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Treatment of gingival recession with coronally advanced flap procedures: a systematic review

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Abstract

Background: The treatment of buccal gingival recessions is a common requirement due to aesthetic concern or root sensitivity. The aim of this manuscript was to systematically review the literature on coronally advanced flap (CAF) alone or in combination with tissue grafts, barrier membranes (BM), enamel matrix derivative (EMD) or other material for treating gingival recession.

Material and Methods: Randomized clinical trials on treatment of Miller Class I and II gingival recessions with at least 6 months of follow-up were identified. Data sources included electronic databases and hand-searched journals. The primary outcome variable was complete root coverage (CRC). The secondary outcome variables were recession reduction, clinical attachment gain, keratinized tissue gain, aesthetic satisfaction, root sensitivity, post-operative patient pain and complications. **Results:** A total of 794 Miller Class I and II gingival recessions in 530 patients from 25 RCTs were evaluated in this systematic review. CAF was associated with mean recession reduction and CRC. The addition of connective tissue graft (CTG) or EMD enhanced the clinical outcomes of CAF in terms of CRC, while BM did not. The results with respect to the adjunctive use of acellular dermal matrix were controversial. **Conclusions:** CTG or EMD in conjunction with CAF enhances the probability of obtaining CRC in Miller Class I and II single gingival recessions.

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Key words: complete root coverage; coronally advanced flap; gingival recession; muco-gingival surgery; root coverage; systematic review

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The treatment of buccal gingival recession is a common requirement due to aesthetic concern or root sensitivity in patients with high standards of oral hygiene (American Academy of Periodontology 1996). The ultimate goal of a root coverage procedure is the complete coverage of the recession defect with

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good appearance related to adjacent soft tissues and minimal probing depth (PD) (Miller 1985, Roccuzzo et al. 2002, Clauser et al. 2003). Previous systematic reviews showed that several surgical procedures such as pedicle flaps, free soft tissue grafts, combinations of pedicle flaps and grafts or barrier membranes (BM) may be indicated to improve the coronal level of the gingival margin on the root surface (Roccuzzo et al. 2002, Clauser et al. 2003, Oates et al. 2003), even if very limited data for epithelialized free gingival graft and laterally positioned flap are available (Roccuzzo et al. 2002). In addition, no difference between resorbable and nonresorbable barriers in terms of mean root coverage was reported (Roccuzzo et al. 2002) and no clinical benefit following root conditioning was detected (Roccuzzo et al. 2002, Cheng et al. 2007). An earlier European Federation of Periodontology Systematic Review on root coverage (Roccuzzo et al. 2002) reported that complete root coverage (CRC) and mean percentage of root coverage varied considerably between studies comparing the same techniques.

The coronally advanced flap (CAF) procedure is a very common approach for root coverage. This procedure is based on the coronal shift of the soft tissues on the exposed root surface (Allen & Miller 1989, Pini Prato et al. 2000). This approach may be used alone or in combination with soft tissue grafts (Wennström & Zucchelli 1996), BM (Pini Prato et al. 1992), enamel matrix derivative (EMD) (Rasperini et al.

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2000), acellular dermal matrix (ADM) (Harris 1998), platelet-rich plasma (PRP) (Marx et al. 1998) and living tissue-engineered human fibroblastderived dermal substitute (HF-DDS) (Wilson et al. 2005).

The purpose of this systematic review was to answer the following question: "What is the clinical benefit of adding to the CAF procedure: connective tissue graft (CTG) or BM or EMD or ADM or PRP or living tissue-engineered HF-DDS in the treatment of Miller Class I and II localized gingival recessions?"

Material and Methods

This systematic review was conducted according to the QUOROM statement instruments for systematic reviews (Moher et al. 1999).

In this systematic review, only randomized-controlled clinical trials (RCTs), including a split-mouth model, of at least 6 months' duration were considered.

Searching

For the identification of the studies investigated in this review and published until December 1999, the register of clinical studies published in previous systematic reviews (Pagliaro et al. 2003, Clauser et al. 2003) was consulted.

For the identification of studies considered for this review and published from January 2000 to August 2007, a search was performed using two electronic evidence sources:

- 1. The National Library of Medicine (MEDLINE by PubMed), on 07.09.2007, using the strategy: ("Gingival Recession/surgery" [Mesh] OR "Gingival Recession/ therapy" [Mesh]) AND ((Humans [Mesh]) AND (Randomized Controlled Trial[ptyp]));
- 2. The Cochrane Oral Health Group Trials Register, on 07.09.2007, using the following strategy: "Gingival Recession" [Search All Text] AND "Root Coverage" [Search All Text].

There was no language restriction.

Hand searching included a complete search of Journal of Clinical Periodontology, Journal of Periodontology, Journal of Periodontal Research, International Journal of Periodontics and Restorative Dentistry and PERIO from January 2000 up to August 2007. References from AAP position paper (American Academy of Periodontology 1996), EFP review article (Wennström 1994) and previous systematic reviews dealing with root coverage procedures (Greenwell et al. 2000, Roccuzzo et al. 2002, Oates et al. 2003, Clauser et al. 2003, Al-Hamdan et al. 2003, Gapski et al. 2005, Hwang & Wang 2006, Cheng et al. 2007) were checked for article identification.

In addition, all authors of the identified studies, clinical experts or researchers in the field of mucogingival surgery were contacted in an attempt to identify unpublished data or studies not yet published.

Selection

The criteria for considering studies for this review were organized by the PICO method (Glossary of Evidence-Based Terms 2007) and were follows:

(P) Types of participants

Patients with a clinical diagnosis of Miller Class I or II localized gingival recession defect.

(I) Types of interventions

The following surgical procedures for the treatment of single recessions were considered:

- CAF,
- CAF plus CTG (CAF+CTG),
- CAF plus Barrier Membrane (CAF+BM),
- CAF plus EMD (CAF+EMD),
- CAF plus ADM (CAF+ADM),
- CAF plus PRP (CAF+PRP),
- CAF plus HF-DDS (CAF+HF-DDS).

RCTs comparing CAF with multiple combinations (i.e. CAF+CTG+EMD, CAF+BM+CTG, CAF+ BM+EMD, etc.) or RCTs comparing variations of the same technique (i.e. CAF with releasing incisions *versus* CAF without releasing incisions) were excluded from the systematic review.

(C) Comparison between interventions

The following comparisons between the selected techniques were investigated:

- CAF versus CAF+CTG,
- CAF versus CAF+BM,
- CAF versus CAF+EMD,
- CAF versus CAF+ADM,
- CAF versus CAF+PRP,
- CAF versus CAF+HF-DDS,

- CAF+CTG versus CAF+BM,
- CAF+CTG versus CAF+EMD,
- CAF+CTG versus CAF+ADM,
- CAF+CTG versus CAF+PRP,
- CAF+CTG versus CAF+HF-DDS,
- CAF+BM versus CAF+EMD,
- CAF+BM versus CAF+ADM,
- CAF+BM versus CAF+PRP,
- CAF+BM versus CAF+HF-DDS,
- CAF+EMD versus CAF+ADM,
- CAF+EMD versus CAF+PRP,
- CAF+EMD versus CAF+HF-DDS,
- CAF+ADM versus CAF+PRP,
- CAF+ADM versus CAF+HF-DDS,
- CAF+PRP versus CAF+HF-DDS.

(O) *Type of outcome measures*

The following outcome measures were considered:

Primary outcome

• Recession defects that obtained **CRC**.

Secondary outcomes

- Change in gingival recession expressed as recession reduction in mm at follow-up visit (**RecRed**),
- Change in clinical attachment level (CAL) expressed as CAL gain in millimetres at follow-up visit (CAL gain),
- Change in width of keratinized tissue (KT) expressed as KT gain in millimetres at follow-up visit (KT gain),
- Biological complications during the post-operative healing period (**Complications**),
- Patient discomfort during the postoperative healing period (**Postoperative pain**),
- Patient preference in terms of aesthetic result at follow-up visit (Aesthetic satisfaction),
- Patient perception of root sensitivity at follow-up visit (**Root sensitivity**).

Validity assessment

The quality assessment of the included trials was independently performed and in duplicate form by two review authors (F. C. and U. P.). According to the *Cochrane Handbook Systematic Review*

of Interventions 4.3.6. (section 6.3) (Higgins & Green 2006), three main quality criteria were examined: allocation concealment, blinding treatment outcomes to outcome assessors and completeness of follow-up.

- 1) Allocation concealment was considered *adequate*, *inadequate* or unclear. Ideally, the surgeon should have known the allocation group just before the treatment was delivered. AC was considered as adequate when it was centralized (allocation by a central office unaware of subjects' characteristics). AC was considered as *adequate* when prenumbered or coded identical containers were serially administered to participants; when there was an onsite computer system combined with allocation kept in a locked unreadable computer file that could be accessed only after the characteristics of an enrolled patient had been entered; when numbers in closed envelopes opened before the surgical procedure were used; when coin flip was used before surgical treatment. AC was considered as inadequate when any procedure was entirely transparent before the treatment was delivered. When details of AC were not provided, it was coded as unclear.
- 2) Treatment blind to outcomes assessors (TB) was recorded as yes, no, unclear and not possible.
- 3) Completeness of follow-up (CF): a clear explanation for drop-outs in each treatment group was searched in the manuscript. CF was evaluated as no drop-outs/yes when authors specified that no drop-outs were detected or when authors specified the numbers of drop-outs and related reasons. CF was evaluated as no when no information on completeness of follow-up was provided.

After quality assessment, studies were grouped into 2 categories:

- A) Low risk of bias, if all 3 quality criteria were met.
- B) High risk of bias, if one or more of the 3 quality criteria were not met.

Data abstraction

The titles and abstracts (when available) of all reports identified through the

electronic and manual searches were screened independently by two review authors (F. C. and U. P.). When studies met the inclusion criteria or when insufficient data from abstracts to evaluate inclusion criteria were gained, the full article was obtained. The full text of all studies of possible relevance was independently assessed by two review authors (F. C and U. P.). All studies meeting the inclusion criteria then underwent quality assessment and data recording. When there was disagreement between the two reviewers, consensus was achieved by discussion with the third reviewer/statistical advisor (M. N.). Then data were independently extracted and entered into a computer by two review authors (F. C and U. P.) using specifically designed data-collection forms. Patient characteristics, treatments, clinical outcomes, complications and study quality were systematically registered. When clinical data on CRC were lacking, authors of the trials were contacted.

When several articles reporting different follow-up durations were published for the same study population, the longest follow-up duration article was considered, but if the number of withdrawals and drop-outs were $\geq 30\%$ of the original sample, the previous article with a shorter follow-up was considered.

Study characteristics

Only RCTs, with or without a splitmouth design, were included in the systematic review.

Eligible RCTs, with a follow-up duration ≥ 6 months, had to compare the results of at least 2 of the investigated surgical techniques in patients with Miller Class I or II gingival recession defects.

CRC had to be expressed as the number or the percentage of treated teeth of each considered study arm that achieved total root coverage at the follow-up visit. RecRed had to be expressed as mean recession reduction in millimetres of the treated teeth of each study arm at the follow-up visit. KT gain had to be expressed as mean KT width increase in millimetres of the treated teeth of each study arm at the follow-up visit. CAL gain had to be recorded as mean CAL in millimetres of the treated teeth of each study arm at the follow-up visit. Complications, Post-operative pain, Aesthetic satisfaction and Root sensitivity had to be described at least in a narrative form.

Quantitative data synthesis

For dichotomous outcomes (*CRC*), the estimates of effect of an intervention were expressed as odds ratios (OR) together with 95% confidence intervals (CI). For continuous outcomes, mean differences and standard deviations were used to summarize the data from each group. In each patient only one site for each technique was permitted. When individual patient data (IPD) were available, multiple sites treated with the same technique in the same patient were eliminated.

OR were combined for dichotomous data and mean differences for continuous data using a random-effect model. Data from split-mouth studies were combined with data from parallel group trials with the method outlined by Elbourne et al. (2002), using the generic inverse variance method in the RevMan. The techniques described by Follmann et al. (1992) were used to calculate the standard error of the difference for splitmouth studies, where the appropriate data were not presented.

The significance of any discrepancies in the estimates of the treatment effects from different trials was assessed by means of Cochran's test for heterogeneity and the I^2 statistic, which describes the percentage total variation across studies that is due to heterogeneity rather than change. It was planned to undertake sensitivity analyses to examine the effect of the study quality for *CRC*.

Results Searching results

The search results are presented in Fig. 1.

The register of clinical studies published in previous systematic reviews (Clauser et al. 2003, Pagliaro et al. 2003) provided **5** articles (Ricci et al. 1996, Jepsen et al. 1998, Trombelli et al. 1998, Zucchelli et al. 1998, Borghetti et al. 1999) published until December 1999 and that met inclusion criteria.

The electronic search in MEDLINE (by PubMed) and in the *Cochrane Collaboration* databases provided, respectively, **120** and **57** articles published from January 2000 until August 2007. Subsequently, after reading all the



Fig. 1. Literature search process and results.

abstracts, **56** articles (51 PubMed and 50 Cochrane) were selected. **Four** (Ito et al. 2000, Kassab et al. 2006, Rahmani & Lades 2006, Barros et al. 2005) of these **56** articles were not published in the journals selected for the hand searching of the present systematic review.

The hand searching found **47** articles and **5** of these were not found by the electronic search.

The search of the "grey literature" (unpublished data) by e-mail contact with all the authors of the identified studies and clinical experts or researchers in the field of mucogingival surgery provided the complete data of **1** trial (Cortellini et al., unpublished data).

Finally, by crossing the literature searches (electronic, manual and unpublished data searches) we were able to select **66** articles (**5** articles published until December 1999 and **61** articles published from January 2000 to August 2007) and **1** still unpublished study.

The full text reading of the **67** articles (5 by register + 56 by electronic search + 5 by hand-search + 1 by "gray literature" search) allowed the selection of **25** studies (**27** reports) (Table 1) that met the inclusion criteria of this systematic review and the exclusion of **40** articles from the analysis. Rejected studies at this stage are listed in Table 2 (characteristics of excluded studies) and the reason for exclusion was recorded.

Tał	ole I	. Т	wenty-five	included	studies	(27	articles	,)
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Study	Comparison
da Silva et al. (2004)	CAF versus CAF+CTG
Cortellini et al., unpublished data	
Lins et al. (2003)	CAF versus CAF+BM
Amarante et al. (2000), Leknes et al. (2005)	
Modica et al. (2000)	CAF versus CAF+EMD
Spahr et al. (2005)	
Del Pizzo et al. (2005)	
Castellanos et al. (2006)	
Pilloni et al. (2006)	
Woodyard et al. (2004)	CAF versus CAF+ADM
Côrtes et al. (2004, 2006)	
Huang et al. (2005)	CAF versus CAF+PRP
Zucchelli et al. (1998)	CAF+CTG versus CAF+BM
Jepsen et al. (1998)	
Trombelli et al. (1998)	
Borghetti et al. (1999)	
Tatakis & Trombelli (2000)	
Romagna-Genon (2001)	
Wang et al. (2001)	
McGuire & Nunn (2003)	CAF+ CTG versus CAF+EMD
Aichelmann-Reidy et al. (2001)	CAF+CTG versus CAF+ADM
Paolantonio et al. (2002)	
Tal et al. (2002)	
Joly et al. (2007)	
Wilson et al. (2005)	CAF+CTG versus CAF+HF-DDS

CAF, coronally advanced flap; CTG, connective tissue graft; BM, barrier membrane; EMD, enamel matrix derivative; ADM, acellular dermal matrix graft; PRP, platelet-rich plasma; HF-DDS, human fibroblast-derived dermal substitute.

