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CLINICAL EVALUATION OF CORONALLY ADVANCED FLAP WITH OR WITHOUT PLATELET RICH FIBRIN FOR THE TREATMENT OF MULTIPLE GINGIVAL RECESSIONS

PhD Thesis

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APPROVAL

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DECLARATION

I hereby declare that this thesis is my own work and that, to the best of my knowledge and belief, it contains no material previously published or written by another person nor material which has been accepted for the award of any other degree except where due acknowledgment has been made in the text.

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ABBREVIATIONS

ADM	Acellular Dermal Matrix
BoP	Bleeding on Probing
CAF	Coronally Advanced Flap
CAL	Clinical Attachment Level
CRC	Complete Root Coverage
CTG	Connective Tissue Graft
EMD	Enamel Matrix Derivatives
GI	Gingival Index
GT	Gingival Thickness
GTR	Guided Tissue Regeneration
KT	Keratinized Tissue Width
MRC	Mean Root Coverage
PD	Probing Depth
PI	Plaque Index
PRF	Platelet Rich Fibrin
PRP	Platelet Rich Plasma
RES	Root Coverage Esthetic Score
RH	Recession Height
RW	Recession Width
XCM	Xenogeneic Collagen Matrix
®	Registered Trademark

ABSTRACT

Kuka, S. (2015). Clinical Evaluation of Coronally Advanced Flap With or Without Platelet Rich Fibrin for the Treatment of Multiple Gingival Recessions. Yeditepe University, Institute of Health Sciences, Department of Periodontology, PhD thesis, Istanbul.

The objective of this controlled study was to assess the clinical effectiveness of platelet rich fibrin (PRF) in combination with coronally advanced flap on root coverage, aesthetics and patient satisfaction compared to coronally advanced flap (CAF) alone for the treatment of multiple Miller Class I gingival recession defects. A total of 20 patients (10 females and 10 males) with 49 Miller Class I multiple recessions ≥3 mm were included and divided into CAF + PRF and CAF groups. At baseline and 6 months after the surgery, plaque and gingival indices, bleeding on probing, probing depth, clinical attachment level, recession height (RH), keratinized tissue height, gingival thickness (GT), and mean and complete defect coverage were evaluated. Patient satisfaction and root coverage aesthetic scores were also assessed. Baseline RH in CAF+PRF and CAF groups was 3,20 ± 0,26 mm and 3,36 ± 0,34 mm, respectively. Intragroup comparisons revealed statistically significant differences at 6 months for all parameters ($p<0.05$). Gingival thickness increased from 0,78 ± 0,06 mm to 1,31 ± 0,07 mm in CAF + PRF group, and from 0,73 ± 0,07 mm to 0,8 ± 0,08 mm in CAF group. Mean root coverage was 79,02% (RH reduction: 2,5±0,53 mm) in CAF + PRF group, and 74,63% (RH reduction: 2,51±0,33 mm) in CAF group. Complete root coverage was achieved 36% of the teeth (9 out of 25 sites) for the CAF + PRF group, while it occurred 33.3% of the teeth (8 out of 24 sites) for the CAF group. Intergroup differences were found to be significant only for GT gain ($p<0.05$). Both techniques were successful in the treatment of multiple Miller Class I gingival recession defects. Tissue thickness significantly increased with the use of PRF graft in CAF + PRF group.

Key Words: Platelet Rich Fibrin, Coronally Advanced Flap, Multiple Gingival Recessions, Root Coverage, Gingival Thickness

ÖZET

Kuka, S. (2015). Çoklu dişeti çekilmelerinin tedavisinde kuronale kaydırılan flep ve trombositten zengin fibrin kombinasyonunun tek başına kuronale kaydırılan flep ile karşılaştırılması. Yeditepe Üniversitesi, Sağlık Bilimleri Enstitüsü, Periodontoloji ABD., Doktora Tezi. İstanbul.

Bu çalışmada, Miller Sınıf I çoklu dişeti çekilmelerinin tedavisinde kuronale kaydırılan flep (KKF) ve trombositten zengin fibrin (TZF) kombinasyonunun tek başına KKF ile klinik, estetik ve hasta memnuniyeti sonuçları açısından karşılaştırılması amaçlandı. Çoklu dişeti çekilmesi ≥ 3 mm olan 20 hastadaki 49 dişeti çekilmesi araştırmaya dahil edildi ve test (KKF + TZF) ile kontrol (KKF) olarak 2 gruba ayrıldı. Çalışmanın başlangıcında ve operasyondan 6 ay sonra, plak ve gingival indeks, sondalamada kanama, sondalanabilir cep derinliği (SCD), klinik ataşman seviyesi (KAS), dişeti çekilmesi miktarı (DÇM), keratinize doku genişliği (KD), dişeti kalınlığı (DK), ortalama ve tam kök kapanma yüzdesi, hasta memnuniyeti ve kök kapanma estetik skoru değerlendirildi. Başlangıç DÇM, KKF+ TZF ve KKF gruplarında sırasıyla 3.20 ± 0.26 mm ve 3.36 ± 0.34 mm olarak saptandı. Başlangıç ve 6. ay verileri karşılaştırıldığında, incelenen tüm parametrelerde, istatistiksel olarak anlamlı değişimler saptandı ($p<0.05$). Dişeti kalınlığı test grubunda 0.78 ± 0.06 mm'den 1.31 ± 0.07 mm'ye; kontrol grubunda 0.73 ± 0.07 mm'den 0.8 ± 0.08 mm'ye değişim gösterdi. Ortalama ve tam kök kapanma yüzdesi test ve kontrol gruplarında sırasıyla 79.02% ve 36% (DÇM azalması: 2.5 ± 0.53 mm); 74.63%ve %33 (DÇM azalması: 2.51 ± 0.33 mm) olarak saptandı. Sadece DK açısından gruplar arasında istatistiksel olarak anlamlı fark saptandı ($p<0.05$). Miller Sınıf I çoklu dişeti çekilmelerinin tedavisinde her iki teknikte başarılı bulundu. Doku kalınlığı, TZF'nin greft olarak kullanıldığı KKF+TZF grubunda anlamlı derecede arttı.

Anahtar Kelimeler: Trombositten Zengin Fibrin, Kuronale Kaydırılan Flap, Çoklu Dişeti Çekilmeleri, Kök Kapanması, Dişeti Kalınlığı

1. INTRODUCTION AND PURPOSE

Gingival recession is defined as an apical shift of the gingival margin from its physiologic position, 1-2 mm coronal to the cemento-enamel junction (1). Gingival recession is a frequent clinical condition in most populations with both good and poor standarts of oral hygiene (2). Patient complaints such as poor esthetics and root sensitivity are considered as the major indications for the treatment of gingival recessions (3). Also if there is a continuing recession that is determined at the recall intervals, the clinician should consider the treatment.

Many techniques have been proposed in periodontal plastic surgery to treat gingival recessions. Coronally advanced flap (CAF) is one of those techniques that is predictable and effective for the treatment of multiple Miller Class I & II gingival recessions with optimum root coverage and esthetics (4-7). Coronally advanced flap approach has been proposed alone (4-15) or in combination with connective tissue graft (CTG) (16-26), guided tissue regeneration (GTR) (barrier membranes) (27-31), enamel matrix derivatives (EMD) (32-40), acellular dermal matrix graft (ADM) (41-47), xenogeneic collagen matrix (XCM) (48, 49), platelet rich plasma (PRP) (50, 51), platelet rich fibrin (PRF) (52-55), orthodontic button application (56) and low intensity laser therapy (57). From these techniques, CAF in combination with CTG is considered as the gold standard technique for the treatment of multiple gingival recessions, obtaining significantly higher percentage of root coverage, gingival thickness (GT) and keratinized tissue height (KT) (58-62). Coronally advanced flap is modified using a trapezoidal flap design. The studies about this technique were ranging from 71.87% (14) to 98.6% (8) for mean root coverage (MRC) and from 33% (l3) to 88.88% (11) for complete root coverage (CRC) with evaluation periods of 6 (9-13,15), 12 (7, 8, 13), 24 (9), 36 (8) and 60 months (13); also 8 (14) and 14 years (13).

Many materials have been proposed to improve the clinical outcomes of CAF procedure (27-51). Platelet rich fibrin is one of those materials that have been used. Platelet-rich fibrin is a second generation platelet concentrate which was developed by Choukroun et al in 2001 (63). Platelet rich fibrin is an autologous fibrin biomaterial and a rich source of platelets and leukocytes (64, 65). Platelet rich fibrin technique has several advantages among the other platelet concentrates such as simplified preparation, ease of application, cost effectiveness, requires neither anticoagulant nor bovine thrombin and composed of dense fibrin matrix (63). Platelet rich fibrin consists of a fibrin three-dimensional matrix polymerized in a trimolecular structure, with the incorporation of platelets, leukocytes, growth factors and circulating stem cells (66). Platelet rich fibrin slowly releases significant amounts of growth factors and other matrix glycoproteins during at least 7 days (67, 68). This structure and composition of PRF supports cell migration, accelerates wound healing, angiogenesis and tissue regeneration (69).

The primary outcome of all root coverage therapies is to obtain CRC (60). Coronally advanced flap + CTG is accepted as the gold standard technique in the treatment of gingival recessions however, the risk of postoperative complications such as palatal necrosis, pain and bleeding, the need for a second surgical procedure to harvest donor tissue which caused patient morbidity/discomfort and prolonged surgical time and difficulty to harvest adequate donor tissue for multiple recession sites limit the clinicians (16, 70, 71). Platelet rich fibrin can be an alternative to CTG for the treatment of multiple gingival recessions, with its unique properties, such as being a biologic mediator that enables early wound healing and eliminates above mentioned complications.

Review of the literature reveals limited number of studies with controversial results for the use of PRF in the treatment of gingival recessions (52-55, 72-77). The studies about CAF + PRF were ranging from 72.1% (77) to 100% (53) for MRC and from 50% (54) to 80% (55) for CRC with evaluation periods of 6 (52-55, 73-76) and 12 months (72, 77). The aim of this randomized controlled clinical study was to evaluate clinical effectiveness of PRF in combination with CAF on root coverage, esthetics and patient satisfaction compared to CAF alone for the treatment of multiple Miller Class I gingival recessions and present 6 months results.

2. LITERATURE REVIEW

2.1. Gingival Recession and Its Classification

Gingival recession is defined as an apical shift of the gingival margin from its physiologic position, 1-2 mm coronal to the cemento-enamel junction (1). Epidemiologic and longitudinal studies have shown that gingival recession is a common clinical manifestation which can be seen in populations with both good and poor oral hygiene (78-91). Marginal tissue recession and attachment loss is observed in populations with high standarts of oral hygiene especially in younger individuals. These defects mostly affect buccal surfaces (84, 85). On the contrary, older patients associated with periodontal disease usually have recession defects, which affect all tooth surfaces (79, 81, 83, 84).

Etiology of gingival recession is complex and its mechanism is not well understood. Improper oral hygiene methods (e.g. excessive tooth brushing, floss, interproximal brush, hard toothbrush use) (92-97), tooth malposition, path of eruption, tooth shape, profile and position in the arch (16, 97), thin gingival biotype (98), alveolar bone dehiscence (99-101), muscle attachment and frenal pull (102, 103), plaque and calculus (104), periodontal treatment (105), orthodontic treatment (106-108), iatrogenic factors related to restorative or operative treatment (109, 110), viral infections (111) and other self-inflicted injuries (e.g. oral piercing, fingernail biting) (112-114) are considered to be the main causative factors and have been associated with the development of gingival recession.

In the literature, several recession classification systems have been proposed by various authors over the years (115-120). Miller’s classification is the most widely used of all the classification systems. It is based on the relationship between the gingival margin and the mucogingival junction, as well as the interproximal alveolar crest and soft tissue height and is useful in predicting the final amount of root coverage (118, 121). Four types of recession defects were categorized on the basis of the evaluation of soft and hard periodontal tissues (118).

Miller's Classification of Recession (118):

Class I: Marginal tissue recession that does not extend to the mucogingival junction. There is no periodontal loss (bone or soft tissue) in the interdental area, and 100% root coverage can be anticipated.

Class II: Marginal tissue recession that extends to or beyond the mucogingival junction. There is no periodontal loss (bone or soft tissue) in the interdental area, and 100% root coverage can be anticipated.

Class III: Marginal tissue recession that extends to or beyond the mucogingival junction. Bone or soft tissue loss in the interdental area is present or there is malposition of the teeth, which prevents the attempting of 100% root coverage. Partial root coverage can be anticipated.

Class IV: Marginal tissue recession that extends to or beyond the mucogingival junction. The bone or soft tissue loss in the interdental area and/or malposition of teeth is so severe that root coverage cannot be anticipated.

2.2. Periodontal Plastic Surgery

The term periodontal plastic surgery was suggested to replace the term mucogingival surgery and adopted by the American Academy of Periodontology in 1989 at World Workshop of Clinical Periodontics, which was first proposed by Miller in 1988 (118, 122, 123). Periodontal plastic surgery is defined as the surgical procedures performed to prevent or correct anatomic, developmental, traumatic or plaque disease-induced deformities of the gingiva, alveolar mucosa or bone (122).

Periodontal plastic surgery procedures comprise gingival and edentulous ridge augmentation, root coverage procedures, correction of mucosal defects at implants, crown lengthening, removal of aberrant frenulum, prevention of ridge collapse associated with tooth extraction, gingival preservation at ectopic tooth eruption and aesthetic correction of interdental papilla (124).

Root coverage procedures in the treatment of gingival recessions are one of the most widely performed indications of periodontal plastic surgery, depending on the patient complaints such as esthetic and dentinal hypersensitivity (60, 125).

Over the decades, numerous surgical techniques have been proposed for root coverage. The use of pedicle or free soft tissue grafts to cover denuded root surfaces were first presented by Younger in 1902, Harlan in 1906 and Rosenthal in 1911 (126), however, these techniques were abandoned at the end of the 1950-es. Surgical procedures used in the treatment of recession defects may basically be classified as pedicle soft tissue graft and free soft tissue graft procedures (127). The autogenous free soft tissue graft procedures may be performed as an epithelialized graft or as a subepithelial connective tissue graft (non-epithelialized graft) (128). The pedicle soft tissue graft procedures are grouped as rotational flap procedures or advanced flap procedures (127). Rotational flap procedures include laterally repositioned flap (128), double papilla flap (129), oblique rotational flap (130), rotational flap (131) and transpositioned flap (132). Advanced flap procedures include CAF (8, 16, 133-137), semilunar coronally repositioned flap (138, 139) and laterally moved and coronally advanced flap (140).

Complete coverage of the recession defect with good appearance related to adjacent soft tissues and minimal probing depth is the ultimate goal of root coverage procedures (141). For the successful treatment of recession defects, it is important to select the most predictable and easy-to-perform surgical technique according to a careful evaluation of the existing clinical factors: single or multiple gingival recession defects, location of the recession defects (maxillary or mandibular) and anatomic morphology of the defect (Recession height (RH), Recession width (RW), amount of KT adjacent to defect, interdental papilla height and width, GT, vestibule depth and presence of frenulum) (142). Additionally, several factors affect the clinical outcomes after root coverage procedures and the percentage of MRC and CRC such as patient related factors: poor oral hygiene, and traumatic tooth brushing (5), smoking (9, 142-145); surgery related factors: root surface preparation techniques (10, 146-150), flap design (151, 152), flap tension (152, 153), postsurgical marginal position (154), clinical experience (155); site related factors: tooth location, defect configurations (155) and anatomy (118), papilla dimension (156), flap thickness (157, 158) and tissue biotype (159).

2.3. Healing After Root Coverage Procedures

Healing nature after root coverage procedures have been investigated in animal studies (160-172) as well as in human histological case reports (173-187).

A number of animal studies have been performed using CAF alone or in combination with CTG, GTR, EMD, ADM and XCM. Similar histological and histomorphometrical findings were reported in these animal studies; connective tissue attachment with new bone and cementum was found in the most apical portion of the root, and long junctional epithelium was observed in the most coronal root surface (160-172).

Several human histological studies have been performed on the use of autogenous free gingival grafts; or CTGs (173-179), GTR (180-183), EMD (179, 184, 185), ADM (186) and XCM (187) with pedicle flaps for root coverage procedures. Autogenous free tissue grafts or combination of pedicle flaps and CTGs demonstrated healing by combination of long junctional epithelium and connective tissue attachment with new cementum and bone after root coverage procedures (173-179). A couple of histological studies revelaed high amounts of periodontal regeneration after the treatment of gingival recessions with GTR (180-182), on the contrary, Harris (183) reported healing by long junctional epithelium in three of the four teeth with recessions that were treated with GTR. Only, in one tooth new cementum and connective tissue attachment was formed but not coronal to the original gingival margin. Histological studies related to the combination of CAF procedure and CTG plus EMD revealed contradictory outcomes (179, 184, 185). Carnio et al. (185) reported attachment consisting of collagen fibers running parallel to the root surface without new cementum or Sharpey's fiber formation; new bone and new cementum were found only in the most apical portion of the root surface. In contrast, Rasperini et al. (184) and McGuire & Cochran (179) reported periodontal regeneration with connective tissue attachment, new bone and cementum formation. Histological studies of CAF procedure and ADM or XCM showed healing by combination of long junctional epithelium and connective tissue adhesion (186,187).

Review of literature revealed that there is no reported animal study or human histological case report about PRF. However, Del Corso et al. (188) explained the healing nature of PRF after root coverage procedures. The property of slow release of growth factors and matrix proteins from the PRF membrane promotes two specific biological mechanisms during root coverage procedures: impregnation and induction.

Firstly, the root surface is impregnated with blood proteins, which are the first biological links between the surface and a new attachment. Secondly, the slow release of molecules from the PRF membrane lasts several days and so it is long enough to trigger a cell induction phenomenon. The growth factors stimulate cell proliferation, neovessels develop within the fibrin matrix, the periosteum is stimulated, the gingival fibroblasts migrate within the fibrin matrix and slowly remodel it, while the membrane guides surface epithelialization if needed: this matrix offers a new scheme of development to the natural tissue. The short-term result is a quick wound closure and healing, with the reduction of postsurgical pain and edema. The long-term result is not only stable root coverage, but also a thicker and stable gingiva.

