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COMPARATIVE EVALUATION OF SECOND-GENERATION PLATELET-RICH FIBRIN (PRF) AND CONNECTIVE TISSUE GRAFT (CTG) IN THE MANAGEMENT OF LOCALIZED MILLER CLASS I AND II GINGIVAL RECESSIONS: A CASE SERIES

ЕФЕКТИВНОСТА НА ВТОРАТА ГЕНЕРАЦИЈА ТРОМБОЦИТНО-ЗБОГАТЕН ФИБРИН PRF ВО ТРЕТМАНОТ НА ЛОКАЛИЗИРАНИТЕ ПОЕДИНЕЧНИ ГИНГИВАЛНИ РЕЦЕСИИ MILLERIИ II ВО ОДНОС НА СУБЕПИТЕЛИЈАЛЕН СВРЗНОТКИВЕН ГРАФТ SCTG (АНАЛИЗА НА СЛУЧАИ)

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Abstract

The mucogingival surgical modality SCTG + CAF (subepithelial connective tissue graft (SCTG) + coronally advanced flap (CAF)) in the treatment of Miller Class I and II gingival recessions is considered the “gold standard” technique for predictable and complete root coverage of gingival defects, with long-term clinical stability of the achieved results. The aim of this study is to evaluate the clinical efficacy of the CAF + PRF combined technique in the treatment of localized single Miller Class I and II gingival recessions in 10 patients, by comparing periodontal clinical parameters measured preoperatively and one month postoperatively, versus results obtained with the CAF + CTG (SCTG) modality in another 10 patients with the same type of recession, over the same time period. **Material and method:** Ten patients were admitted to the Clinic “St. Panteleimon” – Skopje, Department of Oral Surgery, for surgical treatment of localized single Miller Class I and II gingival recessions. Half of the patients were treated with the CAF + PRF technique, while the other half were treated with the CAF + CTG (SCTG) modality. One day preoperatively, periodontal clinical parameters were measured, including vertical gingival recession (RD/VGR), probing pocket depth (PPD/PD), clinical attachment level (CAL), keratinized gingival width (KTW/KMW), and gingival thickness (GT), all measured in millimeters, as well as gingival biotype in all 10 patients. Following mucogingival surgical procedures (CAF + PRF in five patients and CAF + CTG/SCTG in five patients), the same periodontal clinical parameters were recorded one month postoperatively in all patients. These values were then compared with the preoperative measurements both between the groups and within each group over time. **Results:** An insignificant reduction in PPD and CAL, as well as a slight, clinically minor increase in KTW, was observed when comparing measurements taken one day preoperatively and one month postoperatively between the two groups. Similarly, no statistically significant changes in these parameters were observed within the same group over the same time periods. A statistically significant increase in the RD/VR parameter ($Z = 1.984$; $p = 0.0472$) was observed in the SCTG + CAF group one month postoperatively compared with the PRF + CAF group, while other comparisons of this parameter between and within groups were not statistically significant. Regarding the GT parameter, a statistically significant change ($Z = 2.507$; $p = 0.0122$) was observed in the PRF + CAF group when comparing baseline and one-month postoperative values within the same group. However, no statistically significant differences in GT were observed between the two groups at either time point. Changes in gingival biotype from thin to thick were observed only in the PRF + CAF group one month postoperatively in 2 patients (40%). **Conclusion:** Therefore, PRF as a second generation of autologous concentrate is not only an adjuvant and/or replacement of the SCTG- "gold standard" in the treatment of Miller I and II, but is also a superior alternative in the surgical treatment of this type of superficial mucogingival defects.

Keywords: PRF, platelet concentrates, CAF, Miller I and II, gingival recessions, mucogingival surgery.