In 3 of the selected clinical studies, 2 articles with different follow-up durations were published. For the first study, both Amarante et al. (2000) (6-month follow-up) and Leknes et al. (2005) (12and 72-month follow-up) publications were considered to complete data recording; for the second study, Hägewald et al. (2002) publication (12-month follow-up) was not utilized because the

Table 2. Characteristics of the 40 excluded articles

Study	Reason for exclusion
Aimetti et al. (2005)	Not surgical theraphy
Al-Zahrani et al. (2004)	Comparison between variations of a same surgical technique
Barros et al. (2004)	Comparison between variations of a same surgical technique
Barros et al. (2005)	Comparison between variations of a same surgical technique
Barros et al. (2007)	Comparison between variations of a same surgical technique
Berlucchi et al. (2002)	Comparison with a combination of techniques
Bertoldi et al. (2007)	Not study on root coverage
Bittencourt et al. (2006)	Comparison with a surgical techniques not investigated
Bittencourt et al. (2007)	Surgical techniques not investigated in the present systematic review
Burkhardt & Lang (2005)	Surgical techniques not investigated in the present systematic review
Caffesse et al. (2000)	Comparison between variations of a same surgical technique
Çetiner et al. (2003)	More than one treated site for each technique in the same patient
Cheung & Griffin (2004)	More than one treated site for each technique in the same patient
Cueva et al. (2004)	Miller Class III gingival recession defects treated
Dodge et al. (2000)	Comparison with a combination of techniques
Duval et al. (2000)	Comparison with a combination of techniques
Felipe et al. (2007)	Comparison between variations of a same surgical technique
Francetti et al. (2005)	Comparison not investigated in the present systematic review
Hägewald et al. (2002)	Same pool of patients with a shorter follow-up of an included study
	in this systematic review
Harris (2000)	Not RCT
Harris et al. (2005)	Comparison with a surgical techniques not investigated
Henderson et al. (2001)	Comparison between variations of a same surgical technique
Ito et al. (2000)	Comparison with a surgical techniques not investigated
Kassab et al. (2006)	Comparison between variations of a same surgical technique
Kimble et al. (2004)	Comparison with a combination of techniques
Lucchesi et al. (2007)	Comparison between variations of a same surgical technique
McGuire & Nunn (2005)	Not study on root coverage
Moses et al. (2006)	Not RCT
Nemcovsky et al. (2004)	Not RCT
Novaes et al. (2001)	More than one treated site for each technique in the same patient
Paolantonio (2002)	Comparison not investigated in the present systematic review
Pini Prato et al. (2000)	Comparison between variations of a same surgical technique
Rahmani & Lades (2006)	More than one treated site for each technique in the same patient
Ricci et al. (1996)	Comparison not investigated in the present systematic review
Rosetti et al. (2000)	Comparison with a combination of techniques
Shin et al. (2007)	Comparison with a combination of techniques
Silva et al. (2006)	Not KUT
Tozum et al. (2005)	Comparison between variations of a same surgical technique
Trabulsi et al. (2004)	Comparison with a combination of techniques
Zucchelli et al. (2003)	Comparison between variations of a same surgical technique

RCT, randomized clinical trial.

longer duration of the Spahr et al. (2005) publication (24-month follow-up) was used; for the third study, both Côrtes et al. (2006) (24-months follow-up) and Côrtes et al. (2004) (6-months followup) publications were respectively utilized for CRC variable analysis and for all the other variable analyses.

Only 1 (Joly et al. 2007) of all contacted research groups was able to provide additional unpublished data of CRC.

Study characteristics

Included studies

The list of included studies is presented in Table 1.

The 25 selected studies (27 articles) allowed the following comparisons (Fig. 2):

- CAF *versus* CAF+CTG: **2** studies (da Silva et al. 2004, Cortellini et al., unpublished data) (Table 3);
- CAF *versus* CAF+BM: **2** studies (3 articles) (Amarante et al. 2000, Lins et al. 2003, Leknes et al. 2005) (Table 4);
- CAF *versus* CAF+EMD: **5** studies (Modica et al. 2000, Del Pizzo et al. 2005, Spahr et al. 2005, Castellanos et al. 2006, Pilloni et al. 2006) (Table 5);
- CAF *versus* CAF+ADM: **2** studies (3 articles) (Côrtes et al. 2004, 2006, Woodyard et al. 2004) (Table 6);
- CAF *versus* CAF+PRP: **1** study (Huang et al. 2005) (Table 7);
- CAF+CTG *versus* CAF+BM: 7 studies (Jepsen et al. 1998, Trombelli et al. 1998, Zucchelli et al.

1998, Borghetti et al. 1999, Tatakis & Trombelli 2000, Romagna-Genon 2001, Wang et al. 2001) (Table 8);

- CAF+ CTG versus CAF+EMD: 1 study (McGuire & Nunn 2003) (Table 9);
- CAF+CTG *versus* CAF+ADM: 4 studies (Aichelmann-Reidy et al. 2001, Paolantonio et al. 2002, Tal et al. 2002, Joly et al. 2007) (Table 10);
- CAF+CTG *versus* CAF+HF-DDS: 1 study (Wilson et al. 2005) (Table 11).

In the case of Leknes et al. (2005), the article referred to the same pool of patients as the previous publication (Amarante et al. 2000), but reported data with a longer follow-up (12 and 72 months). The 12-month follow-up data were considered for the comparison because in the 72-month follow-up data there were > 30% drop-outs among the participants.

In the case of Modica et al. (2000), 2 of the 12 participants were excluded from meta-analyses because they participated in a split-mouth study with more than 1 pair of bilateral gingival recessions. Hence, IPD of the remaining 10 pair of recession defects were reanalysed.

For all the other possible comparisons investigated in the systematic review, no eligible study was found.

Of the 25 included studies, 18 studies (Jepsen et al. 1998, Trombelli et al. 1998, Borghetti et al. 1999, Amarante et al. 2000, Modica et al. 2000, Tatakis & Trombelli 2000, Aichelmann-Reidy et al. 2001, Romagna-Genon 2001, Wang et al. 2001, Tal et al. 2002, Lins et al. 2003, McGuire & Nunn 2003, Côrtes 2004, 2006, da Silva et al. 2004, Del Pizzo et al. 2005, Leknes et al. 2005, Spahr et al. 2005, Wilson et al. 2005, Joly et al. 2007) had an intra-individual (split-mouth) design, while 7 studies (Zucchelli et al. 1998, Paolantonio et al. 2002, Woodyard et al. 2004, Huang et al. 2005, Castellanos et al. 2006, Pilloni et al. 2006, Cortellini et al., unpublished data) had a parallel group design.

Two studies (Paolantonio et al. 2002, Huang et al. 2005) were completely supported by public institutes for research, **1** study (Cortellini et al. unpublished data) was supported by private institutes for reasearch, **9** studies (Trombelli et al. 1998, Amarante et al. 2000, Tatakis & Trombelli 2000, Aichelmann-Reidy et al. 2001, Wang



CAF: Coronally Advanced Flap; **CTG**: Connective Tissue Graft + CAF; **BM**: Barrier Membrane + CAF; **EMD**: Enamel Matrix Derivative + CAF; **ADM**: Acellular Dermal Matrix + CAF; **PRP**: Platelet-Rich Plasma + CAF; **HF-DDS**: Human Fibroblast-Derived Dermal Substitute + CAF.

Fig. 2. Comparisons of techniques: 25 included studies (27 articles) in the systematic review.

et al. 2001, Tal et al. 2002, McGuire & Nunn 2003, Leknes et al. 2005, Spahr et al. 2005, Wilson et al. 2005) were supported, in part, by companies whose products were being used as interventions in the trials and **13** studies (Jepsen et al. 1998, Zucchelli et al. 1998, Borghetti et al. 1999, Modica et al. 2000, Romagna-Genon 2001, Lins et al. 2003, Côrtes et al. 2004, 2006, da Silva et al. 2004, Woodyard et al. 2004, Del Pizzo et al. 2005, Castellanos et al. 2006, Pilloni et al. 2006, Joly et al. 2007) did not report how the study was supported.

Excluded Studies

See Table 2 (Characteristics of the 40 excluded studies).

There were **40** excluded studies out of which:

• 12 studies reported comparisons between variations of the same surgical technique (Caffesse et al. 2000, Pini Prato et al. 2000, Henderson et al. 2001, Zucchelli et al. 2003, Al-Zahrani et al. 2004, Barros et al. 2004, Barros et al. 2005, Tözüm et al. 2005, Kassab et al. 2006, Barros et al. 2007, Felipe et al. 2007, Lucchesi et al. 2007).

- 7 studies reported comparisons with a combination of techniques (Dodge et al. 2000, Duval et al. 2000, Rosetti et al. 2000, Berlucchi et al. 2002, Kimble et al. 2004, Trabulsi et al. 2004, Shin et al. 2007).
- 7 studies reported comparisons with or between surgical techniques not investigated in the present systematic review (Ricci et al. 1996, Ito et al. 2000, Paolantonio 2002, Burkhardt & Lang 2005, Harris et al. 2005, Bittencourt et al. 2006, Bittencourt et al. 2007).
- 1 study was on non-surgical therapy (Aimetti et al. 2005).
- 1 study treated Miller Class III gingival recession defects (Cueva et al. 2004).
- 1 study evaluated different surgical procedures under an operative microscope (Francetti et al. 2005).
- 4 studies were not RCTs (Harris 2000, Nemcovsky et al. 2004, Moses et al. 2006, Silva et al. 2006).
- 2 studies were not on root coverage (McGuire & Nunn 2005, Bertoldi et al. 2007).
- 4 studies evaluated more than one site for each technique in each patient (Novaes et al. 2001, Çetiner et al. 2003, Cheung & Griffin 2004, Rahmani & Lades 2006).
- 1 study evaluated patients with a shorter follow-up of a study included in the systematic review (Hagewold et al. 2002).

Methodological quality of the included studies

Randomization was reported in all studies included in the present systematic review.

Concealment of the randomization code during patient selection was judged as adequate in **13** studies (Jepsen et al. 1998, Aichelmann-Reidy et al. 2001, Romagna-Genon 2001, Wang et al. 2001, Lins et al. 2003, McGuire & Nunn 2003, da Silva et al. 2004, Del Pizzo et al. 2005, Huang et al. 2005, Spahr et al. 2005, Wilson et al. 2005, Joly et al. 2007, Cortellini et al., unpublished data) and inadequate in all the other studies.

Examiner blinding was described in 14 of the studies (Zucchelli et al. 1998, Amarante et al. 2000, Modica et al. 2000, Tatakis & Trombelli 2000,

Table 3.	Characteristics	of the 2	included	studies	comparing	CAF	versus	CAF+CTG
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Study	da Silva et al. (2004)
Methods	RCT, split mouth design
	2 treatment groups, 6 months duration
Participants	11 individuals, 5 females, mean age 29.2 years (range 18–43)
	with bilateral Miller Class I gingival recessions Non-smokers
Intervention	Control: CAF (11 treated sites)
	Test: CAF+CTG (11 treated sites)
Mean % of root coverage	Control: 68.8%
	Test: 75.3%
Founding	Not reported
Allocation concealment	Adeguate
Examiner blinding	No
Drop-outs	No drop out
Study	Cortellini et al. (unpublished data)
Methods	RCT, parallel study design
	2 treatment groups, 6 months duration
Participants	83 individuals, 48 females, age range 20-59 years, with one
-	Miller Class I or II gingival recession $\ge 2 \text{ mm}$
	21 smokers
Intervention	Control: CAF
	Test: CAF+CTG
Mean % of root coverage	Control: $62\% \pm 44$
	Test: 76% \pm 36
Founding	Supported by A.T.R.O. and ERGOPERIO
Allocation concealment	Adeguate
Examiner blinding	Yes
Drop-outs	2 drop outs

CAF, coronally advanced flap; CTG, connective tissue graft; RCT, randomized clinical trial.

Study	Lins et al. (2003)
Methods	RCT, split mouth design
	2 treatment groups, 6 months duration
Participants	10 individuals, 4 females, mean age 38.2 years (range 25-55)
-	with 2 contralateral Miller Class I or II gingival recessions
	≥2 mm
	Non-smokers
Intervention	Control: CAF (10 treated sites)
	Test: titanium reinforced CAF+BM (10 treated sites)
Mean % of root coverage	Control: 60.0%
_	Test: 45.0%
Founding	Not reported
Allocation concealment	Adeguate
Examiner blinding	No
Drop-outs	No
Study	Leknes et al. (2005)
Methods	RCT, split mouth design
	2 treatment groups, 12 and 72 months duration
	Same patients of the previous article (Amarante et al. 2000)
Participants	20 individuals, 10 females, mean age 38.4 years (range 25–55)
1	with 2 bilateral Miller Class I or II gingival recessions $\ge 3 \text{ mm}$
	8 smokers
Intervention	Control: CAF (20 treated sites)
	Test: CAF+BM (20 treated sites)
Mean % of root coverage	Control: 34.0%
-	Test: 35.0%
Founding	In part by Guidor
Allocation concealment	Inadeguate
Examiner blinding	Yes
Drop-outs	No

CAF, coronally advanced flap; BM, barrier membrane; RCT, randomized clinical trial.

Aichelmann-Reidy et al. 2001, Wang et al. 2001, McGuire & Nunn 2003, Woodyard et al. 2004, Del Pizzo et al. 2005, Huang et al. 2005, Leknes et al. 2005, Spahr et al. 2005, Wilson et al. 2005, Pilloni et al. 2006, Cortellini et al., unpublished data) and was "unclear" or not described in all the other studies.

Only 14 of the 25 included studies reported about drop-outs (Modica et al. 2000, Tatakis & Trombelli 2000, Aichelmann-Reidy et al. 2001, Romagna-Genon 2001, Wang et al. 2001, McGuire & Nunn 2003. Côrtes et al. 2004, 2006, da Silva et al. 2004, Woodyard et al. 2004, Del Pizzo et al. 2005, Huang et al. 2005, Spahr et al. 2005, Wilson et al. 2005, Cortellini et al., unpublished data). The number of drop-outs was 7 for Spahr et al. (2005), 3 for McGuire & Nunn (2003), 2 for Wilson et al. (2005) and 1, respectively, for Tatakis & Trombelli (2000), Romagna-Genon (2001) and Huang et al. (2005).

After quality assessment, **8** RCTs were classified as studies at a low risk of bias (Aichelmann-Reidy et al. 2001, Wang et al. 2001, McGuire & Nunn 2003, Del Pizzo et al. 2005, Huang et al. 2005, Spahr et al. 2005, Wilson et al. 2005, Cortellini et al., unpublished data). All the other studies were classified as studies at a high risk of bias.

