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Is coronally positioned flap procedure adjunct with enamel matrix derivative or root conditioning a relevant predictor for achieving root coverage? A systemic review

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Background and Objective: This study is a systemic review of coronally positioned flap, coronally positioned flap + chemical root surface conditioning, or coronally positioned flap + enamel matrix derivative (EMD) for the treatment of Miller class I and II gingival recession.

Material and Methods: All studies available through the Medline database by the end of October 2005 were used. Each study provided mean clinical attachment level, keratinized tissue, probing pocket depth, gingival recession depth and root coverage percentage before and after treatment with coronally positioned flap alone, coronally positioned flap + chemical root surface conditioning, or coronally positioned flap + EMD. Effectiveness was evaluated by comparing the weighted mean average in gingival recession depth, probing pocket depth, clinical attachment level, keratinized tissue and root coverage percentage achieved with the three treatments.

Results: Seven studies for the coronally positioned flap + EMD group, four studies for the coronally positioned flap + chemical root surface conditioning group, and seven studies for the coronally positioned flap group were retrieved for this weighted mean analysis. The results of clinical attachment level, gingival recession depth, and root coverage percentage in the coronally positioned flap + EMD group were statistically significantly better than the changes in the coronally positioned flap and coronally positioned flap + chemical root surface conditioning group at 6 and 12 mo ($p < 0.001$). There was no significant difference at the 6-mo comparison among clinical attachment level, keratinized tissue, probing pocket depth, and gingival recession depth, except in the root coverage percentage for coronally positioned flap and coronally positioned flap + chemical root surface conditioning groups.

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Conclusion: The results suggest that root coverage by the coronally positioned flap and coronally positioned flap + chemical root surface conditioning procedures were unpredictable but became more predictable when the coronally positioned flap procedure was improved by the modification of adding EMD.

Gingival recession is defined as the location of marginal periodontal tissues apical to the cemento–enamel junction (1). An ideal periodontal plastic surgery procedure for root coverage should re-establish esthetics and function, and provide a sulcus exhibiting no bleeding on probing and a depth of ≤ 2 mm (2). The coronally positioned flap has also been shown to be effective in covering recession-type defects (3,4). However, as gingival fibroblasts tend to repopulate the root surface faster than periodontal ligament cells, healing will generally not lead to the formation of a functional periodontal ligament but instead to new attachment. In fact, there is some risk of root resorption in roots directly exposed to gingival fibroblasts during healing (5). Enamel matrix derivative (EMD; Emdogain®; Biora AB, Malmö, Sweden), harvested from embryonic porcine teeth, has been extensively studied in animals and humans, and has provided evidence of tissue regeneration (6–9). Numerous studies have reported that EMD promotes the formation of the acellular cementum that attaches to the dentin and alveolar bone (6,7,10,11). Three human biopsy reports revealed that true periodontal regeneration could be achieved with the topical application of EMD (12–14).

Recently, clinical studies have shown that it is possible to apply EMD adjunct to coronally positioned flap procedures (15–17) to achieve root coverage, as well as periodontal regeneration on a previously exposed root surface. Cueva *et al.* recently reported significant increases in the root coverage percentage and keratinized tissue 6 mo after surgery, in marginal tissue recessions (Miller classes I, II, and III) treated with coronally positioned flap + EMD compared with coronally positioned flap without EMD (18). However, Modica *et al.* observed that root coverage and the clinical attachment level were slightly (but not significantly) improved when using coronally positioned flap + EMD compared with coronally positioned flap alone in the treatment of gingival recession (19). There are conflicting results regarding the clinical benefit of the combined procedure. Based on this evidence, it seems that using EMD in combination with coronally positioned flap or coronally positioned flap alone for treating Miller class I and II recession defects is still controversial.

Chemical root surface conditioning has been introduced, using a variety of agents, in order to detoxify, decontaminate and demineralize the root surface, thereby removing the smear layer and exposing the collagenous matrix of dentin and cementum (20–23). Various acids have been used for chemical root surface conditioning, including citric and phosphoric acids (24), ethylenediaminetetraacetic acid (EDTA) (25) and tetracycline hydrochloride (26). These procedures in an animal model are believed to be able to induce cementogenesis and enhance attachment either by connective tissue ingrowth and/or demineralization (27,28). However in human studies, no clinical advantages were observed (29,30). The clinical relevance of root conditioning with an acid agent in routine periodontal surgery is still questionable.

There being no explicit critical appraisal has created controversy and confusion about the positive or negative uses of these agents. Therefore, the aim of the present systematic review was to assess the efficacy of EMD and root conditioning on the root coverage with coronally positioned flap, in terms of changes in clinical attachment level, keratinized tissue, probing pocket depth, gingival recession depth, and root coverage percentage.