Апстракт

Мукогингивалниот хируршки модалитет SCTG + CAF (субепителијален сврзно-ткивен графт (SCTG) + коронарно позициониран флап (CAF)) во третманот на Miller Class I и II гингивални рецесии се смета за „златен стандард", односно техника за предвидливо и за комплетно коренско покривање на гингивалните дефекти, со долгорочна клиничка стабилност на постигнатите резултати. Целта на овој труд е евалуација и компарација на клиничката ефикасност на комбинираната техника CAF + PRF во однос на техниката SCTG + CAF, во третманот на локализирани поединечни Miller Class I и II гингивални рецесии, преку споредба на вредностите на пародонталните клинички параметри мерени предоперативно и 1 месец постоперативно. **Материјал и метод:** Во оваа кохортна студија се вклучени 10 испитаници од двата пола, поделени во 2 групи. Првата, контролна група од 5 испитаници беше третирана со хируршкиот модалитет SCTG + CAF, додека кај втората, тест/експериментална група од 5 испитаници беше изведен PRF + CAF оперативниот модус при третман на Miller Class I и II рецесии. Студијата е изведена на Клиниката за орална хирургија при ЈЗУ-УСКЦ "Св. Пантелејмон" – Скопје. Предоперативно беа извршени мерења на следниве пародонтални клинички параметри: вертикална димензија на гингивална рецесија (RD/VGR), длабочина на пародонтален џеб (PPD/PD), клиничко ниво на припоена гингива (CAL), ширина на кератинизирана гингива (KTW/KMW) и дебелина на гингива (GT), сите мерени во mm, како и определување на гингивалниот биотип. Како хируршки пристап беше применет терапискиот модалитет CAF (coronally advanced flap) за третман на гингивалниот дефект. Еден месец постоперативно повторно беа измерени истите клинички пародонтални параметри, и нивните вредности беа споредени со предоперативните мерења. **Резултати:** При мерењата изведени еден ден предоперативно и еден месец постоперативно беа забележани несигнификантна редукција на вредностите на PPD и CAL, како и незначајна промена на вредностите на KTW, како помеѓу двете групи, така и при интрагрупна споредба во истите временски интервали. Еден месец по интервенцијата, групата SCTG + CAF имаше статистички сигнификантно повисока вредност на RD/VR (Z = 1,984; p = 0,0472) споредено со групата PRF + CAF, додека другите резултати добиени од овој параметар, компарирани интра- и интергрупно, беа статистички несигнификантни. Што се однесува до параметарот GT, статистички значајна промена на вредноста (Z = 2,507; p = 0,0122) беше забележана кај пациентите третирани со модалитетот PRF + CAF, при интрагрупна споредба помеѓу еден ден предоперативно и еден месец постоперативно, што укажува на значајно зголемување на дебелината на гингивата кај PRF-оперативниот модус. При компарацијата помеѓу двете групи во истите временски интервали, не беа пронајдени статистички сигнификантни промени на вредностите на GT-параметарот. Промена на гингивалниот биотип од тенок во дебел беше забележана само во групата PRF + CAF, еден месец постоперативно, кај 2 пациенти (40%). **Заклучок:** PRF, како втора генерација на автологни тромбоцитни концентрати, не само што претставува адјувант и/или алтернатива на SCTG – „златниот стандард" во третманот на MillerClassI и II рецесии, туку претставува и потенцијално супериорна алтернатива во хируршкиот третман на овој тип плитки мукогингивални дефекти. **Клучни зборови:** PRF, тромбоцитни концентрати, CAF, MillerClassI и II, гингивални рецесии, мукогингивална хирургија.