Results of the Analyses

A total of 794 Miller Class I and II gingival recessions in 530 patients from 25 RCTs were evaluated in this systematic review.

Complete Root Coverage (CRC)

The primary outcome variable was CRC. When considering CAF as the control surgical procedure, 5 comparisons were possible.

- Comparison between CAF+CTG versus CAF (2 studies) showed better results for CAF+CTG, p = 0.03 (OR = 2.49; 95% CI from 1.10 to 5.68) (Fig. 3);
- Only one study compared CAF+BM versus CAF, reporting no significant difference, *p* = 0.41 (OR = 0.58; 95% CI from 0.16 to 2.08) (Fig. 4);
- Four studies compared CAF+EMD *versus* CAF. Meta-analysis showed better results for CAF+EMD,

Table 5. Characteristics of the 5 included studies comparing CAF versus CAF+EMD

Study	Modica et al. (2000)
Methods	RCT, split mouth design
	2 treatment groups, 6 months duration
Participants	10 individuals, 5 females, mean age 33.8 years (range 20-50)
-	with 2 bilateral Miller Class I or II gingival recessions $\ge 3 \text{ mm} (2 \text{ mm})$
	patients excluded from meta-analyses because participated to
	study with more than 1 pair of recessions)
	Non-smokers
Intervention	Control: CAF (10 treated sites)
	Test: CAF+EMD (10 treated sites)
Mean % of root coverage	Control: $80.9\% \pm 21.3$
	Test: $91.2\% \pm 1.55$
Founding	Not reported
Allocation concealment	Inadeguate
Examiner blinding	Yes
Drop-outs	No drop outs
Study	Del Pizzo et al. (2005)
Methods	RCT, split mouth design
	2 treatment groups, 24 months duration
	Same patients of the previous article (Hägewald et al. 2002)
Participants	30 individuals, 12 females, mean age 36.5 years (range 23-62)
	with one pair of bilateral Miller Class I or II gingival recessions
	≥3 mm
	5 smokers
Intervention	Control: CAF+Placebo (30 treated sites)
	Test: CAF+EMD (30 treated sites)
Mean % of root coverage	Control: 67%
	Test: 84%
Founding	In part by Biora AB/Straumann Biologics
Allocation concealment	Adeguate
Examiner blinding	Yes
Drop-outs	7 drop outs
Study	Spahr et al. (2005)
Methods	RCT, split mouth design
	2 treatment groups, 24 months duration
Participants	15 individuals, 11 females, mean age 39.46 years (range 18–56)
-	with bilateral Miller Class I (28 sites) or II (2 sites) gingival
	recessions
	Non-smokers
Intervention	Control: CAF (15 treated sites)
	Test: CAF+EMD (15 treated sites)
Mean % of root coverage	Control: $86.67\% \pm 18.29$
	Test: $90.67\% \pm 16.99$
Founding	Not reported
Allocation concealment	Adeguate
Examiner blinding	Yes
Drop-outs	no arop out
Study	Castellanos et al. (2006)
Methods	RCT, parallel study design
~	2 treatment groups, 12 months duration
Participants	22 individuals, 13 females, mean age 42.5 years (range 28–71)
	with 1 Miller Class I or II gingival recession $>2 \text{ mm}$
*	Non-smokers
Intervention	Control: CAF (11 treated sites)
	Test: CAF+EMD (11 treated sites)
Mean % of root coverage	Control: 62.2%
E l'	1est: 88.6%
Founding	Not reported
Anocation concealment	No
Drop outs	No
Drop-outs	110

p = 0.003 (OR = 3.89; 95% CI from 1.59 to 9.50) (Fig. 5);

- Two studies compared CAF+ADM *versus* CAF. Meta-analysis reported no significant difference between therapies, *p* = 0.31 (OR = 4.83; 95% CI from 0.23 to 99.88) (Fig. 6).
- Only one study compared CAF+PRP *versus* CAF reporting no significant difference, p = 0.79 (OR = 1.25; 95% CI from 0.23 to 6.71) (Fig. 7).

Therefore, only CAF+CTG and CAF+EMD provided better results in terms of Complete Root Coverage (CRC) compared with CAF alone.

When considering CAF+CTG as a comparative surgical procedure, 4 comparisons were performed.

- No significant difference in comparing CAF+BM versus CAF+CTG was reported (6 RCTs included), although a trend favouring CAF+CTG was detected, p = 0.06 (OR = 0.45; 95% CI from 0.20 to 1.04) (Fig. 8).
- Only one study compared CAF+ EMD *versus* CAF+CTG, reporting no significant difference *p* = 0.31 (OR = 2.31; 95% CI from 0.45 to 11.74) (Fig. 9).
- Four studies compared CAF+ADM *versus* CAF+CTG. Meta-analysis reported no significant difference for CRC, although a trend favouring CAF+CTG was detected, p = 0.06 (OR = 0.49; 95% CI from 0.23 to 1.03) (Fig. 10).
- Only one study compared CAF+HF-DDS *versus* CAF+CTG, reporting no significant difference, p = 1.00 (OR = 1.00; 95% CI from 0.02 to 50.40) (Fig. 11).

Therefore, no combined therapy was more effective than CAF+CTG for CRC.

The secondary outcome variables in this systematic review were Recession Reduction, Clinical Attachment gain, KT gain, Root Sensitivity, Aesthetic Satisfaction, Post-operative Pain and Complications including sites with PD > 3 mm at 6 months following therapy.

Recession Reduction

For *Recession Reduction (RecRed)*, 5 comparisons were possible considering CAF as the control surgical procedure.

• Two studies compared CAF+CTG *versus* CAF. Meta-analysis reported

Study	Pilloni et al. (2006)
Methods	RCT, parallel design
	2 treatment groups, 18 months duration
Participants	30 individuals, 13 females, with age ranged from 19 to 67 years,
-	with one Miller Class I or II gingival recession
	Non-smokers
Intervention	Control: CAF (15 treated sites)
	Test: CAF+EMD (15 treated sites)
Mean % of root coverage	Control: $65.5\% \pm 26.03$
-	Test: 93.8% ± 12.90
Founding	Not reported
Allocation concealment	Inadeguate
Examiner blinding	Yes
Drop-outs	No

CAF, coronally advanced flap; EMD, enamel matrix derivative; RCT, randomized clinical trial.

Table 6	Characteristics	of the 2 included	l studies (3 articles)	comnaring	CAEver	rsus CAF+AI	эM
Tuble 0.	Characteristics	of the 2 merudee	a studies (5 articles)	comparing	CHI VEI	Sus Chi + hL	1111

Study	Woodyard et al. (2004)
Methods	RCT, parallel study design
	2 treatment groups, 6 months duration
Participants	24 individuals, 14 females, mean age 34.6 years with one Miller
	Class I (17 sites) or II (7 sites) gingival recessions $\ge 3 \text{ mm}$
	Non-smokers
Intervention	Control: CAF (12 treated sites)
	Test: CAF+ADM (12 treated sites)
Mean % of root coverage	Control: $67\% \pm 27$
	Test: 99% ± 5
Founding	Not reported
Allocation concealment	Inadeguate
Examiner blinding	Yes
Drop-outs	No drop outs
Study	Côrtes et al. 2006
Methods	RCT, split mouth design
	2 treatment groups, 24 months duration
	Same patients of the previous article (Côrtes et al. 2004)
Participants	13 individuals, 7 females, mean age 32.8 years (range 25–55)
1	with 2 bilateral Miller Class I gingival recessions $\ge 3 \text{ mm}$
	Non-smokers
Intervention	Control: CAF (13 treated sites)
	Test: CAF+ADM (13 treated sites)
Mean % of root coverage	Control: 55.98% ± 23.00
-	Test: $68.04\% \pm 17.87$
Founding	Not reported
Allocation concealment	Inadeguate
Examiner blinding	No
Drop-outs	No drop out

CAF: coronally advanced flap; ADM, acellular dermal matrix; RCT, randomized clinical trial.

better results for CAF +CTG, p = 0.005 (mean difference = 0.49 mm; 95% CI from 0.14 to 0.83) (Fig. 12);

- No significant difference was reported in comparing CAF+BM *versus* CAF (2 studies included), p = 0.11 (mean difference = -0.27mm; 95% CI from -0.60 to 0.06) (Fig. 13).
- CAF+EMD provided better results than CAF alone (5 RCTs included), p = 0.002 (mean difference = 0.58 mm; 95% CI from 0.21 to 0.95) (Fig. 14).
- Two studies compared CAF+ADM versus CAF. Meta-analysis reported no significant difference p = 0.29 (mean difference = 0.60 mm; 95% CI from -0.52 to 1.73); for this

comparison, the test for heterogeneity was statistically significant (p = 0.005) (Fig. 15).

• Only one study compared CAF+ PRP versus CAF, reporting no difference p = 0.57 (mean difference = -0.20 mm; 95% CI from -0.89 to 0.49) (Fig. 16).

Therefore, 2 combinations, CAF+CTG and CAF+EMD, provided better results than CAF in terms of *RecRed*.

When considering CAF+CTG as the control comparative surgical procedure, 2 comparisons were performed.

- Six studies compared CAF+BM versus CAF+CTG. Meta-analyses reported better results for CAF+CTG, p = 0.008 (mean difference = -0.38 mm; 95% CI from -0.65 to -0.10) (Fig. 17).
- No significant differences were reported comparing CAF+ADM *ver*sus CAF+CTG (4 RCTs included), p = 0.24 (mean difference = -0.40 mm; 95% CI from -1.07to 0.26); for this comparison, the test for heterogeneity was statistically significant (p = 0.002) (Fig. 18).

Comparison in terms of *RecRed* between CAF+EMD *versus* CAF+ CTG and CAF+HF-DDS *versus* CAF+CTG was not possible due to data presentation in the original articles (McGuire & Nunn 2003, Wilson et al. 2005), even though no statistically significant difference was reported by the authors.

Therefore, no combination was more effective than CAF+CTG for *RecRed*.

CAL gain

For *CAL gain*, 5 comparisons were possible considering CAF as the control surgical procedure.

- Two studies compared CAF+CTG *versus* CAF. Meta-analysis reported better results for CAF+CTG, *p* = 0.05 (mean difference = 0.38 mm; 95% CI from 0.01 to 0.75) (Fig. 19);
- No statistically significant differences were reported comparing CAF+BM versus CAF (2 studies included), although a trend favouring CAF was detected, p = 0.06 (mean difference = -0.33 mm; 95% CI from -0.68 to 0.02) (Fig. 20);

Table 7. Characteristics of the included study comparing CAF+PRP versus CAF

Study	Huang et al. (2005)
Methods	RCT, parallel study design
	2 treatment groups, 6 months duration
Participants	23 individuals, 17 females, mean age 43.8 years (range 24–63)
-	with 1 Miller Class I gingival recession $\ge 2 \text{ mm}$
	Non-smokers
Intervention	Control: CAF (12 treated sites)
	Test: CAF+PCG (11 treated sites)
Mean % of root coverage	Control: $83.5\% \pm 21.8$
c .	Test: $87.1\% \pm 21.4$
Founding	Supported by the University of Michigan Periodontal Graduate
-	Student Research Fund and the 2003 Dental Master's Thesis
	Award Program from the Delta Dental Fund, Okemos, Michigan.
Allocation concealment	Adeguate
Examiner blinding	Yes
Drop-outs	1 drop out

CAF, coronally advanced flap; PRP, platelet-rich plasma; RCT, randomized clinical trial.

Table 8.	Characteristics	of the 7	included	studies	comparing	CAF+CTG	versus CAF+BN

Study	Zucchelli et al. (1998)			
Methods	RCT, parallel study design			
	3 treatment groups, 12 months duration			
Participants	54 individuals, 29 females, mean age 28.2 years (range 23-33)			
	with one Miller Class I or II gingival recessions $\ge 5 \text{ mm}$			
	16 smokers			
Intervention	Control: CTG+CAF (18 treated sites)			
	Test: Bioabsorbable BM+CAF (18 treated sites)			
	Test: Unresorbable BM+CAF (18 treated sites)			
Mean % of root coverage	Control (CAF+CTG): 93.5 % ± 8.6			
-	Test (Bioabsorbable CAF+BM): 85.7 $\% \pm 13.8$			
	Test (Unresorbable CAF+BM): $80.5\% \pm 14.9$			
Founding	Not reported			
Allocation concealment	Inadeguate			
Examiner blinding	Yes			
Drop-outs	No			
Study	Jepsen et al. (1998)			
Methods	RC1, split mouth design			
	2 treatment groups, 12 months duration			
Participants	15 individuals, 9 females, mean age 40 years (range 20–62) with			
	two Miller Class I or II gingival recessions located in different			
	quadrants			
	No data on smoking habits			
Intervention	Control: CAF+CTG (15 treated sites)			
	Test: CAF+titanium reinforced ePTFE Membrane (15 treated			
	sites)			
Mean % of root coverage	Control: 86.9% \pm 15.4			
	Test: $87.1\% \pm 13.8$			
Founding	Not reported			
Allocation concealment	Adeguate			
Examiner blinding	No			
Drop-outs	No			
Study	Trombelli et al. (1998)			
Methods	RCT split mouth design			
	2 treatment groups 6 months duration			
Participants	12 individuals 10 females mean age 34 years (range 23-58) with			
Turterpants	2 controlateral Miller Class L or II gingival recessions			
	No data on smoking habits			
Intervention	Control: $CAE \perp CTG$ (12 trooted sites)			
	Control. CALTECTO (12 treated sites) Test: $CAE \pm DM$ (12 treated sites)			
N. CI C	Test. CAFT DM (12 treated sites)			
wean % of root coverage				
	1est: 48%			

- CAF+EMD provided better results than CAF alone (5 RCTs included), p = 0.0001 (mean difference = 0.53 mm; 95% CI from 0.26 to 0.80) (Fig. 21).
- Comparison between CAF+ADM versus CAF (2 studies included) resulted in no significant difference p = 0.22 (mean difference = 0.28 mm; 95% CI from -0.16 to 0.72) (Fig. 22).
- Only one study compared CAF+PRP versus CAF, reporting no difference p = 0.39 (mean difference = -0.50 mm; 95% CI from -1.64 to 0.64) (Fig. 23).

Therefore, 2 combinations, CAF+CTG and CAF+EMD, provided better results than CAF in terms of *CAL gain*.

When considering CAF+CTG as the comparative surgical procedure, 2 comparisons were performed.

- No significant differences were reported comparing CAF+BM *ver*sus CAF+CTG (6 studies included), p = 0.73 (mean difference = -0.05 mm; 95% CI from -0.32 to 0.22) (Fig. 24).
- Four studies compared CAF+ADM versus CAF+CTG. Meta-analysis reported no significant difference, p = 0.20 (mean difference = -0.39 mm; 95% CI from -1.00 to 0.21); for this comparison, the test for heterogeneity was statistically significant (p = 0.03) (Fig. 25).

Comparison in terms of *CAL gain* between CAF+EMD versus CAF+ CTG and CAF+HF-DDS versus CAF+ CTG was not possible due to data presentation in the original articles (McGuire & Nunn 2003, Wilson et al. 2005), even though no statistically significant difference was reported by the authors.