This systematic review follows a well-defined protocol whereby a clearly formulated question is addressed using systematic and specific methods to identify, select, critically appraise and summarize relevant research. It may provide clinicians with an expanded and unbiased appraisal of human experimental studies. The purpose of this report was to present the results of the searched papers, and to evaluate the methods and quality of the systematic reviews, in order to facilitate clinical decision-making in the choice of coronally positioned flap alone, coronally positioned flap + chemical root surface conditioning, or coronally positioned flap + EMD for the treatment of gingival recession.

Material and methods

Strategy for data collection

Studies in the medical literature, available through the Medline database by the end of October 2005, were screened for this meta-analysis. We used the following interventions: coronally positioned flap, coronally positioned flap + chemical root surface conditioning, or coronally positioned flap + EMD, for the treatment of Miller class I and II gingival recession (Fig. 1). Only full-length original journal articles were considered; abstracts or unpublished studies were not included. Hand searching of journals for missed trials was not carried out. The search was restricted to studies published in English language journals and those conducted on human subjects. The contents of full-text articles identified during the literature search were reviewed to determine whether they met the inclusion criteria.

Criteria for including studies

The following inclusion criteria were set after detailed discussion between two reviewers:

- human trials;

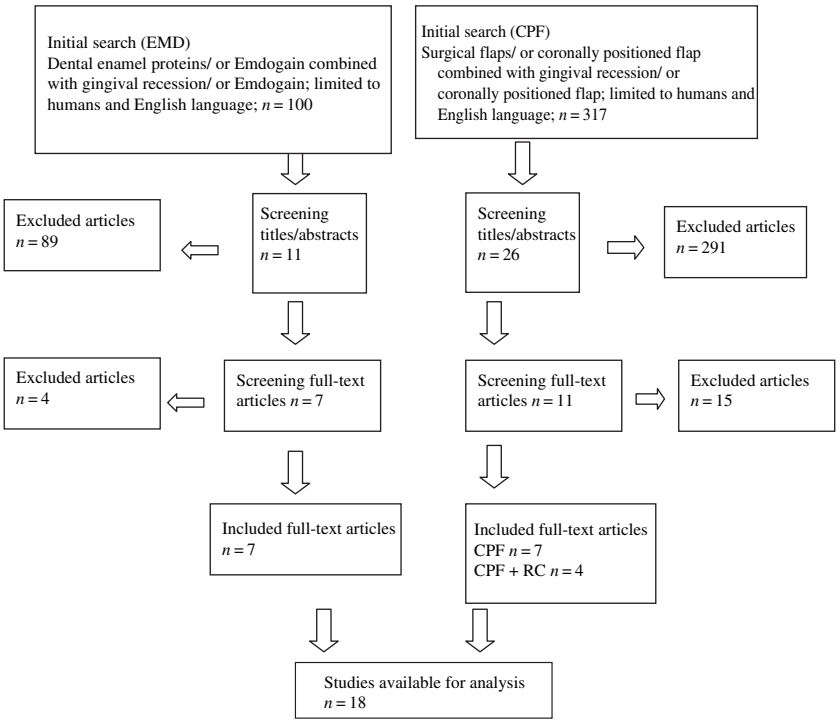

Fig. 1. The flow for selecting the articles. CPF, coronally positioned flap; EMD, enamel matrix derivative; RC, chemical root surface conditioning.

- patients with a clinical diagnosis of gingival recession of > 2 mm (class I and II according to the Miller classification);
- treatment with coronally positioned flap, coronally positioned flap + chemical root surface conditioning, or coronally positioned flap + EMD;
- a randomized controlled trial, controlled clinical trial, or care series report with at least a 6- to 12-mo interval between the initial and final measurements; and
- baseline and final measurements of buccal recession depth.

Criteria for excluding studies

Exclusion criteria for these procedures included:

- lack of any of the outcome variables at the baseline or on the final visit;
- animal studies;
- abstracts;
- histological studies;
- studies with insufficient data;
- laterally moved, coronally advanced flap; and
- root coverage with the design of a semilunar coronally positioned flap.

Quality assessment

Two independent reviewers screened titles and abstracts to identify eligible studies and reviewed a full text of studies to assess their suitability for inclusion in a systematic review database. Any disagreement in the choice of studies of possible relevance was resolved by discussion among the reviewers. Three aspects were analyzed:

- the adequacy of the method of randomization;
- the existence of blinding of the examiners for the variable type of treatment; and
- the existence and treatment of lost cases.

After a preliminary evaluation of the selected articles, considerable heterogeneity was found in the study methodologies, characteristics of the included patients, types of treatments provided, outcome variables registered and results. Nevertheless, it was still possible to make a quantitative synthesis of the data and the consequent weighted mean analysis following the predetermined flow chart (Fig. 1).