Introduction

Approximately 90% of the world population up to 60 years of age hasat least one tooth with recession up to 1mm. The distribution of recessions greater than 3mm is about 40% of the entire population[1].Gingival recession is defined as theapical dislocation of the marginal gingiva towards the cemento-enamel junction-CEJ[2,3] associated with subsequent exposure of the root surfaces, root caries, hypersensitivity, plaque accumulation, and aesthetic compromise[4]. The etiology is complex; it includes traumatic occlusion, deficient or improper oral hygiene (e.g., grough tooth brushing), older prosthetic constructions or dental fillings (with inadequate marginal closure), as well as a high-inserted upper or lower labial frenulum, or a shallow vestibule, caused by muscle attachments andstrong muscle traction[5]. Malocclusions and malpositioned teeth, as orthodontic anomalies, and the peiod following treatment with fixed appliances, are conditions that presentanatomical challenge to the mucogingival complex as part of the periodontal apparatus, and these, combined with the thin biotype of the gingiva, are also etiological causes contributing to gingival recession[6]. The most common clinical manifestation of recession is the loss of vestibular/palatal "attachment loss"[7,8,9].The principles of modern aesthetic mucogingival surgery using autologous grafts (SCTG or PRF) are based on complete and predictable coverage of exposed root surfaces[10], the establishment of homeostasis of the mucogingival complex, regeneration of the lost attachment, including the formation of new cementum through the insertion of connective tissue fibers, and regeneration of the alveolar bone[11]. The most widely used and most commonly used surgical technique is the coronally advanced flap (CAF). The CAF is a simple "pedicle" flap that provides excellent root coverage in the treatment of Miller Class I and Class II gingival recessions[12, 13, 14]. The current "gold standard" or technique of choice is the use of CAF and SCTG, with a predictability of root coverage of 73-96% and graft stability for up to 20 years[15,16,17,18].The reported percentage of predictable root coverage achieved with CAF and PRF ranges from 75 to 91%[19].

In modern regenerative mucogingival surgery, the focus on the application of the second generation of autologous platelet concentrates is increasingly being emphasized. These autologous blood derivatives are divided into fourcategories/classes (according to the content of leukocytes and fibrin): P-PRP (Pure Platelet Rich Plasma); L-PRP (Leukocyte Platelet Pure Plasma), P-PRF(Pure Platelet-Rich Fibrin) and L-PRF (Leukocyte Platelet-Rich Fibrin)[20]. On the other hand, these fourclasses are divided into threegenerations of platelet concentrates[21].

PRF(platelet-rich fibrin; thrombocyte-enriched fibrin) represents the second generation of autologous platelet concentrates (APCs) embeddedinto a fibrin matrix. The

founder of the second generation ATCs, PRF, is Dr. Choukroun, who introcused it in 2001, and for the first time they were described by Dohan et al.[22]. In addition to the conventional Choukroun protocol, modifications have been developed overthe last two decades, conditioned by the aforementioned protocol variations. These new modalities are as follows:

A-PRF (Choukroun, 2004) - the protocol is characterized by a lower centrifugation speed and a longer centrifugation time (1300rpm/8min) in sterile, ordinary glass-coated vacuum collectiontubes (A-PRF).

I-PRF (Choukroun, 2004) (injectible platelet-rich fibrin) is prepared by centrifugation at 700 rpm for 3min-plastic tubes without any coating[23,24].

Microscopically, PRF consists of a three-dimensional (3D) fibrin network compoesed of thin, elastic, mature, and densely polymerized fibrin fibers, in which a multitude of cells, predominantly platelets, as well as concentrates of growth factors and cytokines are trapped. The physiological (natural) polymerization of PRF allows for enhanced trapping of circulating cytokines, which are released only when the 3D fibrin matrix is remodeled, due to the slow, prolonged, and controlled release of growth factors for a period of up to 28 days[25]. This 3D fibrin network, in addition to stimulating the activity of the trapped regulatory cytokines, also enables the adhesion of new blood vessels. Therefore, PRF can be considered as an ideal biomaterial for tissue engineering: it contains a network that behaves like a three-dimensional matrix, viable cells for tissue population as well as molecules that stimulate repair[26]. In addition to the fact that platelet-rich fibrin concentrate (PRF) contains platelets, leukocytes, and circulating stem cells, it is also a reservoir of a large number of slow-releasing growth factors (released over 7, 10, 21 to 28 days), cytokines, and matrix glycoproteins (thrombospondin-1) that influence the regeneration process of soft and hard tissues, stimulating neoangiogenesis and fibroblast/osteoblast migration.

Material and Methods

This prospective cohort study was performed at the Clinic of Oral Surgery and Implantology, University Surgical Clinic "St. Panteleimon", Skopje, the Laboratory of the Faculty of Dentistry, Ss. Cyril and Methodius University in Skopje (UKIM), as well as the Institute of Pathological Anatomy, Faculty of Medicine, Skopje.