KT gain

For *KT gain*, 5 comparisons were possible considering CAF as the comparative surgical procedure.

• Comparison between CAF+CTG versus CAF (2 studies included) resulted in better outcomes for CAF+CTG, p = 0.0001 (mean difference = 0.73 mm; 95% CI from 0.35 to 1.10) (Fig. 26).

Table 8.	(Cont.)
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Study	Trombelli et al. (1998)
Founding	In part by GORE and Associates Inc. and by MURST (Italian Department of scientific Research and Technology)
Allocation concealment Examiner blinding	Inadequate No
Drop-outs	No
Study	Borghetti et al. (1999)
Methods	RCT, split mouth design
Participants	14 individuals, 11 females, mean age 37.5 years (range 20–55) with 14 pair of bilateral Miller Class I gingival recessions $\geq 2 \text{ mm}$
Intervention	No data on smoking habits Control: CAF+CTG (14 treated sites)
Mean % of root coverage	Test: CAF+BM (14 treated sites) Control: 76%
Founding	Test: 70.2% Not reported
Allocation concealment	Inadequate
Examiner blinding	No
Drop-outs	No
Study	Tatakis & Trombelli (2000)
Methods	RCT, split mouth design
Participants	12 individuals, 8 females, mean age 38 years (range 22–48) with 2 controlateral Miller Class I or II gingival recessions $\ge 2 \text{ mm}$, with no more than 1 mm difference between the two defects
Intervention	Non-smokers Control: CAF+CTG (12 treated sites) Test: CAF+BM (12 treated sites)
Mean % of root coverage	Control: 96% Test: 81%
Founding	In part by Guidor, USA and by Loma Linda University School of Dentistry
Allocation concealment	Inadequate
Examiner blinding	Yes
Drop-outs	1 drop out
Study	Romagna-Genon (2001)
Methods	RCT, split mouth design
Participants	20 individuals, 19 females, mean age 37 years (range 21–54) with one pair of controlateral Miller Class I or II gingival recessions
Intervention	Non-smokers Control: CAF+CTG (20 treated sites)
Mean % of root coverage	Control: 84.84%
Founding	Not reported
Allocation concealment	Adequate
Examiner blinding	No
Drop-outs	1 drop out
Study	Wang et al. (2001)
Methods	RCT, split mouth design
Participants	16 individuals, 10 females, mean age 40.6 years (range 30–54) with 2 bilateral Miller Class I or II gingival recessions $\ge 3 \text{ mm}$
Intervention	Non-smoking Control: CAF+CTG (16 treated sites) Test: CAF+BM (16 treated sites)
Mean % of root coverage	Control: $84\% \pm 25$ Test: $73\% \pm 26$
Founding	In part by Sulzer Calcitek Inc., Carlsbad, California

- Two studies compared CAF+ BM versus CAF: meta-analysis reported no significant difference, p = 0.30 (mean difference = 0.15 mm; 95% CI from -0.13 to 0.42) (Fig. 27).
- CAF+EMD achieved better outcomes than CAF alone (5 RCTs included), p = 0.0007 (mean difference = 0.42 mm; 95% CI from 0.18 to 0.66) (Fig. 28).
- No difference was reported between CAF+ADM versus CAF (2 studies included), p = 0.19 (mean difference = 0.31 mm; 95% CI from -0.15 to 0.78) (Fig. 29).
- Only one study compared CAF+ PRP versus CAF, reporting no significant difference p = 0.38 (mean difference = -0.30 mm; 95% CI from -0.97 to 0.37) (Fig. 30).

The additional effect of CTG or EMD in combination with CAF was associated with better outcomes in terms of *KT gain* than CAF alone.

When considering CTG+CAF as the control surgical procedure, 2 comparisons were possible for *KT gain*.

- Comparison between CAF+BM versus CAF+CTG (6 studies included) resulted in better outcomes for CTG+CAF, p = 0.004(mean difference = -1.18 mm; 95% CI from -1.98 to -0.39). For this comparison, the test for heterogeneity was found to be statistically significant (p < 0.00001) (Fig. 31).
- Comparison between CAF+ADM versus CAF+CTG (4 studies included) resulted in better outcomes for CAF+CTG, p = 0.004 (mean difference = -0.90 mm; 95% CI from -1.51 to -0.28) (Fig. 32).

Comparison in terms of KT gain between CAF+EMD versus CAF+CTG and CAF+HFDDS versus CAF +CTG was not possible due to data presentation in original articles (McGuire & Nunn 2003, Wilson et al. 2005). However, McGuire & Nunn (2003) reported higher KT gain for CAF+CTG than EMD+CAF (p < 0.001) one year following therapy, while Wilson et al. (2005) reported no difference.

Therefore, no therapy was found to be more effective than CAF+CTG in *KT* gain.

Table 8. (Cont.)

Allocation concealment	Adequate
Examiner blinding	Yes
Drop-outs	No drop outs

CAF, coronally advanced flap; CTG, connective tissue graft; BM, barrier membrane; RCT, randomized clinical trial.

Table 9. Characteristics of the included study comparing CAF+CTG versus CAF+EMD

Study	McGuire & Nunn (2003)
Methods	RCT, split mouth design
	2 treatment groups, 12 months duration
Participants	17 individuals, 10 females, mean age 44.9 years (range 23-62)
-	with 2 contralateral Miller Class II gingival recessions $\ge 3 \text{ mm}$
	Non-smokers
Intervention	Control: CAF+CTG (17 treated sites)
	Test: CAF+EMD (17 treated sites)
Mean % of root coverage	Control: 93.8%
-	Test: 95.1%
Founding	In part by Biora AB, Malmo, Sweden
Allocation concealment	Adequate
Examiner blinding	Yes
Drop-outs	3 drop outs

CAF, coronally advanced flap; CTG, connective tissue graft; EMD, enamel matrix derivative; RCT, randomized clinical trial.

	Table 10.	Characteristics	of the 4	included	studies	comparing	CAF+	CTG	versus	CAF+	-ADM
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Study	Aichelmann-Reidy et al. (2001)
Methods	RCT, split mouth design
	2 treatment groups, 6 months duration
Participants	22 individuals, 15 females, mean age 47.2 years (range 24–67) with 22 pair of bilateral Miller Class I or II gingival recessions >2 mm
	Non-smokers
Intervention	Control: CAE+CTG (22 treated sites)
intervention	Test: $CAE + ADM$ (22 treated sites)
Mean % of root coverage	Control: $74.1\% + 38.3$
Weat % of foot coverage	Test: 65.0% \pm 46.7
Founding	In part by LifeCell Corp. and by the Louisiana Periodoptics
Touliding	Support Fund
Allocation concealment	Adequate
Examiner blinding	Ves
Drop-outs	No drop outs
Study	Paolantonio et al. (2002)
Methods	RCT, parallel design
	2 treatment groups, 12 months duration
Participants	30 individuals, 19 females, mean age 34.5 years (range 29–51)
	with one Miller Class I or II gingival recession $\ge 3 \text{ mm}$
	Non-smokers
Intervention	Control: CAF+CTG (15 treated sites)
	Test: CAF+ADM (15 treated sites)
Mean % of root coverage	Control: 88.80% ± 11.65
	Test: $83.33\% \pm 11.40$
Founding	Supported by Italian Ministry of University and Scientific
	Research (ex MURST 60%)
Allocation concealment	Inadequate
Examiner blinding	No
Drop-outs	No
Study	Tal et al. (2002)
Methods	RCT, split mouth design

ds RCT, split mouth design 2 treatment groups, 12 months duration

Root sensitivity

Very few studies evaluated *Root sensitivity* following root coverage procedures. No meta-analysis was performed for this variable due to the fact that data were few and heterogeneous. Cortellini et al. (unpublished data) compared CAF+CTG *versus* CAF, reporting no statistically significant differences for root sensitivity (12% in the test group and 12% in the control group) six months following therapy. McGuire & Nunn (2003) reported root sensitivity in only one case treated with CAF+EMD and none for CAF+CTG one year following therapy.

Aesthetic satisfaction

Few studies evaluated aesthetic satisfaction following therapy. No meta-analysis was performed for this variable because data were few and heterogeneous. Romagna-Genon (2001) compared CAF+BM versus CAF+CTG in a split-mouth study, reporting that one patient was not satisfied by either treatment. In the study by Wang et al. (2001), a double aesthetic evaluation was performed by a periodontist blinded to the treatment and by the patient. The periodontist evaluated treatment outcomes at 6 months, rating 15 out of 16 BM sites as an excellent colour match, while 11 CTG sites reported a similar score. Patient satisfaction with aesthetics (colour match, overall satisfaction and amount of root coverage) was the same for both treatments, although overall satisfaction greater was expressed for BM sites compared with CTG sites. Aichelmann-Reidy et al. (2001) compared CAF+ADM versus CAF+CTG in a split-mouth study in 22 patients by performing a double aesthetic evaluation (blinded clinician and patient). Clinicians considered sites with CAF + ADM to have better results in 11 cases, while the other 11 were similar to CAF+CTG. Patients considered CAF+ADM to have better aesthetics in 9 cases out of 22; in 12 cases, they considered it similar to CAF+CTG; and only 1 patient preferred the site with CAF+CTG. A keloid formation was reported in one case of CTG+CAF.

Post-operative pain and complications

Pain and complications (including sites with PD > 3 mm) were unusual follow-

Table 10. (Cont.)

Review.

Recession and CAF

Study	Tal et al. (2002)
Participants	7 individuals, 5 females, mean age 47.3 years (range 23–54) with one pair of bilateral Miller Class I or II gingival recessions ≥4 mm
	Non-smokers
Intervention	Control: CAF+CTG (7 treated sites)
	Test: CAF+ADM (7 treated sites)
Mean % of root coverage	Control: 88.7%
	Test: 89.1 %
Founding	Supported by the Gerald A. Niznick Chair of Implant Dentistry at Tel Aviv University, School of Dental Medicine and by Perimed, Ba'anana Jerael
Allocation concealment	Inadequate
Examiner blinding	Unclear
Drop-outs	No
Study	Joly et al. (2007)
Methods	RCT. split mouth design
	2 treatment groups, 6 months duration
Participants	10 individuals, 4 females, age range 27–51 years, with one pair of bilateral Miller Class I or II gingival recessions ≥3 mm
	Non-smokers
Intervention	Control: CAF+CTG (10 treated sites)
	Test: CAF+ADM (10 treated sites)
Mean % of root coverage	Control: 79.5%
	Test: 50.0%
Founding	Not reported
Allocation concealment	Adequate
Examiner blinding	No
Drop-outs	No

CAF: coronally advanced flap; CTG: connective tissue graft; ADM: acellular dermal matrix graft; RCT: randomized clinical trial.

Study	Wilson et al. (2005)
Methods	RCT, split mouth design
	2 treatment groups, 6 months duration
Participants	10 individuals, 11 females, mean age 47.7 years (range 38–60) with
-	2 bilateral Miller Class I or II gingival recessions $\ge 3 \text{ mm}$
	Non-smoking
Intervention	Control: CAF+CTG (10 treated sites)
	Test: CAF+HF-DDS (13 treated sites)
Mean % of root coverage	Control: $64.4\% \pm 31.9$
-	Test: $56.7\% \pm 27.8$
Founding	In part by Advanced Tissue Science, Inc., La Jolla, Ca,
Allocation concealment	Adequate
Examiner blinding	Yes
Drop-outs	2 drop outs

CAF, coronally advanced flap; CTG, connective tissue graft; **HF-DDS**, human fibroblast-derived dermal substitute; **RCT**, randomized clinical trial.

01 CAF+CTG v s CAF 01 CRC					
CAF+CTG N	CAF N	log(Odds Ratio) (SE)	Odds Ratio (random) 95% Cl	Weight %	Odds Ratio (random) 95% Cl
11	11	0.7965 (1.1493)	-	13.35	2.22 [0.23, 21.14]
41	42	0.9318 (0.4511)	⊢ ∎−	66.65	2.54 [1.05, 6.15]
52	53		-	100.00	2.49 [1.10, 5.68]
enenity: Chr² = 0.01, df = 1 (P effect: Z = 2.18 (P = 0.03)	= 0.91), I* = 0	6			
		0.01	0.1 1 10	100	
	01 CAF+CTG v s CAF 01 CRC CAF+CTG N 11 41 52 encity : Chi₹ = 0.01, df = 1 (P effect: Z = 2.18 (P = 0.03)	01 CAF+CTG v s CAF 01 CRC CAF+CTG CAF N N 11 11 41 42 52 53 encity : Chr ² = 0.01, df = 1 (P = 0.91), l ² = 0? effect: Z = 2.18 (P = 0.03)	01 CAF+CTG v s CAF 01 CRC CAF+CTG CAF N N bg[Odds Ratio] (SE) 11 11 0.7965 (1.1493) 41 42 0.9318 (0.4511) 52 53 encity : Chi ² = 0.01, df = 1 (P = 0.91), I ² = 0% effect: Z = 2.18 (P = 0.03) 0.01	$\begin{array}{c c c c c c c c c c c c c c c c c c c $	$\begin{array}{c c c c c c c c c c c c c c c c c c c $

analysis was performed for this variable due to the fact that data were few and heterogeneous. Da Silva et al. (2004) reported no complication on comparing CAF+CTG versus CAF. Cortellini et al. (unpublished data) reported 3 cases of haematoma in 43 patients treated with CAF, while 5 cases of haematoma were reported in 42 patients treated with CAF+CTG. A higher number of cases of swelling were reported for the CAF+CTG group, and these differences were statistically significant (CAF+CTG 32.2 ± 28.4 and CAF 17.8 ± 19.9 using visual analogue scale-(VAS), p = 0.0068). No statistically significant differences for pain were reported between two groups $(23.8 \pm 19.4 \text{ for CAF and } 31.4 \pm 24.6)$ for CAF+CTG, using VAS

p = 0.0811). No treated sites reported

ing root coverage procedures. No meta-

PD > 3 mm 6 months following therapy.Studies using BM reported membrane exposure as a frequent complication. Amarante et al. (2000) reported exposure of several membranes in CAF+BM sites, while Lins et al. (2003) reported the exposure of all membranes in all treated sites (10/10). PD $\leq 2 \text{ mm}$ resulted following therapy. In comparbetween CAF+BM versus isons CAF+CTG, membrane exposure was reported as a possible complication (7/ 15 Jepsen et al. 1998, 2/12 Trombelli et al. 1998, 5/12 Tatakis & Trombelli 2000). Jepsen et al. (1998) reported a similar incidence of post-operative pain for both treatments (5/15 patients) with final PD ≤2.8 mm. Tatakis & Trombelli (2000) reported 7 cases of swelling in 12 patients treated with CAF+BM and none for CAF+CTG; the final PD was ≤ 2 mm. On the other hand, no complication for CAF+BM was reported by Wang et al. (2001): they reported one swelling and one ecchymosis in the CAF+CTG Romagna-Genon arm.

Fig. 3. Comparison CAF+CTG versus CAF for CRC. CAF, coronally advanced flap; CTG, connective tissue graft; CRC, complete root coverage.