Data extraction and outcome measures

For each trial, the following data were recorded: year of publication, details on the type of defects, the number of subjects, the chemical root surface modifier, details of the outcomes report and time intervals. A data extraction sheet was used to collect information that was then entered into a database. Primary outcome measures included changes in clinical attachment levels, keratinized tissue, probing pocket depths, gingival recession depths and root coverage percentage. Mean values were used for continuous data for primary variables.

Data analyses

Data from studies were combined in order to evaluate the treatment effect of coronally positioned flap, coronally positioned flap + chemical root surface conditioning, or coronally positioned flap + EMD for root coverage. Each study provided the mean clinical attachment level, keratinized tissue, probing pocket depth, gingival recession depth, and root coverage percentage before and after treatment with coronally positioned flap, coronally positioned flap + chemical root surface conditioning, or coronally positioned flap + EMD. Effectiveness was evaluated by comparing the average changes in clinical attachment level, keratinized tissue, probing pocket depth, gingival recession depth and root coverage percentage with these three treatments. Analysis was performed by using a random-effects model, and the results are expressed as weighted mean difference with 95% confidence interval. A weighted mean difference method (Weighted mean = Σ[(Mean1.n1/n1 + n2 + … + nf) + (Mean2.n2/n1 + n2 + ... + nf) + … + (Meanf.nf/n1 + n2 + ... + nf)]) was used to pool continuous data of the relevant outcomes. In studies where the standard deviation of the studied outcome data was not pooled, statistical analysis was carried out with SPSS software (version 12.0; SPSS, Chicago, IL, USA) to fit the models. The results of the systemic review were analyzed as weighted mean differences and stand-

ard deviations. The effect size was estimated using the reported *p*-values. A *p*-value of < 0.001 was considered statistically significant.

Results

Study characteristics

According to the flow chart shown in Fig. 1, our search provided 100 potentially relevant publications for coronally positioned flap + EMD and 317 for coronally positioned flap alone. Of these, 89 for coronally positioned flap + EMD and 291 for coronally positioned flap alone were clearly not relevant to the review because they addressed completely different research questions, involved animal research only, or they were review articles after screening titles and abstracts. Eleven studies for coronally positioned flap + EMD and 26 studies for coronally positioned flap were retrieved for detailed evaluation. After review of the full text of the coronally positioned flap + EMD articles, two studies did not meet the inclusion criteria (18,31), leaving seven trials that were appropriate for the meta-analysis (Table 1) (15-17, 19, 32–34). In 26 trials for coronally positioned flap, 11 publications were available for data abstraction. Of these, three studies used tetracycline for root conditioning and one study used EDTA for root conditioning (Table 2) (19, 33, 35–43). Fifteen articles were excluded following the exclusion criteria set up for coronally positioned flap and coronally positioned flap + etching groups (18,44–57).

Clinical attachment level

At 6 mo, the mean gains in clinical attachment level were 2.42 ± 0.70 mm (chi-square for heterogeneity: 88.925 ± 6, $p < 0.05$) in the coronally positioned flap group, 2.22 ± 0.36 mm (chi-square for heterogeneity: 0.182 ± 2, $p = 0.913$) in the coronally positioned flap + chemical root surface conditioning group, and 4.01 ± 0.77 mm (chi-square for heterogeneity: 1.000 ± 2, $p = 0.607$) in the coronally positioned flap + EMD group (Table 3). At 12 mo, the mean gains in clinical attachment level were 1.69 ± 0.15 mm (chi-square for heterogeneity: 2.613 ± 1, $p = 0.106$) in the coronally positioned flap group, 3.10 ± 0.00 mm in the coronally positioned flap + chemical root surface conditioning group, and 3.61 ± 0.50 mm (chi-square for heterogeneity: 24.303 ± 3, $p < 0.05$) in the coronally positioned flap + EMD group (Table 4). At 6 mo, analysis of variance measures demonstrated a statistically significant difference ($p < 0.001$) between the coronally positioned flap + EMD group compared with the coronally positioned flap group and coronally positioned flap + chemical root surface conditioning group. The change in the coronally positioned flap + EMD group was statistically significantly better than those in the coronally positioned flap + chemical root surface conditioning and coronally positioned flap groups at 6 mo. The mean gain in clinical attachment level in the coronally positioned flap group was better than that in the coronally positioned flap + chemical root surface conditioning group, but did not differ statistically significantly at 6 mo ($p = 0.111$). At 12 mo, differences in the gain in clinical attachment level of root coverage were statistically significant ($p < 0.001$) among all groups. The change in the coronally positioned flap + EMD group was better than that in the coronally positioned flap + chemical root surface conditioning group, and the change in the coronally positioned flap + chemical root surface conditioning group was better than that in the coronally positioned flap group at 12 mo.

