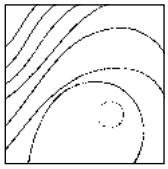
Split-Mouth Comparison of a Coronally Advanced Flap With or Without Enamel Matrix Derivative for Coverage of Multiple Gingival Recession Defects: 6- and 24-month Follow-up



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The aim of this study was to evaluate whether the use of enamel matrix derivative (EMD) improves clinical results of the coronally advanced flap (CAF) procedure in the treatment of multiple gingival recession defects. Ten patients presenting at least two adjacent buccal gingival recession defects affecting symmetric teeth on both sides of the maxilla were included in this study. Each set of multiple recession defects was assigned randomly to the test or control group. A bilateral simultaneous CAF procedure with vertical releasing incisions, with the adjunct of EMD for test sites, was performed. Clinical measurements (recession length, keratinized tissue, probing depth, and clinical attachment level) were assessed at baseline and 6 and 24 months after surgery by a blinded examiner. At the 6-month evaluation, both treatment procedures displayed good results with significant root coverage gain (CAF, 80.7% ± 20%; CAF + EMD, 82.8% ± 14%). A similar amount of relapse was noted at the 24-month evaluation when compared with the 6-month results (CAF, 71.0% ± 22%; CAF + EMD, 74.8% ± 16%). The use of EMD does not seem to significantly improve the results of the CAF procedure for root coverage in treatment of multiple recessions. (Int J Periodontics Restorative Dent 2012;32:e10–e20.)

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Various surgical techniques for root coverage have been proposed in the past,[1–3] such as the free gingival graft,[4,5] different types of laterally positioned flaps,[6–8] the coronally advanced flap,[9] the rotated flap,[10] the double papillae flap,[11] the subpedicle connective tissue graft,[12] and the subepithelial connective tissue graft.[13] The choice among these techniques as to which to use could be influenced by operator experience and skill, together with site- and patient-related factors.[14]

The coronally advanced flap (CAF) is a well-documented procedure[15–17] showing predictable results,[18–20] provided that some anatomical features are present, such as an adequate dimension of keratinized tissue and the preservation of the interdental soft and hard tissues.[21] It also has been suggested that the best results for this technique are obtained in the maxilla.[22]

Bioabsorbable membranes have been used in combination with a CAF[23,24] to induce regeneration of the periodontal attachment and have shown no significant improvement when compared with a CAF alone in short- and long-term studies.[25,26]

Histologic analysis on human extracted teeth showed that the use of a nonresorbable membrane in adjunct with a CAF procedure could determine the presence of new connective tissue attachment, new cementum, and newly formed bone.[27,28] The regenerative potential of the combination of enamel matrix derivative (EMD) with a CAF in the treatment of localized gingival recessions has been investigated.[29] The data obtained in some comparative studies on single recession-type defects showed that the addition of EMD did not improve the results of a traditional CAF technique in short-term evaluations,[30,31] and it did not show better outcomes when compared to a connective tissue graft (CTG).[32,33] Other authors, however, achieved significantly increased percent root coverage in defects treated with the CAF + EMD procedure in split-mouth[34] or controlled studies.[35,36] Although the results vary, some histologic analyses displayed the presence of new cementum, connective tissue fibers anchored in the new cementum, and islands of condensed bone[37,38] on teeth treated with EMD for root coverage therapy. Gingival recession defects often affect adjacent teeth, forming groups of multiple exposed roots; bilateral distribution of multiple recession defects is also common.[39–41] The treatment of multiple adjacent recession-type defects with a single-layer technique is not largely described in the literature, even though Zucchelli and De Sanctis obtained excellent short- and long-term results using a modified CAF procedure.[14,42]

The aim of this clinical study was to evaluate the effects of EMD when used in combination with the CAF procedure in the treatment of multiple gingival recession defects.

Method and materials

Patient and site selection

A split-mouth, randomized, blinded clinical trial was designed to compare the clinical performance of CAFs with or without the use of EMD for the trearment of multiple gingival recession defects. The study was performed at the Department of Periodontics and Implant Dentistry, George Eastman Dental Hospital, Rome, Italy.

