate
Castellanos et al. (2006)	inad	un	un	N	N	High
Cordaro et al. (2012)	ad	un	Y	N	N	Moderate
Cortellini et al. (2009)	ad	ad	Y	Y	N	Low
Cueva et al. (2004)	ad	un	N	N	Y	High
Da Silva et al. (2004)	ad	un	N	N	N	Moderate
Del Pizzo et al. (2005)	ad	un	Y	N	N	Moderate
Kuis et al. (2013)	ad	un	Y	N	N	Moderate
Mc Guire et al. (2003)	ad	un	Y	N	N	Low
Mc Guire et al. (2014)	ad	un	Y	N	N	Moderate
Modica et al. (2000)	ad	un	Y	N	N	Moderate
Roman et al. (2013)	ad	ad	Y	N	N	Low
Salhi et al. (2014)	ad	un	N	N	N	Moderate
Spahr et al. (2005)	un	un	Y	N	N	Moderate
Zucchelli et al. (2014, 41 S. 396-403)	ad	un	Y	N	N	Moderate
Zucchelli et al. (2014, 41 S. 806-813)	ad	un	Y	N	N	Moderate

ad: adequate; inad: inadequate; y: yes, n: no,
un: unclear;

REFERENCES

[1] Abolfazli N, Saleh-Saber F, Eskandari A, Lafzi A. A comparative study of the long term results of root coverage with connective tissue graft or enamel matrix protein: 24-month results. Medicina oral, patología oral y cirugía bucal 2009;14;304–309.

[2] Academy Report. Oral reconstrucitve and corrective considerations in periodontal therapy. J Periodontol 2005;76;1588-1600.

[3] Alkan EA, Parlar A. EMD or subepithelial connective tissue graft for the treatment of single gingival recessions: A pilot study. J Periodontol Res 2011; 46;637–642.

[4] Alkan EA, Parlar A. Enamel matrix derivative (emdogain) or subepithelial connective tissue graft for the treatment of adjacent multiple gingival recessions: a pilot study. Int J Perio Rest Dent 2013;33;619–25.

[5] Allen E, Miller P. Coronal positioning of existing Gingiva : Short term results in the treatment of shallow marginal tissue recession. J Periodontol 1989;60;316–319.

[6] Aroca S, Molnár B, Windisch P, Gera I, Salvi GE, Nikolidakis D, Sculean A. Treatment of multiple adjacent Miller class I and II gingival recessions with a Modified Coronally Advanced Tunnel (MCAT) technique and a collagen matrix or palatal connective tissue graft: A randomized, controlled clinical trial. J Clin Periodontol 2013;40;713–720.

[7] Boyd RL. Mucogingival considerations and their relationship to orthodontics. J Periodontol 1978;49;67–76.

[8] Cairo F, Cortellini P, Tonetti M, Nieri M, Mervelt J, Cincinelli S, Pini-Prato G.

[9] Coronally advanced flap with and without connective tissue graft for the treatment of single maxillary gingival recession with loss of interdental attachment. A randomized controlled clinical trial. J Clin Periodontol, 2012;39;760–768.

[10] 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;44–62.

[11] Cairo F, Pagliaro U, Nieri M. Treatment of gingival recession with coronally advanced flap procedures: A systematic review. J Clin Periodontol 2008; 35 Suppl. 8;136–162.

[12] Cardaropoli D, Tamagnone L, Roffredo A, Gaveglio L. 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;321–328.

[13] Castellanos A, de la Rosa M, de la Garza M, Caffesse RG. Enamel matrix derivative and coronal flaps to cover marginal tissue recessions. J Periodontol 2006;77;7–14.

[14] Chambrone L, Sukekava F, Araújo M, Pustiglioni F, Chambrone L, Lima, L. Root coverage procedures for the treatment of localized recession-type defects: A Cochrane Systematic Review. J Periodontol 2009;81;452–78.

[15] Chambrone L, Tatakis DN. Periodontal soft tissue root coverage procedures: a systematic review from the AAP Regeneration Workshop. J Periodontol 2015;86;8-51.