Keratinized tissue

At 6 mo, the mean gains in keratinized tissue were −0.04 ± 0.37 mm (chi-square for heterogeneity 87.898 ± 5, $p < 0.05$) in the coronally positioned flap group, 0.14 ± 0.47 mm (chi-square for heterogeneity 0.182 ± 2, $p = 0.913$) in the coronally positioned flap + chemical root surface conditioning group, and 0.59 ± 0.20 mm (chi-square for heterogeneity 11.164 ± 2, $p < 0.05$) in the coronally positioned flap + EMD group (Table 3). At 12 mo, the mean gains in keratinized tissue were 0.10 ± 0.41 mm (chi-square for heterogeneity: 2.613 ± 1, $p = 0.106$) in the coronally positioned flap group, 0.30 ± 0.00 mm in the coronally positioned flap + chemical root surface conditioning group, and 0.61 ± 0.14 mm (chi-square for heterogeneity: 53.647 ± 2, $p < 0.05$) in the coronally positioned flap + EMD group (Table 4). The change in the coronally positioned flap + EMD group was statistically significantly better than those in the coronally positioned flap and coronally positioned flap + chemical root surface conditioning groups at 6 mo ($p < 0.001$) and 12 mo ($p < 0.001$). The mean gain in keratinized tissue in the coronally positioned flap + chemical root surface conditioning group was better than that in the coronally positioned flap group, but they did not differ statistically significantly at 6 mo ($p = 0.018$) or 12 mo ($p = 0.005$).

Probing depth

At 6 mo, the probing pocket depth mean values were 1.04 ± 0.38 mm (chi-square for heterogeneity: 212.014 ± 4, $p < 0.05$) in the coronally positioned flap group, 1.09 ± 0.14 mm (chi-square for heterogeneity: 0.182 ± 2, $p = 0.913$) in the coronally positioned flap + chemical root surface conditioning group, and 1.16 ± 0.15 mm (chi-square for heterogeneity: 11.444 ± 3, $p < 0.05$) in the coronally-positioned flap + EMD group (Table 3). At 12 mo, the probing pocket depth mean values were 0.98 ± 0.02 mm (chi-square for heterogeneity: 2.613 ± 1, $p = 0.106$) in the coronally positioned flap group, 1.4 ± 0.00 mm in the coronally positioned flap + chemical root surface conditioning group, and 1.41 ± 0.33 mm (chi-square for heterogeneity: 24.739 ± 4, $p < 0.05$) in the coronally-positioned flap + EMD group (Table 4). The probing pocket depths of the three groups were all < 2 mm at 6 and 12 mo.

Gingival recession depth

The gingival recession depth in the coronally positioned flap + EMD

Table 1. Characteristics of the included studies for the coronally positioned flap plus enamel matrix derivative (CPF + EMD) group

Reference	Year	Study description	Defects	Subjects	Interventions	Cleaning of root surface	Duration	Outcomes
Abbas (32)	2003	Clinical trial	Miller class I recession of at least 4 mm in depth	Six patients with six sites	CPF + EMD	A polishing paste and rubber cup, 24% ethylenediaminetetraacetic acid (EDTA) gel, pH 6.7, for 2 min	12 mo	Mucogingival surgery in combination with the application of EMD resulted in predictable root coverage and gain of clinical attachment while maintaining shallow pockets
Berlucchi (15)	2002	Random assignment	Gingival recession depth > 2 mm Miller class I or II	14 patients with 26 sites	CPF + CTG + EMD; CPF + EMD	EDTA 24% for 2 min	6 mo	EMD for the treatment of Miller class I or II gingival recessions displayed good clinical results in combination with CPF or CPF + CTG
Berlucchi (16)	2005	Clinical trial	Gingival recession depth ≥ 2 mm; Miller class I or II	30 patients with 30 sites	CPF + EMD	Scaled and planed by ultrasonic instruments and Gracey curets; EDTA gel 24% for 2 min	12 mo	CPF + EMD gave excellent results when treating Miller class I or II recession, with 91.7% root coverage obtained at 12 mo and a mean attachment gain of 3.23 mm
Hägewald (33)	2002	A blinded, split-mouth, placebo-controlled, randomized design	≥ 3-mm buccal recession defects Miller class I or II	24 patients with 2 paired defects	CPF + vehicle solution CPF + EMD	Hand instruments and a rubber cup; conditioning with 24% EDTA gel (PrefgelA, BIORA) for 2 min	1 and 3 wk, and 3, 6, and 12 mo	There was no clear benefit of combining Emdogain with this surgical technique
McGuire (34)	2003	Randomized, controlled, single-center, split-mouth protocol	Miller class II in incisors or bicuspids	17 patients 34 sites	CPF + CTG CPF + EMD	Conditioning with 24% EDTA	12 mo	The addition of EMD to the coronally advanced flap resulted in root coverage similar to the CTG
Modica (19)	2000	Randomized, controlled, split-mouth protocol	Miller class I or II	12 patients 24 sites	CPF; CPF + EMD	Conditioning with 24% EDTA	12 mo	EMD did not seem to improve significantly the clinical outcomes of gingival recession treated by means of CPF
Nemcovsky (17)	2004	Randomized, controlled, split-mouth protocol	Miller class I or II in anterior or premolar teeth	70 patients 30 sites with EMD 40 sites with CTG	CGF; CPF + EMD	Conditioning with 24% EDTA	6 and 12 mo	The CTG procedure was superior to the coronally positioned flap with the addition of EMD in percentage of coverage and increase in width of keratinized tissue