Material

This study included 20 subjects (10 men and 10 women) indicated for mucogingival surgical correction of isolated gingival recession: 10 subjects in the test group (CAF+PRF) and 10 subjects in the control group (CAF+SCTG).

Group I: CAF + second-generation platelet-rich fibrin (A-PRF and I-PRF) (Choukroun et al., 2004)

Group II: CAF + subepithelial connective tissue graft (SCTG)

The inclusion criteria for the study group were: age 18–60 years, absence of acute diseases, systemically healthy patients (ASA I and II, American Society of Anesthesiologists), patients with localized, single, unilateral or bilateral Miller Class I and Class II gingival recessions on any teeth in both jaws, patients with an identifiable cemento-enamel junction, and subjects who understood the nature of the intervention and were able to attend subsequent follow-up examinations.

The general (systemic) exclusion criteria for members of the study group were as follows: patients receiving anticoagulant therapy, smokers, individuals with substance use disorders, patients with coagulopathies, cardiovascular diseases, hepatic disorders, malignancies, those undergoing chemotherapy, immunodeficiency conditions, and pregnant or lactating women.

The local exclusion criteria were as follows: patients with bad habits and unsatisfactory oral hygiene, mobile teeth, non-vital teeth, local signs of infection (bleeding, redness, pain, swelling), presence of restorative materials in the area to be treated, gingival thickness (GT) $\leq$ 0.8 mm, keratinized gingival width (KTW) $\leq$ 2 mm, and insufficient palatal tissue thickness $\leq$ 2.5 mm (for participants in the control group).

All patients signed an Informed Consent Form and completed a questionnaire, in accordance with the Declaration of Helsinki (1998/2008, revised). Preoperative preparation (initial therapy) included mechanical decontamination/debridement, scaling and root planing, elimination of premature contacts (traumatic occlusion) and other bad habits etiologically associated with recession. The teeth were cleaned with an abrasive paste and then polished. Patients were instructed on proper oral hygiene maintenance.

Before the surgical intervention, patients rinsed their mouths with 10 mL of 0.05% cetylpyridinium chloride. The antibiotic protocol included the administration of metronidazole 400 mg tablets (1 tablet three times daily), initiated 3 days before the intervention and continued for an additional 7 days. Instructions were given regarding postoperative oral hygiene, including a liquid and soft diet during the first week and rinsing with 0.05% cetylpyridinium chloride (3 times daily for 1 minute) for 14 days. The teeth in the surgical field were cleaned with cotton pellets, gently removing soft dental plaque while avoiding brushing until the sutures were removed after 3 weeks. Brushing with an ultra-soft toothbrush was recommended after the

first month. Non-steroidal anti-inflammatory drugs (NSAIDs) were prescribed for pain control, as well as vitamin C (1000 mg/day) and vitamin D3 (1000 IU/day, once daily) for 4–6 months.

Method

Surgical protocol:

The design of the CAF (coronally advanced flap) consists of sulcular incisions that merge with horizontal incisions in the area of the adjacent interdental papillae. The mesial and distal horizontal incisions start from the bases of the anatomical papillae of the adjacent teeth up to the CEJ of the tooth with recession, and their positioning from the tip of the papillae to the marginal gingiva of the affected tooth is equal to the sum of RD + 1 mm, without violating the integrity of the marginal edge of the adjacent teeth (method of de Sanctis & Zucchelli[27,28]). These horizontal incisions are connected with two oblique vertical incisions that start at the corners of the adjacent teeth and continue slightly divergently towards the alveolar mucosa of the vestibular fornix, crossing the mucogingival junction, resulting in a coronal-apical trapezoidal partial-thickness flap (Figures 1 and 2).