Findings of these studies reveal that wound healing after root coverage procedures mostly result as a soft tissue repair by formation of long junctional epithelium and connective tissue attachment at the most apical part. On the other hand regeneration by formation of new cementum and periodontal ligament at the most apical portion of the defect can be observed with GTR and EMD. Finally, a recent systematic review showed that although GTR, EMD, autogenic, allogenic and xenogenic soft tissue substitutes in combination with root coverage procedures were able to enhance new attachment however, none of them shown complete regeneration (189).

2.4. Coronally Advanced Flap for the Treatment of Single & Multiple Recession Defects

The CAF procedure is a very common approach for root coverage, and based on the coronal shift of the soft tissues on the exposed root surfaces (137, 153, 190). The technique was initially described by Norberg and subsequently reported by Allen & Miller (190). Recently, it was modified using a trapezoidal flap design and a split-full-split thickness flap elevation approach (8, 190). The condition required to perform the CAF are the presence of adequate keratinized tissue (height and thickness) apical to the root exposure (8, 123).

Coronally advanced flap has been used alone (4-15) or in combination with CTG (16-26), GTR (27-31), EMD (32-40), ADM (41-47), XCM (48, 49), PRP (50, 51), PRF (52-55), recombinant human platelet derived growth factor (191, 192), anorganic bone mineral/peptide-15 (193), living tissue-engineered human fibroblast-derived dermal substitute (194), button application (56), and low intensity laser therapy (57).

Coronally advanced flap procedure is a very common approach for the treatment of gingival recessions. It can be used either for single and multiple gingival recessions.

This part will focus on the CAF procedure in single gingival recessions.

De Sanctis & Zucchelli (8) reported the long-term clinical results following a modification of the CAF, utilizing a split–full–split surgical technique (split thickness flap with releasing vertical incisions) on 40 single maxillary Miller Class I or II recession defects ≥ 2mm and initial KT ≥ 1 mm. Clinical parameters assessed included RH, KT, probing depth (PD), and clinical attachment level (CAL). Baseline RH and KT was 3.82 ± 1.2 mm and 1.34 ± 0.6 mm, respectively. Recession height reduction was 3.72 ± 1.0 mm and 3.64 ± 1.1 mm, representing to a MRC of 98.6 % and 96.7 % and mean KT increase was 0.70 ± 0.20 mm and 1.78 ± 0.90 mm at 1 and 3 year evaluations, respectively. Keratinized tissue significantly increased at 1 and 3 years ($p<0.05$). Probing depth remained almost unchanged in the observation periods (1 and 3 years). They concluded that the modified CAF technique was effective in the treatment of localized gingival recessions in the upper jaw.

Santana et al. (11) compared the clinical outcomes of CAF (control group) and laterally repositioned flap technique (test group) in the treatment of 36 patients with single maxillary Miller Class I recession defects. Clinical parameters assessed included RH, KT, PD and CAL. Baseline RH in test and control groups was 3.4 ± 0.6 mm and 3.2 ± 0.5 mm. Recession height reduction was 3.26 ± 0.4 mm and 3.09 ± 0.5 mm in test and control groups, representing to a MRC of 95.5 % and 96.6 % at 6 months evaluation, respectively. Complete root coverage was achieved 83.33 % and 88.88% in test and control groups. Mean root coverage and CRC were not statistically significant between the procedures. Baseline KT in test and control groups was 4.3 ± 0.6 mm and 4.5 ± 0.6 mm. Keratinized tissue increase was 2.9 ± 1.7 mm and 0.2 ± 1.7 mm in test and control groups at 6 months evaluation, respectively. Inter-group comparisons demonstrated statistically significant KT gain in favor of the test group ($p<0.05$). Both flap techniques were effective in treating recession defects resulting in similar improvements for percentage of root coverage and frequency of CRC. The laterally repositioned flap resulted in significantly more KT gain than the CAF. The authors concluded that the results obtained 6 months after the surgery by CAF in the treatment of Miller Class I maxillary recession defects were clinically similar to the laterally repositioned flap.

Santana et al. (12) compared the clinical outcomes of CAF (control group) and semilunar coronally repositioned flap (test group) procedure in the treatment of 22 patients with single maxillary Miller Class I recession defects ≤ 5 mm and baseline KT

≥ 2 mm. Clinical parameters assessed included RH, KT, PD and CAL. Baseline RH in test and control groups was 2.9 ± 0.4 mm and 3.1 ± 0.6 mm, respectively. Recession height reduction was 1.2 ± 0.5 mm and 2.6 ± 0.7 mm in test and control groups, representing to a MRC of 41.38 % and 83.87 % at 6 months evaluation, respectively. Complete root coverage was achieved 9.03 % and 63.64 % in test and control groups, respectively. Baseline KT in test group and control groups was 4.3 ± 0.6 mm and 4.5 ± 0.6 mm, respectively. Keratinized tissue increase was 0.9 ± 0.7 mm in the test group, however, in the control group, this value decreased at 6 months evaluation (0.2 ± 0.9 mm). Inter-group comparisons demonstrated statistically significant RH reduction in favor of the control group, however, for KT, the significance was in favor of the test group ($p<0.05$). Both flap procedures were effective in obtaining and maintaining a coronal displacement of the gingival margin. Root coverage obtained in the immediate post-surgical period of test sites, but was not maintained throughout the subsequent evaluations. The authors concluded that root coverage was significantly better with CAF compared to the semilunar coronally repositioned flap procedure in the treatment of shallow maxillary Miller Class I recession defects in terms of percentage of root coverage and frequency of CRC at 6 months postoperatively.

Pini Prato et al. (14) evaluated the results of CAF procedures performed for the treatment of 60 patients (11 smokers) with single Miller Class I & II maxillary gingival recession defects ≥ 2 mm in long-term (8-year) case series study, followed for 6 months and 8 years. Clinical parameters assessed included RH, CRC and KT. Baseline RH was 3.2 ± 1.1 mm. Recession height reduction from baseline to 8 years was 2.3 ± 1.1 mm ($p<0.001$), however, in 53 % of the sites, gingival recessions were observed between 6 months and 8 years (0.5 ± 0.7 mm; $p<0.001$). Mean root coverage was 90.62 % at 6 months and 71.87 % at 8 years. The percentage of sites with CRC decreased from 55 % at 6 months to 35 % at 8 years ($p<0.05$). Fifteen sites with CRC at 6 months showed a recurrent recession at 8 years, in contrast 3 patients with residual recession at 6 months showed CRC at 8 years. Baseline KT was 2.7 ± 1.1 mm. The amount of KT tended to decrease from baseline to 8 years (0.6 ± 0.8 mm; $p<0.0001$). Sex, age and smoking were not associated with RH reduction at 8 years. The authors concluded that the CAF procedure was effective in the treatment of gingival recessions. However, recession relapse and KT reduction occurred during the follow-up period. Also, the baseline KT was a predictive factor for recession reduction: the greater the width of KT, the greater the reduction of the recession.

Moka et al. (15) compared the clinical outcomes of CAF (control group) and semilunar coronally repositioned flap (test group) procedure in the treatment of 20 patients with single maxillary Miller Class I recession defects ≤ 3 mm and baseline KT ≥ 2 mm. Clinical parameters assessed included RH, KT, PD and CAL. Baseline RH in test and control groups was 2.10 ± 0.31 mm and 2.30 ± 0.42 mm. Recession height reduction in test and control groups was 1.30 mm and 2.20 mm, representing to a MRC of 66.75 % and 93.48 % at 6 months evaluation, respectively. Complete root coverage was achieved 50 % and 70 % in test and control groups, respectively. Baseline KT in test group and control groups was 2.90 ± 0.31 mm and 3.05 ± 0.64 mm, respectively. Keratinized tissue increase was 0.85 mm and 0.75 mm in test and control groups, at 6 months evaluation, respectively. Inter-group comparisons demonstrated statistically significant RH reduction in favor of the control group, however, for KT, the significance was in favor of the test group ($p<0.05$). The authors concluded that CAF was found to be superior when the MRC and CRC were taken into account. However, there is a significant increase in KT in semilunar coronally repositioned flap compared to CAF group.

Review of literature revealed successful results with CAF alone procedure. The reported studies about CAF procedure alone in the treatment of single recession defects were ranging from 71.87 % (14) to 98.6 % (8) for MRC and from 33 % (13) to 88.88 % (11) for CRC with evaluation periods of 6 (9-13, 15), 12 (7, 8, 13), 24 (9) 36 (8) and 60 months (13); also 8 (14) and 14 years (13).

When multiple recessions affect adjacent teeth, root coverage should be undertaken with one surgical procedure. Coronally advanced flap has been reported to present successful clinical outcomes not only in the treatment of single gingival recessions but also in multiple gingival recessions.

Zucchelli & De Sanctis (4) evaluated the effectiveness of CAF without vertical releasing incisons (envelope type flap) in the treatment of 22 patients with 73 multiple maxillary Miller Class I or II recession defects ≥ 2 mm in a case series study. Clinical parameters assessed included RH, KT, PD and CAL. Recession height decreased from 2.8 ± 1.1 mm at baseline to 0.1 ± 0.3 mm at 12 months, reduction of 2.7 ± 0.8 mm, representing to a MRC of 97 %, respectively. Complete root coverage in all recessions was achieved in 16 out of 22 patients (73 %). There was no statistically significant relationship between the root coverage results and the number of recession defects treated in each patient. Keratinized tissue increased from 1.8 ± 0.9 mm at baseline to 2.4

± 0.8 mm at 12 months, gain of 0.6 ± 0.1 mm, respectively. Keratinized tissue increase was inversely correlated with the amount of presurgical KT ($p<0.001$). At 6 months evaluation, the intra-group difference was statistically significant in terms of RH, KT and CAL gain ($p < 0.05$). The multiple regression analysis showed that the final result, in terms of root coverage, was significantly affected by the initial RH ($p<0.001$) and KT ($p<0.01$). The authors concluded that envelope type CAF technique was very effective for the treatment of multiple gingival recessions in esthetic areas and successful root coverage could be obtained irrespective to both the number of recessions simultaneously treated and the presence of preoperative minimal KT amount (≤ 1mm).

In 2005, Zucchelli & De Sanctis (5) reported the 5-year clinical outcomes of the previous study (4). At 5 years evaluation, RH reduction was 2.56 ± 1.00 mm, representing to a MRC of 94 %, respectively. Complete root coverage in all recessions was almost stable in 15 out of 22 patients (68 %). Keratinized tissue increase was 1.38 ± 0.90 mm at 5 years evaluation. Increase in KT at 5 years was correlated negatively with the baseline amount of KT and positively with RH. The authors concluded that CAF in the treatment of multiple recession defects were well maintained over the 4 years evaluation period. Additionally, lack of compliance with a supportive care program and individual susceptibility to gingival recession were significantly associated with the recurrence in gingival recession. Lastly, KT increase following the CAF procedure may be attributed to the tendency of the mucogingival junction line to regain its genetically determined position.

Zucchelli & De Sanctis (6) evaluated the clinical efficacy of the CAF modification in the treatment of 6 patients with 25 multiple maxillary anterior Miller Class I & II recession defects ≥ 2 mm. Clinical parameters assessed included RH, KT, PD and CAL. Baseline RH was 2.84 ± 1.0 mm. Recession height reduction was 2.72 ± 0.9 mm at 12 moths, representing to a MRC and CRC of 97 % and 67 %, respectively. Baseline KT was 1.76 ± 0.6 mm and KT increase was 0.64 ± 0.6 mm at 12 months evaluation. At 12 months, there was statistically significant difference in terms of RH reduction; KT increase and CAL gain ($p<0.05$). The authors concluded that the modification of the CAF was effective for the treatment of multiple gingival recessions affecting the anterior teeth in patients with aesthetic demands, and these results were successful both in terms of RH decrease and KT increase.

Zucchelli et al. (7) compared two different CAF approaches: the flap with vertical releasing incisions (control group) and the envelope type flap (test group) in the treatment of 32 patients with 92 multiple maxillary Miller Class I & II (at least two on the same quadrant) recession defects ≥ 1 mm to evaluate root coverage and esthetic outcomes. The patient's postoperative morbidity was assessed 1 week after the surgery, whereas the esthetic evaluation, made by the patient and independent periodontist, and the clinical evaluation (RH, PD, CAL, KT) were made 1 year later. In test and control groups, RH decreased from 2.59 ± 1.03; 2.55 ± 0.92 mm at baseline to 0.10 ± 0.04 mm; 0.22 ± 0.42 mm at 12 months, reductions of 2.49 ± 0.93 mm; 2.33 ± 0.85 mm, representing to a MRC of 97.27 ± 8.08 % and 92.64 ± 14.25 %, respectively. No statistically significant difference was demonstrated between two groups in terms of RH reduction. Complete root coverage was achieved 89.3 % and 77.7 % in test and control groups, respectively. In test and control groups, KT increased from 1.70 ± 0.50 mm; 1.60 ± 0.49 mm at baseline to 2.38 ± 0.49 mm; 2.04 ± 0.47 mm, gain of 0.68 ± 0.51 mm; 0.44 ± 0.50 mm, respectively. A statistically greater probability of CRC and a greater increase in buccal KT were observed with the test group ($p<0.05$). Patient satisfaction with esthetics (overall satisfaction, color match, and amount of root coverage) was very high in both treatment groups, with no statistically significant differences between the groups. Better results in terms of postoperative course and esthetic evaluation by an independent expert periodontist were obtained in patients treated with the test group. Keloids, which may form along the vertical releasing incisions, contributed to the worst esthetic evaluation made by the expert periodontist. Also, surgical time was significantly shorter in the test group. The authors concluded that both CAF techniques were effective in RH reduction. However, the envelope type of CAF was associated with an increased probability of achieving CRC and with a better postoperative course.

Overall, the reported studies about CAF procedure alone in the treatment of multiple recession defects were ranging from 94 % (5) to 97 % (4, 6) for MRC and from 67 % (6) to 77.7 % (7) for CRC with evaluation periods of 12 months (4, 6, 7) and 60 months (5).

2.4.1. Coronally advanced flap in combination with connective tissue graft for the treatment of single & multiple recession defects

Among the various treatment modalities, CAF in combination with CTG for the treatment of recession defects are the most widely performed procedure and hold the most promising results in the literature (16-26). Systematic reviews revealed that CTG with CAF provided the most predictable and long-term stable results in terms of CRC and RH reduction in the treatment of single & multiple gingival recessions (58-62, 125, 141, 195-200).

Wennström & Zucchelli (16) compared the clinical outcomes of CAF alone (control group) and in combination with CTG (test group) in the treatment of 67 patients with 103 single Miller Class I recession defects ≥ 3 mm. Clinical parameters assessed included PD, CAL, RH and KT. Baseline RH in test and control groups was 4.0 ± 1.0 mm and 4.1 ± 0.9 mm, respectively. Recession height reduction was 3.8 ± 0.7 mm and 3.9 ± 0.5 mm for test and control groups, representing to a MRC of 96.1 % and 96.4 % at 6 months evaluation, respectively. Complete root coverage was observed at 72 % of the test and 74 % of the control sites. Mean root coverage and CRC in test and control groups were 98.9 % and 80 %; 97.1 % and 88 % at 24 months evaluation, respectively. Baseline KT in test and control groups was 0.9 ± 0.5 mm and 1.1 ± 0.5 mm, respectively. Keratinized tissue increase in test and control groups was 2.6 ± 0.1 mm and 0.4 ± 0.5 mm at 6 months and 2.8 ± 0.1 mm and 1.1 ± 0.1 mm at 24 months evaluation, respectively. There was no difference among groups at the 24 follow-up examination ($p>0.05$), except KT increase was significant in favour of the test group both at 6 and 24 months ($p<0.05$). The authors concluded that both surgical procedures resulted in similar degree of root coverage and that changes of tooth brushing habits might be of greater importance than increased gingival thickness for long-term maintenance of the surgically established position of the gingival margin.

Da Silva et al. (17) compared the clinical outcomes of CAF alone (control group) and in combination with CTG (test group) in the treatment of 11 non-smoking patients with single Miller Class I recession defects ≥ 3 mm. Clinical parameters assessed included RH, PD, CAL, KT, and GT. Baseline RH in test and control groups was 4.20 ± 0.78 mm and 3.98 ± 0.62 mm, respectively. Recession height reduction was 3.16 ± 0.86 mm and 2.73 ± 0.99 mm for test and control groups, representing to a MRC of 75 % and 69 % at 6 months evaluation, respectively. Complete root coverage was observed at 56 % of the test and 45 % of the control sites. Baseline KT in test and control groups was 2.79 ± 0.93 mm and 3.38 ± 1.23 mm, respectively. Keratinized tissue increase in the test and decrease in the control groups was 0.55 ± 0.91 mm and 0.21 ± 0.63 mm at 6 months evaluation period, respectively. Baseline GT in test and control groups was 1.34 ± 0.28 mm and 1.27 ± 0.29 mm, respectively. Gingival thickness increase in test and control groups was 0.44 ± 0.37 mm and 0.01 ± 0.32 mm at 6 months postoperatively, respectively. The test group showed a statistically significant gain in KT and GT compared to the control group at 6 months postoperatively ($p<0.05$). The authors concluded that both surgical approaches were effective in terms of root coverage; however, CAF combined with CTG should be used if the desired outcomes are KT and GT increase.