Table 2. Characteristics of the 11 included studies for coronally positioned flap (CPF) and coronally positioned flap plus chemical root surface conditioning (CPF + RC) groups

Reference	Year	Study description	Defects	Subjects	Interventions	Cleaning of root surface	Duration	Outcomes
Amarante (35)	2000	A blinded, split-mouth, randomized design	≥ 3-mm buccal recession; Miller class I or II in cuspids or bicuspids	20 patients 40 sites	CPF; CPF + membrane	Polished with a rubber cup and an abrasive paste	3 and 6 mo	CPF offered a predictable, simple and convenient approach as a root coverage procedure in Miller class I and II recession defects Combining CPF with a bioabsorbable membrane did not seem to improve the results
Côrtes (36)	2004	A blinded, split-mouth, randomized design	Miller class I gingival recession (≥ 3.0 mm)	13 patients 26 sites	CPF; CPF + ADM	Curets and washed with a saline solution	6 mo	Both techniques provided significant root coverage in class I gingival recessions; however, a greater keratinized tissue thickness could be expected with ADM
Gurgan (37)	2004	Clinical trial	≥ 1-mm buccal recession defects; Miller class I	24 patients 24 sites	CPF	None	1, 6, 12, and 60 mo	After the CPF procedure, the MGJ was observed to move back to its original position in the 60-mo follow-up
Hägewald (33)	2002	A blinded, split-mouth, placebo-controlled, randomized design	≥ 3-mm buccal recession defects Miller class I or II	24 patients with two paired defects	CPF + vehicle solution; CPF + EMD	Hand instruments and a rubber cup; conditioning with 24% EDTA gel (PrefgelA, BIORA) for 2 min	1 and 3 wk, and 3, 6, and 12 mo	There was no clear benefit to combine EMD with this surgical technique
Leknes (38)	2005	Randomized, split-mouth protocol	Miller class I or II in cuspids or bicuspids	20 patients 40 sites	CPF; CPF + biodegradable membrane	Polished with a rubber cup and an abrasive paste	6 and 12 mo, and 6 years	The CPF procedure offered a simple and reliable treatment alternative as a root coverage procedure. Placement of a biodegradable membrane underneath the flap did not improve either the short- or long-term results
Lins (39)	2003	Randomized, split-mouth protocol	Miller class I or II in cuspids or bicuspids	10 patients 20 sites	CPF; CPF + tr-ePTFE	Scaled and planed; conditioned with 50 mg/ml tetracycline for 3 min	6 mo	The amount of root coverage obtained with CPF was greater than that observed with GTR

Table 2. Continued

Reference	Year	Study description	Defects	Subjects	Interventions	Cleaning of root surface	Duration	Outcomes
Modica (19)	2000	Randomized, controlled, split-mouth protocol	Miller class I or II	12 patients 24 sites	CPF; CPF + EMD	None	12 mo	EMD did not seem to improve significantly the clinical outcomes of gingival recession treated by means of CPF
Pini Prato (40)	2005	Clinical trial	≥ 2-mm buccal recession defects Miller class I	60 patients 60 sites	CPF	None	6 mo	The location of the gingival margin relative to the cemento–enamel junction following CPF procedure seemed to affect CRC
Silva (41)	2004	Randomized, controlled, split-mouth protocol	Miller class I in anterior or premolar teeth	11 patients 22 sites	CPF; CPF + SCTG	None	6 mo	Both surgical approaches were effective in addressing root coverage, but CPF + SCTG was better in increasing KT
Thromelli (42)	1996	Randomized, controlled, split-mouth protocol	Class I or II recession defects	11 patients 22 sites	CPF CPF + fibrin glue	Tetracycline in sterile water (100 mg/ml) for about 4 min	6 mo	There were no clinical or statistically significant differences between the treatments
Woodyard (43)	2004	Randomized, controlled, blinded, clinical investigation	Miller class I or II buccal recession defects of ≥ 3 mm treated	24 subjects; 12 for CPF and 12 for CPF + ADM	CPF; CPF + ADM	Tetracycline in sterile water (100 mg/ml) for about 4 min	6 mo	Treatment with a CPF plus an ADM allograft significantly increased gingival thickness when compared with a CPF allograft alone