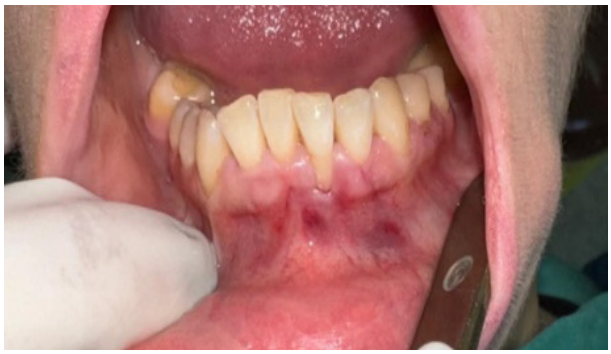

Figure 1

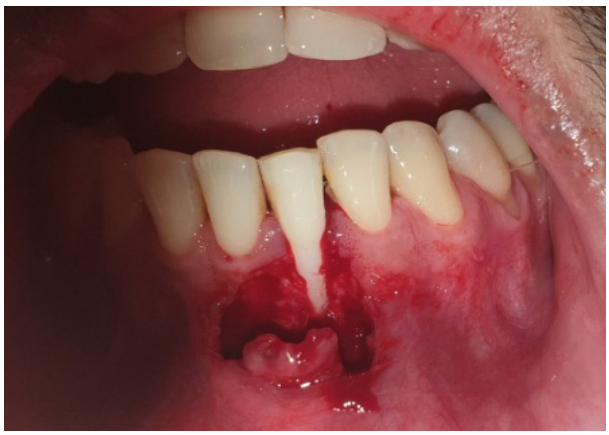

Figure 2

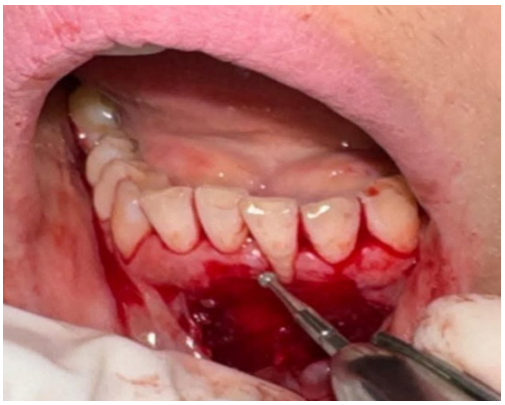

Figure 3

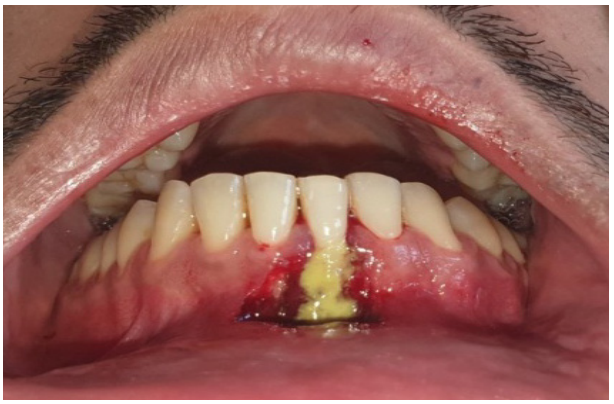

Figure 4

The exposed root surface is mechanically debrided using Gracey curettes, and then refined with a diamond bur. The root surface is conditioned with 24% EDTA for 2 minutes, and subsequently treated with a concentrated solution of doxycycline for 2 minutes (Figures 3 and 4).

The SCTG autograft is harvested after application of anesthesia (3% mepivacaine [Scandonest]) from the palatal side of the patient using a No. 15 scalpel blade. SCTG can be harvested with 1, 2, or 3 incisions or as a FGG with 4 incisions, which must then be de-epithelialized (Figures