Review: Comparison: Outcome:	Recession and CAF 02 CAF+EMvs CAF 01 CRC					
Study or sub-category	CAF+EM v N	CAF N	log[Odds Ratio] (SE)	Odds Ratio (random) 95% Cl	Weight %	Odds Ratio (random) 95% Cl
Leknes 2005	20	20	-0.5390 (0.6487)		100.00	0.58 [0.16, 2.08]
Total (95% CI) Test for hetero Test for overal	20 geneity: not applicable l effect: Z = 0.83 (P = 0.41)	20			100_00	0.58 [0.16, 2.08]
			0.0)1 0.1 1 10 FavoursCAF FavoursCAF	100 +BM	

Fig. 4. Comparison CAF+BM versus CAF for CRC. CAF, coronally advanced flap; CRC, complete root coverage; BM, barrier membranes.

Review: Comparison: Outcome:	Recession and CAF 03 CAF+EMD v s CAF 01 CRC						
Study or sub-category	CAF+EM N	D CAF N	log(Odds Ratio) (SE)	Odds F	Catio (random) 95% Cl	Weight %	Odds Ratio (random) 95% Cl
Modica 2000	10	10	0.0000 (1.0000)		+	16.13	1.00 [0.14, 7.10]
Del Pizzo 2005	15	15	1.6094 (1.5492)	_		→ 8.15	5.00 [0.24, 104.14]
Spahr 2005	30	30	1.3231 (0.4950)			53.41	3.76 [1.42, 9.91]
Piloni 2006	15	15	2.5619 (0.9361)			20_32	13.00 [2.07, 61.47]
Total (95% CI)	70	70			-	100.00	3.69 [1.59, 9.50]
Test for heterog Test for overal	eneily: Chi ^z = 3.54, df = 3 effect: Z = 2.99 (P = 0.00	3) (P = 0.32), P =	15.2%				
				0.01 0.1	1 10	100	
				Favours CA	F Favours CA	+EMD	

Fig. 5. Comparison CAF+EMD versus CAF for CRC. CAF, coronally advanced flap; CRC, complete root coverage; EMD, enamel matrix derivative.

Review: Comparison: Outcome:	Recession a 04 CAF+ADI 01 CRC	nd CAF Mivs CAF					
Study or sub-category	,	CAF+ADM N	CAF N	log[Odds Ratio] (SE)	Odds Ratio (random) 95% Cl	Weight %	Odds Ratio (random) 95% C1
Cortes 2004 Woodyard 200	04	13 12	13 12	0.0000 (1.2849) 3.0910 (1.2107)		49-03	1.00 [0.06, 12.41] 22.00 [2.05, 236.02]
Total (95% CI)		25	25			100.00	4.83 [0.23, 99.88]
Test for heteroy Test for overal	geneity: Chi# = effect: Z = 1.	= 3.07, df = 1 (P = .02 (P = 0.31)	0.08), I* = 67	4%			
					0.01 0.1 1 10 Eavours CAF Eavours CAF	100 ADM	

Fig. 6. Comparison CAF+ADM versus CAF for CRC. CAF, coronally advanced flap; CRC, complete root coverage; ADM, acellular dermal matrix.

Review. Comparison: Outcome:	Recession and CAF 05 CAF+FRP vs CAF 01 CRC					
Study or sub-category	CAF+PRP N	CAF N	log(Odds Ratio) (SE)	Odds Ratio (randon 95% Cl	n) Weight %	Odds Ratio (random) 95% Cl
Huang 2005	11	12	0.2231 (0.8577)	-+	100.00	1.25 [0.23, 6.71]
Total (95% CI) Test for heterog Test for overal	11 eneity: not applicable effect: Z = 0.26 (P = 0.79)	12		-	100.00	1.25 [0.23, 6.71]
			Q	0.01 0.1 1 Eavours CAE Eavour	10 100 s CAE+PRP	

Fig. 7. Comparison CAF+PRP versus CAF for CRC. CAF, coronally advanced flap; CRC, complete root coverage; PRP, platelet-rich plasma.

(2001) described postoperative discomfort for the palatal donor site for the CTG. Sites treated with BM were more frequently symptom-free compared with CTG sites. None of the sites showed exposure of the membrane.

No complication was reported in comparisons among CAF+EMD versus

CAF (Modica et al. 2000), CAF+ADM versus CAF (Côrtes et al. 2004, Woodyard et al. 2004) and CAF+ADM versus CAF+CTG (Joly et al. 2007) with

Review: Comparison: Outcome:	Recession and CAF 09 CAF+BMvs CAF+CTG 01 CRC					
Study or sub-category	CAF+BM N	CAF+CTG N	log[Odds Ratio] (SE)	Odds Ratio (random) 95% Cl	Weight %	Odds Ratio (random) 95% Cl
Jepsen 1998	15	15	0.0000 (0.6165)		17.60	1.00 [0.20, 4.95]
Zucchelli 1998	36	18	-1.3863 (0.6124)		25.13	0.25 [0.08, 0.83]
Borghetti 1999	14	14	0.0000 (0.7303)		20.54	1.00 [0.24, 4.16]
Trombelli 1998	12	12	-2.5802 (1.0753)	←→	11.95	0.08 [0.01, 0.62]
Tatakis 2000	12	12	-1.9459 (1.5119)	←	6.79	0.14 [0.01, 2.77]
Wang 2001	16	16	0.0000 (0.6165)	+	17.60	1.00 [0.20, 4.95]
lotal (95% CI)	105	87			100.00	0.45 [0.20, 1.04]
lest for heterog	eneaty: Chi≇ = 7.34, df = 5 (P	= 0.20), P = 31	.9%	-		
Test for overal	effect: Z = 1.87 (P = 0.06)	-				
				0.01 0.1 1 10	100	
				Eavours CAE+CTG Eavours CAE	+EM	

Fig. 8. Comparison CAF+BM *versus* CAF+CTG for CRC. CAF, coronally advanced flap; CTG, connective tissue graft; CRC, complete root coverage; BM, BM, barrier membranes.

Review: Comparison: Outcome:	Recession an 06 CAF+EMD 01 CRC	d CAF vs CAF+CTG							
Study or sub-category	,	CAF+EMD N	CAF+CTG N	log[Odds Ratio] (SE)		OddsRa 95	tio (random 7% Cl) Weight %	Odds Ratio (random) 95% Cl
McGuire & Nu	rn 2003	17	17	0.8362 (0.8299)		-	-	- 100.00	2.31 [0.45, 11.74]
Total (95% CI) Test for helero; Test for overal	geneity:notapp effect:Z=1.0	17 ficable 11 (P = 0.31)	17			-		- 100.00	2.31 [0.45, 11.74]
				1	0.01	0.1	1 1	0 100	

Favours CAF+CTG Favours CAF+EMD

Fig. 9. Comparison CAF+EMD versus CAF+CTG for CRC. CAF, coronally advanced flap; CTG, connective tissue graft; CRC, complete root coverage; EMD, enamel matrix derivative.

Review. Comparison: Outcome:	Recession a 07 CAF+AD 01 CRC	nd CAF Avs CAF+CTG								
Study or sub-category	,	CAF+ADM N	CAF+CTG N	log[Odds Ratio] (SE)		Odds Rat 95	io (random) % Cl	Weight %	Odds Ratio (random) 95% C1	
AicheimannRe	sidy 2001	22	22	-0.7621 (0.5463)			L	48.26	0.47 [0.16, 1.36]	_
Padantonio 2	002	15	15	-0.8781 (0.7802)			L	23.66	0.42 [0.09, 1.92]	
Tal 2002		7	7	0.0000 (0.8165)				21.60	1.00 [0.20, 4.95]	
Joly 2007		10	10	-2.1972 (1.4907)	←		+	6.48	0.11 [0.01, 2.06]	
Total (95% Cl) Test for hetero Test for overal	geneity: Chi¥ = l effect: Z = 1.	54 = 1.81, df = 3 (P = 89 (P = 0.06)	54 = 0.61), 1² = 0%			•		100.00	0.49 [0.23, 1.03]	
					0.01	0.1	1 10	100		_
					Favou	s CAF+CTG	Favours C	AF+ADM		

Fig. 10. Comparison CAF+ADM *versus* CAF+CTG for CRC. CAF, coronally advanced flap; CTG, connective tissue graft; CRC, complete root coverage; ADM, acellular dermal matrix.

Review: Comparison: Outcome:	Recession a 08 CAF+HFI 01 CRC	nd CAF DDS vs CAF+CT	G				
Study or sub-calegory		CAF+HFDDS N	CAF+CTG N	log(Odds Ratio) (SE)	Odds Ratio (rando 95% Cl	m) Weight %	Odds Ratio (random) 95% Cl
Wilson Jr 2008	5	10	10	0.0000 (2.0000)		100.00	1.00 [0.02, 50.40]
Total (95% CI) Test for heterog Test for overal	jeneity:nota; effect:Z=D	10 pplicable DD (P = 1.00)	10			100.00	1.00 [0.02, 50.40]
					0.01 0.1 1 Favours CAF+CTG Favou	10 100 IIS CAF+HFDDS	

Fig. 11. Comparison CAF+HF-DDS versus CAF+CTG for CRC. CAF, coronally advanced flap; CTG, connective tissue graft; CRC, complete root coverage; HF-DDS, human fibroblast-derived dermal substitute.

Review: Comparison: Outcome:	Recession a 01 CAF+CTC 02 RecRed	nd CAF ∋vsCAF						
Study or sub-category	,	CAF+CTG N		Mean difference (SE)	Mean diffe 9	rence (random) 5% Cl	Weight X	Mean difference (random) 95% Cl
Da Silv a 2004	l	11	11	0.1100 (0.2700)		+	42.05	0.44 [-0.09, 0.97]
Contellini		41	42	0.5200 (0.2300)		+-	57.95	0.52 [0.07, 0.97]
Total (95% CI)		52	53			•	100.00	0.49 [0.14, 0.63]
Test for heterog Test for ov eral	geneity:Chi*= effect:Z=2.	:0.05, df = 1 (P = 78 (P = 0.005)	0.82), I* = 0%					
				_	4 -2	0 2	4	
					Favours CAF	Favours CAF#	CTG	

Fig. 12. Comparison CAF+CTG versus CAF for RecRed. CAF, coronally advanced flap; CTG, connective tissue graft.

Review: Comparison: Outcome:	Recession an 02 CAF+BM v 02 RecRed	1 CAF s CAF									
Study CAF+BM or sub-category N		CAF+BM N	CAF N	Mean difference (SE)		Mean difference (random) 95% Cl		Weight %	Mean difference (random) 95% Cl		
Amarante 200 Lins 2003	0	20 10	20 10	-0.2000 (0.2100) -0.4000 (0.2900)]				65.60 34.40	-0.20 [-0.61, 0.21] -0.40 [-0.97, 0.17]	
Total (95% CI)		30	30		,				100.00	-0.27 [-0.60, 0.06]	
Test for heterog Test for overal	peneily: Chi ^a = 0 effect: Z = 1.5).31, df = 1 (P = B (P = 0.11)	0.58), I* = 09	6							
					-4	-2 Favours	0 CAF Fa	2 VOURS CAF+	4 814		

Fig. 13. Comparison CAF+BM versus CAF for RecRed. CAF, coronally advanced flap; BM, BM, barrier membranes.

Review: Recession Comparison: 03 CAF+E Outcome: 02 RecRe		d CAF vsCAF							
Study		CAF+EMD	CAF		_	Mean diff	erence (random)	Weight	Mean difference (random)
or sub-category		N	N	Mean difference (S	E)		95% CI	*	95% CI
Modica 2000		10	10	0.9000 (0.4300)			_	13.11	0.90 [0.06, 1.74]
Del Pizzo 200	5	15	15	0.0700 (0.2500)			+	23.91	0.07 [-0.42, 0.56]
Spahr 2005		30	30	0.3770 (0.2300)			↓	25.56	0.38 [-0.07, 0.63]
Castellanos 2	006	11	11	0.9100 (0.4400)				12.71	0.91 [0.05, 1.77]
Piloni 2006		15	15	0.9300 (0.2400)				24.72	0.93 [0.46, 1.40]
Total (95% CI)		61	61				•	100.00	0.58 [0.21, 0.95]
Test for heterog	genenity:Chi²=8	8.09, df = 4 (P =	0.09), P = 50	.5%			-		
Test for overal	effect: Z = 3.0	6 (P = 0.002)	-						
					-4	_2	0 2	4	
						Favours CA	F Favours CAF+	MD	

Fig. 14. Comparison CAF+EMD versus CAF for RecRed. CAF, coronally advanced flap; EMD, enamel matrix derivative.

Review: Comparison: Outcome:	Recession a D4 CAF+AD 02 RecRed	nd CAF MivsCAF					
Study or sub-category	,	CAF+ADM N	CAF N	Mean difference (SE)	Mean difference (ran 95% Ci	dam) Weight %	Mean difference (random) 95% Cl
Cortes 2004 Woody ard 200	м	13 12	13 12	0.0800 (0.1600) 1.2300 (0.3800)	† -•	54.49 45.51	0.08 [-0.23, 0.39] 1.23 [0.49, 1.97]
Total (95% CI) Test for helerog Test for overall	geneily: Chi ^z = effect: Z = 1.	25 = 7.78, df = 1 (P = 05 (P = 0.29)	25 D.005), Iª = 8	7.1%	-	► 100_00	0.60 [-0.52, 1.73]
				-4	-2 0 Favours CAF Favou	2 4 rs CAF+ADM	

Fig. 15. Comparison CAF+ADM versus CAF for RecRed. CAF, coronally advanced flap; ADM, acellular dermal matrix.

Review: Comparison: Outcome:	Recession and CAF 05 CAF+PRPvs CAF 02 RecRed					
Study or sub-category	CAF+PRP N	CAF N	Mean Difference (SE)	Mean Difference (random) 95% Cl	Weight %	Mean Difference (random) 95% Cl
Huang 2005	11	12	-0.2000 (0.3500)	-	100.00	-0.20 [-0.89, 0.49]
Total (95% CI) Test for heterog Test for overall	11 geneity: not applicable leffect: Z = 0.57 (P = 0.57)	12		•	100.00	-0.20 [-0.69, 0.49]
			-4	-2 0 2 Favours CAF Favours CAF+F	4 RP	

Fig. 16. Comparison CAF+PRP versus CAF for RecRed. CAF, coronally advanced flap; PRP, platelet-rich plasma.