ADM, acellular dermal matrix allograft; EMD, enamel matrix derivative; KT, keratinized tissue; MGJ, mucogingival junction; tr-ePTFE, titanium-reinforced expanded polytetrafluoroethylene; SCTG, subepithelial connective tissue graft.

Table 3. Mean (± SD) of clinical attachment level (CAL), keratin thickness (KT), probing pocket depth (PD) and gingival recession depth (GRD) for 6 mo of follow-up

		6-mo follow-up					
		Study *n*	Subjects	Baseline weighted mean ± SD (mm)	6 mo mean ± SD (mm)	Difference mean ± SD (mm)	
CAL	CPF	7	147	6.67 ± 3.69	4.25 ± 4.23	2.42 ± 0.70	*
	CPF + RC	3	33	4.63 ± 0.24	2.41 ± 0.12	2.22 ± 0.36	*
	CPF + EMD	3	42	5.26 ± 0.76	1.25 ± 0.03	4.01 ± 0.77	*
KT	CPF	7	147	2.68 ± 0.47	2.64 ± 0.49	−0.04 ± 0.37	*
	CPF + RC	3	33	2.47 ± 0.72	2.57 ± 0.78	0.14 ± 0.47	*
	CPF + EMD	3	55	1.43 ± 0.37	2.02 ± 0.34	0.59 ± 0.20	*
PD	CPF	7	147	1.19 ± 0.14	1.04 ± 0.38	0.15 ± 0.30	*
	CPF + RC	3	33	1.30 ± 0.29	1.09 ± 0.14	0.22 ± 0.22	*
	CPF + EMD	4	72	1.49 ± 0.26	1.16 ± 0.15	0.33 ± 0.17	*
GRD	CPF	7	147	3.36 ± 0.36	0.80 ± 0.42	2.56 ± 0.43	*
	CPF + RC	4	69	3.62 ± 0.29	1.17 ± 0.25	2.46 ± 0.48	*
	CPF + EMD	5	108	3.91 ± 0.35	0.62 ± 0.36	3.29 ± 0.43	*

SD, between studies; *, $p < 0.001$.
CPF, coronally positioned flap; CPF + EMD, coronally positioned flap plus enamel matrix derivative; CPF + RC, coronally positioned flap plus chemical root surface conditioning.

Table 4. Mean (± SD) of clinical attachment level (CAL), keratin thickness (KT), probing pocket depth (PD) and gingival recession depth (GRD) for 12 mo of follow-up

		12-mo follow-up					
		Study *n*	Subjects	Baseline weighted mean ± SD (mm)	12 mo mean ± SD (mm)	Difference mean ± SD (mm)	
CAL	CPF	2	31	9.54 ± 4.33	7.85 ± 4.18	1.69 ± 0.15	*
	CPF + RC	1	36	5.50 ± 0.00	2.40 ± 0.00	3.10 ± 0.00	= *
	CPF + EMD	4	89	5.37 ± 0.72	1.76 ± 0.44	3.61 ± 0.50	* *
KT	CPF	2	31	2.87 ± 0.37	2.97 ± 0.04	0.10 ± 0.41	*
	CPF + RC	1	36	2.40 ± 0.00	2.70 ± 0.00	0.30 ± 0.00	*
	CPF + EMD	4	102	1.86 ± 0.50	2.47 ± 0.44	0.61 ± 0.14	* *
PD	CPF	2	31	1.30 ± 0.00	0.98 ± 0.02	0.31 ± 0.02	*
	CPF + RC	1	36	1.60 ± 0.00	1.40 ± 0.00	0.20 ± 0.00	*
	CPF + EMD	5	119	1.57 ± 0.29	1.41 ± 0.33	0.16 ± 0.29	*
GRD	CPF	2	31	3.18 ± 0.57	1.37 ± 0.04	1.82 ± 0.53	*
	CPF + RC	1	36	3.90 ± 0.00	1.00 ± 0.00	2.90 ± 0.00	= *
	CPF + EMD	5	119	3.91 ± 0.42	0.72 ± 0.40	3.16 ± 0.41	* *

SD, between studies; *, $p < 0.001$.
CPF, coronally positioned flap; CPF + EMD, coronally positioned flap plus enamel matrix derivative; CPF + RC, coronally positioned flap plus chemical root surface conditioning.