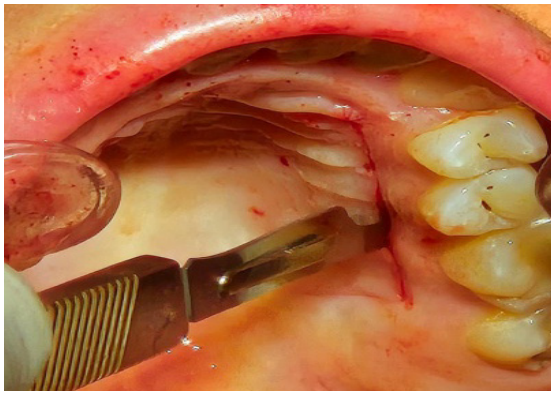

Figure 5

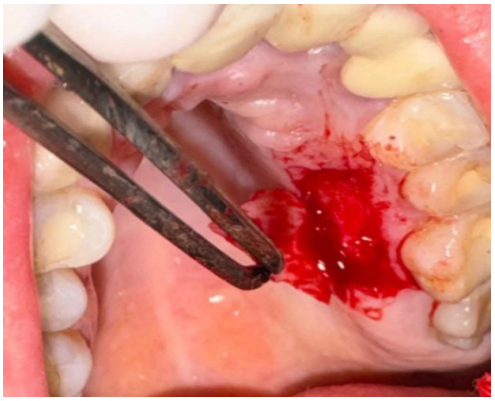

Figure 6

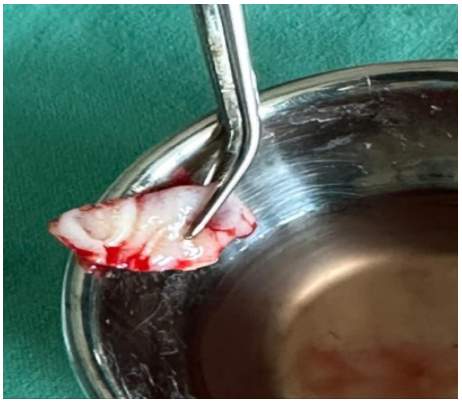

Figure 7

5,6,7). "W"-sutures are placed at the donor site using a locking technique (Figure 8). The autograft is fixed with absorbable Vicryl 5-0 sutures using a horizontal mattress suture technique for the adjacent soft tissue in the apical direction, and vertical mattress sutures for the de-epithelialized surgical papillae.

The surgical manipulation of the A-PRF membrane involves several stages. By venipuncture, 20 mL of venous blood is collected from the antecubital vein using a Vacutainer system into two sterile, glass-coated vacuum

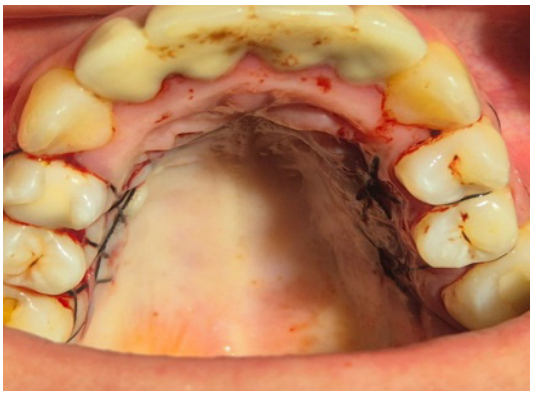

Figure 8

Figure 9

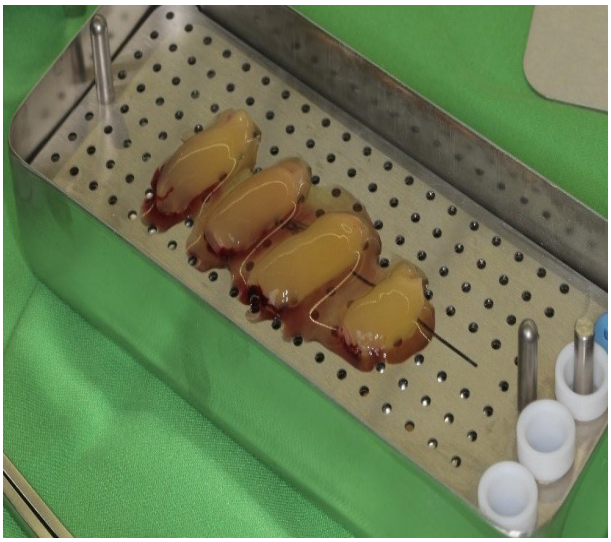

Figure 10

tubes (A-PRF), without anticoagulants or citrate. The entire manipulation should be rapid, and immediately after blood collection, the tubes are centrifuged according to the protocol of Dr. Choukroun from 2004, which is characterized by a lower centrifugation speed but a longer centrifugation time (1300 rpm for 8 minutes), in a specially designed centrifuge (BIOBASE LC-H4K, Biobase, Jinan, Shandong, China). After centrifugation, the tubes are placed on a laboratory rack and then left to stand for 5 minutes, covered with sterile gauze. With anatomical tweezers, the two fibrin clots are removed from the tubes and then placed in the PRF box for membrane preparation. The membranes can be placed coronally up to 1 mm coronal to the CEJ and, due