Cortellini et al. (21) compared the clinical outcomes of CAF alone (control group) and in combination with CTG (test group) in the treatment of 85 patients with single Miller Class I & II gingival recession defects ≥ 2 mm. Clinical parameters assessed included RH, KT, PD, CAL, and dentine hypersensitivity. Baseline RH in test and control groups was 2.7 ± 0.7 mm and 2.4 ± 0.7 mm, respectively. Recession height reduction was 2.0 ± 1.0 mm and 1.5 ± 1.1 mm for test and control groups, representing to a MRC of 74.1 % and 62.5 % at 6 months evaluation, respectively. Complete root coverage was observed at 60 % of the test and 37 % of the control sites. Baseline KT in test and control groups was 2.7 ± 1.2 mm and 3.2 ± 1.3 mm, respectively. Keratinized tissue increase and decrease in test and control groups at 6 months evaluation period was 0.6 ± 1.1 mm and 0.1 ± 1.2 mm, respectively. Even RH reduction was not different between the two groups, significantly greater probability of CRC was observed after CAF + CTG combination ($p<0.05$). Both treatments were effective in providing a significant reduction in RH and dentine hypersensitivity, with only limited intra-operative and post-operative morbidity and side effects. The authors concluded that adjunctive application of CTG under a CAF increased the probability of achieving CRC in maxillary Miller Class I & II defects.

Cairo et al. (24) evaluated the adjunctive benefit of CTG (test group) to CAF alone (control group) in the treatment of 29 patients with 1 gingival recession associated with inter-dental clinical attachment loss equal or smaller to the buccal attachment loss. Outcome measures assessed included RH, CRC, root coverage esthetic score (RES), intra-operative and post-operative morbidity and root sensitivity. Baseline RH in test and control groups was 2.9 ± 0.7 mm and 2.6 ± 0.6 mm, respectively. Recession height reduction was 2.6 ± 0.7 mm and 2.0 ± 0.7 mm for test and control groups at 6 months evaluation, respectively. No difference was detected in term of RH reduction between groups. Test group resulted in better outcomes in terms of CRC than control group ($p<0.05$). Four of 14 treated cases in the control group showed CRC, whereas in the test group, it was 8 of 14 treated cases at 6 months evaluation. Complete root coverage was observed more than 80 % of the treated cases in the test group when the baseline amount of inter-dental CAL was ≤ 3 mm. Test group was associated with longer surgical-time, higher number of days with post-operative morbidity and the need for a greater number of analgesics than control group ($p<0.05$). No difference for final RES score was detected between the groups ($p>0.05$). The authors concluded that both CAF in combination with CTG and CAF alone could provide CRC in single gingival recession with inter-dental CAL loss. The application of CTG under CAF resulted in predictable CRC when inter-dental CAL was ≤ 3 mm.

Kuis et al. (25) compared the long-term (5-year) clinical outcomes of CAF alone (control group) and in combination with CTG (test group) in the treatment of 37 patients with 114 bilateral, single Miller Class I & II gingival recession defects. Clinical parameters assessed included RH, KT, CRC and MRC. Baseline RH in test and control groups was 2.63 ± 0.72 mm and 2.63 ± 0.75 mm, respectively. Recession height reduction was 2.54 ± 0.38 mm and 2.38 ± 0.24 mm for test and control groups, representing to a MRC of 97.2 ± 10.6 % and 91.9 ± 16.4 % at 6 months evaluation, respectively. Complete root coverage was observed at 93 % of the treated cases in the test group and 78.9 % of the cases in the control group. Baseline KT in test and control groups was 1.33 ± 1.17 mm and 1.33 ± 1.19 mm, respectively. Keratinized tissue increase in test and control groups was 1.13 ± 0.57 mm and 0.76 ± 0.48 mm at 6 months evaluation, respectively. There was a significant reduction in RH and increase in KT after surgery in both groups ($p<0.05$). Test group showed significantly better results for all evaluated clinical parameters in 6, 12, 24 and 60 months follow-up periods ($p<0.05$). Miller Class I defects showed better results in terms of RH reduction, CRC, and MRC, whereas Miller Class II defects showed better results in KT, both in favor of the test group ($p<0.05$). Miller Class I defects showed better results than Miller Class II gingival recession defects regardless of the surgical procedure used. The authors concluded that both surgical procedures were effective in the treatment of single Miller Class I and II gingival recession defects. The CAF in combination with CTG provided better long-term outcomes (60 months postoperatively) than CAF alone. Long-term stability of the gingival margin is less predictable for Miller Class II gingival recession defects compared to those of Class I.

As a result, the reported studies about CAF procedure in combination with CTG in the treatment of single recession defects were ranging from 74.1 % (21) to 98.9 % (16) for MRC and from 56 % (17) to 97.1 % (16) for CRC with evaluation periods of 6 (16, 17, 21, 24, 25) and 24 months (16).

Cetiner et al. (18) reported the clinical outcomes of CAF in combination with expanded mesh CTG in the treatment of 10 patients with 52 multiple Miller Class I & II recession defects ≥ 3 mm in a case series study. Clinical parameters assessed included PD, CAL, RH, KT and RW. Baseline RH was 3.11 ± 0.80 mm. Recession height reduction was 3.0 ± 0.53 mm at 12 months, representing to a MRC of 96.1 %. Complete root coverage was achieved in 80 % of the treated sites. Keratinized tissue increased from 3.93 ± 0.72 mm to 5.11 ± 0.76 mm, with a gain of 1.18 ± 0.35 mm at 12 months evaluation. Baseline RW was 3.07 ± 0.65 mm. Recession width reduction was 0.11 ± 0.27 mm at 12 months. There was statistically significant difference in terms of RH and RW reduction; KT and CAL gain at 12 months when compared to baseline ($p<0.05$). The authors concluded that expanded mesh CTG in combination with CAF procedure provided highly predictable root coverage in multiple gingival recessions.

Chambrone & Chambrone (19) reported the clinical outcomes of CAF in combination with CTG in the treatment of 28 patients with 69 multiple Miller Class I & II recession defects ≥ 3 mm in a case series study. Clinical parameters assessed included PD, CAL, RH and KT. Recession height decreased from 3.84 ± 1.50 mm to 0.14 ± 0.23 mm at 6 months, with a reduction of 3.7 ± 1.27 mm, representing to a MRC of 96.35 %, respectively. Complete root coverage was achieved in 71 % of the treated sites. Keratinized tissue increased from 1.66 ± 1.09 mm to 3.82 ± 0.91 mm at 6 months, with a gain of 2.16 ± 0.18 mm. There was statistically significant difference in terms of RH reduction; KT and CAL gain at 6 months when compared to baseline ($p<0.05$). Maxillary recessions showed statistically better clinical outcomes than mandibular recessions ($p<0.05$). The authors concluded that CTG in combination with CAF was an effective procedure for the coverage of multiple gingival recessions.

Carvalho et al. (20) reported the clinical outcomes of CAF without vertical releasing incisions (Modified CAF) in combination with CTG in the treatment of 10 patients with 29 multiple Miller Class I & II recession defects ≥ 1 mm in a case series study. Clinical parameters assessed included PD, CAL, RH and KT. Recession height decreased from 2.10 ± 0.82 mm to 0.07 ± 0.26 mm at 6 months, with a reduction of 2.03

± 0.78 mm, representing to a MRC of 96.7 %. Complete root coverage was achieved in 93.1 % of the treated sites (9 of 10 patients). Keratinized tissue increased from 2.34 ± 1.47 mm to 3.65 ± 0.94 mm at 6 months, with a gain of 1.31 ± 1.23 mm. There was statistically significant difference in terms of RH reduction; KT and CAL gain at 6 months when compared to baseline (p<0.05). The authors concluded that CAF without vertical releasing incisions in combination with CTG was effective and predictable to obtain root coverage in multiple gingival recessions.

Pini-Prato et al. (22) compared the long-term (5-year) clinical outcomes of CAF alone (control group) and in combination with CTG (test group) in the treatment of 13 patients with 93 bilateral multiple maxillary Miller Class I, II & III recession defects. Clinical parameters assessed included RH and CRC. In test and control groups, RH decreased from 3.6 ± 1.3 mm; 2.9 ± 1.3 mm to 0.6 ± 0.5 mm; 0.4 ± 0.5 mm at 6 months, with a reduction of 3.0 ± 1.3 mm; 2.6 ± 1.3 mm, representing to a MRC of 89.65% and 83.33%, respectively. Complete root coverage was achieved in 57% and 34% of the treated cases in the test and control groups at 6 months, respectively. There was no statistically significant difference between groups in terms of RH reduction and CRC at 6 months (p>0.05). At the 5-year follow-up, test group showed a higher percentage of sites with CRC (52%) than CAF alone group (35%). An apical relapse of the gingival margin in the control group was observed whereas a coronal displacement of the margin was noted in the test group between the 6-month and 5-year follow-ups. The authors concluded that CAF in combination with CTG achieved better outcomes in terms of CRC than CAF alone in the treatment of multiple gingival recessions at the 5-year follow-up.

De Sanctis et al. (23) reported the clinical outcomes of CAF in combination with CTG in the treatment of 10 patients with 26 multiple mandibular posterior Miller Class I & II recession defects ≥ 2 mm in a case series study. Clinical parameters assessed included PD, CAL, RH and KT. Recession height decreased from 3.40 ± 0.83 mm to 0.28 ± 0.32 mm, with a reduction of 2.12 ± 0.50 mm, representing to a MRC of 91.2 % at 1-year evaluation. Complete root coverage of the defects and patients was 50 % and 10 % at 1-year evaluation, respectively. Keratinized tissue increased from 0.57 ± 0.46 mm to 3.05 ± 0.71 mm at 1-year. There was statistically significant difference in terms of RH and RW reduction; KT and CAL gain at 1-year (p<0.05). The authors concluded that CAF in combination with CTG could be a valid treatment approach for mandibular posterior multiple recession defects.

Zucchelli et al. (26) compared short- and long-term (5-year) clinical and esthetic outcomes of CAF alone (control group) and in combination with CTG (test group) in the treatment of 50 patients with multiple maxillary Miller Class I & II gingival recession defects ≥ 2 mm. Parameters assessed included RH, PD, CAL, KT, post-operative morbidity and esthetics. In test and control groups, mean RH decreased from 3.15 mm; 3.05 mm to 0.10 mm; 0.06 mm at 6 months, with reductions of 3.05 mm; 2.99 mm, respectively. In the control group, among the 73 treated defects, CRC was achieved in 68 (at 6 months), 65 (at 1 year) and 57 (at 5 years) defects whereas in the test group among the 76 treated defects, CRC was achieved in 68 (at 6 months), 66 (at 1 year) and 69 (at 5 years) defects. In test and control groups, mean KT increased from 1.47 mm; 1.43 mm to 1.84 mm; 1.51 mm at 6 months evaluation, respectively. No statistically significant difference was demonstrated between the two groups in terms of RH reduction and CRC at 6 months and 1 year ($p<0.05$). At 5 years, statistically greater RH reduction and probability of CRC, greater increase in buccal KT and better contour were observed in the test group ($p<0.05$). Better post-operative course and better colour match were demonstrated in CAF alone group both at 1 and 5 years. The authors concluded that CAF plus CTG provided better CRC at 5 years; however, keloid formation due to graft exposure was responsible for the worse colour match evaluation in CAF plus CTG procedure.

In conclusion, the reported studies about CAF procedure in combination with CTG in the treatment of multiple recession defects were ranging from 89.65 % (22) to 98.9 % (16) for MRC and from 34 % (22) to 97.1 % (16) for CRC with evaluation periods of 6 (19, 20, 22, 26), 12 (18, 23, 26) and 60 months (22, 26).

Although the CAF in combination with CTG is a predictable and versatile technique, there are some disadvantages of CTG such as; limited amount of tissue that can be harvested from the palate especially for the treatment of the multiple gingival recessions, increased patient morbidity and prolonged surgical time may limit the clinician (16, 70, 71, 190). Thus, substitutes to CTG might be a choice for the clinicians that may ease the surgery and reduce patient morbidity.

2.4.2. Coronally advanced flap and different combinations for the treatment of single & multiple recession defects

CAF has been also used in combination with different materials as an alternative to CTG such as; GTR (27-31), EMD (32-40), ADM (41-47), XCM (48, 49), PRP (50, 51), orthodontic button application (56) and low intensity laser therapy (57).

The use of GTR with barrier membranes in the treatment of gingival recessions was first reported by Tinti et al. (201) and Pini Prato et al. (202) in 1992. The aim of using barrier membranes for root coverage procedures was to prevent the migration of epithelial cells along the root surface and stimulate the proliferation of periodontal ligament cells on the root surface for the formation of new bone and cementum, so called periodontal regeneration (203). Comparative studies demonstrated no difference between resorbable and nonresorbable barriers in terms or root coverage (194). Recently, a sytematic review indicated that the additional use of GTR was not effective to improve the clinical results of CAF procedure (125). Additionally, the high incidence of complications such as membrane exposure and financial cost should be considered (2, 190). Case selection is critical. Better results are achieved with Miller Class I defects with a tissue thickness of > 1 mm (203).

Enamel matrix derivatives in combination with CAF procedure in the treatment of gingival recessions was introduced by Modica et al. (32) to enhance root coverage and promote periodontal regeneration. In the literature, systematic reviews showed that CAF in combination with EMD improved the clinical outcomes in terms of percentage of CRC, KT gain and RH reduction (141, 195, 199, 204). Recent systematic reviews also indicated that EMD improved the clinical efficacy of CAF alone and might be used as an alternative in the treatment of gingival recessions (61, 62, 141). However, the true clinical rationale behind the use of EMD with CAF is unclear, therefore, its application should be performed critically (2, 190).

Acellular dermal matrix graft has also been used to treat gingival recessions in combination with CAF (41-47). In patients with shallow palate or thin palatal tissues, and also for the treatment of multiple recession defects, it becomes difficult to harvest sufficient donor tissue. To overcome these disadvantages ADM has been used a successful alternative to CTG. Recent systematic reviews indicated that studies using ADM with CAF showed a large heterogeneity (125, 141, 198). Acellular dermal matrix graft has shown to provide stable grafting when added to CAF for multiple recession defects, being only minimally inferior to CTG (205-210). The cost-effectiveness of the material should be considered for the clinician and the patient.

Another option for the clinicians is to use the recently developed XCM in the treatment of gingival recessions in combination with CAF (48, 49). Although, according to a recent systematic review, XCM might improve the efficacy of CAF, there is limited evidence that this material may be used as alternative to other materials (62, 125).

Platelet rich plasma has been proposed in the treatment of gingival recessions with CAF in limited number of studies (50, 51). Platelet rich plasma is highly concentrated in platelets. Platelets contain many autogeneous growth factors including platelet derived growth factor (PDGF), transforming growth factor-beta (TGF-β), vascular endothelial growth factor (VEGF), insulin-like growth factor (IGF) and epithelial growth factor (EGF) (50). These growth factors regulate several biologic activities such as tissue repair (mitogenesis and angiogenesis) at both genetic and cellular levels (2, 50). On the other hand, the preparation protocol of PRP is complex which requires biochemical blood handling (bovine thrombin and anticoagulants) and it is time consuming (211). Very limited number of studies are available about PRP application for the treatment of gingival recessions (50, 51).

Huang et al. (50) compared the clinical outcomes of CAF procedure alone (control group) and in combination with PRP (test group) in the treatment of 24 patients with single Miller Class I gingival recession defects ≥ 2 mm. Clinical parameters assessed included RH, RW, KT, GT, PD and CAL. In test and control groups, RH decreased from 2.8 ± 0.2 mm; 2.9 ± 0.5 mm to 0.5 ± 0.7 mm; 0.5 ± 0.6 mm at 6 months, with reductions of 2.3 ± 0.9 mm; 2.5 ± 0.8 mm, representing to a MRC of 81 % and 83.5 %, respectively. In test and control groups, KT increased from 2.7 ± 1.2 mm; 2.7 ± 1.4 mm to 3.1 ± 0.7 mm; 3.2 ± 1 mm at 6 months, with gains of 0.3 ± 0.9 mm; 0.6 ± 0.7 mm, respectively. In test group, GT increased from 1.1 ± 0.4 mm to 1.7 ± 0.5 mm at 6 months, with a gain of 0.6 ± 0.4 mm, whereas in the control group GT decreased from 1.1 ± 0.2 to 1.4 ± 0.4 mm at 6 months, with a loss of 0.3 ± 0.4 mm. At 6 months evaluation, there was no statistically significant difference between the groups in terms of all evaluated clinical parameters ($p>0.05$). The authors concluded that the application of PRP in CAF for root coverage provides no clinically measurable improvements on the final clinical outcomes of CAF in Miller Class I recession defects.

Lafzi et al. (51) compared the clinical outcomes of CAF procedure alone (control group) and in combination with PRP (test group) in the treatment of 6 non-smoker patients with 20 bilateral, single Miller Class I gingival recession defects ≥ 2 mm. Clinical parameters assessed included RH, RW, KT, PD and CAL. In test and control groups, RH decreased from 3.3 ± 0.8 mm; 3.6 ± 0.9 mm to 1.3 ± 0.7 mm; 2.4 ± 0.2 mm at 3 months, with reductions of 2.0 ± 0.1 mm; 1.2 ± 0.7 mm, corresponding to a MRC of 61.8 % and 65.0 %, respectively. In test and control groups, KT decreased from 2.9 ± 0.9 mm; 2.4 ± 0.7 mm to 2.8 ± 0.8 mm; 2.3 ± 0.5 mm at 3 months, with losses of 0.1 ± 0.1 mm; 0.1 ± 0.2 mm, respectively. At 3 months, both treatment protocols led to a significant improvement in all measured variables compared to the baseline values, except KT. However, there was no statistically significant difference between the groups in terms of all evaluated parameters (p>0.05). The authors concluded that while PRP improved the outcomes of CAF especially throughout the first month post-operatively, it showed no clinical advantage over CAF alone during the subsequent 2 months.

2.4.3. Coronally advanced flap in combination with platelet rich fibrin for the treatment of single & multiple recession defects

The gold standard for the treatment of gingival recessions is the bilaminar technique, which mainly consists of CAF covering CTG because the adjunctive use of CTG increases the likelihood of CRC with respect to the CAF alone especially in the long-term follow-up (190). Although limited dimension is required for single type of defects, the same cannot be assumed for multiple recession defects and difficulty to harvest adequate donor tissue from shallow or thin palate is a problem for the clinician (16, 70, 71, 190). Furthermore, the enhanced possibility of dehiscence in the covering flap as a result of the increasing dimension of the CTG is particularly unacceptable in patients with esthetic demands. The color, texture and surface characteristic of the exposed grafted area might be different from the adjacent soft tissue (190). In this view, the utilization of substitutes for the CTG's is strongly encouraged (190). In this aspect, PRF with enhanced wound healing and decreased complications seems to be one of the recently proposed alternatives to CTG for the treatment of multiple gingival recessions.