group decreased from 3.91 ± 0.35 to 0.62 ± 0.36 mm (chi-square for heterogeneity: 21.537 ± 4, $p < 0.05$) at 6 mo (Table 3) and decreased from 3.91 ± 0.42 to 0.72 ± 0.40 mm (chi-square for heterogeneity: 24.739 ± 4, $p < 0.05$) at 12 mo (Table 4). In the coronally positioned flap group, the gingival recession depth decreased from 3.36 ± 0.36 to 0.80 ± 0.42 mm (chi-square for heterogeneity: 76.469 ± 5, $p < 0.05$) at 6 mo (Table 3) and decreased from 3.18 ± 0.57 to 1.37 ± 0.04 mm (chi-square for heterogeneity: 2.613 ± 1, $p = 0.106$) at 12 mo (Table 4). In the coronally positioned flap + chemical root surface conditioning group, gingival recession depth decreased from 3.62 ± 0.29 to 1.17 ± 0.25 mm (chi-square for heterogeneity: 27.290 ± 3, $p < 0.05$) at 6 mo (Table 3) and decreased from 3.90 ± 0.00 to 1.00 ± 0.00 mm at 12 mo (Table 4). The change in the coronally positioned flap + EMD group was statistically significantly better ($p < 0.001$) than those in the coronally positioned flap and coronally positioned flap + chemical root surface conditioning groups at 6 and 12 mo. At 6 mo, the mean reduction in the coronally positioned flap group was better than that in the coronally positioned flap + chemical root surface conditioning group, but this was not statistically significant ($p = 0.112$). At 12 mo, the change in the coronally positioned flap + chemical root surface conditioning group was statisti-

cally significantly better ($p < 0.001$) than that in the coronally positioned flap group.

Root coverage percentage

The results in the coronally positioned flap group were 74.12 ± 15.80% (chi-square for heterogeneity: 88.952 ± 6, $p < 0.05$) root coverage percentage at 6 mo and 54.16 ± 0.00% root coverage percentage at 12 mo. In the coronally positioned flap + chemical root surface conditioning group, the results were 60.88 ± 5.12% (chi-square for heterogeneity: 0.182 ± 2, $p = 913$) root coverage percentage at 6 mo and 79.00 ± 0.00% root coverage percentage at 12 mo. In the coronally positioned flap + EMD group, the results were 84.33 ± 7.72% (chi-square for heterogeneity 21.537 ± 4, $p < 0.05$) root coverage percentage at 6 mo and 84.42 ± 8.75% (chi-square for heterogeneity 25.000 ± 5, $p < 0.05$) root coverage percentage at 12 mo (Table 5). The root coverage percentage of the coronally positioned flap + EMD group was statistically significantly better ($p < 0.001$) than those of the coronally positioned flap and coronally positioned flap + chemical root surface conditioning groups at 6 and 12 mo. At 6 mo, the root coverage percentage of the coronally positioned flap group was statistically significantly better ($p < 0.001$) than that of the coronally positioned flap + chemical root surface conditioning group. At 12 mo, the root coverage percentage of the coronally positioned flap + chemical root surface conditioning group was statistically significantly better ($p < 0.001$) than that of the coronally positioned flap group.

Discussion

Clinically, the present analysis demonstrated that all three groups are useful in treating Miller's class I and II recession defects. All three groups achieved considerable root coverage and gains in clinical attachment, and maintained the amount of keratinized tissue and shallow probing pocket depths. The application of EMD to denuded root surfaces treated with the coronally positioned flap procedure significantly increased the percentage of root coverage and the attachment level compared with coronally positioned flap alone and the coronally positioned flap + chemical root surface conditioning procedure. In the present study, the coronally positioned flap and coronally positioned flap + chemical root surface conditioning groups resulted in root coverage percentage values ranging from 55 to 75%. The mean root coverage percentage of coronally positioned flap + EMD-treated sites ranged from 71.7 to 95.1%. This implies that coronally positioned flap alone for root coverage may be technique-sensitive, and the success of root coverage is overwhelmingly influenced by the condition of the surgical sites, such as the soft-tissue thickness (15,44). The coronally positioned flap procedure, combined with EMD for root coverage, showed improved and more consistent results.