Review: Comparison: Outcome:	Recession and CAF 09 CAF+EMvs CAF+CTG 02 RecRed													
Study or sub-category	CAF+BM N	CAF+CTG N	Mean	difference (SE)		Mean diff !	erena 95%	ce (rando Cl	m)	Weight %	M	an diffen 95	ence (random % Cl	I)
Jepsen 1998	15	15	-0.0100	(0.2300)			+			16.77	-0.01	[-0.16,	0_11]	
Trombelli 1998	12	12	-0.9000	(0.2600)			- 1			16.50	-0.90	[-1.41,	-0.39]	
Zucchelii 1998	16	36	-0.6000	(0_2100)		-	⊢			20.45	-0.60	[-1.01,	-0.19]	
Borghetti 1999	14	14	0.0000	(0.3700)		-	+	_		10.51	0.00	[-0.73,	0.73]	
Tatakis 2000	12	12	-0.1000	(0_2400)		-	•			17.97	-0.40	[-0.87,	0_07]	
Wang 2001	16	16	-0.2000	(0.2700)		-	•			15.81	-0.20	[-0.73,	0.33]	
otal (95% CI)	87	105					•			100.00	-0.38	[-0.65,	-0.10]	
est for heterog est for ov erall	eneity: Chi² = 9.19, df = 5 (P effect: Z = 2.66 (P = 0.008)	= 0.10), P = 45.	6%				-					-	_	
					-4	-2	ò			4				
					Favours	CAF+CT	G	Favours	CAF+BM					

Fig. 17. Comparison CAF+BM versus CAF+CTG for RecRed. CAF, coronally advanced flap; CTG, connective tissue graft; BM, barrier membranes.

Review Comparison: Outcome:	Recession a 07 CAF+AD 02 RecRed	d CAF I vs CAF+CTG									
Study or sub-category	,	CAF+ADM N	CAF+CTG N	Mean differe	maae (SE)		lican diff	incince (n 15% Cl	adaa)	Weight %	Mean difference (random) 99% Cl
Aichda an R	eidy 2001	22	22	-0.5000 (0.29	300)		-	-		25.98	-0.50 [-1.07, 0.07]
Padantonio 2	002	15	15	-0.2000 (0.3	500)		_	•		23.91	-0.20 [-0.89, 0.49]
Tal 2002		7	7	0.2900 (0.22	200)			+		29.26	0.29 [-0.14, 0.72]
Jaly 2007		10	10	-1.4000 (0.4)	LDO)					21.84	-1.40 [-2.20, -0.60]
Total (95% CI)		54	54				-			100.00	-0.10 [-1.07, 0.26]
Test for hetero	geneily: Chi ² -	14.99, df = 3 (P	= 0.002), I*= 7	9.4%				-			
Test for overal	effect Z = 1	18 (P = 0.24)									
					-	4	-2	0	2	4	
						Favours	CAF+CT	G Fav	CAF+	ADM	

Fig. 18. Comparison CAF+ADM versus CAF+CTG for RecRed. CAF, coronally advanced flap; CTG, connective tissue graft; ADM, acellular dermal matrix.

Recession an 01 CAF+CTG 05 CALGain	d CAF vs CAF					
	CAF+CTG N	CAF N	Mean Difference (SE)	Mean Difference (random) 95% Ci	Weight %	Mean Difference (random) 95% Ci
	11	11	0.3200 (0.3800)		25.10	0.32 [-0.42, 1.06]
	41	42	0.4000 (0.2200)	-	74_90	0.40 [-0.03, 0.83]
	52	53		•	100.00	0.38 [0.01, 0.75]
eneily:Chi≇=0 effect:Z=2.0	0.03, df = 1 (P = 0 (P = 0.05)	0.86), 1ª = 0%				
			-4	-2 0 2	4	
	Recession an DI CAF+CTG D5 CALGain eneily: Chi ^a = (effect: Z = 2.0	Recession and CAF D1 CAF+CTG vs CAF 05 CALGain CAF+CTG N 11 41 52 eneity: Chi ^a = 0.03, df = 1 (P = effect: Z = 2.00 (P = 0.05)	Recession and CAF D1 CAF+CTG vs CAF CAF+CTG CAF N N 11 11 41 42 52 53 eneity: Chi ² = 0.03, of = 1 (P = 0.86), I ^a = 0% effect: Z = 2.00 (P = 0.05)	Recession and CAF D1 CAF+CTG vs CAF CAF D5 CALGain CAF+CTG CAF 11 11 0.3200 (0.3800) 11 12 0.4000 (0.2200) 52 53 53 54 eneity: Chi ² = 0.03, df = 1 (P = 0.86), I ² = 0% 12 = 0% -4	Recession and CAF DI CAF+CTG vs CAF DI CAF+CTG vs CAF DS CALCain CAF+CTG CAF Mean Difference (se) Mean Difference (random) 11 11 0.3200 0.3800)	Recession and CAF DI CAF+CTG vs CAF DI CAF+CTG vs CAF DS CALCain CAF+CTG N CAF Mean Difference (sE) Mean Difference (random) Weight % 11 11 0.3200 (0.3800) - - 25.10 11 12 0.4000 (0.2200) - 74.90 52 53 - 100.00 6reety: Chi ² = 0.03, of = 1 (P = 0.86), I ² = 0% - - 0 2 4 -4 -2 0 2 4

Fig. 19. Comparison CAF+CTG versus CAF for CAL gain. CAF, coronally advanced flap; CTG, connective tissue graft; CAL, clinical attachment level.

Review: R Comparison: 0 Outcome: 0	ecession and CAF 2 CAF+BM vs CAF 1 CALGain							
Study or sub-category	CAF+BM N	CAF N	Mean difference (SE)	Mean difference (random) 95% Cl	Weight %	Mean difference (random) 95% Cl		
Amarante 2000	20	20	-0.2000 (0.2400)	-	55.86	-0.20 [-0.67, 0.27]		
Lins 2003	10	10	-0.5000 (0.2700)		44.14	-0.50 [-1.03, 0.03]		
Total (95% CI)	30	30		•	100.00	-0.33 [-0.68, 0.02]		
Test for heterogen Test for overall eff	sty: Chi ^p = 0.69, df = 1 (P = ect: Z = 1.85 (P = 0.06)	0.41), I²=I	0%					
			_4	-2 0 2 Eavours CAE Eavours CAE	4 8M			

Fig. 20. Comparison CAF+BM versus CAF for CAL gain. CAF, coronally advanced flap; BM, barrier membranes; CAL, clinical attachment level.

Review: Recession and CAF Comparison: D3 CAF+EMD vs CAF Outcome: D5 CALGain									
Study or sub-category	,	CAF+EMD N	CAF N	Mean difference (SE)	Mean (difference (random) 95% Cl	Weight %	Mean difference (random) 93% Cl
Modica 2000		10	10	0.9000 (0.4300)				9.83	0.90 [0.06, 1.74]
Del Pizzo 200	5	15	15	0.2000 (0.2200)				33.79	0.20 [-0.23, 0.63]
Spahr 2005		30	30	0.4900 (0.2700)				23.50	0.49 [-0.04, 1.02]
Castellanos 2	006	11	11	0.9700 (0.5600)			—	5.89	0.97 [-0.13, 2.07]
Pillani 2006		15	15	0.7400 (0.2500)				26.99	0.74 [0.25, 1.23]
Total (95% CI)		81	81				•	100.00	0.53 [0.26, 0.80]
Test for helero	geneily: Chi ^a =	4.33, df = 4 (P =	0.36), I ^x = 7.6	*					
Test for overa	effect: Z = 3.8	94 (P=0.0001)							
					-4	-2	0 2	4	
					-4	Esware		-	

Fig. 21. Comparison CAF+EMD versus CAF for CAL gain. CAF, coronally advanced flap; EMD, enamel matrix derivative.

Review: Comparison: Outcome:	Recession a 04 CAF+AD 04 CALGain	nd CAF M vs CAF					
Study or sub-category	,	CAF+ADM N	CAF N	Mean difference (SE)	Mean difference (random) 95% Cl	Weight %	Mean difference (random) 95% Ci
Cortes 2004		13	13	0.1900 (0.2700)		69.75	0.19 [-0.34, 0.72]
Woody ard 200	D4	12	12	0.4800 (0.4100)	+• -	30.25	0.48 [-0.32, 1.28]
Total (95% CI) Test for hetero;	geneity: Chi≭⊧	25 = 0.35, df = 1 (P =	25 0.55), I² = 0%		+	100.00	0.28 [-0.16, 0.72]
Test for overa	effect: Z = 1	.23 (P = 0.22)					
				-4	-2 0 2 Favours CAF Favours CAF#	4 10M	

Fig. 22. Comparison CAF+ADM versus CAF for CAL gain. CAF, coronally advanced flap; CAL, clinical attachment level; ADM, acellular dermal matrix.

Review: Recession and CAF Comparison: 05 CAF+PRP vs CAF Outcome: 04 CALGain							
Study or sub-category	,	CAF+PRP N	CAF N	Mean difference (SE)	Mean difference (random) 95% Ci	Weight %	Mean difference (random) 95% Cl
Huang 2005		11	12	-0.5000 (0.5800)		100.00	-0.50 [-1.64, 0.64]
Total (95% CI) Test for heterog Test for overal	geneity: not appli effect: Z = 0.86	11 cable (P=0.39)	12			100.00	-0.50 [-1.64, 0.64]
				-4	-2 0 2 Favours CAF Favours CAF	4 +PRP	

Fig. 23. Comparison CAF+PRP versus CAF for CAL gain. CAF, coronally advanced flap; PRP, platelet-rich plasma; CAL, clinical attachment level.

Review

Recession and CAF

Comparison: Outcome:	09 CAF+BM vs CAF+CTG 05 CALGain										
Study or sub-category	CAF+EM N	CAF+CTG N	Mean diffe	rence (SE)	Mea	ndiffere 937X	nce (ran 6 Cl	tom)	Weight %	Mean differ 95	ence (random) % Cl
Jepsen 1998	15	15	-0.0300 (0.2	2700)		_	_		16.60	-0.03 [-0.56,	0.50]
Trambelli 1998	12	12	-0.6000 (0.2	2700)					16.60	-0.60 [-1.13,	-0.07]
Zucchelli 1998	36	18	0.1000 (0.2	2200)		_	-		21.04	0.10 [-0.33,	0.53]
Barghetti 1999	14	14	0.1500 (0.4	1400)		_			8.13	0.15 [-0.71,	1.01]
Tatakis 2000	12	12	-0.2000 (0.2	2200)			-		21.04	-0.20 [-0.63,	0.23]
Wang 2001	16	16	0.4000 (0.2	2700)		-	•		16.60	0.40 [-0.13,	0.93]
Total (95% CI)	105	87				•	•		100.00	-0.05 [-0.32,	0_22]
Test for heterog	eneity: Chi ^a = 8.07, df = 5 (P	² = 0. 15), 1 ² = 38.	0%			1					
Test for overa	effect: Z = 0.34 (P = 0.73)										
					4 _2)	2	4		
					avours CA	F+CTG	Favou	S CAF+B	M		

Fig. 24. Comparison CAF+BM *versus* CAF+CTG for CAL gain. CAF, coronally advanced flap; CTG, connective tissue graft; CAL, clinical attachment level; BM, barrier membranes.

Review: Recession and CAF Comparison: 07 CAF+ADM vs CAF+CTG Outcome: 05 CALGain													
Study or sub-category	,	CAF+ADM N	CAF+CTG N	Mean diffe	rrence (SE)	Me	an differe 953	nce (rando X. Cl	om)	Weight %	Mean diff	erence (random) 95% Cl	
AichelmannRe	eidy 2001	22	22	-0.1000 (0.	2800)		1	_		28.63	-0.10 [-0.6	5, 0.45]	
Paolantonio 2	002	15	15	-0.2700 (0.	4100)			L		22.58	-0.27 [-1.0	7, 0.53]	
Tal 2002		7	7	0.0700 (0.	3400)		-	—		25.77	0.07 [-0.6	0, 0.74]	
Joly 2007		10	10	-1.4000 (0.	4000)	-	•			23.02	-1.40 [-2.1	8, -0.62]	
Total (95% CI)		54	54				-	•		100.00	-0.39 [-1.0	0, 0.21]	
Test for hetero Test for overal	geneity:Chi² = l effect:Z = 1.3	9.24, df = 3 (P = 27 (P = 0.20)	= 0.03), 1* = 67.	5%			-						
					_	4 -	2	0	2	4			
						Favo	urs CTG	Favours	ADM	•			

Fig. 25. Comparison CAF+ADM versus CAF+CTG for CAL gain. CAF, coronally advanced flap; CTG, connective tissue graft; CAL, clinical attachment level; ADM, acellular dermal matrix.

Review: Comparison: Outcome:	Recession a D1 CAF+CT0 D3 KTGain	nd CAF Gvs CAF					
Study or sub-category	,	CAF+CTG N	CAF N	Mean difference (SE)	Mean difference (random) 95% Cl	Weight %	Mean difference (random) 95% Ci
Da Silva 2004	1	11	11	0.7600 (0.2900)		42.63	0.76 [0.19, 1.33]
Cartelini		41	42	0.7000 (0.2500)	-	57.37	0.70 [0.21, 1.19]
Total (95% CI)		52	53		•	100.00	0.73 [0.35, 1.10]
Test for heteror Test for overal	geneily: Chi ^a = I effect: Z = 3;	0.02, df = 1 (P = 83 (P = 0.0001)	0.88), I×=0%				
				-4	-2 0 2 Esugers CAE Esugers CAE	4	

Fig. 26. Comparison CAF+CTG versus CAF for KT gain. CAF, coronally advanced flap; CTG, connective tissue graft; KT, keratinized tissue.

Review. Camparison: Outcame:	Recession an 02 CAF+EM v 03 KTGain	I CAF s CAF					
Study or sub-category	,	CAF+BM N	CAF N	Mean difference (SE)	Mean difference (random) 95% Cl	Weight %	Mean difference (random) 95% Cl
Amarante 200 Lins 2003	0	20 10	20 10	0.1000 (0.1500) 0.5000 (0.4100)	*-	88.20 11.80	0.10 [-0.19, 0.39] 0.50 [-0.30, 1.30]
Total (95% CI) Test for helero Test for overal	geneity: Chi²= effect: Z = 1.0	30).84, df = 1 (P = 5 (P = 0.30)	30 0.36), 1* = 0%		•	100_00	0.15 [-0.13, 0.42]
				_4	-2 0 2 Favours CAF Favours CAF+	4 BM	

Fig. 27. Comparison CAF+BM versus CAF for KT gain. CAF, coronally advanced flap; KT, keratinized tissue.

tudy r sub-category	CAF+EMD N	CAF N	Mean difference (SE)	Mean difference (random) 95% Cl	Weight %	Mean difference (random 95% Cl
Modica 2000	10	10	0.6000 (0.2200)	-	17.77	0.60 [0.17, 1.03]
Del Pizzo 2005	15	15	0.5300 (0.2600)	⊢	14.52	0.53 [0.02, 1.04]
Spahr 2005	30	30	0.3170 (0.2000)	+	19.70	0.32 [-0.07, 0.71]
Castellanos 2006	11	11	0.8600 (0.3000)	 →	11.96	0.86 [0.27, 1.45]
Piloni 2006	15	15	0.1900 (0.0700)	•	36.06	0.19 [0.05, 0.33]
iotal (95% CI)	61	61		•	100.00	0.42 [0.18, 0.66]
est for heterogeneity	Chi≇ =8.46, df =4 (P	= 0.08), I* = 52	27%	ľ		
est for overall effect	Z = 3.38 (P = 0.0007)					

Fig. 28. Comparison CAF+EMD versus CAF for KT gain. CAF, coronally advanced flap; KT, keratinized tissue; EMD, enamel matrix derivative.