Platelet-rich fibrin is a second-generation platelet concentrate and defined as an autologous leukocyte- and PRF biomaterial (64, 65, 212, 213). Choukroun et al. developed PRF in 2001 for the use in oral and maxillofacial surgery in France (63).

Obtaining PRF is not complex unlike the other platelet concentrates (i.e. PRP) since it does not require anticoagulants or bovine thrombin. The absence of anticoagulant implies the activation in a few minutes of most platelets of the blood sample incontact with the tube walls and the release of the coagulation cascades. Fibrinogen is initially concentrated in the high part of the tube, before the circulating thrombin transforms it into fibrin (212). The protocol is quite simple and inexpensive: blood is collected in dry glass tubes or glass-coated plastic tubes and immediately softly centrifuged. Three layers are formed: a red blood cell base at the bottom, acellular plasma (platelet poor plasma) and a PRF clot in the middle. This clot combines many healing and immunity promoters present in the initial blood harvest. It can be used directly as a clot or after compression as a strong membrane (214).

Platelet rich fibrin consists of a three-dimensional fibrin matrix polymerized in a trimolecular or equilateral structure, with the incorporation of platelets, leukocytes, growth factors (PDGF, TGF-β, VEGF, IGF) and circulating stem cells (66, 212). This specific fibrin polymerization mode of PRF provides a flexible fibrin network which is able to support cytokine enmeshment and cellular migration and results in flexible, elastic and resilient membrane (212). Also, this mode of PRF allows slow release of significant amounts of growth factors and other matrix glycoproteins (Thrombospondin-1) during at least 7 days (67, 68, 214). This structure and composition of PRF supports cell migration, accelerates wound healing and tissue regeneration (69). In vitro studies showed proliferative effects of PRF on different types of cells such as osteoblasts (69), gingival and periodontal ligament fibroblasts (215).

Potential clinical use of PRF in periodontal procedures includes intrabony defects (216), furcation defects (217), sinus floor augmentation (218) and single and multiple gingival recessions (52-55, 72-77).

Aroca et al. (52) compared the clinical outcomes of modified CAF alone (control group) and in combination with PRF (test group) in the treatment of 20 patients with 67 multiple Miller Class I and II gingival recession defects ≥ 2 mm. Clinical parameters assessed included RH, KT, RW, GT, PD and CAL. Mean root coverage was 80.7 % ± 14.7 % and 91.5 % ± 11.4 % in test and control groups at 6 months, respectively. Complete root coverage was achieved in 52.23 % and 74.62 % of the treated sites in test and control groups at 6 months evaluation, respectively. In test and control groups, KT decreased from 2.78 ± 1.08 mm; 2.85 ± 1.23 mm to 2.54 ± 1.28 mm; 2.37 ± 0.89 mm at 6 months, respectively. In the test group, GT increased from 1.1

± 0.4 mm to 1.4 ± 0.5 mm at 6 months whereas in the control group GT remained the same value (1.1 ± 0.3 mm). In test and conrol groups, RW reduction was 66.2 % ± 37.5 % and 82.4 % ± 33 % at 6 months, respectively. At 6 months evaluation, the differences between test and control groups were statistically significant in terms of RH and RW reduction and were in favor of the control group ($p<0.05$); whereas GT and CAL gain differ significantly between groups and the significance was in favor of the test group ($p<0.05$). The changes in PD and KT did not differ significantly between test and control groups ($p>0.05$). The authors concluded that modified CAF was a predictable treatment for Miller Class I or II multiple gingival recessions. The use of a PRF membrane positioned under the modified CAF did not provided additive effects in terms of root coverage but an additional gain in GT.

Padma et al. (53) compared the clinical outcomes of CAF alone (control group) and in combination with PRF (test group) in the treatment of 15 patients with 30 bilateral, single Miller Class I and II gingival recession defects ≥ 3 mm. Clinical parameters assessed included RH, KT and CAL. In test and control groups, RH decreased from 3.44 ± 1.09 mm; 3.44 ± 1.21 mm to 0.00 ± 0.00 mm; 0.13 ± 0.72 mm at 6 months, with reductions of 3.44 ± 1.09 mm; 2.31 ± 0.49 mm, representing to a MRC of 100.00 ± 0.00 % and 68.44 ± 17.42 %, respectively. In test and control groups, KT increased from 2.94 ± 0.77 mm; 2.44 ± 0.81 mm to 5.38 ± 1.67 mm; 4.63 ± 0.81 mm at 6 months, with gains of 2.44 ± 0.90 mm; 2.19 ± 0.00 mm, respectively. At 6 months evaluation, the differences between test and control groups were statistically significant in terms of RH reduction; KT and CAL gain, which were in favor of the test group ($p<0.05$). The study indicated that CAF is a predictable treatment for isolated Miller Class I and II recession defects. The use of PRF membrane with CAF provides superior root coverage with additional benefits of gain in CAL and KT at 6 months postoperatively.

Thamaraiselvan et al. (54) compared the clinical outcomes of CAF alone (control group) and in combination with PRF (test group) in the treatment of 20 patients with 20 single Miller Class I and II gingival recession defects ≥ 2 mm. Clinical parameters assessed included RH, KT, RW, GT, PD and CAL. In test and control groups, RH decreased from 2.30 ± 0.67 mm; 2.20 ± 0.91 mm to 0.70 ± 0.94 mm; 0.90 ± 0.99 mm at 6 months, representing to a MRC of 74.16 ± 28.98 % and 65 ± 44.47 %, respectively. Complete root coverage was achieved in 50 % of the defects at 6 months evaluation both in test and control groups. In test and control groups, KT increased from

2.30 ± 0.82 mm; 2.40 ± 0.69 mm to 2.70 ± 0.67 mm; 2.80 ± 0.91 mm at 6 months, respectively. In test and control groups, RW decreased from 3.40 ± 0.69 mm; 3.50 ± 0.84 mm to 1.50 ± 1.64 mm; 1.40 ± 1.64 mm at 6 months, respectively. In test and control groups, GT increased from 0.95 ± 0.14 mm; 0.93 ± 0.18 mm to 1.25 ± 0.23 mm; 0.96 ± 0.18 mm at 6 months, respectively. At 6 months, there were no statistically significant differences between test and control groups in terms of RH and RW reductions; KT and CAL gains ($p>0.05$); whereas GT increase differ significantly between groups, and this increase was in favor of the test group ($p<0.05$). The authors concluded that CAF was a predictable treatment for isolated Miller Class I and II recession defects. However, the use of PRF membrane with CAF provided no additional advantage in terms of recession coverage except for an increase in GT.

Gupta et al. (55) compared the clinical outcomes and clinical efficacy of CAF alone (control group) and in combination with PRF (test group) in the treatment of 26 patients with 30 single Miller Class I and II gingival recession defects ≥ 2 mm. Clinical parameters assessed included RH, KT, GT, PD and CAL. In test and control groups, RH decreased from 2.80 ± 0.41 mm; 2.47 ± 0.64 mm to 0.27 ± 0.59 mm; 0.40 ± 0.74 mm at 6 months, with reductions of 2.53 ± 0.64 mm; 2.07 ± 0.59 mm, representing to a MRC of 91 ± 19.98 % and 86.60 ± 23.83 %, respectively. Complete root coverage was achieved in 80 % and 11 % of the defects in test and control groups at 6 months, respectively. In test and control groups, KT increased from 5.07 ± 0.46 mm; 5.0 ± 0.66 mm to 6.67 ± 0.49 mm; 6.40 ± 0.51 mm at 6 months, with gains of 1.60 ± 0.63 mm; 1.40 ± 0.51 mm, respectively. In test and control groups, GT increased from 1.33 ± 0.20 mm; 1.31 ± 0.19 mm to 1.40 ± 0.18 mm; 1.35 ± 0.16 mm at 6 months, with gains of 0.07 ± 0.03 mm; 0.04 ± 0.05, respectively. At 6 months, there were no statistically significant differences between test and control groups in terms of RH reduction, KT, GT, and CAL gains ($p>0.05$). The authors concluded that the addition of PRF membrane to CAF did not provide any added advantages in terms of recession coverage in Miller Class I and II recessions.

Aleksic et al. (72) compared the clinical efficacy of CAF in combination with CTG (control group) or PRF (test group) in the treatment of 38 single Miller Class I and II gingival recession defects ≥ 2 mm. Clinical parameters assessed included RH, KT, PD, CAL and Healing Index. In test and control groups, RH decreased from 3.49 ± 0.67 mm; 3.41 ± 0.73 mm to 0.70 ± 0.49 mm; 0.39 ± 0.51 mm at 12 months, with reductions of 2.79 ± 0.41 mm; 3.02 ± 0.28 mm, representing to a MRC of 79.94 % and 88.56 %, respectively. In test and control groups, KT increased from 1.30 ± 0.59 mm; 1.43 ± 0.50 mm to 2.09 ± 0.46 mm; 2.87 ± 0.43 mm at 12 months, with gains of 0.79 ± 0.68 mm; 1.44 ± 0.64 mm, respectively. After 12 months, the differences between test and control groups were not statistically significant in terms of RH reduction, PD change and CAL gain ($p>0.05$). The changes in KT differ significantly between the groups in favor of the test group ($p<0.05$). Additionally, the values of healing index recorded in the first and second week postoperatively were significantly enhanced in the test group ($p<0.05$). The authors concluded that both procedures were effective in solving gingival recession problems. Also, the utilization of the PRF resulted in a decreased postoperative discomfort and advanced tissue healing.

Jankovic et al. (73) compared the clinical outcomes achieved by CAF in combination with CTG (control group) or PRF (test group) in the treatment of 15 patients with single Miller Class I and II gingival recession defects ≥ 3 mm. Clinical parameters assessed included RH, KT, PD, CAL and Healing Index. In test and control groups, RH decreased from 3.51 ± 0.70 mm; 3.45 ± 0.84 mm to 0.68 ± 0.45 mm; 0.38 ± 0.48 mm at 6 months, with reductions of 2.83 ± 0.37 mm; 3.07 ± 0.30 mm, representing to a MRC of 88.68 % ± 10.65 % and 91.96 % ± 15.46 %, respectively. Complete root coverage was 75.85 % and 79.56 % in test and control groups, respectively. In test and control groups, KT increased from 1.32 ± 0.66 mm; 1.41 ± 0.58 mm to 2.20 ± 0.54 mm; 2.85 ± 0.45 mm at 6 months, with gains of 0.88 ± 0.71 mm; 1.44 ± 0.63 mm, respectively. There were no statistically significant differences between test and control groups in terms of RH reduction, PD change and CAL gain ($p>0.05$) whereas KT differ significantly between groups, and this significance was in favor of the test group ($p<0.05$). In addition, healing index recordings in the first and second week postoperatively were significantly superior in the test group ($p<0.05$). Greater gain in KT was obtained in the CAF plus CTG group whereas enhanced wound healing was associated with the CAF plus PRF group.

Uraz et al. (74) compared the clinical efficiency of CAF in combination with CTG (control group) or PRF (test group) in the treatment of 15 patients with 106 multiple Miller Class I and II gingival recession defects ≥ 2 mm. Clinical parameters assessed included RH, KT, RW, PD and CAL. In test and control groups, RH decreased from 4.73 ± 1.30 mm; 3.11 ± 0.80 mm to 1.17 ± 1.47 mm; 0.11 ± 0.27 mm at 6 months, corresponding to a MRC of 95 % and 96.1 %, respectively. Complete root coverage was achieved as 73.3 % and 80 % in test and control groups at 6 months, respectively. In test and control groups, KT increased from 3.45 ± 1.05 mm; 3.93 ± 0.72 mm to 4.63 ± 0.86 mm; 5.11 ± 0.76 mm, respectively. RW decreased from 2.92 ± 0.36 mm; 3.07 ± 0.65 mm to 0.96 ± 0.62 mm; 0.11 ± 0.27 mm at 6 months, in test and control groups, respectively. 6 months after surgery, there were no statistically significant differences between test and control groups in terms of RH and RW reduction, KT and CAL gain (p>0.05). The authors concluded that both treatments were effective and predictable treatment modalities for the management of multiple gingival recessions.

Eren and Atilla (75) compared the clinical efficiency of CAF in combination with CTG (control group) or PRF (test group) in the treatment of 22 patients with 44 single Miller Class I and II gingival recession defects ≥ 2 mm. Clinical parameters assessed included RH, KT, RW, GT, PD and CAL. In test and control groups, RH decreased from 2.67 ± 0.61 mm; 2.61 ± 0.67 mm to 0.18 ± 0.32 mm; 0.16 ± 0.33 mm at 6 months, representing to a MRC of 92.7 % and 94.2 %, respectively. Complete root coverage was 72.7% and 77.3 % in test and control groups, respectively. In test and control groups, KT increased from 2.58 ± 1.37 mm; 2.41 ± 1.20 mm to 3.51 ± 1.28 mm; 3.63 ± 1.43 mm; RW decreased from 3.70 ± 0.60 mm; 3.49 ± 0.67 mm to 0.64 ± 1.17 mm; 0.43 ± 1.08 mm; GT increased from ± 0.18 mm; ± 0.23 mm at baseline to 1.59 ± 0.53 mm; 1.68 ± 0.57 mm at 6 months, respectively. There were no statistically significant differences between test and control groups in terms of RH and RW reduction, KT and GT gain (p>0.05). The study indicated that localized gingival recessions could be successfully treated with CAF plus PRF as well as CAF plus CTG.

Keçeli et al. (76) compared the clinical outcomes of CAF in combination with CTG (control group) and CAF in combination with CTG plus PRF (test group) in the treatment of 40 patients with 40 single Miller Class I and II gingival recession defects ≥ 3 mm. Clinical parameters assessed included RH, KT, RW, GT, PD and CAL. In test and control groups, RH decreased from 3.35 ± 0.43 mm; 3.20 ± 0.34 mm to 0.35 ± 0.52 mm; 0.65 ± 0.59 mm, representing to a MRC of 89.6 % and 79.9 %, respectively. Complete root coverage was 55 % and 35 % in test and control groups, respectively. In test and control groups, KT increased from 3.25 ± 1.17 mm; 2.85 ± 1.03 mm to 4.43 ± 1.48 mm; 3.63 ± 1.37 mm; RW decreased from 3.45 ± 1.04 mm; 2.93 ± 0.80 mm to 0.60 ± 0.94 mm; 0.95 ± 0.84 mm, respectively. Gingival thickness increased from 0.85 ± 0.33 mm; 0.83 ± 0.31 mm to 1.96 ± 0.34 mm; 1.55 ± 0.37 mm in test and control groups, respectively. At 6 months, there were no statistically significant differences between test and control groups in terms of RH and RW reduction, KT and CAL gain, and PD change (p>0.05) whereas GT gain differs significantly between groups, and this significance was in favor of the test group (p<0.05). The authors concluded that the addition of PRF membrane did not improve the outcomes of CAF plus CTG treatment except increasing the GT.

Jankovic et al. (77) compared the clinical efficiency of CAF in combination with EMD (control group) or PRF (test group) in the treatment of 20 patients with single Miller Class I and II gingival recession defects ≥ 3 mm. Clinical parameters assessed included RH, KT, PD and Healing Index. In test and control groups, RH decreased from 4.10 ± 1.05 mm; 3.90 ± 1.0 mm to 1.05 ± 0.45 mm; 0.15 ± 0.65 mm at 12 months, reductions of 3.05 ± 0.76 mm; 2.75 ± 0.61 mm, corresponding to a MRC of 72.1 ± 9.55 % and 70.5 ± 11.76 %, respectively. Complete root coverage was 65 % and 60 % in test and control groups, respectively. In test and control groups, KT increased from 1.45 ± 0.86 mm; 1.30 ± 0.56 mm to 1.62 ± 0.28 mm; 1.90 ± 0.81 mm, with gains of 0.17 ± 0.68 mm; 0.60 ± 0.41 mm, respectively. At 12 months, there were no statistically significant differences between test and control groups in terms of RH reduction and PD change (p>0.05) whereas KT gain differs significantly between the groups, and this significance was in favor of the control group (p<0.05). In addition, healing index recordings in the first week postoperatively was significantly superior in the test group (p<0.05), however in the second week both groups showed a high level of equivalence (p>0.05). The authors concluded that the study did not succeed in demonstrating any clinical advantage of the use of PRF compared to EMD in the coverage of gingival recession with the CAF procedure.

As discussed above, review of the existing literature reveals controversial results for the use of PRF in the treatment of gingival recessions (52-55, 72-77). Results ranged from the significant enhancement of healing to a null effect. Locally delivered platelet concentrates, such as PRF, are supposed to increase the proliferation of connective tissue progenitors to stimulate fibroblast and osteoblast activity and enhance angiogenesis, all of which are fundamental to tissue healing. Platelets also play a role in the host defense mechanism at the wound site by delivering signaling molecules that attract macrophage cells. The antimicrobial activity of platelet concentrates against several bacterial species involved in oral infections was also reported (219). In the recent years, there has been a growing interest in the use of PRF for the treatment of many intraoral clinical conditions, including gingival recessions and the subject warrants further investigation. Therefore, the aim of this randomized controlled clinical study was to evaluate clinical effectiveness of PRF in combination with CAF on defect coverage, esthetics and patient satisfaction compared to CAF alone for the treatment of Miller Class I multiple gingival recessions and to present 6 months results.

3. MATERIALS AND METHODS

3.1. Study Population

Patients seeking treatment at Yeditepe University's Faculty of Dentistry and Dental Hospital for gingival recession defects made up the selected study population, which comprised of 20 patients (10 females and 10 males), with at least 2 sites indicating Miller Class I multiple buccal recession defects ≥3 mm. All the risks and benefits involved in the procedures were explained to the patients prior to signing an informed consent form.