The average root coverage of coronally positioned flap plus EMD amounted to 84.33 ± 7.72% after 6 mo and 84.42 ± 8.75% at 12 mo. The outcome of coronally positioned flap + EMD was better than coronally positioned flap alone after 6 mo (74.12 ± 15.80%) and 12 mo (54.16 ± 0.00%); the outcomes were also better than coronally positioned flap + chemical root surface conditioning after 6 mo (60.88 ± 5.12%) and 12 mo (79.00 ± 0.00%). The amount of root coverage obtained was quite stable between 6 and 12 mo in the coronally positioned flap + EMD group for root coverage. This suggests that root coverage procedures in the coronally positioned flap alone and coronally positioned flap + chemical root surface conditioning procedures were unpredictable. They became more predictable when the coronally positioned flap procedure was improved by the modification of adding EMD. In the present study, we did not discuss the relationship between the thickness of the flap and the amount of root coverage after coronally positioned flap alone or coronally positioned flap in combination with chemical root surface conditioning or EMD. Neither this nor the other studies detected any significant impact of pre-operative clinical parameters (tissue thickness, recession width, papilla height and width, vestibular bone height, anatomic factors, smoking, or others) on root coverage procedures. More evidence is required to determine which pre-operative clinical parameters can influence the recession reduction following coronally positioned flap surgery.

Root surface conditioning is a prerequisite of the EMD protocol on the premise that root surface conditioning removes the smear layer and allows the EMD to precipitate onto a surface free of organic remnants. The use of EDTA seems to improve the quality as well as quantity of the available root surface before EMD use, by removing the smear layer and exposing the collagen fibers (58). However, three quasi-

Table 5. Mean (± SD) of root coverage percentage for 6 and 12 mo of follow-up

	6-mo follow-up			12-mo follow-up		
	Study *n*	Subjects	RCP (%)	Study *n*	Subjects	RCP (%)
CPF	7	147	74.12 ± 15.80 *	1	11	54.16 ± 0.00 * *
CPF + RC	3	33	60.88 ± 5.12 *	1	36	79.00 ± 0.00 *
CPF + EMD	3	55	84.33 ± 7.72 *	6	149	84.42 ± 8.75 *

SD, between studies; *, $p < 0.001$.

CPF, coronally positioned flap; CPF + EMD, coronally positioned flap plus enamel matrix derivative; CPF + RC, coronally positioned flap plus chemical root surface conditioning; RCP, root coverage rate percentage.

experimental studies examined the effects of a solution containing 24% EDTA at a pH of between 7.0 and 7.2. The EDTA was applied to root surfaces for either 2 or 3 min, and the study duration was 6 mo. In all three studies, there were no differences in probing pocket depth, clinical attachment level, gingival recession depth, or probing bone levels between EDTA treatment and control root surfaces (59–61). In Mariotti's systematic review, the use and application of citric acid, tetracycline, or EDTA to modify the root surface provided no clinical benefit to the patient with respect to reduction of probing depths or gain in clinical attachment levels (62). It was confirmed in the present study that clinical outcomes for root coverage do not depend on the use of root conditioning. There were no statistically significant differences between coronally positioned flap alone group and the coronally positioned flap + chemical root surface conditioning group in the amount of root coverage and increase of clinical attachment level at 6 mo. Obviously, chemical root surface conditioning used alone therefore cannot be considered as beneficial for root coverage (63). Although the root coverage and increase of clinical attachment level in the coronally positioned flap + chemical root surface conditioning group was statistically significantly better than that of the coronally positioned flap group at 12 mo, it was justified by only one study that was included in our study. It needs more evidence to verify the above point.

The postoperative measurement period of 6 mo is sufficient to determine the long-term results of the method studied because it has been shown that a stable tissue relationship exists after the first postoperative month following root coverage procedures, and that was the reason why we decided to examine data at 6 and 12 mo on a short-term basis (64). In order to provide a definitive comparison of the results of coronally positioned flap alone and coronally positioned flap + chemical root surface conditioning procedures for root coverage, changes in clinical results between these two procedures were distinguished in this analysis. There was no significant difference at the 6-mo comparison time-point among clinical attachment level, keratinized tissue, probing pocket depth and gingival recession depth, except for root coverage percentage. However, there were certain contrariwise differences between coronally positioned flap and coronally positioned flap + chemical root surface conditioning in terms of clinical attachment level, probing pocket depth, gingival recession depth and root coverage percentage at the 12-mo follow-up. We cannot draw any firm conclusions about the respective data owing to the limited number of studies included in the 12-mo follow-up. More evidence is required to determine definitively whether root conditioning improves the results of root coverage for the coronally positioned flap procedure.

It is still not clear which biological mechanism is involved in the regeneration of periodontal tissue during healing in root coverage. Finally, histological reports are needed to gain greater insights into the tissue-healing process and prove that EMD is really responsible for improving the percentage of regenerated vs. repaired tissues compared with other techniques.

From this systemic analysis, it can be concluded that root coverage manipulated by the coronally positioned flap and coronally positioned flap + chemical root surface conditioning procedures were unpredictable. The results can be modified by adding EMD to increase significantly the clinical outcomes of gingival recession.

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