A total of 10 consecutive patients (age range, 18 to 60 years) requiring root coverage therapy for esthetic or hypersensitivity reasons were evaluated. General inclusion criteria were good general health conditions and no contraindications for periodontal surgery. Smoking was allowed if limited to 10 or less cigarettes per day. Only maxillary recession defects were treated.

Patients presenting at least two adjacent, buccal gingival recession defects affecting symmetric teeth on both sides of the maxilla were included in this study. Only Miller Class I and II recession defects with a minimum length of 2 mm limited to the incisors, canines, and premolars were selected for the study. Each group of multiple recession defects was comparable in size with the contralateral defects, ie, the mean recession length of one group did not differ more than 2 mm from the mean recession length of the contralateral group in the same patient.

Other inclusion criteria were: presence of a clearly identifiable cementoenamel junction (CEJ), absence of deep abrasion, absence of restorations of the root surface, and indication for a CAF procedure. All patients received oral hygiene instructions and motivation, full-mouth scaling and root planing, and two hygiene control visits; at periodontal reevaluation, all patients presented full-mouth plaque scores < 20%, full-mouth bleeding scores < 20%, and probing depths ≤ 3 mm.

Nine patients were assigned for treatment of bilateral groups of 3 adjacent recession defects, and one patient was assigned for treatment of bilateral groups of 2 adjacent recession defects, for a total of 58 recession defects affecting 6 lateral incisors, 20 canines, 20 first premolars, and 12 second premolars.

The sample size was decided in advance by performing a calculation based on expected outcomes of the parameter to be measured (mean coverage gain) with a difference of 0.6 mm to be detected between test and control sites at alpha equal to 0.5 and a beta error equal to 0.2.

This study was approved by the ethical committee of the ASL RMA/ Eastman Dental Hospital, and all patients signed an informed consent form specific to this study.

Fig 1 (left) *Baseline clinical photograph of a control site. The right canine and premolars were to be treated with a CAF.*

Fig 2 (right) *Baseline clinical photograph of a test site. The left canine and premolars were to be treated with CAF + EMD therapy.*

Fig 3 (right) *Trapezoidal flap design.*

Surgical procedure

In each patient, one set of multiple recession defects was randomly assigned to the test group and the other to the control group using a coin toss. Randomization was performed only after preoperative measurements were taken. The same operator treated all patients.

A CAF procedure was performed for test and control sites, with the adjunct of EMD in test sites. Both sites were treated in the same surgical session (Figs 1 and 2). After local anesthesia (mepivacaine with epinephrine 1:100,000), an intrasulcular incision was made at each recession and was continued in a horizontal incision at the base of the adjacent interdental papilla, thus forming a continued horizontal incision that included the mesial papilla of the mesial tooth to be treated and the distal papilla of the distal tooth. The vertical position of the horizontal incision placed on the papillae was determined by the height of the adjacent recession defects. Two oblique, beveled incisions were made at the mesial and distal extremities of the incision and extended beyond the mucogingival line, outlining a trapezoidal flap (Fig 3).

A full-thickness dissection was made apical to the recession extending to the mucogingival line; a split-thickness dissection was made in the papillary area and apical to the mucogingival junction. The muscular fibers were dissected undermining the mucogingival area mesial and distal to the flap to obtain tension-free coronal displacement of the flap. The interdental papillae were de-epithelialized using a blade or bur. The exposed roots at test and control sites were scaled in the most coronal area, carefully avoiding damage to the residual marginal bone.

In test sites, a 24% ethylenediaminetetraacedic acid gel (PrefGel, Straumann) was applied for 2 minutes on the exposed root surfaces, and the entire area was then carefully rinsed with a sterile saline solution. EMD (Emdogain, Straumann) was then applied starting from the most apical point until the entire root surface was covered. In control sites, no chemical conditioning of the root was performed nor was any other medication added.