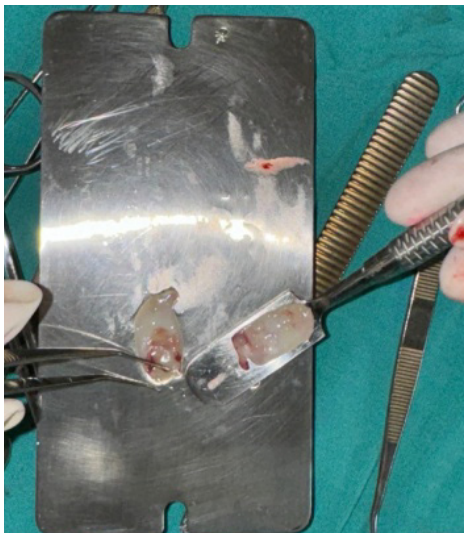

Figure 11

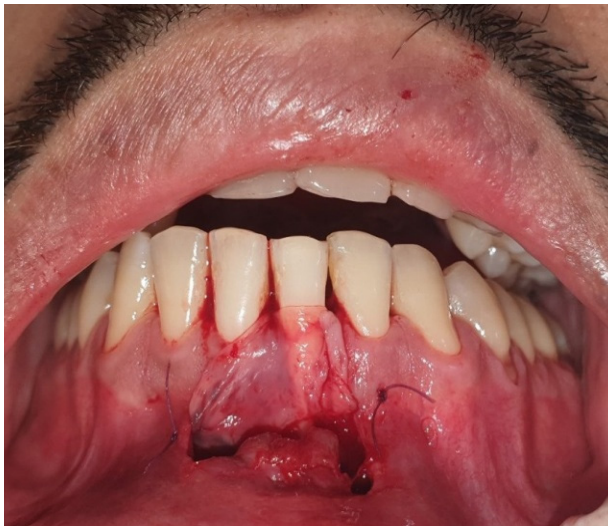

Figure 12

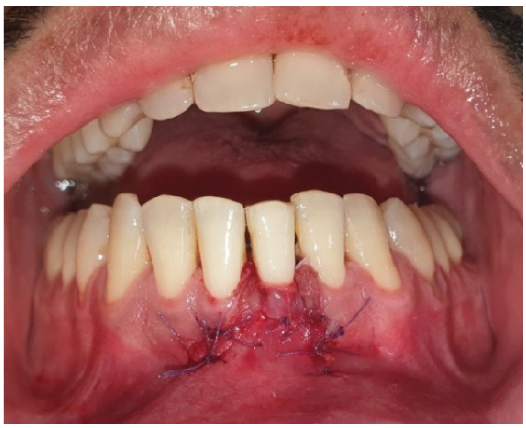

Figure 13

Figure 12

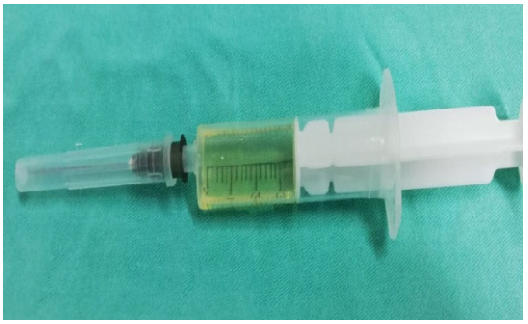

Figure 14

Figure 15

to their adhesive properties, they are not sutured but gently adapted under the mesiodistal borders of the recipient site (Figure 12).