Review: Comparison: Outcome:	Recession a 04 CAF+ADI 03 KTGain	nd CAF Nivs CAF					
Study or sub-category	,	CAF+ADM N	CAF N	Mean difference (SE)	Mean difference (random) 95% Cl	Weight %	Mean difference (random) 95% Cl
Cortes 2004 Woodyard 20	04	13 12	13 12	0.2300 (0.2900) 0.4600 (0.4100)	*	66.65 33.35	0.23 [-0.34, 0.60] 0.46 [-0.32, 1.26]
Total (95% CI) Test for hetero Test for overal	geneity:Chi²= Ieffect:Z=1.	25 : 0.25, df = 1 (P = 32 (P = 0.19)	25 0.62), P = 0%		→	100.00	0.31 [-0.15, 0.78]
				-4	–2 0 2 FavoursCAF FavoursCAF+	4 VDM	

Fig. 29. Comparison CAF+ADM versus CAF for KT gain. CAF, coronally advanced flap; KT, keratinized tissue; ADM, acellular dermal matrix.

Review: Comparison: Outcome:	Recession and CAF 05 CAF+PRPvs CAF 03 KTGain					
Study or sub-category	CAF+PRI N	P CAF N	Mean difference (SE)	Mean difference (random) 95% Cl	Weight %	Mean difference (random) 95% Cl
Huang 2005	11	12	-0.3000 (0.3400)		100.00	-0.30 [-0.97, 0.37]
Total (95% CI) Test for heterog Test for overal	11 eneity: not applicable effect: Z = 0.88 (P = 0.38	12		•	100.00	-0.30 [-0.97, 0.37]
				-4 -2 0 2 FavoursCAF FavoursCAF	4 +PRP	

Fig. 30. Comparison CAF+PRP versus CAF for KT gain. CAF, coronally advanced flap; KT, keratinized tissue; PRP, platelet-rich plasma.

PD $\leq 1 \text{ mm}$ (Joly et al. 2007) or $\leq 2.5 \text{ mm}$ (Tal et al. 2002). In a comparison between CAF+EMD *versus* CAF+CTG, McGuire & Nunn (2003) reported higher discomfort for CTG procedure (p = 0.011) 1 month following therapy, while no difference between the two approaches was reported at the 1-year follow-up.

No statistically significant differences for complications were reported on comparing CAF+PRP *versus* CAF (Huang et al. 2005) using a Wound Healing Index $(1.3 \pm 0.5$ for CAF and 1.2 ± 0.4 for CAF+PRP).

Sensitivity analysis on CRC

Following methodological analysis, some studies showed a low risk of bias (Aichelmann-Reidy et al. 2001, Wang et al. 2001, McGuire & Nunn 2003, Del Pizzo et al. 2005, Spahr et al. 2005, Wilson et al. 2005, Hwang & Wang 2006, Cortellini et al. unpublished data). A sensitivity analysis to assess possible differences was performed considering only the primary outcome variable (CRC) comparing studies at a low risk *versus* at a high risk of bias. For sensitivity analysis, only 4 comparisons were possible:

- CAF+CTG versus CAF (Fig. 33)
- CAF+BM versus CAF+CTG (Fig. 34)
- CAF+EMD versus CAF (Fig. 35)
- CAF+ADM *versus* CAF+CTG (Fig. 36)

The results of sensitivity analysis showed no marked difference between studies at a low risk and at a high risk of bias in terms of CRC.

Discussion

In the era of evidence-based medicine, systematic reviews provide concise

Review Comparison Outcome:	Recession and CAF 09 CAF+BM vs CAF+CTG 03 KTGain							
Slady orsalo-callegory	CAF+BM N	CAF+CTG N	lican difference (S	E)	lican difference () 95% Cl	andom)	Weight %	lifean difference (andom) 95% Cl
Jepsen 1998	15	15	-0.9300 (0.4900)				14.64	-0.93 [-1.89, 0.03]
Trombelli 1998	12	12	-1.0000 (0.3400)				16.95	-1.00 [-1.67, -0.33]
Zucchelli 1998	36	19	-2.4500 (0.1700)	-	⊢		18.00	-2.45 [-2.78, -2.12]
Bargheiti 1999	14	14	-1.6100 (0.2900)				16.98	-1.61 [-2.18, -1.04]
Tatatis 2000	12	12	-0.6000 (0.3300)				16.96	-0.60 [-1.25, 0.05]
Wang 2001	16	16	-0.4000 (0.2500)				17.37	-0.40 [-0.89, 0.09]
Tatal (95% CI)	105	87					100.00	-1.19 [-1.96, -0.39]
Test for helerog Test for overall	cacity: Chi² = 61.66, df = 5 (F effect: Z = 2.91 (P = 0.004)	P < 0.00001), P	= 91.9%					
				-4	-2 0	2	4	
				Favours	CAF+CTG Fan	OURS CAF+		

Fig. 31. Comparison CAF+BM versus CAF+CTG for KT gain. CAF, coronally advanced flap; KT, keratinized tissue; BM, barrier membranes; CTG, connective tissue graft.

Review: Comparison: Outcome:	teview: Recession and CA Comparison: 07 CAF+ADM vs (Sulcome: 03 KTGain							
Sludy or sub-calegory	,	CAF+ADM N	CAF+C1KG N	Mean ofference (SE	Mean dilfere 2) 99	ance (random) KiCl	Weight %	Mean difference (random) 95% Cl
AichelmannRe	sidy 2001	22	22	-0.4000 (0.5200)		L	20.71	-0.40 [-1.42, 0.62]
Paolantonio 2	002	15	15	-1_4000 (0.3000)			33.53	-1.40 [-1.99, -0.81]
Tal 2002		7	7	-1.2900 (0.4700)			23.14	-1.29 [-2.21, -0.37]
Jaly 2007		10	10	-0.2000 (0.4800)		<u> </u>	22.63	-0.20 (-1.14, 0.74)
Total (95% CI)		54	54		•		100.00	-0.90 [-1.51, -0.28]
Test for helero	geneily: Chi ² =	6.27. df = 3 (P =	0.10). F = 52.	7%				
Test for overal	effect Z = 2	87 (IP = 0.004)						
					-4 -2	0 2	4	
					Favours CAF+CTG	Favours GAF+	ADM	

Fig. 32. Comparison CAF+ADM versus CAF+CTG for KT gain. CAF, coronally advanced flap; CTG, connective tissue graft; KT, keratinized tissue; ADM, acellular dermal matrix.

Review: Comparison: Outcome:	Recession and C 01 CAF+CTG vs 04 CRC Sensitiv	AF CAF ily					
Study or sub-category	, (CAF+CTG N	CAF N	log[Odds Ratio] (SE)	Odds Ratio (rando 95% Cl	m) Weight %	Odds Ratio (random) 95% Cl
01 Low Risk of	Bias						
Cottellini		41	42	0.9316 (0.4511)		86.65	2.54 [1.05, 6.15]
Subtotal (95% C	CI)	41	42			86.65	2.54 [1.05, 6.15]
Test for heteros Test for overal	geneity: not applic l effect: Z = 2.07 (able P = 0.04)					
02 High Risk of	f Blas						
Da Silva 2004		11	11	0.7915 (1.1493)		13.35	2.21 [0.23, 20.99]
Subtotal (95% C	CI)	11	11			13.35	2.21 [0.23, 20.99]
Test for heteroy Test for overal	geneity: not applic leffect: Z = 0.69 (able P = 0.49)					
Total (95% CI)		52	53			100.00	2-49 [1.09, 5-68]
Test for hetero Test for overal	geneity: Chi² = 0.0 leffect: Z = 2.17 (1, df = 1 (P = P = 0.03)	0.91), I² = 0%				
				(1 0.2 0.5 1 2 FavoursCAF Favou	5 10 rs CAF+CTG	

Fig. 33. Sensitivity analysis comparing CAF+CTG versus CAF considering CRC. CAF, coronally advanced flap; CTG, connective tissue graft.

information from the available literature using a clearly formulated question (Needleman 2002). The focused question of this systematic review evaluating only RCTs in Miller Class I and II gingival recessions was: "What is the clinical benefit of adding to the CAF procedure, CTG or BM or EMD or ADM or PRP or living tissue-engineered HF-DDS in the treatment of Miller Class I and II localized gingival recessions?" Therefore, CAF was selected as a reference treatment and then possible combinations (CAF+ CTG; CAF+EMD; CAF+BM, etc) were compared with it, although no multiple combinations were evaluated, due to difficulties in detecting the

itudy r sub-category	CAF+EMI N	CAF+CTG N	log[Odds Ratio] (SE)	Odds Ratio (random) 95% Cl	Weight %	Odds Ratio (random) 95% Cl
Low Risk of Bias						
Wang 2001	16	16	0.0000 (0.8165)	_	17.80	1.00 [0.20, 1.95]
ubtotal (95% CI)	16	16			17.60	1.00 [0.20, 4.95]
est for heterogeneity: not ap	plicable			_T_		
est for overall effect: Z = 0.	00 (P = 1.00)					
? High Risk of Bias						
Jepsen 1998	15	15	0.0000 (0.6165)	_	17.60	1.00 [0.20, 4.95]
Frombelli 1998	12	12	-2.5802 (1.0753)	→ 1	11.95	0.08 [0.01, 0.62]
Zucchelli 1998	36	16	-1.3863 (0.6124)	←− −−	25.13	0.25 [0.08, 0.83]
Borghetti 1999	14	14	0.0000 (0.7303)		20.54	1.00 [0.24, 4.18]
Tatakis 2000	12	12	-1.9459 (1.5119)	↔ → →	6.79	0.14 [0.01, 2.77]
ubtotal (95% CI)	89	71			82.20	0.38 [0.15, 0.96]
est for heterogeneity: Chi* = est for overall effect: Z = 2.	: 6.28, df = 4 (P 00 (P = 0.05)	P = 0. 18), I² = 36 .3	3%			
otal (95% CI)	105	67			100.00	0.45 [0.20, 1.04]
est for hetemoeneity: Chi ² =	7.34 df = 5 fP	= 0.20) P = 31	976			
et for averal effect: 7 = 1	87 (P = 0.06)					

Fig. 34. Sensitivity analysis comparing CAF+BM *versus* CAF+CTG considering CRC. CAF, coronally advanced flap; CTG, connective tissue graft; CRC, complete root coverage; BM, barrier membranes.

Recession and CAF 03 CAF+EMD v s CAF 04 CRC Sensitivity	:									
CAF+I N	EMD CAF N	log[O	ids Ratio] (SE)		Odds I	Ratio (ran 95% CI	dom)	Weight %	Odds R 9	atio (random) 5% Cl
lias										
1	15 15	1.6094	(1.5492)			_	•	6.15	5.00 [0.24,	104.14]
1	30 30	1.3231	(0.4950)			I –	-	- 53.41	3.76 [1.42,	9.91]
9	45 45					- I -		61.56	3.86 [1.53,	9.72]
eneity: Chi ² = 0.03, df	= 1 (P = 0.86), P	= 0%								
effect: Z = 2.86 (P = 0	.004)									
Bias										
1	10 10	0.0000	(1.0000)	_		+		16.13	1.00 [0.14,	7.10]
1	15 15	2.5649	(0.9364)					20.32	13.00 [2.07,	61.47]
a	25 25							36.44	3.69 [0.30,	45.58]
eneitv: Chi≇ = 3.51. df	= 1 (P = 0.06), P	= 71.5%								-
effect: Z = 1.02 (P = 0	.31)									
	70 70						-	- 100.00	3.89 [1.59,	9.50]
eneity: Chi² = 3.54. df	= 3 (P = 0.32) P	= 15.2%								-
ffect: Z = 2.99 (P = 0	.003)									
				01 0	2 05	1	2 5	10		
				V.I U.		Е Е		D		
	Recession and CAF 03 CAF+EMD v s CAF 04 CRC Sensitivity CAF+ N Bias () eneity: Chi ² = 0.03, df effect: Z = 2.86 (P = 0 Bias () eneity: Chi ² = 3.51, df effect: Z = 1.02 (P = 0 eneity: Chi ² = 3.54, df effect: Z = 2.99 (P = 0	$\begin{tabular}{lllllllllllllllllllllllllllllllllll$	Recession and CAF 03 CAF+EMD vs CAF CAF+EMD CAF N log[Cn Bias 15 15 1.6094 30 30 30 1.3231 i) 45 45 eneity: Ch ² = 0.03, df = 1 (P = 0.86), P = 0% eneity: Ch ² = 3.66 (P = 0.004) Bias 10 10 0.0000 15 15 2.5649 25 reneity: Ch ² = 3.51, df = 1 (P = 0.06), P = 71.5% affect: Z = 1.02 (P = 0.31) reneity: Ch ² = 3.54, df = 3 (P = 0.32), P = 15.2% affect: Z = 2.99 (P = 0.003)	Recession and CAF 03 CAF+EMD vs CAF CAF+EMD CAF N log[Odds Ratio] (SE) Bias 15 15 1.6094 (1.5492) a0 30 30 1.3231 (0.4950) b) 45 45 eneity: Ch ² = 0.03, df = 1 (P = 0.86), P = 0% eneity: Ch ² = 3.66 (P = 0.004) Bias 10 10 0.0000 (1.0000) 15 15 2.5649 (0.9364) 25 Provide the state of the stateo	Recession and CAF 03 CAF+EMD vs CAF OAF+EMD CAF N log(Odds Ratio) (SE) Bias 15 1.6094 (1.5492) a0 30 1.3231 (0.4950) b) 45 45 enoity: Ch ² = 0.03, df = 1 (P = 0.86), P = 0% enoity: Ch ² = 3.54, of = 1 (P = 0.06), P = 0% Bias 10 10 0.0000 (1.0000) 15 i) 25 25 25 enoity: Ch ² = 3.51, of = 1 (P = 0.06), P = 71.5% of 70 of 70 of 70 enoity: Ch ² = 3.54, of = 3 (P = 0.32), P = 15.2% of 70 of 70 enoity: Ch ² = 3.54, of = 3 (P = 0.03) 0.1 0.1	Recession and CAF 03 CAF+EMD vs CAF Odds F Odds F <td>Recession and CAF 03 CAF +EMD vs CAF Odds Ratio (ran N log(Odds Ratio) (SE) 95% C1 Sias 15 15 1.6094 (1.5192) 30 30 1.3231 (0.4950) 30 30 1.3231 (0.4950) 30 30 1.3231 (0.4950) 30 30 1.3231 (0.4950) 30 30 1.3231 (0.4950) anointy: Ch² = 0.03, df = 1 (P = 0.86), P = 0% Bias 10 0.0000 (1.0000) 15 15 2.5649 (0.9364) (1) 25 25 area 70 70 70 area 70 70 area 91 15.2% area 91 92 92 1 0.1 0.2 0.5 1</td> <td>Recession and CAF 03 CAF+EMD vs CAF Odds Ratio (random) N N log(Odds Ratio) (SE) 95% C1 Sias 15 15 1.6094 (1.5492) 95% C1 Sias 10 1.3231 (0.4950) 95% C1 Sias 10 10 0.4950) 15 15 2.5649 (0.9364) Bias 10 10 0.0000 (1.0000) 15 15 2.5649 (0.9364) Of 70 emeity: Ch² = 3.51, df = 1 (P = 0.06), I⁴ = 71.5% affect: Z = 1.02 (P = 0.31) 70 0.1 0.2 5 Of 70 emeity: Ch² = 3.54, df = 3 (P = 0.32), I⁴ = 15.2% of 70 Of 70</td> <td>Recession and CAF 03 CAF+EMD vs CAF 04 CRC Sensitivity CAF+EMD vs CAF 04 CRC Sensitivity CAF N log(Odds Ratio (SE) Odds Ratio (random) 95% C1 Weight % Size 15 15 1.6094 (1.5492) 30 95% C1 % Size 0 1.3231 (0.4950) 6.15 53.41 (1) 45 45 45 eneity: Ch² = 0.03, df = 1 (P = 0.86), P = 0% 61.56 61.56 Bias 10 10 0.0000 (1.0000) 16.13 (1) 25 25 25 38.44 eneity: Ch² = 3.51, df = 1 (P = 0.06), P = 71.5% 4fect: Z = 1.02 (P = 0.31) 100.00 100.00 eneity: Ch² = 3.54, df = 3 (P = 0.32), P = 15.2% 0.1 0.2 0.5 1 2 5 10 Energy: Ch² = 3.54, df = 3 (P = 0.32), P = 15.2% 0.1 0.2 0.5 1 2 5 10 Energy: Ch² = 3.54, df = 3 (P = 0.32), P = 15.2% 0.1 0.2 0.5 1 2 5 10 Energy: Ch² = 3.54, df = 3 (P = 0.32), P = 15.2% 0.1 0.5 1 2 5 10 <td>Recession and CAF 03 CAF+EMD vs CAF 04 CRC Sensitivity CAF+EMD vs CAF 04 CRC Sensitivity CAF log[Odds Ratio] (SE) Odds Ratio (random) 95% C1 Weight % Odds Ratio 3ias 15 15 1.6094 (1.5492) 53.41 3.76 [1.42, 30 30 1.3231 (0.4950) (1) 45 45 45 61.56 3.86 [1.53, 61.56 3.86 [1.53, 61.56 3.86 [1.53, 61.56 3.86 [1.53, 61.56 3.86 [1.53, 61.56 3.86 [1.53, 61.56 3.86 [1.53, 38.44 3.69 [0.30, 20.32 31.00 [2.07, 38.44 3.69 [0.30, 61 10.000 3.89 [1.59, 61 10.000 10.000 3.89 [1.59, 61 10.000 10.000 10.000 10.5 10.000 10.5 10.000 10.5 10.000 10.5 10.000 10.5 10.5 10.5 10.5 10.5</td></td>	Recession and CAF 03 CAF +EMD vs CAF Odds Ratio (ran N log(Odds Ratio) (SE) 95% C1 Sias 15 15 1.6094 (1.5192) 30 30 1.3231 (0.4950) 30 30 1.3231 (0.4950) 30 30 1.3231 (0.4950) 30 30 1.3231 (0.4950) 30 30 1.3231 (0.4950) anointy: Ch ² = 0.03, df = 1 (P = 0.86), P = 0% Bias 10 0.0000 (1.0000) 15 15 2.5649 (0.9364) (1) 25 25 area 70 70 70 area 70 70 area 91 15.2% area 91 92 92 1 0.1 0.2 0.5 1	Recession and CAF 03 CAF+EMD vs CAF Odds 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Fig. 35. Sensitivity analysis comparing CAF+EMD versus CAF considering CRC. CAF, coronally advanced flap; CRC, complete root coverage; EMD, enamel matrix derivative.