The study was designed as a randomized, parallel and controlled clinical trial. Ten patients were treated by a combination of CAF with PRF, as a test group, and 10 patients were treated by CAF as a control group. Patients were randomly assigned to treatment groups using a coin toss. First, a flip was performed for the purpose of assigning the treatment group. The sides of the coin were assigned to the specific treatment (heads: CAF+PRF, tails: CAF). Subsequently, another flip of the coin was made for the purpose of distributing patients to a group.

3.2. Patient Selection

Patient inclusion criteria used is as follows:

1. Presence of at least two Miller Class I multiple buccal recession defects ≥ 3 mm on maxillary or mandibular incisors, canines or premolars,
2. PD <3 mm,
3. Absence of non-vital teeth, caries, advanced non-caries lesions, occlusal trauma and previous root coverage procedure,
4. When cemento enamel junction (CEJ) is not identifiable, CEJ was determined according to Zucchelli et al. (220) (If the facial CEJ cannot be found, the interdental soft tissue was prodded with a probe to observe the CEJ point angle, where the CEJ intersects with interdental papilla),
5. Non-smoker,
6. Not pregnant,
7. No systemic diseases that could influence the outcome of the therapy.

3.3. Study Design

Each patient received a comprehensive periodontal examination and full diagnostic evaluation including comprehensive full mouth periapical radiographs, study casts, and intraoral photographs. Before surgical procedures commenced, detailed oral hygiene instructions were given, scaling and root planning were performed using ultrasonic devices[1] , and Gracey curettes[2], and occlusal adjustment were performed, if necessary. The patients were instructed to employ a non-traumatic brushing technique (roll) using an ultra-soft toothbrush, in combination with interdental flossing twice daily. Patients were revaluated 8 weeks after the initial therapy and only patients with PI scores ≤1 were included (221). In order to record the clinical measurements of CAL, PD, RH and KT, individual acrylic occlusal stents were prepared for probe positioning. Additionally, gingival thickness and RW were also measured at the baseline and at the 6 monthmark following surgery. The study design as such is explained in Figure 1.

[1] **Piezon® OEM built-in kit**, EMS, Nyon, Switzerland.
[2] **Gracey** SG ¾, $^{5}/_{6}$, $^{7}/_{8}$, **Mini-Five SAS ¾**, Hu-Friedy, Chicago, USA.

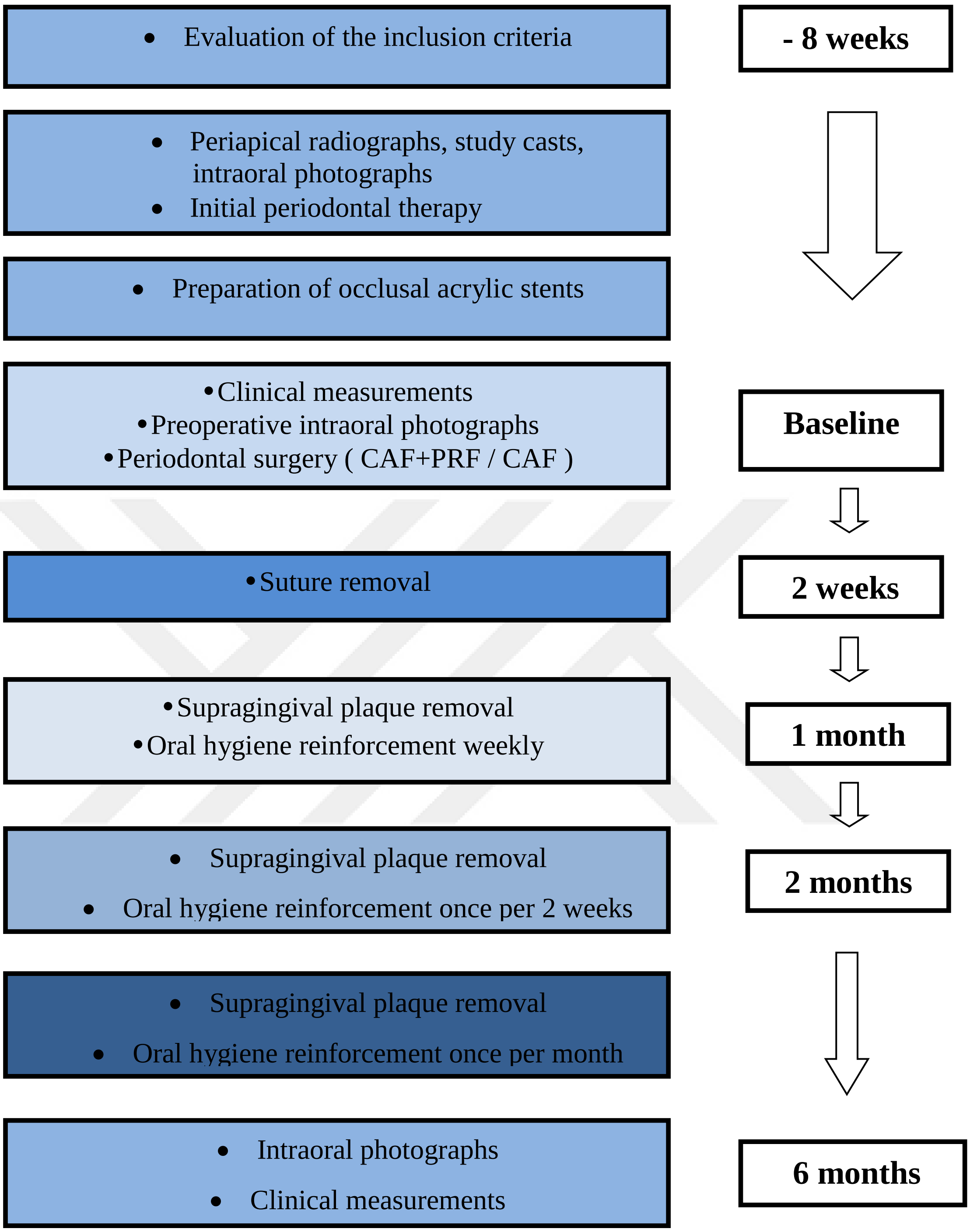


Figure 1. Study Design.

3.4. Clinical Parameters and Measurements

All measurements were performed by the same calibrated examiner at baseline and at 6 months post-surgery. Before the start of the study, intra-examiner reproducibility was tested in 5 patients, not included in the study. The examiner measured at least 6 teeth in every 5 patients, on two occasions at 48-hour intervals. The examiner was accepted as calibrated if measurements at baseline and at 48 hours were similar to the mm at $\geq$90%. Individually prepared acrylic occlusal stents were used and thus served as the constant points in order to align the probe properly and reduce errors associated with probe placement at different time intervals. The occlusal stent was made to cover the occlusal surfaces of all teeth being treated in maxilla and mandibula. It was also extended apically on the buccal and lingual surfaces to cover the coronal third of the teeth. A groove was marked at the midpoint of the related tooth so post-surgical measurements at the same position and angulation as those taken prior to surgery could be recorded. All measurements were taken with a 0.4 mm diameter, 15 mm calibrated periodontal probe[3] and, with the exception of GT, all measurements were rounded to the nearest 1 mm, a digital caliper was used to measure GT.

The following indices and measurements were used:

3.4.1. Plaque index

Teeth were isolated by cotton rolls, and after drying by air syringe, the microbial dental plaque was evaluated by the explorer on 4 tooth surfaces (mesio-buccal, mid-buccal, disto-buccal and mid-palatinal) and scores between 0-3 were given for each point (222).

The scoring system was as follows:

0 – No microbial dental plaque in the gingival area.

1 – A film of microbial dental plaque adhering to the free gingival margin and adjacent area of the tooth, was recognized only by running a probe across the tooth surfaces.

2 – Moderate accumulation of soft deposits within the gingival pocket and on the gingival margin and/or adjacent tooth surfaces that can be seen by the naked eye.

3 – Abundance of soft matter within the gingival pocket and/or on the gingival margin and on the adjacent tooth surface.

[3] **PCP 15 UNC**, Hu-Friedy, Chicago, USA.

3.4.2. Gingival index

The periodontal probe was used to assess the bleeding potential of tissues from 4 tooth surfaces (mesio-buccal papilla, mid-buccal margin, disto-buccal papilla and mid-palatinal margin) and scores between 0-3 were given for each point (223).

Scoring was as follows:

0 – Normal gingiva.

1 – Mild inflammation, slight change in color, slight edema; no bleeding on probing.

2 – Moderate inflammation, redness, edema, and glazing; bleeding on probing.

3 – Severe inflammation, marked redness and edema, ulcerations; tendency to bleed spontaneously.

3.4.3. Bleeding on probing (BoP) (%)

The periodontal probe was used to assess bleeding after probing 4 tooth surfaces (mesio-buccal papilla, mid-buccal margin, disto-buccal papilla and mid- palatinal margin) and scored as either positive (+) or negative (-) bleeding at each point (224).

3.4.4. Probing depth (mm)

The depth of the probing on the recession defect was measured by the periodontal probe at the mid-buccal surface of the related tooth, at the distance between the gingival margin and the bottom of the gingival sulcus (Figure 2).

3.4.5. Clinical attachment level (mm)

Clinical attachment level of the recession defect was measured by the periodontal probe at the mid-buccal surface of the related tooth and it was defined as the distance between the cemento-enamel junction and the bottom of the gingival sulcus (Figure 2).

3.4.6. Recession height (mm)

Recession height was measured by the periodontal probe at the mid-buccal surface of the related tooth at the distance between the cemento-enamel junction and the most apical point of the gingival margin (Figure 2).

3.4.7. Recession width (mm)

Recession width of the defect was measured by the periodontal probe at the horizontal distance from one border of the recession to another in the mesio-distal direction at the level of the cemento-enamel junction (Figure 2).

3.4.8. Keratinized tissue height (mm)

Keratinized tissue height of the recession defect was measured by the periodontal probe at the mid-buccal surface of the related tooth at the distance between the mucogingival junction to the gingival margin (Figure 2).

3.4.9. Gingival thickness (mm)

Gingival thickness was measured at the mid-point location between the gingival margin and mucogingival junction (Figure 2), using an #25 endodontic spreader[4] (Figure 3). Under the local anesthesia, the spreader was pierced perpendiculary to the mucosal surface until a hard surface was felt. The silicone disk stop was then placed in tight contact with the external soft tissue surface. After carefully removing the spreader, penetration depth was measured with a digital caliper[5] at the distance between the tip of the spreader and the inner border of the silicone disk stop (42) (Figure 4).

All measurements were recorded in personal data sheets prepared for the research (Figure 5, 6).

[4] **MANI Endodontic Spreader #25, 25 mm**, Tochigi, Japan.
[5] **SHAN 75 mm Stainless Steel Digital Caliper**, Cincinnati, USA.

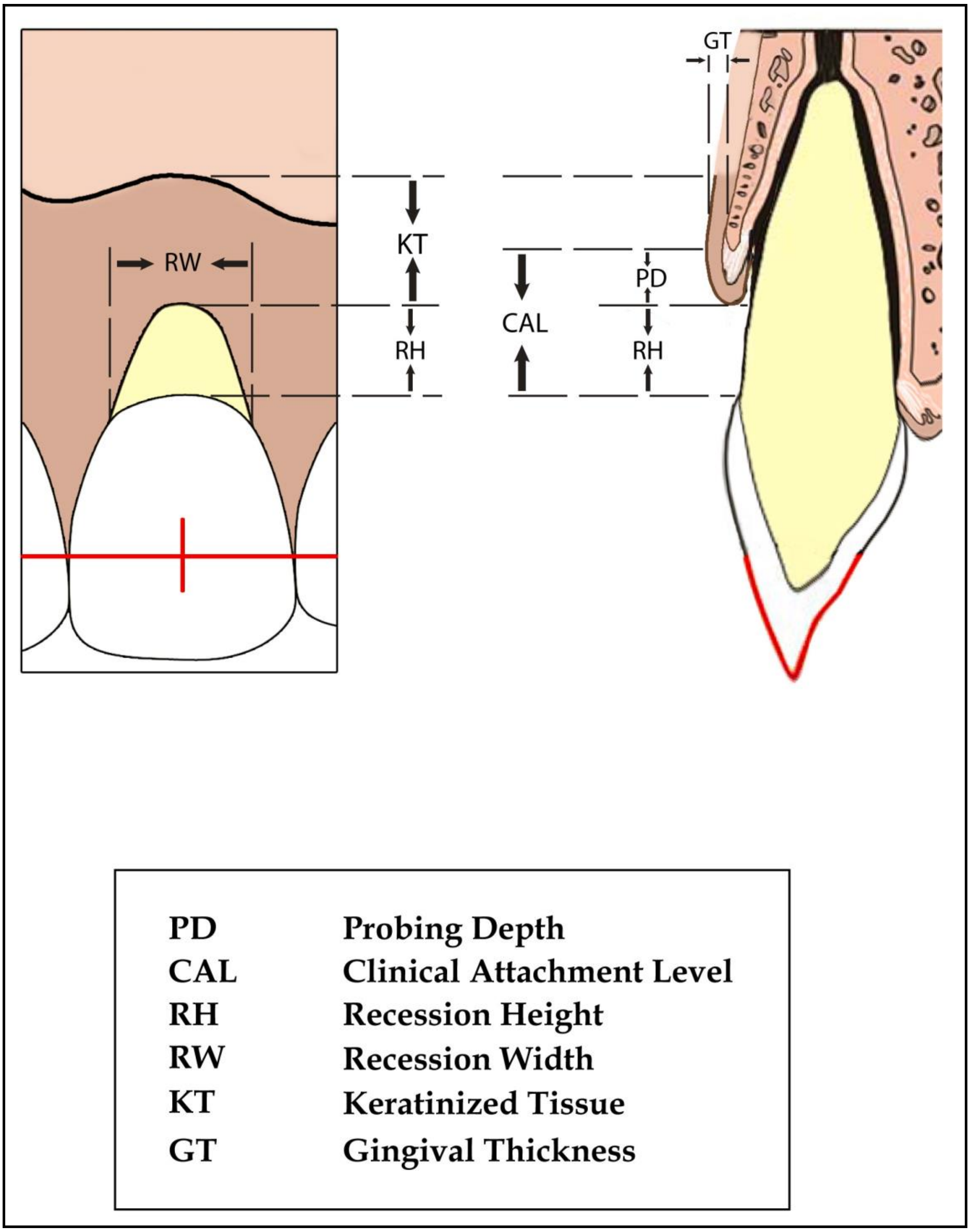


Figure 2. Schematic drawing representing clinical indices and measurements.

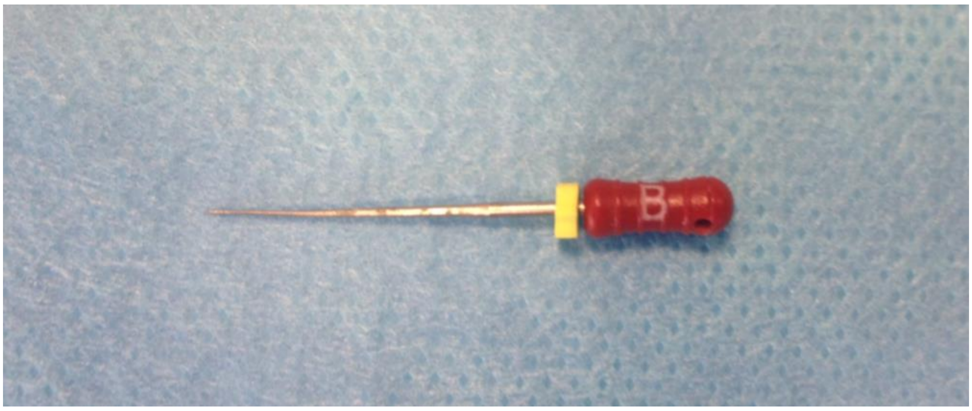
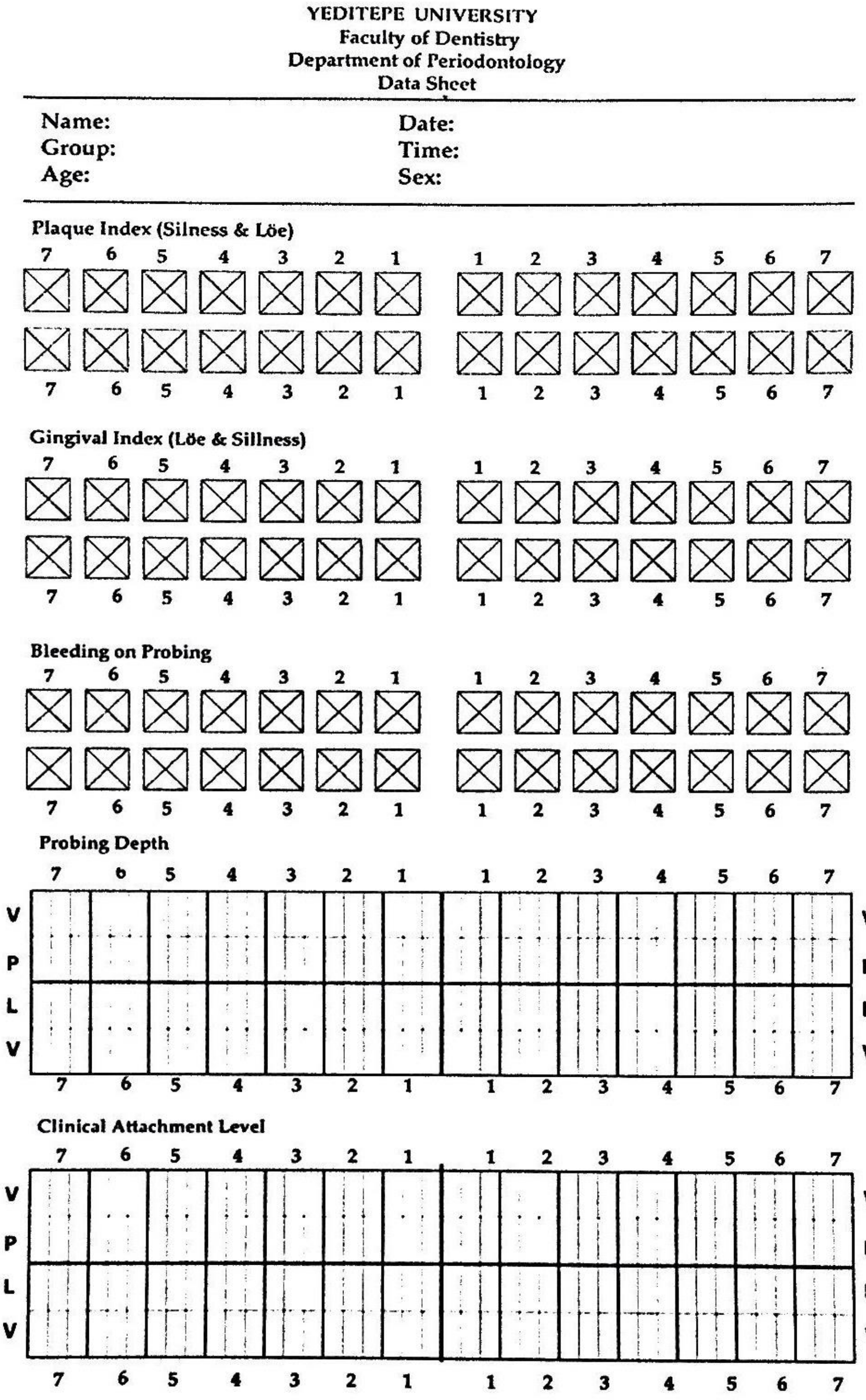


Figure 3. Endodontic spreader.