Once it was verified that the repositioning was tension-free, the flap was positioned coronally just above the CEJ and secured with 5-0 resorbable sutures on both sides.

Fig 4 (left) *Control site treated with CAF 6 months after surgery.*

Fig 5 (right) *Test site treated with CAF + EMD 6 months after surgery.*

Fig 6 (left) *Control site treated with CAF 24 months after surgery (compare to Fig 1).*

Fig 7 (right) *Test site treated with CAF + EMD 24 months after surgery (compare to Fig 2).*

Postoperative care

Anti-inflammatory/analgesic therapy was prescribed (nimesulide 100 mg twice a day for 3 days). A cold liquid diet was recommended for the first 2 days, with soft food for 5 days after that. Patients were also asked to avoid any traumatic movement of the upper lip until suture removal.

Patients were instructed not to brush the teeth in proximity to the surgical areas for 4 weeks and to rinse with 0.2% chlorhexidine digluconate three times a day for 1 minute until suture removal. Sutures were removed 14 days after surgery; in that visit, a professional supragingival cleaning was performed, and new hygiene instructions were given. It was recommended to rinse with 0.12% chlorhexidine digluconate three times a day for 1 minute for an additional 2 weeks and to begin to brush the teeth 4 weeks after surgery using a super-soft toothbrush and the roll technique. All patients were recalled at weeks 6, 12, and 18 for control visits, hygiene instructions, and prophylaxis and every 6 months thereafter (Figs 4 and 5) until the final examination, which was 24 months after surgery (Figs 6 and 7).

Measurements

An examiner blinded to the surgical protocol recorded all clinical parameters.

The following data were collected for the sites examined:

- Recession length (REC): Distance between the gingival margin and the CEJ (one point per tooth on the midbuccal aspect)
- Probing depth (PD): Distance between the gingival margin and the tip of the probe inserted with calibrated power (six points per tooth)
- Clinical attachment level (CAL): Distance between the CEJ and the tip of the probe inserted with calibrated power (one point per tooth on the midbuccal aspect)
- Keratinized tissue (KT): Distance between the gingival margin and the mucogingival line (one point per tooth on the midbuccal aspect)

All measurements were assessed using a periodontal probe (CP UNC 15, Hu-Friedy) and were rounded to the nearest 0.5 mm. Plaque Index and the Bleeding Index scores were recorded at the surgical sites. Full-mouth bleeding and plaque scores were also recorded.

Table 1 Statistical comparison between test and control groups for REC (mm)

	Baseline	6 mos	Gain	% coverage	24 mos	Gain	% coverage
CAF	2.93	0.64	2.29	80.7% ± 20%	0.90	2.03	71.0% ± 22%
CAF + EMD	3.12	0.62	2.50	82.8% ± 14%	0.81	2.31	74.8% ± 16%
Overall	3.02	0.63	2.40	81.8% ± 19%	0.86	2.17	72.9% ± 22%
Difference	0.19	0.02	0.21	1.9%	0.09	0.28	3.8%
*P**	NS	NS	NS	NS	NS	NS	NS

REC = recession length; CAF = coronally advanced flap; EMD = enamel matrix derivative.
*Mann-Whitney test. Test and control grups were not statistically significantly different (NS) at any stage in this study.

Table 2 Mean REC values (mm) at the different stages of the study and mean recession gain values (mm) at 6 and 24 mo compared with baseline and 6 mo†