weight of a single therapy in the overall clinical outcome. *CRC* was considered to be the treatment goal and, consequently, the primary outcome variable.

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This systematic review confirms that the CAF procedure is a safe and reliable approach in periodontal plastic surgery and is associated with consistent recession reduction and frequently with CRC. The results of meta-analyses showed that only two combinations (CAF+CTG and CAF+EMD) provided better results than CAF alone. CAF+CTG resulted in better clinical outcomes for both *CRC* (OR = 2.49) and *RecRed* (+0.49 mm) compared with CAF, and no other therapy provided better results than CAF+CTG. Possible biological reasons to explain the clinical outcomes of CAF +CTG may be related to (i) the ability of the bilaminar blood supply from both the periosteal surface and the overlaying flap in promoting survival of CTG on the root surface (Langer & Langer 1985) and (ii) the capacity of CTG to reduce the apical relapse of the coronally positioned gingival margin during the healing phase of the CAF procedure (Pini Prato et al. 2005).

The combination of CAF+EMD was associated with a higher probability to obtain *CRC* (OR = 3.89) and a higher amount of *RecRed* (0.58 mm) than CAF.

A single study on a sample of 17 patients with 2 bilateral recessions compared CAF +EMD versus CAF+CTG (McGuire & Nunn 2003). This study was at a low risk of bias and reported no significant difference in terms of *CRC* between the two approaches. Unfortunately, no meta-analysis was possible for *RecRed* due to the data presentation, although the authors (McGuire & Nunn 2003) reported no difference in terms of the mean amount of root coverage. Further RCTs with a high power comparing CAF+EMD versus CAF+CTG are needed.

A possible benefit following root coverage procedures may be the aug-

Recession and CAF 07 CAF+ADMvs CAF+CTG

Review

Comparison

Study	CAF+ADM	CAF+CTG		Odds Ratio (random)	Weight	Odds Ratio (random)
or sub-category	N	N	log[Odds Ratio] (SE)	95% CI	*	95% CI
)1 Low Risk of Bias						
AichelmannReidy 2001	22	22	-0.7621 (0.5463)	_	48.26	0.47 [0.16, 1.36]
Subtotal (95% CI)	22	22			48.26	0.47 [0.16, 1.36]
lest for heterogeneity: not a	applicable					
lest for overall effect: $Z = \frac{1}{2}$	1.40 (P = 0.16)					
2 High Risk of Elias						
Paolantonio 2002	15	15	-0.8781 (0.7802)	←	23.66	0.42 [0.09, 1.92]
Tai 2002	7	7	0.0000 (0.8165)		21.60	1.00 [0.20, 1.95]
Joly 2007	10	10	-2.1972 (1.4907)	←	6.48	0.11 [0.01, 2.06]
subtotal (95% CI)	32	32			51.74	0.51 [0.16, 1.43]
est for heterogeneity: Chi* est for overall effect: Z =	= 1.79, df = 2 (P 1.28 (P = 0.20)	= 0.41), I* = 0%				
Total (95% CI)	54	54			100-00	0.49 [0.23, 1.03]
fest for heterogeneity: Chi ²	= 1.81, df = 3 (P	= 0.61), I ² = 0%				
lest for overall effect: Z =	1.89 (P = 0.06)					
				\rightarrow \rightarrow \rightarrow \rightarrow \rightarrow \rightarrow \rightarrow \rightarrow \rightarrow		
				0.1 0.2 0.5 1 2 5	10	
				Favours CAF+CTG Favours CAF+	ADM	

Fig. 36. Sensitivity analysis comparing CAF+ADM *versus* CAF+CTG considering CRC. CAF, coronally advanced flap; CTG, connective tissue graft; CRC, complete root coverage; ADM, acellular dermal matrix.

mentation of KT. This systematic review showed that CAF+CTG was associated with better clinical outcomes in terms of *KT gain* following therapy.

The decision on whether to select CTG or EMD in conjunction with CAF may be only partially explained by the systematic review. Further studies with higher power for assessing possible interactions between prognostic factors (baseline recession, baseline KT, etc.) and the surgical techniques are needed. However, the ability of the CAF+CTG procedure to increase KT may suggest this approach when KT augmentation with recession reduction is the treatment goal. In fact, this systematic review showed that CAF+CTG was associated with better clinical outcomes in terms of KT gain. On the contrary, CAF+EMD appears to be an easier procedure than CAF+CTG and does not require a donor area for CTG harvest, which generally implies greater post-operative discomfort in the first month following therapy (McGuire & Nunn 2003). On the other hand, the cost/benefit ratio of CAF+EMD should be carefully evaluated.

ADM was introduced in mucogingival surgery as an alternative to CTG in order to reduce the patient discomfort (Harris 1998). Meta-analyses showed that no statistically significant difference between CAF+ADM *versus* CAF in terms of *CRC*, *RecRed* and *KT gain* was detected, suggesting that no additional benefit over CAF alone may be provided by ADM. Similarly, the comparison between CAF +ADM *versus* CAF+CTG showed no statistically sig-

nificant differences for CRC (p = 0.06, OR = 0.49) and *RecRed* (p = 0.24, mean difference = -0.40 mm), even if a tendency favouring CTG was observed for both variables. Moreover, statistically significant differences for KT gain favouring CTG (p = 0.004, mean difference = -0.90 mm) were detected. Meta-analyses of the selected studies (Côrtes et al. 2004, Woodyard et al. 2004) showed a large heterogeneity in RecRed for both comparisons (CAF+ ADM versus CAF and CAF+CTG versus CAF), thus indicating the possible influences of patient's related factors, operator skill and recession severity on the clinical outcomes. On the other hand, CAF+ADM resulted in better overall aesthetic outcomes for both blinded clinicians and patients compared with CAF+CTG, even if it showed less CRC than CAF+CTG (Aichelmann-Reidy et al. 2001). This finding may be related to different colour matches with adjacent tissues for ADM and CTG or poorer healing for CTG where size exceeds the bone dehiscence (Zucchelli et al. 2003).

This systematic review showed that the use of BM in conjunction with CAF (CAF+BM) did not improve the result of CAF in terms of *CRC* and *RecRed*. When comparing CAF +BM *versus* CAF+CTG, statistically significant differences favouring CAF+CTG were detected for both *RecRed* (p = 0.008, mean difference = -0.38 mm) and *KT* gain (p = 0.004, mean difference = -1.18 mm). Therefore, the use of BM for the root coverage procedure appears to be unadvisable, especially considering the high incidence of complications (i.e. membrane exposure) related to the use of BM for root coverage (Jepsen et al. 1998, Trombelli et al. 1998, Tatakis & Trombelli 2000).

Only one RCT (Huang et al. 2005) comparing CAF+PRP versus CAF was identified, with no statistically significant differences reported in terms of CRC, RecRed and KT gain. Similarly, only one RCT (Wilson et al. 2005) analysed the addition of HF-DDS in conjunction with CAF compared with CAF+CTG, reporting no difference for CRC, RecRed and KT gain. Even if further studies are needed to better understand the potential benefits of these innovative approaches, current evidence does not support the introduction of PRP or HF-DDS under CAF as a routine root coverage procedure due to both cost/benefit ratio and practicality.

Aesthetics and root sensitivity are the sole indications for the root coverage procedure (American Academy of Periodontology 1996) but are generally poorly investigated. Nonetheless, it is reasonable to hypothesize that complete root coverage is associated with a higher reduction of root sensitivity than partial root coverage, thus supporting CRC as the treatment goal. In addition, CRC may be associated with greater patient satisfaction, especially when the root surface shows a colour contrast with the enamel surface was completely covered, but it does not completely assess overall aesthetic satisfaction. In fact, in an RCT comparing two CAF+CTG techniques, a CTG with size exceeding the distance between the most apical

extension of buccal bone crest and cemento-enamel junction (bone dehiscence) was associated with poorer aesthetic outcomes compared with CRC in sites where the CTG was equal to the bone dehiscence (Zucchelli et al. 2003). The authors suggested that possible reasons may be related to difficulties in vascular exchanges between the covering flap and CTG with excessive size/ thickness, favouring statistically significant flap dehiscence and graft exposure with poorer aesthetic outcomes (Zucchelli et al. 2003). Therefore, the achievement of CRC associated with poor colour match, inadequate integration with adjacent tissues or a flat gingival contour may affect the aesthetic perception of treatment (Aichelmann-Reidy et al. 2001, Zucchelli et al. 2003). Moreover, the possible association between KT gain and aesthetic satisfaction has to be tested. Future RCTs in the field of root coverage procedures must consider patient satisfaction as one of the treatment outcomes towards a better understanding of the potential benefit of the tested techniques.

Post-operative pain and complications following therapy were difficult to investigate in this systematic review due to data heterogeneity. CAF+BM was frequently associated with membrane exposure (Jepsen et al. 1998, Amarante et al. 2000, Tatakis & Trombelli 2000, Lins et al. 2003) even if others did not report exposure (Romagna-Genon 2001). CTG+CAF was frequently associated with swelling (Cortellini et al. unpublished data) and pain at the donor site (Romagna-Genon 2001), even if these side effects were not confirmed by others (Jepsen et al. 1998, Tatakis & Trombelli 2000). Possible reasons may be related to different approaches in the harvesting technique or suturing modalities in different studies. On the other hand, CAF+EMD seemed to have limited post-operative discomfort. No RCT included in this systematic review describes PD >3 mm following root coverage procedures.

The methodological assessment performed in this systematic review showed that most RCTs included were at a high risk of bias (17/25). On the other hand, sensitivity analysis, whenever possible, did not show a marked difference between studies at a low risk and at a high risk of bias in terms of *CRC*. Research protocols for future RCTs in the field of root coverage procedure minimizing the risk of bias (i.e. based on CONSORT guidelines) are advisable.

Few RCTs included in this systematic review evaluated clinical outcomes over a 1-year follow-up (Del Pizzo et al. 2005, Leknes et al. 2005, Spahr et al. 2005, Côrtes et al. 2006, Pilloni et al. 2006). Interestingly, a study by Leknes et al. (2005) reported 1- and 6-year follow-ups of the CAF procedure with and without resorbable BM. In the metaanalysis, only data of the 1-year followup were considered due to the high drop-out rate at the 6-year follow-up. Leknes et al. (2005) reported a significant reduction in the number of sites with CRC and a decrease in mean RecRed for both treatments at the 6-year follow-up compared with the 1-year and 6-month follow-ups (Amarante et al. 2000). These detrimental effects were thought to be associated with traumatic tooth brushing: in fact, new gingival recessions in non-treated sites were identified at the last followup. These observations suggest that careful maintenance may be the key for long-term stability of the gingival margin.

Conclusions

- 1. CAF is a safe and predictable approach for root coverage.
- 2. CTG or EMD in conjunction with CAF procedure enhances the probability to obtain *CRC* and to improve recession reduction in Miller Class I and II single gingival recession.
- 3. BM do not improve the clinical benefits of CAF alone.
- 4. Contradictory results were associated with use of ADM in conjunction with CAF.

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Clinical Relevance

Scientific rationale for the study: To investigate the potential benefit of adding tissue grafts, BM, EMD or other material under CAF.

Coronally advanced flap procedure for root coverage. Flap with tension *versus* flap without tension: a randomized controlled clinical study. *Journal of Periodontology* **71**, 188–201.

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Principal findings: The additional use of CTG and EMD enhanced the clinical outcomes of CAF, while BM did not. Controversial results were found with the adjunctive use of ADM.

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Practical implications: CTG or EMD should be considered in conjunction with CAF to improve the probability of obtaining CRC.

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