Figure 4. Stainless steel digital caliper.



YEDITEPE UNIVERSITY
Faculty of Dentistry
Department of Periodontology
Data Sheet

Name: Date:
Group: Time:
Age: Sex:

Plaque Index (Silness & Löe)
7 6 5 4 3 2 1 1 2 3 4 5 6 7
7 6 5 4 3 2 1 1 2 3 4 5 6 7

Gingival Index (Löe & Sillness)
7 6 5 4 3 2 1 1 2 3 4 5 6 7
7 6 5 4 3 2 1 1 2 3 4 5 6 7

Bleeding on Probing
7 6 5 4 3 2 1 1 2 3 4 5 6 7
7 6 5 4 3 2 1 1 2 3 4 5 6 7

Probing Depth
7 6 5 4 3 2 1 1 2 3 4 5 6 7
V P L V
7 6 5 4 3 2 1 1 2 3 4 5 6 7

Clinical Attachment Level
7 6 5 4 3 2 1 1 2 3 4 5 6 7
V P L V
7 6 5 4 3 2 1 1 2 3 4 5 6 7

Figure 5. Data sheet 1

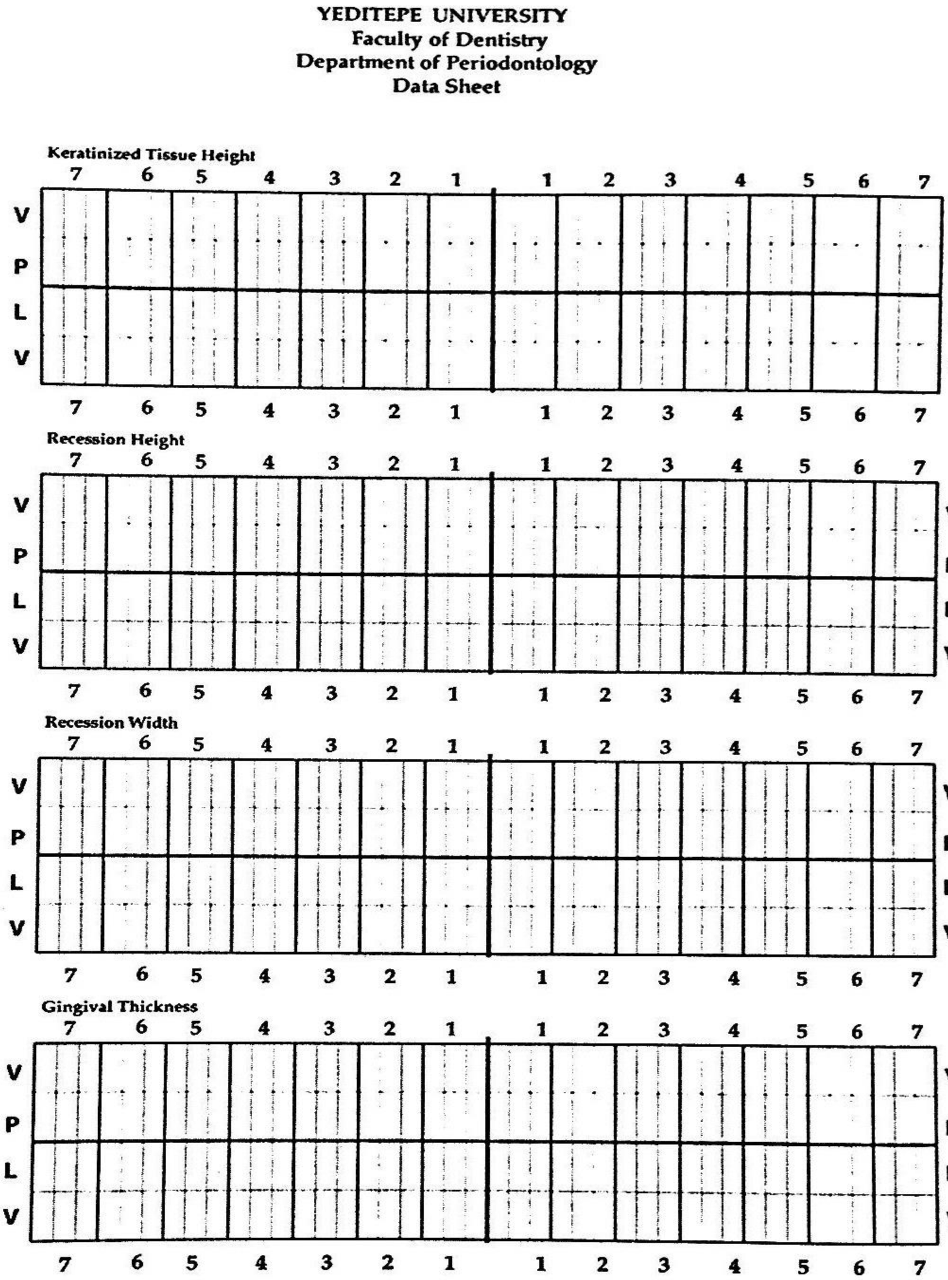


Figure 6. Data sheet 2

3.4.10. Root coverage

Mean root coverage (%) was calculated at patient level as follows:

[(RH baseline – RH 12 months) / RH baseline] x 100%.

Complete root coverage (%) was calculated as the percentage of teeth with defects having complete defect coverage achieved as the gingival margin at the cemento-enamel junction or coronal level.

Percentage of CRC was calculated as follows:

[(Teeth with complete root coverage) / (All treated teeth)] × 100.

3.4.11. Patient satisfaction score

Patients were asked about his/her satisfaction with regard to the folowing patient-centered criteria: root coverage attained, relief from dentinal hypersensitivity, color of gums, shape and contour of gums, surgical procedure in terms of pain during surgery and the discomfort experienced related to the duration of the procedure and handling by the operator, post-surgical pain, swelling, and post-operative complications; and value of the treatment where cost and time invested were concerned (44). A three-point system was utilized to rate patient satisfaction: 3 indicated ‘‘fully satisfied’’; 2 ‘‘satisfied’’; and 1 ‘‘unsatisfied’’.

3.4.12. Root coverage esthetic score

In order to fully assess the esthetic outcomes following root coverage procedures, a root coverage esthetic score was given. The following criteria were evaluated: gingival margin level**,** marginal tissue contour**,** soft tissue texture**,** mucogingival junction alignment as well as gingival color were evaluated without magnification (225). Zero, 3 and 6 points were used for the evaluation of the position of the gingival margin, and scores of either 0 or 1 point were assigned to the other variables (Table 1), with the ideal score being 10. If the final position of gingival margin was equal or apical to the previous recession depth (failure of root coverage procedure), irrespective of color, the presence of scar tissue, marginal tissue contour, or mucogingival junction, or if a partial or total loss of interproximal papilla (black triangle) occurred post-treatment, then 0 points was thus given.

Table 1. RES variables and definitions.

Gingival Margin Level	**0**	Root coverage failure (Gingival margin apical or equal to the baseline recession)
	3	Partial root coverage
	6	CRC
Marginal Tissue Contour	**0**	Irregular gingival margin (Does not follow cemento-enamel junction)
	1	Proper marginal contour/scalloped gingival margin (Follows cemento-enamel junction)
Soft Tissue Texture	**0**	Scar formation and/or keloid like appearance
	1	Absence of scar or keloid formation
Mucogingival Junction Alignment	**0**	Mucogingival junction not aligned with the junction of adjacent teeth
	1	Mucogingival junction aligned with the junction of adjacent teeth
Gingival Color	**0**	Color of tissues varies from gingival colours on adjacent teeth
	1	Normal color and integration in adjacent soft tissues

3.5. Platelet Rich Fibrin Preparation Protocol

Prior to surgery, PRF was prepared as follows: intravenous blood was collected from the antecubital vein in 10-ml glass-coated plastic tubes[6] without anticoagulant and were immediately centrifuged[7] at 3.000 revolutions per minute for 10 minutes (Figure 7). The fibrin clot formed in the middle part of the tube. In the upper portion of the tube acellular plasma appeared, and, the bottom portion consisted red corpuscles. Subsequently, the fibrin clot was removed, and the red blood cells that were attached to it were seperated using a pair of scissors. Then, the clots were placed on a grid in the PRF box[8] and compressed with a cover to create a fibrin membrane (Figure 8).

Figure 7. Blood collection and centrifugation machine.

[6] **VACUETTE 10 ml blood collection tube no additive**, Greiner bio-one, North Carolina, USA.
[7] **Hettich EBA 20 Centrifuge**, Tutlingen, Germany.
[8] **PRF box**, Istanbul, Turkey.

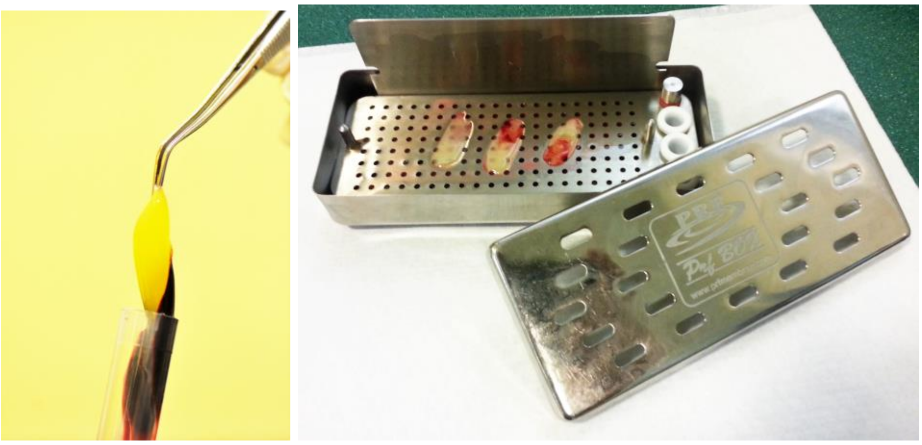


Figure 8. Fibrin clot in the tube and fibrin membranes**.**

3.6. Surgical Procedure

The same operator performed all of the treatments and procedures. After local anesthesia[9] was administered, an intra-sulcular incision using a 15C blade[10] was made at the buccal aspect of the teeth to be treated. Horizontal incisions were made at the level of cementoenamel junction of the interdental papillae, without interfering with the neighboring teeth’s gingival margins. Two vertical incisions were extended at the distal ends of the horizontal incisions across the mucogingival line reaching the alveolar mucosa. A split-full-split thickness flap was elevated to expose at least 3 mm of the marginal bone apical to the dehiscence area, and to allow for a tension-free coronal repositioning of the flap, releasing incisions were made. Also, for better tissue bed vascularization, papillas were deepithelialized. The exposed root surface was then thoroughly planed with hand instruments to obtain a smoother and harder surface and then rinsed with saline solution. In the CAF + PRF group, the PRF was adapted to cover the root surface to the level of cementoenamel junction and extended approximately 3 mm beyond the osseous defect margins. Platelet rich fibrin was sutured

[9] **Ultracain DS Fort 2 ml** , Aventis Pharma Istanbul, Turkey.
[10] **Scalpel Blade 15C**, KLS Martin Group**,** Tuttlingen, Germany.

in using the sling suture technique with 5–0 resorbable polyglyconate monofilament sutures[11]. The flap was coronally positioned at the level of coronal to cementoenamel junction and sutured to completely cover the PRF using the sling suture technique with 5-0 non-resorbable polypropylene monofilament sutures[12]. The releasing incisions were closed with interrupted sutures. Gentle pressure was applied to achieve hemostasis, and a close adaptation of the flap to the underlying surface. In addition, no surgical dressing was used. The surgical procedures for the CAF group turned out to be nearly identical, except for the PRF placement. Clinical photographs were taken to document all aforementioned procedures[13] (Figure 9).

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[11] **Coated Vicryl 5-0 sutures, Ethicon,** Johnson & Johnson, New Jersey, USA.
[12] **Prolene 5-0 sutures, Ethicon,** Johnson & Johnson, New Jersey, USA.
[13] **Kohler Surgical Instruments**, Stockach, Austria.

Figure 9. Surgical instruments.

3.7. Post-Surgical Medication and Care

Post surgical care was directed to the maintenance of wound stability, pain and infection control. In the interest of the patient's wound stability, as well as pain and infection prevention control, post-surgical care was outlined in the form of written and oral post-operative instructions, elaborating on home care and medication dosing. The patients received post-operative systemic antibiotic therapy for a period of 5 days (2x1000 mg, amoxicillin clavulanate/day)[14]. Oral analgesics (550 mg tablets every 8 hours as necessary, naproxen sodium)[15] were also prescribed. Additionally, patients were instructed to avoid brushing and avoid heavy chewing in surgical areas until suture removal. Lastly, patients were instructed to rinse twice daily with a 0,2% chlorhexidine gluconate[16] solution for the next 4 weeks.

[14] **Augmentin BID 1000 mg**; GlaxoSmithKline Pharmaceuticals Istanbul, Turkey.
[15] Apranax Forte Tablets 550 mg; Abdi Ibrahim, Istanbul, Turkey.
[16] **Klorhex Oral Rinse % 0,2;** Drogsan Pharmaceuticals, Istanbul, Turkey.

Sutures were removed after a recovery and healing period of approximately two weeks. All patients were allowed to initiate mechanical plaque control using an ultra soft toothbrush and a roll technique 4 weeks after the operation. The patients were asked to return for a weekly supragingival plaque removal, tooth polishing and oral hygiene reinforcement during the first month, then bi-monthly until the third month, and then, monthly until the study's conclusion. Neither subgingival instrumentation nor probing of the operated areas was performed in the 6 months following. Upon the conclusion of the 6-month evaluation period, all baseline clinical measurements and intraoral photographs were repeated.

3.8. Data Analysis

The statistical analysis was performed using commercially available software[17]. With the exception of CRC, subject-level analysis was performed for each parameter. Mean & standard deviations (mean ± SD) and median values for the clinical parameters were calculated. Data analysis was done for full mouth for PI, GI and BoP, whereas defect site measurements were used for PD, CAL, RH, GT and KT. All the parameters were measured at baseline and at six months. Age- and gender- balanced groups were tested via Student's t-test and Continuity (Yates) correction, respectively. Parameters without normal distribution were evaluated using the Mann Whitney U-test and the Wilcoxon sign test. More specifically, the Wilcoxon sign tests focused on evaluating intragroup differences, and conversely, the Mann-Whitney U tests aimed to evaluate intergroup differences. The primary outcome variable was CRC. Mean root coverage, root coverage esthetics and patient satisfaction and changes in other parameters (RH reduction, KT and GT increase) were considered as secondary outcome variables. For the sample size calculation, RH was used. The power analysis results indicate that, 7 subjects from each group were defined at 80 % statistical power and $\alpha=0.05$ to detect $\Delta=0.66$, standard deviation (SD): 0.39 (47). The value of $p<0.05$ is considered to be the level of significance.

[17] **IBM SPSS Statistics 22**, New York, USA.

4. RESULTS

4.1. Demographic results / Recession location

Twenty patients aged between 21-41 years (mean age of 32.35 ± 6.41) with 49 Miller I buccal multiple gingival recession defects ≥3 mm fulfilling the selection criteria were included in this study. The recessions were located in 25 incisors, and 14 canines 10 premolars. Age and gender of the patients, and recession location are presented in Tables 2 & 3, accordingly.

Table 2. Age and gender distribution of the patients

		CAF + PRF	**CAF**	***p***
Age		33.50 ± 7.57	31.20 ± 5.16	**0.438⁺**
Gender	**Female**	6 (%60)	4 (%40)	**0.655⁺⁺**
	Male	4 (%40)	6 (%60)	

⁺Student's t-test, ⁺⁺Continuity (Yates) Correction, not-significant: $p>0.05$.

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Table 3. Location of the recession defects

CAF + PRF	**Incisors**	**Canines**	**Premolars**
Maxilla	7	5	3
Mandible	6	2	2
CAF	**Incisors**	**Canines**	**Premolars**
Maxilla	8	4	3
Mandible	4	3	2

4.2. Clinical results

All patients completed the study and none of them was excluded from the study. Healing was uneventful in all patients and one representative case from each group was documented in Figures 10 a-f and 11 a-e.

4.2.1. Baseline parameters

No statistically significant differences were observed between the groups at baseline in terms of all evaluated parameters (Table 4, p>0.05).