[16] Cheng GL, Fu E, Tu YK, Shen EC, Chiu HC, Huang RJ, Yuh DY, Chiang CY. 2014. Root coverage by coronally advanced flap with connective tissue graft and/or enamel matrix derivative : a meta-analysis. J Periodont Res 2014;501-11.

[17] Cordaro L, di Torresanto VM, Torsello F. Split-mouth comparison of a coronally advanced flap with or without enamel matrix derivative for coverage of multiple gingival recession defects: 6- and 24-month follow-up. Int J Perio Rest Dent 2012;32;10–20.

[18] Cortellini P, Tonetti M, Baldi C, Francetti L, Rasperini G, Rotundo R, Nieri M, Franceschi D, Labriola A, Pini Prato G. 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;68–79.

[19] Cueva M, Boltchi FE, Hallmon WW, Nunn ME, Rivera-Hidalgo F, Rees T. A comparative study of coronally advanced flaps with and without the addition of enamel matrix derivative in the treatment of marginal tissue recession. J Periodontol 2004;75;949–956.

[20] Gorman W. Prevalence and etiology of ginigival recession. J Periodontol 1967; 38;316–322.

[21] Grupe H, Warren R. Repair of gingival defects by a sliding flap operation. J Periodontol 1956;27;92–95.

[22] Hägewald S, Spahr A, Rompola E, Haller B, Heijl L, Bernimoulin JP. Comparative study of Emdogain and coronally advanced flap technique in the treatment of human gingival recessions. A prospective controlled clinical study. J Clin Periodontol 2002;29;35–41.

[23] Higgins JP, Green S. 2011. Cochrane Handbook at http://handbook.cochrane.org/.

[24] Hofmänner P, Alessandri R, Laugisch O, Sculean A. Predictability of surgical techniques used for coverage of multiple adjacent ginigval recessions. A systematic review. Quintessence International 2012;43;545–554.

[25] Jaiswal G, Khatri P, Bhongade M, Kumar R, Jaiswal S. The effectiveness of enamel matrix protein (Emdogain®) in combination with coronally advanced flap in the treatment of multiple marginal tissue recession: A clinical study. Journal of Indian Society of Periodontol 2012;16;224-230.

[26] Kuis D, Sciran I, Lajnert V, Snjaric D, Prpic J, Pezelj-Ribaric S, Bosnjak A. Coronally advanced flap alone or with connective tissue graft in the treatment of single gingival recession defects: a long-term randomized clinical trial. J Periodontol 2013;84;1576–85.

[27] Kumar GNV, Murthy KRV. A comparative evaluation of subepithelial connective tissue graft (SCTG) versus platelet concentrate graft (PCG) in the treatment of gingival recession using coronally advanced flap technique: A 12-month study. Journal of Indian Society of Periodontology 2013;17;771–776.

[28] Langer B, Langer L. Subepithelial connective tissue graft technique for root coverage. J Periodontol 1985;56;715–720.

[29] McGuire MK, Scheyer ET. Xenogeneic collagen matrix with coronally advanced flap compared to connective tissue with coronally advanced flap for the treatment of dehiscence-type recession defects. J Periodontol 2010;81;1108–1117.

[30] McGuire MK, Scheyer ET, Snyder MB. Evaluation of recession defects treated with coronally advanced flaps and either recombinant human platelet-derived growth factor-BB plus Beta Tricalcium Phosphate or Connective Tissue: Comparison of clinical parameters at 5 Years. J Periodontol 2014;85;1361-1370.

[31] McGuire, Nunn. Evaluation of human recession defects treated with coronally advanced flaps. J Periodontol 2003;74;1126–1135.

[32] Miller PD. A classification of marginal tissue recession. Int J Periodont Rest Dent 1985;5;8–13.

[33] Miller PD, Allen EP. The development of periodontal plastic surgery. J Periodontol 1996;11;7-17.

[34] Modica F, Del Pizzo M, Roccuzzo M, Romagnoli R. Coronally advanced flap for the treatment of buccal gingival recessions with and without enamel matrix derivative. A split-mouth study. J Periodontol 2000;71;1693–1698.

[35] Oates TW, Robinson M, Gunsolley GC. Surgical therapies for the treatment of gingival recessions: A systematic review. Ann Periodontol 2003;8;303-320.