	Mean	SD	95% CI	Median	Range
Baseline					
CAF	2.93	0.83	2.42 to 3.45	3.00	2 to 6
CAF + EMD	3.12	1.11	2.43 to 3.81	3.00	2 to 6
6 mo					
CAF	0.64	0.78	0.16 to 1.12	0.50	0 to 3
CAF + EMD	0.62	0.58	0.26 to 0.98	0.50	0 to 2
Gain from baseline					
CAF	2.29*	0.62	1.91 to 2.68	2.00	1.0 to 3.5
CAF + EMD	2.50*	0.73	2.05 to 2.95	2.00	1.5 to 4.0
24 mo					
CAF	0.90	0.81	0.40 to 1.40	1.00	0 to 3
CAF + EMD	0.81	0.56	0.46 to 1.16	1.00	0 to 2
Gain from baseline					
CAF	2.03*	0.69	1.60 to 2.46	2.00	0.5 to 3.5
CAF + EMD	2.31*	0.87	1.77 to 2.85	2.00	1 to 4
Gain from 6 mo					
CAF	–0.26**	0.39	–0.52 to –0.03	0.00	–1.0 to 0.5
CAF + EMD	–0.19**	0.31	–0.37 to –0.01	0.00	–1 to 0

REC = recession length; CAF = coronally advanced flap; EMD = enamel matrix derivative; SD = standard deviation; CI = confidence interval.
*$P < .01$.
**$P < .05$.
†Wilcoxon test used to determine statistical significance for intraclass correlations.

Descriptive statistical analysis was performed. The Mann-Whitney test was performed to compare the parameters studied between test and control groups. The Wilcoxon test was performed to assess intragroup comparisons.

Results

Recession defects

At baseline, no significant differences in REC were found between test and control groups ($P > .05$). After 6 months, both procedures displayed good results with statistically significant root coverage gain (control, 80.7% ± 20%; test, 82.8% ± 14%), in accordance with data obtained in other studies. Mean root coverage (MRC) was 2.29 ± 0.62 mm in control sites and 2.50 ± 0.73 mm in test sites. Complete root coverage was obtained in 45% (13 of 29) of defects in the control group and 31% (9 of 29) of defects in the test group. After 24 months, root coverage gain was 71.0% ± 22% in the control group with an MRC of 2.03 ± 0.69 mm; in the test group, root coverage gain was 74.8% ± 16% and MRC was 2.31 ± 0.87 mm. Results at 24 months reported complete root coverage in 7 of 29 sites (24%) in the control group and 5 of 29 sites (17%) in the test group. It should be noted that there were no statistically significant differences between the test and control groups ($P > .05$) at any stage of this study.

The intragroup comparison showed a statistically significant difference in recession coverage between baseline and 6-month visits for both groups ($P < .01$), which was still significant after 24 months ($P < .01$). These data suggest that a significant improvement in gingival recession defects was achieved in both groups and that the adjunctive use of EMD did not affect the treatment results (Tables 1 and 2).

Table 3 Statistical comparison between test and control groups for CAL and KT (mm)

	Baseline	6 mo	Difference	24 mo	Difference
CAL					
CAF	4.34	2.02	−2.32	2.17	−2.17
CAF + EMD	4.64	2.07	−2.57	2.12	−2.52
Difference	0.30	0.05	0.25	0.05	0.35
*P**	NS	NS	NS	NS	NS
KT					
CAF	2.78	3.09	0.31	3.19	0.41
CAF + EMD	2.72	3.00	0.28	3.09	0.36
Difference	0.06	0.09	0.03	0.10	0.05
*P**	NS	NS	NS	NS	NS

CAL = clinical attachment level; KT = keratinized tissue; CAF = coronally advanced flap; EMD = enamel matrix derivative.
*Mann-Whitney test. Test and control grups were not statistically significantly different (NS) at any stage in this study.

Probing depth (PD)

Baseline values did not show significant differences between the two groups for PD ($P > .05$). No statistically significant differences were found at any stage of the study ($P > .05$).

Clinical attachment level (CAL)

CAL values at baseline did not differ between test and control groups ($P > .05$). The values recorded 6 and 24 months after treatment showed no statistically significant differences when test and control groups were compared. However, a significant reduction in CAL values was recorded in both groups at 6 and 24 months when compared with baseline values ($P < .01$). After 24 months, mean CAL gain was 2.17 ± 0.84 mm in the control group and 2.52 ± 0.93 mm in the test group (Tables 3 and 4).