Table 4. Comparison of baseline parameters of CAF + PRF and CAF groups

	CAF + PRF Mean±SD (Median)	**CAF Mean±SD (Median)**	***+p***
PI	0.48 ± 0.08 (0.48)	0.49 ± 0.05 (0.49)	**0.850**
GI	0.49 ± 0.06 (0.49)	0.51 ± 0.07 (0.48)	**0.596**
BoP (%)	8.70 ± 0.82 (8.5)	8.80 ± 1.03 (9)	**0.749**
PD (mm)	1.18 ± 0.24 (1)	1.10 ± 0.21 (1)	**0.529**
CAL (mm)	4.54 ± 0.30 (4.5)	4.30 ± 0.35 (4.25)	**0.099**
RH (mm)	3.20 ± 0.26 (3)	3.36 ± 0.34 (3.5)	**0.240**
RW (mm)	3.39 ± 0.73 (3.5)	3.15 ± 0.24 (3)	**0.127**
GT (mm)	0.78 ± 0.06 (0.8)	0.73 ± 0.07 (0.7)	**0.121**
KT (mm)	2.95 ± 1.01 (2.5)	2.60 ± 0.77 (2.25)	**0.393**

+Mann Whitney U test, not-significant: p>0.05.

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4.2.2. Plaque index

The mean & standard deviations and median values of PI scores at baseline and after 6 months, and intra-group comparisons are presented in Table 5. Intra-group comparisons revealed statistically significant differences in PI values in both groups at 6 months ($p<0.05$). Inter-group difference was not statistically significant for PI scores at 6 months ($p>0.05$).

Table 5. Mean & standard deviations and median values of PI at baseline and 6 months after treatment, and intra- and inter-group comparisons

		CAF+PRF Mean±SD (Median)	CAF Mean±SD (Median)	^{+}p
PI	**Baseline**	0.48 ± 0.08 (0.48)	0.49 ± 0.05 (0.49)	**0.850**
	6 months	0.40 ± 0.06 (0.42)	0.41 ± 0.06 (0.41)	**0.879**
	^{++}p	**0.005**	**0.005**	

$^{+}$Mann Whitney U test, $^{++}$ Wilcoxon Sign Test, significant: $p<0.05$, not-significant: $p>0.05$.

4.2.3. Gingival index

The mean & standard deviations and median values of GI scores at baseline and after 6 months, and intra-group comparisons are presented in Table 6. Intra-group comparisons revealed statistically significant differences in GI values in both groups at 6 months ($p<0.05$). Inter-group difference was not statistically significant for GI values at 6 months ($p>0.05$).

Table 6. Mean & standard deviations and median values of GI at baseline and 6 months after treatment, and intra- and inter-group comparisons

		CAF+PRF Mean±SD (Median)	CAF Mean±SD (Median)	^{+}p
GI	**Baseline**	0.49 ± 0.06 (0.49)	0.51 ± 0.07 (0.48)	**0.596**
	6 months	0.44 ± 0.06 (0.44)	0.46 ± 0.07 (0.42)	**0.621**
	^{++}p	**0.005**	**0.005**	

$^{+}$Mann Whitney U test, $^{++}$Wilcoxon Sign Test, significant: $p<0.05$, not-significant: $p>0.05$.

4.2.4. Bleeding on probing

The mean & standard deviations and median values of BoP scores at baseline and after 6 months, and intra-group comparisons are presented in Table 7. Intra-group comparisons revealed statistically significant differences in BoP values in both groups at 6 months ($p<0.05$). Inter-group difference was not statistically significant for BoP scores at 6 months ($p>0.05$).

Table 7. Mean & standard deviations and median values of BoP at baseline and 6 months after treatment, and intra- and inter-group comparisons

		CAF+PRF Mean±SD (Median)	CAF Mean±SD (Median)	^{+}p
BoP (%)	**Baseline**	8.70 ± 0.82 (8.5)	8.80 ± 1.03 (9)	**0.749**
	6 months	7.40 ± 0.70 (7)	7.75 ± 1.36 (8)	**0.236**
	^{++}p	**0.004**	**0.011**	

$^{+}$Mann Whitney U test, $^{++}$Wilcoxon Sign Test, significant: $p<0.05$, not-significant: $p>0.05$.

4.2.5. Probing depth

The mean & standard deviations and median values of PD measurements at baseline and after 6 months, and intra-group comparisons are presented in Table 8. There was a statistically significant increase in PD measurements in test and control groups at 6 months (Table 8, $p<0.05$). Inter-group difference was not statistically significant for PD at 6 months ($p>0.05$).

Table 8. Mean & standard deviations and median values of PD at baseline and 6 months after treatment, and intra- and inter-group comparisons

		CAF+PRF Mean±SD (Median)	CAF Mean±SD (Median)	^{+}p
PD (mm)	**Baseline**	1.18 ± 0.24 (1)	1.10 ± 0.21 (1)	**0.529**
	6 months	1.95 ± 0.37 (2)	1.65 ± 0.24 (1.5)	**0.017**
	^{++}p	**0.006**	**0.002**	

$^{+}$Mann Whitney U test, $^{++}$Wilcoxon Sign Test, significant: $p<0.05$, not-significant: $p>0.05$.

4.2.6. Clinical attachment level

The mean & standard deviations and median values of CAL scores at baseline and after 6 months, and intra-group comparisons are presented in Table 9. There was a statistically significant decrease in CAL scores, revealing attachment gain, in both groups at 6 months (p<0.05). Inter-group difference was not statistically significant for CAL at 6 months (p>0.05).

Table 9. Mean & standard deviations and median values of CAL measurement at baseline and 6 months after treatment, and intra- and inter-group comparisons

		CAF+PRF Mean±SD (Median)	**CAF Mean±SD (Median)**	^{+}p
CAL (mm)	**Baseline**	4.54 ± 0.30 (4.5)	4.30 ± 0.35 (4.25)	**0.099**
	6 months	2.80 ± 0.35 (3)	2.35 ± 0.85 (2.25)	**0.247**
	^{++}p	**0.005**	**0.005**	

$^{+}$Mann Whitney U test, $^{++}$Wilcoxon Sign Test, significant: p<0.05, not-significant: p>0.05.

4.2.7. Recession height

The mean & standard deviations and median values of RH scores at baseline and after 6 months, and intra-group comparisons are presented in Table 10. Intra-group comparisons for RH reduction was statistically significant in both groups at 6 months (p<0.05). Recession height reduction was 2.5 ± 0.53 mm and 2.51 ± 0.33 mm in CAF + PRF and CAF groups at 6 months, respectively (Table 14, p>0.05). Inter-group comparison for RH values was not statistically significant in both groups at 6 months (p>0.05).

Table 10. Mean & standard deviations and median values of RH measurement at baseline and 6 months after treatment, and intra- and inter-group comparisons

		CAF+PRF Mean±SD (Median)	**CAF Mean±SD (Median)**	^{+}p
RH (mm)	**Baseline**	3.20 ± 0.26 (3)	3.36 ± 0.34 (3.5)	**0.240**
	6 months	0.70 ± 0.67 (1)	0.85 ± 0.24 (1)	**0.519**
	^{++}p	**0.005**	**0.004**	

$^{+}$Mann Whitney U test, $^{++}$Wilcoxon sign test, significant: p<0.05, not-significant: p>0.05.

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4.2.8. Recession width (mm)

The mean & standard deviations and median values of RW at baseline and after 6 months, and intra-group comparisons are presented in Table 11. Intra-group comparisons revealed statistically significant differences for RW in both groups at 6 months ($p<0.05$). Recession width reduction was 2.09 ± 0.69 mm and 2.00 ± 0.91 mm in CAF + PRF and CAF groups at 6 months, respectively (Table 14, $p>0.05$). Inter-group comparison for RW value was not statistically significant between groups at 6 months ($p>0.05$).

Table 11. Mean & standard deviations and median values of RW measurements at baseline and 6 months after treatment, and intra- and inter-group comparisons

		CAF+PRF Mean±SD (Median)	**CAF Mean±SD (Median)**	^{+}p
RW (mm)	**Baseline**	3.39 ± 0.73 (3.5)	3.15 ± 0.24 (3)	**0.127**
	6 months	1.25 ± 0.49 (1)	1.15 ± 1.03 (1.5)	**0.938**
	^{++}p	**0.005**	**0.005**	

$^{+}$Mann Whitney U test, $^{++}$Wilcoxon sign test, significant: $p<0.05$, not-significant: $p>0.05$.

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4.2.9. Keratinized tissue height

The mean & standard deviations and median values of KT scores at baseline and after 6 months, and intra-group comparisons are presented in Table 12. Intra-group comparisons revealed statistically significant differences for KT in both groups at 6 months ($p<0.05$). Keratinized tissue gain was 0,65 ± 0,47 mm and 0,63 ± 0,40 mm in CAF + PRF and CAF groups, at 6 months, respectively (Table 14, $p>0.05$). Inter-group comparison for KT gain was not statistically significant between groups at 6 months ($p>0.05$).

Table 12. Mean & standard deviations and median values of KT measurements at baseline and 6 months after treatment, and intra- and inter-group comparisons

		CAF+PRF Mean±SD (Median)	CAF Mean±SD (Median)	^{+}p
KT (mm)	Baseline	2.95 ± 1.01 (2.5)	2.60 ± 0.77 (2.25)	**0.393**
	6 months	3.60 ± 1.29 (3.5)	3.23 ± 1.00 (3)	**0.529**
	^{++}p	**0.011**	**0.011**	

$^{+}$Mann Whitney U test, $^{++}$Wilcoxon sign test, significant: $p<0.05$, not-significant: $p>0.05$.

4.2.10. Gingival thickness

The mean & standard deviations and median values of GT scores at baseline and after 6 months, and intra-group comparisons are presented in Table 13. Intra-group comparisons revealed statistically significant increase in GT values in both groups at 6 months ($p<0.05$). Gingival thickness increase was 0.53 ± 0.05 mm and 0.07± 0.05 mm in CAF + PRF and CAF groups at 6 months, respectively (Table 14, $p<0.05$). Inter-group comparison for GT value was statistically significant in favor of the CAF+PRF group at 6 months ($p<0.05$).

Table 13. Mean & standard deviations and median values of GT measurements of the recession defect at baseline and 6 months after treatment, and intra- and inter-group comparisons

		CAF+PRF Mean±SD (Median)	CAF Mean±SD (Median)	^{+}p
GT (mm)	Baseline	0.78 ± 0.06 (0.8)	0.73 ± 0.07 (0.7)	**0.121**
	6 months	1.31 ± 0.07 (0.8)	0.80 ± 0.08 (0.8)	**0.001**
	^{++}p	**0.004**	**0.008**	

$^{+}$Mann Whitney U test, $^{++}$Wilcoxon sign test, significant: $p<0.05$, not-significant: $p>0.05$.

4.2.11. Inter-group comparison of changes related to all clinical parameters

Inter-group comparisons of all measurements are presented in Table 14. Inter-group differences were found to be statistically significant for GT gain ($p<0.05$), and insignificant for PI, GI, BoP, PD change, RH reduction, CAL and KT gain at 6 months ($p>0.05$).

Table 14. Inter-group comparisons of PI, GI, BoP, PD change, RH and RW reduction, CAL, KT and GT gain measurements at 6 months after treatment

	CAF+PRF Mean±SD (Median)	**CAF Mean±SD (Median)**	**^{+}p**
PI	0.08 ± 0.03 (0.07)	0.08 ± 0.04 (0.08)	**0.732**
GI	0.05 ± 0.01 (0.05)	0.05 ± 0.02 (0.05)	**0.396**
BoP (%)	1.30 ± 0.48 (1)	1.05 ± 0.69 (1)	**0.464**
PD Change (mm)	0.78 ± 0.34 (1)	0.57 ± 0.19 (1)	**0.086**
CAL Gain (mm)	1.74 ± 0.24 (1.71)	1.95 ± 0.69 (2)	**0.436**
RH Reduction (mm)	2.50 ± 0.53 (2.5)	2.51 ± 0.33 (2.5)	**0.905**
RW Reduction (mm)	2.09 ± 0.69 (2.5)	2.00 ± 0.91 (1.8)	**0.908**
GT Gain (mm)	0.53 ± 0.05 (0.5)	0.07 ± 0.05 (0.1)	**0.001**
KT Gain (mm)	0.65 ± 0.47 (0.50)	0.63 ± 0.40 (0.63)	**1.000**

$^{+}$Mann Whitney U test, significant: $p<0.05$, not-significant: $p>0.05$.

4.2.12. Root coverage (%)

Mean root coverage, and CRC in both groups are presented in Tables 15 & 16. Mean root coverage was 79.02 % in CAF + PRF group, whereas this value was 74.63 % in CAF group. At 6 months, CRC was obtained in 9 out of 25 recessions with CAF + PRF approach, whereas in 8 out of 24 recessions with CAF. Inter-group comparison for MRC and CRC was not statistically significant between groups (Tables 15&16, p>0.05).

Table 15. Inter-group comparison of mean root coverage

	Mean Root Coverage (%) Mean ± SD (Median)	***+p***
CAF+PRF	79.02 ± 19.88 (71.4)	**0.700**
CAF	74.63 ± 8.05 (71.8)	

+Mann Whitney U test, not-significant: p>0.05.

Table 16. Inter-group comparison of complete root coverage at tooth level

	Complete Root Coverage (%)	***+p***
CAF+PRF	36.0±48.99 (0)	**0.846**
CAF	33.33±48.15 (0)	

+Mann Whitney U test, not-significant: p>0.05.

4.2.13. Patient satisfaction score

Inter-group comparisons of overall patient satisfaction scores at 6 months after treatment are presented in Table 17. Inter-group comparison revealed that overall patient satisfaction was similar in both groups (p>0.05).

Table 17. Inter-group comparison of patient satisfaction scores.

	Patient Satisfaction Score	+*p*
CAF+PRF	18.00 ± 2.83 (18)	**0.938**
CAF	18.00 ± 2.87 (18)	

+Mann Whitney U test, not-significant (p>0.05)

4.2.14. Root coverage esthetic score

The results of RES in both groups are presented in Table 18. Inter-group comparison for RES was not statistically significant between the groups at 6 months (p>0.05).

Table 18. Inter-group comparison of RES

	Root Coverage Esthetic Score	+*p*
CAF+PRF	7.20 ± 1.75 (7)	**1.000**
CAF	7.00 ± 0.00 (7)	

+Mann Whitney U test, not-significant (p>0.05)

Figure 10a. Preoperative clinical view.

Figure 10b. Flap design and incisions.

Figure 10c. Flap elevation.

Figure 10d. PRF stabilization with 5-0 resorbable sutures.

Figure 10e. Suturing with 5-0 non-resorbable sutures.

Figure 10f. Postoperative view at 6 months.

Figure 11a. Preoperative clinical view.

Figure 11b. Flap design and incisions.

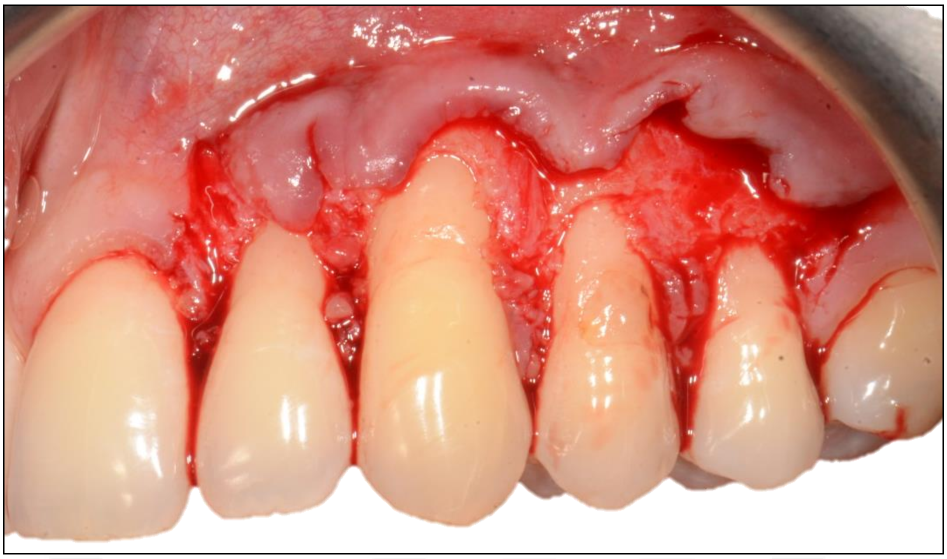

Figure 11c. Flap elevation.

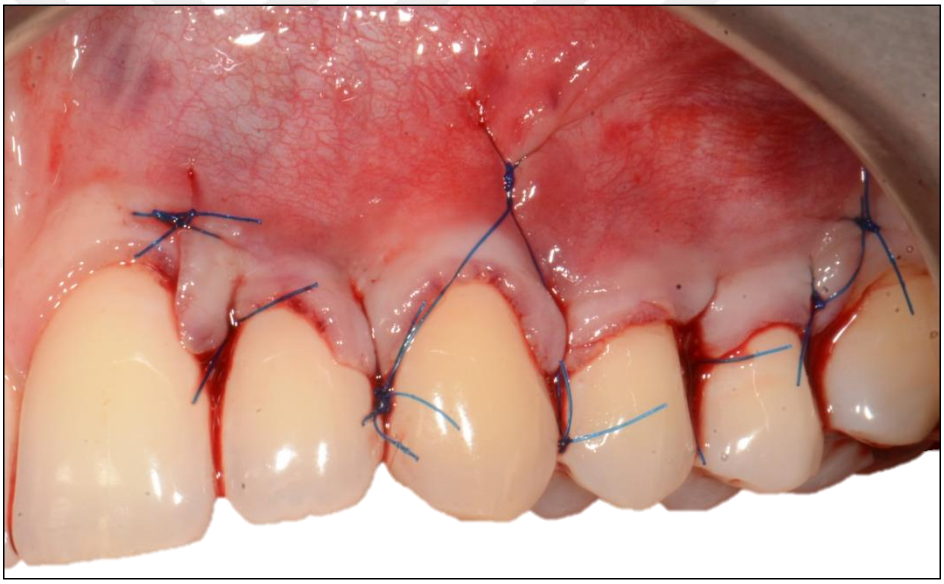

Figure 11d. Suturing with 5-0 non-resorbable sutures.