[36] Pini-Prato G, Nieri M, Pagliaro U, Giorgi TS, La Marca M, Franceschi D, Buti J, Giani M, Weiss JH, Padeletti L, Cortellini P, Chambrone L, Barzagli L, Defraia E, Rotundo R. Surgical treatment of single gingival recessions: clinical guidelines. European journal of oral implantology 2014;7;9–43.

[37] Del Pizzo M, Zucchelli G, Modica F, Villa R, Debernardi C. Coronally advanced flap with or without enamel matrix derivative for root coverage: A 2-year study. J Clin Periodontol 2005;32;1181–1187.

[38] Roccuzzo M, Bunino M, Needleman I, Sanz M. Periodontal plastic surgery for treatment of localized gingival recessions: a systematic review. J Clin Periodontol 2002a; 29 Suppl 3;178–196.

[39] Roccuzzo M, Bunino M, Needleman I, Sanz M. Periodontal plastic surgery for treatment of localized ginigval recessions: a systematic review. J Clin Periodontol 2002b;29;178–194.

[40] Roman, Soancă, Kasaj, Stratul SI. 2013. Subepithelial connective tissue graft with or without enamel matrix derivative for the treatment of Miller class I and II gingival recessions: A controlled randomized clinical trial. J Periodontol Res 2013;48;563–572.

[41] Sagnes G, Gjermo P. Prevalence of oral soft and hard tissue lesions related to mechanical tooth cleaning procedures. Community Dent Oral Epidemiol 1976;4;77–83.

[42] Salhi L, Lecloux G, Seidel L, Rompen E, Lambert F. Coronally advanced flap versus the pouch technique combined with a connective tissuegraft to treat Miller's class I gingival recession: A randomized controlled trial. J Clini Periodontol 2014;41;387–395.

[43] Sayar F, Akhundi N, Gholami S. Connective tissue graft vs. emdogain: A new approach to compare the outcomes. J Dent Res 2013;10;38–45.

[44] Sculean A, Cosgarea R, Stähli A, Katsaros C, Arweiler N, Brecx M, Deppe H. The modified coronally advanced tunnel combined with an

enamel matrix derivative and subepithelial connective tissue graft for the treatment of isolated mandibular Miller Class I and II gingival recessions: A report of 16 cases. Quintessence International 2014;10;829–835.

[45] da Silva RC, Joly JC, de Lima AFM, Tatakis DN. Root coverage using the coronally positioned flap with or without a subepithelial connective tissue graft. J Periodontol 2004;75;413–419.

[46] Spahr A, Haegewald S, Tsoulfidou F, Rompola E, Heijl L, Bernimoulin J, Ring C, Sander S, Haller B. 2005. Proteins versus coronally advanced flap technique : A 2-year report. J Periodontol 2005;76;1871–1880.

[47] Sullivan H, Atkins J. Free autogenous ginigval grafts. I. Principles of successful grafting. J Periodontics 1968;6;121–129.

[48] Tarnow DP. Semilunar coronally repositioned flap. J Clin Periodontol 1986;13;182–185.

[49] Tinti C, Vincenzi G, Cortellini P, Pini Prato G, Clauser C. Guided tissue regeneration in the treatment of human facial recession. A 12-case report. J Periodontol 1992;63;554–60.

[50] Wennström J. Mucogingival therapy. Annals of periodontology 1996;1;671–701.

[51] Wolf HF, Rateitschak EM, Rateitschak KH. Farbatlanten der Zahnmedizin 1, Parodontologie. 3. Auflage, Georg Thieme Verlag, 2004.

[52] Zucchelli G, Marzadori M, Mounssif I, Mazzotti C, Stefanini M. Coronally advanced flap + connective tissue graft techniques for the treatment of deep gingival recession in the lower incisors. A controlled randomized clinical trial. J Clin Periodontol 2014;41;806–813.

[53] Zucchelli G, Mounssif I, Mazzotti C, Stefanini M, Marzadori M, Petracci E, Montebugnoli L. 2014. 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;396–403.

[54] Zuhr, Hürzeler. Plastisch- ästhetische Parodontal- Implantatchirurgie. 1. Auflage, Quintessenz Verlags- GmbH 2011.