Table 4 **Mean CAL values (mm) at the different stages of the study and mean CAL gain at 6 and 24 mo compared with baseline and 6 mo†**

	Mean	SD	95% CI	Median	Range
Baseline					
CAF	4.34	1.13	3.64 to 5.05	4.00	3 to 8
CAF + EMD	4.64	1.31	3.83 to 5.45	4.50	3 to 7
6 mo					
CAF	2.02	0.98	1.41 to 2.62	2.00	0 to 3
CAF + EMD	2.07	0.89	1.55 to 2.66	2.00	0 to 2
Gain from baseline					
CAF	2.32*	0.71	1.89 to 2.77	2.00	1 to 4
CAF + EMD	2.57*	0.84	2.01 to 3.06	2.00	1 to 4
24 mo					
CAF	2.17	1.05	1.52 to 2.82	1.00	0 to 3
CAF + EMD	2.12	0.83	1.61 to 2.64	1.00	0 to 2
Gain from baseline					
CAF	2.17*	0.84	1.65 to 2.69	2.00	0.5 to 3.5
CAF + EMD	2.52*	0.93	1.94 to 3.09	2.00	1 to 4
Gain from 6 mo					
CAF	–0.15**	0.60	–0.53 to 0.22	0.00	–1.0 to 1.5
CAF + EMD	–0.05**	0.49	–0.32 to 0.29	0.00	–1 to 1

CAL = clinical attachment level; CAF = coronally advanced flap; EMD = enamel matrix derivative; SD = standard deviation; CI = confidence interval.
*$P < .01$.
**$P < .05$.
†Wilcoxon test used to determine statistical significance for intraclass correlations.

Keratinized tissue (KT)

Baseline analysis showed no significant differences between the study groups ($P > .05$). At the 24-month evaluation, KT dimensions showed improvment of 0.41 ± 0.42 mm in the control group (baseline, 2.78 ± 0.65 mm; 6 months, 3.09 ± 0.63 mm; 24 months, 3.19 ± 0.59 mm); in the EMD group, an improvement of 0.36 ± 0.44 mm was recorded (baseline, 2.72 ± 0.61 mm; 6 months, 3.00 ± 0.58 mm; 24 months, 3.09 ± 0.57 mm). The difference in KT values was not statistically different between test and control groups ($P > .05$) (Tables 3 and 5).

Discussion

The purpose of this clinical research was to evaluate whether the adjunct of EMD would enhance the outcome of a CAF procedure in the treatment of multiple gingival recession defects. A split-mouth design was used to minimize the bias potentially determined by

Table 5 **Mean KT values (mm) at the different stages of the study and mean KT difference at 6 and 24 mo compared with baseline and 6 mo†**

	Mean	SD	95% CI	Median	Range
Baseline					
CAF	2.78	0.65	2.37 to 3.18	3.00	1.5 to 4.0
CAF + EMD	2.72	0.61	2.35 to 3.10	3.00	2 to 4
6 mo					
CAF	3.09	0.63	2.70 to 3.48	3.00	2 to 5
CAF + EMD	3.00	0.58	2.64 to 3.36	3.00	2 to 5
Difference from baseline					
CAF	0.31*	0.51	0.01 to 0.61	0.00	–1 to 1
CAF + EMD	0.28*	0.41	0.02 to 0.53	0.00	0 to 1
24 mo					
CAF	3.19	0.59	2.82 to 3.55	3.00	2 to 5
CAF + EMD	3.09	0.57	2.73 to 3.44	3.00	2 to 5
Difference from baseline					
CAF	0.41*	0.42	0.15 to 0.68	0.50	0 to 1
CAF + EMD	0.36*	0.44	0.09 to 0.64	0.00	0.0 to 1.5
Difference from 6 mo					
CAF	0.10**	0.25	–0.05 to 0.26	0.00	0 to 1
CAF + EMD	0.09**	0.19	–0.03 to 0.21	0.00	0.0 to 0.5