Figure 11e. Postoperative view at 6 months.

5. DISCUSSION

The aim of this randomized controlled clinical study was to evaluate the clinical effectiveness of PRF in combination with CAF on root coverage, esthetics and patient satisfaction compared to CAF alone for the treatment of Miller Class I multiple gingival recessions. The mean root coverage obtained at 6 months was 79.02 ± 19.88 % and 74.63 ± 8.05 % in CAF + PRF and CAF groups, respectively ($p>0.05$). Complete root coverage was achieved 36% of the teeth (9 out of 25 sites) for the CAF + PRF group, while it occurred 33.3% of the teeth (8 out of 24 sites) for the CAF group. Both procedures provided clinical improvements for the patients in terms of RH reduction, KT and GT gain, MRC, CRC, patient satisfaction and RES compared to baseline ($p<0.05$). Gingival thickness was significantly higher in CAF + PRF group compared to CAF alone ($p<0.05$). From a clinical point of view, better soft tissue healing was observed in the CAF + PRF group.

Multiple adjacent recession-type defects present a further challenge because at least two recessions must be treated at a single surgical session to minimize patient discomfort. The most reported techniques are CAF, modified CAF and tunnel technique (59, 60). In patients with esthetic requests, CAF is recommended when there is adequate keratinized tissue apical to the recession defect. In CAF approach the soft tissue utilized to cover root exposure is similar to that originally present at the buccal aspect of the tooth with the recession defect and thus the esthetic result is satisfactory (190). Recent evidence indicates CAF and its modifications as an effective surgical procedure for the treatment of multiple gingival recessions in terms of MRC and long-term stability (4-7). Therefore, in this study CAF was chosen as a technique to treat multiple gingival recessions and combined with PRF considering the claimed benefits induced by the material for soft tissue wound healing in the treatment of Miller Class I recession defects.

In this study, we aim to compare CAF + PRF with CAF. It has been suggested that additional grafting may provide a scaffold to support wound healing with increasing the thickness of the wound area (60, 157). Mainly, CTG is the choice of the clinicians. However, CTG harvesting may lead to patient morbidity associated with the second surgical site, prolonged surgical time, and possibility of postoperative complications such as palatal necrosis, pain and bleeding (16, 70, 71, 190). Also, in the treatment of multiple gingival recessions, to obtain adequate donor tissue might be a major problem for the clinician. Additionally, anatomical limitations such as thin or shallow palate may be a problem. Platelet rich fibrin has been used in this study to overcome above mentioned problems of CTG and also to utilize the proposed effects of PRF, such as stimulation of fibroblast activity and enhancement of angiogenesis, on soft tissue wound healing (52-55).

Several reviews demonstrated that all periodontal plastic surgical procedures can treat Miller Class I and II multiple recessions predictably (58-62). However, the best treatment outcomes in terms of MRC and CRC is provided in the presence of keratinized tissue apical to the root exposure with an adequate height and thickness (8, 123, 190). Thus, only Miller Class I multiple recessions were included in the study.

It has been reported that a 6-month postoperative measurement period is sufficient to evaluate the stability of gingival margin after CAF procedure due to the existence of a stable tissue relationship even after the first post-operative month (204). Furthermore, according to systematic reviews (141, 195), 6 months evaluation period for root coverage was considered adequate to provide soft tissue stability and maturation. Therefore, in this study 6 months was chosen as the evaluation period.

In this study simple randomization was used. This technique maintains complete randomness of the assignment of a person to a particular group (226). However, randomization results could be problematic in small sample size clinical trials, resulting in an unequal number of participants among groups. In this study, the patients were consecutively treated by random allocation to the two treatment groups until 10 patients belonging either of the groups were operated. Then, the rest of the patients were allocated to the other group in order to achieve groups of equal size.

Systematic reviews revealed CAF as an effective surgical approach for the treatment of multiple gingival recessions in terms of MRC, CRC, esthetics and long-term stability (60-62). Optimum root coverage, good color blending with adjacent soft tissues, and aesthetic results can be obtained by using this surgical procedure (4-15). A recent systematic review (125) about CAF procedure in the treatment of single recession defects reported ranges from 34.2 % (29) to 96.6 % (11) for MRC and from 7.7 % (42,43) to 88.88 % (11) for CRC with evaluation periods of 6 (11, 42), 12 (29, 42) and 24 months (43), respectively. Another recent systematic review (60) about CAF procedure in the treatment of multiple recession defects reported ranges from 23.8 % (40, 46) to 77.7 % (7) for CRC and mean value 82.65 % (7, 40) for MRC with evaluation periods of 6 (46), 12 (7) and 24 (40) months, respectively. In this study, MRC obtained at 6 months was 74.63 ± 8.05 % in the CAF group (p>0.05). Complete root coverage was achieved 33.3% of the teeth (8 out of 24 sites). The results obtained in this study in terms of MRC and CRC are in accordance with the results of the previous studies concerning multiple recessions with CAF alone procedure.

When CAF + PRF technique was considered, limited data is available for multiple recessions (52, 74). In single recessions, MRC was in the range of 72.1 % (77) to 100 % (53) and CRC was in the range of 50 % (54) to 80 % (55) with evaluation periods of 6 (55, 73, 75, 76) and 12 months (72, 77). In multiple recessions, MRC was in the range of 80.7 % (52) to 95 % (74) and CRC was in the range of 52.23 % (52) to 73.3 % (74) with evaluation periods of 6 months (52, 74). These studies reported successful defect coverage after CAF + PRF application in the treatment of multiple gingival recessions (52, 74). In this study, MRC obtained at 6 months was 79.02 ± 19.88 % in CAF+PRF group (p>0.05). Complete defect coverage was achieved 36% of the teeth (9 out of 25 sites). The results obtained in this study are in accordance with the results of the previous studies with CAF + PRF combination concerning multiple recessions in terms of MRC (54, 77).

When we look at the comparative data of CAF to CAF + PRF approach controversial results exist in the literature (52-55). The studies rarely considered multiple gingival recessions (52, 74). Padma et al. (53) treated and 30 single Miller Class I and II bilateral gingival recessions in 15 patients with CAF + PRF and CAF alone. Mean root coverage was 100.00 ± 0.00 % and 68.44 ± 17.42 % in the CAF + PRF and CAF groups at 6 months evaluation, respectively. Thamaraiselvan et al. (54) treated 20 single Miller Class I and II gingival recessions with CAF + PRF and CAF alone in 20 patients. Mean root coverage was 74.16 ± 28.98 %; 65 ± 44.47 % and CRC was 50 % in the CAF + PRF and CAF groups at 6 months evaluation, respectively. Gupta et al. (55) treated 30 single Miller I and II gingival recessions with CAF + PRF and CAF alone in 26 patients. At 6 months, MRC and CRC were 91 ± 19.98 %; 86.60 ± 23.83 % and 80 %; 11 % in the CAF + PRF and CAF groups, respectively. Aroca et al. (52) treated 67 Miller Class I and II multiple gingival recessions with CAF alone and CAF + PRF in 20 patients. After 6 months, MRC and CRC were 80.7 % ± 14.7 %; 91.5 % ± 11.4 % and 52.23 %; 74.62 % in the CAF + PRF and CAF groups, respectively. Padma et al.’s study (53) concluded that the use of PRF membrane with CAF provides superior root coverage with additional benefits of gain in CAL and KT at 6 months postoperatively. On the other hand other studies considering single and multiple recessions concluded that the use of PRF membrane with CAF provided no significant advantage in terms of recession coverage except for an increase in GT (52, 54, 55). In this study, when a comparison was performed between CAF + PRF to CAF, similar clinical outcomes were achieved with above mentioned studies. Although a significant difference was not achieved between the groups in terms of root coverage, enhanced soft tissue healing in terms of color and tissue texture was observed in the PRF group. Platelet rich fibrin contains plethora of cytokines involved in the wound healing process that have the potential to greatly enhance soft tissue healing. It has been reported that the intrinsic incorporation of cytokines within the fibrin mesh allows for their progressive release over time as the network of fibrin disintegrates. In addition, the PRF membrane acts like fibrin bandage, serving as a matrix to accelerate the healing of wound edges (227). All these statements might explain the early wound maturation and early clinical esthetic result of the periodontal soft tissues.

Recession height is the main parameter considered in the evaluation of MRC and CRC. In the present study, the mean baseline RH in CAF + PRF and CAF groups were 3.2 ± 0.26 mm and 3.36 ± 0.34 mm, respectively. Intra-group comparisons revealed statistically significant differences for RH reduction, at 6 months after surgery ($p<0.05$). Recession height reductions were 2.5 ± 0.53 mm and 2.51 ± 0.33 mm in the CAF + PRF and CAF groups, respectively. When the mean baseline RH ≥ 3 mm, RH reductions for CAF procedure were reported in a range from 2 mm (30) to 3.89 mm in single and multiple recessions (56) (26, 30, 39, 56). For CAF + PRF group reported RH reduction range was from 1.60 mm (54) to 3.56 mm in single and multiple recessions (74) (52-55, 72-75, 77). The findings of this study in terms of RH reduction is in accordance with the previous studies in the literature.

The number of defects, their location and depth guide the surgical design, being one design with (trapezoidal type) and the other without vertical releasing incisions (envelope type) in the treatment of multiple recession defects (152). Zucchelli et al. (7) compared two different CAF approaches: the flap with vertical releasing incisions (control group) and the envelope type flap (test group) in the treatment of 32 patients with 92 maxillary Miller Class I and II multiple defects ≥ 1 mm. At 12 months evaluation, both techniques were equally effective in providing a consistent reduction in the baseline RH and gain in CAL, but with statistically greater probability of CRC with envelope type of CAF. In the study of Uraz et al. (74), trapezoidal type of CAF was used and represented a MRC and CRC of 95 % and 73.3 % in the CAF + PRF group, respectively, whereas, in the study of Aroca et al. (52), envelope type of CAF was used and resulted with a MRC and CRC of 80.7 ± 14.7 % and 52.23 % in the CAF + PRF group, respectively. Although it is directly impossible to compare these two studies; from a clinical point of view, in the study in which trapezoidal type of CAF was used, better MRC and CRC were achieved (74). In this study, CAF technique was applied with vertical incisions. Trapezoidal CAF design was used to reduce flap tension and provide more coronal repositioning of the flap. Even though it has been suggested that better clinical outcomes can be achieved due to improved vascularization in envelope type of CAF (7, 228, 229), there is not enough evidence to avoid vertical incisions (230). Furthermore, it has been reported that the main blood supply of the gingiva is directed from vestibule to gingival margin might providing that more blood vessels, nutrients and source cells can provide better integration of the graft material into the host's tissues (231).

The clinicians have used chemical root-surface conditioning by variety of agents in order to decontaminate the root surface to achieve better results. The aim is to expose the collagenous matrix of dentin and cementum. Although in animal studies, it has been reported that chemical agents used for root decontamination enhance attachment by connective tissue ingrowth, in human studies, no clinical advantages were observed (190). A recent systematic review suggested that the root should be mechanically debrided to allow a decontaminated smooth surface and stated that the use of chemical conditioning has not demonstrated an additional clinical value (152). Therefore, in this study root surface biomodification was not applied, but root surfaces debrided carefully with curette.

Gingival thickness is considered to be an important parameter in the achievement of CRC (155,157,158). Baldi et al. (157) proposed ≥ 0.8 mm as the critical flap thickness when the expected clinical outcome is CRC, whereas tissue with less thickness is more prone to additional recession and may require a graft. Also, Ahmedbeyli et al. (47) showed significant positive correlation between GT and defect coverage. When GT ≥ 1.3 mm, higher percentage of CRC was achieved (47). In the present study, baseline GT values were close to ≥ 0.8 mm threshold level that reported by Baldi et al. (157), and GT increase was 0.53 ± 0.05 mm, from 0.78 ± 0.06 mm to 1.31 ± 0.07 mm in CAF + PRF group; and 0.07 ± 0.05 mm from 0.73 ± 0.07 mm to 0.8 ± 0.08 mm in CAF group, with significant difference between the groups which was in favor of the CAF + PRF group ($p<0.05$). Previous studies in the literature reported GT gain for CAF + PRF approach in a range from 0.07 mm (55) to 0.3 mm (52, 54) with inital GT from 0.95 mm (54) to 1.33 mm (55) (52, 54, 55, 75) and in a range from 0.05 mm (232) to 0.24 mm (42) with initial thickness from 0.75 mm (41) to 1.27 mm (17) (17, 41, 42, 232) for CAF approach, respectively. Our results are in accordance with these studies in regard to CAF group, whereas show superior GT gain in comparison to other CAF + PRF groups. This difference can be explained by the discrepancies in the measurement methods of GT. In the studies of Aroca et al. (52), Thamaraiselvan et al. (54), Gupta et al. (55) and Eren & Atilla (75), GT was measured 3 mm (52, 54, 55) and 2 mm (75) below the gingival margin at the attached gingiva or alveolar mucosa, respectively, whereas in our study, GT was measured at the middle of the apico-coronal width of keratinized tissue. Furthermore PRF preparation differed between the studies. Aroca et al. (233), after centrifugation, placed PRF over a dry gauze and stored the gauze in a refrigerator at 4°C until used which might lead to dehydration of the PRF membrane. In this study, PRF preparation protocol recommended by the promoter/ manufacturer of the technique, followed carefully.

In the present study, KT increase was 0.65 ± 0.47 mm, from 2.95 ± 1.01 mm to 3.60 ± 1.29 mm in CAF + PRF group; and 0.63 ± 0.40 mm from 2.60 ± 0.77 mm to 3.23 ± 1.00 mm in CAF group, without statistically significant difference between the groups ($p>0.05$). These findings are in accordance with the previous studies in the literature reported KT gains for CAF + PRF group in a range from -0.24 mm (52) to 2.44 mm (53) (52-55, 72-75, 77) and in a range from -0.48 mm (52) to 1.2 mm (16) for CAF group, respectively. Mechanism of KT increase after CAF + PRF procedure is not clear. The increase in KT can be explained as a result of a tissue manifestation of the proliferation of gingival or periodontal fibroblasts by the influence of the growth factors from the platelets entrapped in the fibrin mesh (73, 75). On the other hand, KT increase after CAF could be explained as the tendency for the mucogingival junction line to regain its ‘‘genetically determined’’ original position after repositioning, or the capability of the connective tissue, deriving from the periodontal ligament, to participate in the healing processes taking place at the dento-gingival interface (234).

In the present study, baseline PD in CAF + PRF and CAF group was 1.18 ± 0.24 mm and 1.10 ± 0.21 mm, respectively. Probing depth increase was 0.78 ± 0.34 mm in CAF + PRF group and 0.57 ± 0.19 mm in CAF group, without statistically significant difference between the groups ($p>0.05$). In this study, 1.74 ± 0.24 mm and 1.95 ± 0.69 mm attachment gain was obtained in CAF + PRF and CAF groups, respectively, without statistically significant difference between the groups (p>0.05). These findings are in accordance with the previous studies in the literature, reporting attachment gain from 1.50 mm to 3.93 mm for CAF + PRF and CAF groups (29, 52-56, 72-75).

A previous study has indicated that maxillary sites might respond better than the mandibular sites (74). Width of keratinized tissue, difficulty of achieving the same degree of flap release and passive coronal positioning, the difference in the thickness of gingiva of maxilla and mandible might be considered as potential factors in the difference between jaws. In the present study CAF + PRF group consisted of 15 maxillary and 10 mandibular teeth, whereas CAF group consisted of 15 maxillary and 9 mandibular teeth. The teeth are distributed homogenously between the groups.

In the present study, esthetic outcome of the treatments was evaluated with RES system, because just the achievement of CRC cannot be considered as full success without aesthetic appearance (225). Level and tissue contour of the gingival margin, texture of the soft tissue, mucogingival line alignment and color of the gingiva were evaluated by the RES system. In the present study, the mean RES in CAF + PRF and CAF groups were 7.20 ± 1.75 and 7.00 ± 0.00, respectively, without statistically significant difference between the groups (p>0.05). We questioned all patients about their satisfaction with regard to the following patient-centered criteria: root coverage; dentinal hypersensitivity; color, shape and contour of gums; pain, discomfort and handling during surgery; post surgical pain, swelling and complications; cost effectiveness in terms of time and money spent for the surgery (44). Satisfaction was assessed using a three-point rating scale: fully satisfied (3 points); satisfied (2 points); and unsatisfied (1 point). Overall patient satisfactions for CAF + PRF and CAF groups were 18.00 ± 2.83 and 18.00 ± 2.87, respectively, and there was no statistically significant difference between the groups (p>0.05). Up to now, there is no published study evaluating RES and patient satisfaction score after CAF + PRF approach. Therefore, it is impossible to compare the results of CAF + PRF approach with the literature. On the other hand, in recent years, a couple of studies concerning CAF approach evaluated the patient related outcomes, since patient feedback should be recognized as a legitimate method of evaluating periodontal plastic surgical procedures (47). The RES score of CAF group of this study is in accordance with the esthetic outcomes of previous clinical trials that reported mean RES with a range between 7.30 (235) and 7.43 (56) for multiple recessions treated with CAF.

Within the limits of this study, it can be concluded that both CAF + PRF and CAF procedures were successful in root coverage of multiple Miller Class I gingival recessions ≥ 3 mm. From a clinical point of view, the CAF + PRF procedure resulted in better early soft tissue healing. Tissue thickness significantly increased with the use of PRF membrane. Further studies will be valuable to reach a conclusion about how tissue thickness affects root coverage stability (no change, further recession, creeping attachment) with greater follow-up times. Platelet rich fibrin might be an alternative to different grafting materials for the treatment of multiple gingival recessions; however, to present insight to the subject, more randomized controlled studies are required.

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Oral &Poster Presentations Presented in International Congresses

1) In vitro evaluation of the effects of diferrent Er:YAG laser tips on the root surface roughness: A SEM Analysis

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2) Clinical Evaluation of Coronally Advanced Flap With or Without Platelet Rich Fibrin for the Treatmanet of Multiple Gingival Recessions

   CED-IADR-2015 Oral Presentation, Antalya, Turkey