KT = keratinized tissue; CAF = coronally advanced flap; EMD = enamel matrix derivative; SD = standard deviation; CI = confidence interval.
*$P < .01$.
**$P < .05$.
†Wilcoxon test used to determine statistical significance for intraclass correlations.

individual factors. Other trials[31] used Propylene Glycol Alginate, an acidic carrier present in Emdogain, in the control sites, but this approach was not performed in the present study because of its proven antibacterial effects (pH between 4 and 5).[43,44]

Recession defects showing comparable clinical aspects with their contralateral defects were included, and the statistical analysis confirmed the homogeneity of test and control groups at baseline; no significant differences (Mann-Whitney test) were found for REC, PD, CAL, or KT.

The rationale for the use of EMD in root coverage procedures is to stimulate regeneration of periodontal attachment on denudated roots, as shown in histologic evaluations on human biopsies to achieve true regeneration rather than periodontal repair.[37,38,45,46] Histologic analysis has demonstrated that a CTG with a pedicle flap in root coverage heals by repairing the periodontal tissue,[47] revealing connective tissue attachment between the tooth and graft but without

histologic evidence of cementum, bone, or periodontal ligament.[38] On the contrary, the use of EMD in combination with a CAF and CTG could promote periodontal regeneration (ie, new cementum, organized periodontal ligament fibers, and islands of condensed bone).[37,38]

Clinical studies demonstrated that CTG + CAF and CAF + EMD procedures show similar results. It should be considered that the CAF + EMD approach produces real benefits in terms of patient comfort resulting from the absence of a donor site, its early healing aspect, and the feasibility of the surgical procedure. Some studies have compared the outcomes of CAFs with or without the use of EMD in the correction of single recession defects. Two split-mouth studies reported 24-month results. Del Pizzo et al[48] obtained no statistically significant differences between test and control groups, even though complete root coverage was achieved in 73.33% in the CAF + EMD group and in 60% in the CAF only group. However, Spahr et al[49] achieved some significant differences concerning result stability in favor of the CAF + EMD group: 47% of recession defects treated only with CAFs deteriorated in the second year after therapy compared with 22% of recession defects in the test group. According to the authors, these data could be related to histologic differences in the healing pattern.[49]

The present study compared the outcome of CAF and CAF + EMD procedures in multiple recession defects. The data reported show good root coverage values (CAF + EMD, 2.31 ± 0.87 mm; CAF, 2.03 ± 0.69 mm), consistent with data from other controlled clinical studies.[48,49] No statistically significant differences could be detected between the two treatment groups. These results show significant root coverage with both procedures at 6 and 24 months of follow-up. The improvements are consistent with the results of Spahr et al[49] (84% in the EMD group, 67% in the placebo-treated group) and Del Pizzo et al[48] (90.6% test, 86.6% control) who performed similar spilt-mouth tests on single-recession defects. On the other hand, when comparing the overall 24-month results for MRC (72.9%), the present study's results are significantly inferior to the long-term outcome that other authors achieved in the treatment of multiple recessions with a modified CAF approach (94% MRC and 85% complete root coverage).[42] It may be speculated that the modified and more conservative approach presented by Zucchelli and De Sanctis[41] could improve the outcome of root coverage procedures.

It should be noted that, even if statistically significant improvements in REC were found in both test and control groups, no statistically significant differences between the two treatment modalities could be determined for any of the clinical parameters evaluated in the study. These results indicate that, in spite of the better histologic results shown in previous studies, the addition of EMD to the CAF procedure did not determine a clinically relevant benefit in this study.

In the present report, the comparison of measurements taken 6 months and 24 months after surgery showed a trend toward a slight relapse of the surgical correction for both test and control groups. This tendency is well documented for each surgical approach. It should be noted that both groups demonstrated similar behaviors and that no statistically significant differences were found for the amount of relapse between 6 and 24 months ($P > .05$).

Conclusion

According to the reported data, the additional use of EMD together with the CAF technique for multiple recession coverage did not improve the overall clinical outcome at the 24-month evaluation.

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