The repositioning and suturing of the flap over both autologous graft variants is identical. The flap is positioned coronally and its marginal edge should end at the enamel, i.e. approximately 1 mm coronal to the cementoenamel junction (CEJ). The flap is sutured with non-absorbable polypropylene (5-0) suture using a horizontal sling suture technique as well as individual interrupted sutures for the adjacent soft tissue and previously de-epithelialized interdental papillae (Figure 13). Gentle pressure is applied for 3 minutes to minimize the thickness of the blood clot.

Injectable platelet-rich fibrin (I-PRF) is obtained by centrifuging 20 mL of venous blood according to the protocol of Dr. Choukroun (2004) at 700 rpm for 3 minutes in specially designed plastic tubes without any coating (I-PRF tubes). After centrifugation of both I-PRF tubes, a light yellow supernatant is observed in the upper part, which is aspirated and used as an injectable form of platelet concentrate. The remaining I-PRF is gently used to rinse the entire surgical area (flap and sutures) (Figure 14). After the intervention, an extraoral compression bandage is placed, to reduce postoperative edema (Figure 15).

Clinical periodontal parameters were recorded 1 day before the intervention and 1 month postoperatively. The following parameters were measured:

- recession depth (GR/GD/VGR – distance from the cementoenamel junction (CEJ) to the marginal gingiva)
- periodontal pocket depth (PPD/PD – distance from the marginal gingiva to the base of the periodontal pocket)
- clinical attachment level (CAL = GR + PPD; distance from the CEJ to the base of the periodontal pocket)
- keratinized gingival width (KTW/KMW/WKG – distance from the marginal gingiva to the mucogingival junction (MGJ), according to Lang & Löe)
- gingival biotype (thin ≤ 1.5 mm; thick ≥ 2.5 mm) according to Ochsenbein & Ross
- gingival thickness (GT – distance from the gingival surface to the underlying bone surface, measured in millimeters)

GR, CAL, KTW, and PPD measurements were performed using a Williams graduated periodontal probe (HuFriedy, Chicago, IL, USA) with a rounded tip. GT measurements were performed on the mid-buccal surface of the affected tooth by transgingival probing (TGP) (Vandana & Savitha) using a #15 endodontic reamer with a rubber stop.

After application of surface anesthesia, in the middle of the attached gingiva, at the midpoint of the distance between the mucogingival junction and the base of the interdental papilla, the reamer was inserted into the tissue to a depth of 1–2 mm apical to the marginal gingiva, perpendicular to the tooth axis, until bone contact was reached. The rubber stop was then positioned flush with the gingival surface, and the distance from the tip of the reamer to the inner border of the stopper was measured using a digital Vernier caliper or micrometer.

Results

One day before and one month after the surgical intervention, the following clinical periodontal parameters were measured in the 10 patients:

Statistical analysis

Quantitative parameters were analyzed using mean, median, minimum and maximum values, and standard deviation. Qualitative data were presented as frequencies and percentages. The normality of data distribution was assessed using the Shapiro-Wilk W-test. The Mann-Whitney U test was used to determine differences between the two groups in terms of selected parameters. The data obtained in the study were processed using the SPSS software package (version 22.0 for Windows; SPSS Inc., Chicago, IL, USA). Statistical significance was set at $p<0.05$, using a two-tailed test.

Comparison of therapeutic effect

The comparison of the two groups (SCTG + CAF vs. PRF + CAF) in terms of the PPD parameter indicated that there was no statistically significant difference between the two groups preoperatively ($Z = -1.775$; $p = 0.0758$) as well as one month postoperatively ($Z = -0.940$; $p = 0.3472$). The comparison of the change from baseline to 1 month in each of the two groups (SCTG + CAF vs. PRF + CAF) in terms of PPD also did not indicate a significant difference ($Z = -1.567$; $p = 0.1172$) (Tables 1 and 2).

The comparison of the groups (SCTG + CAF vs. PRF + CAF) in terms of the RD/VR parameter indicated that there was no statistically significant difference between the two groups preoperatively ($Z = 1.358$; $p = 0.1745$), whereas one month postoperatively, the SCTG + CAF group had a significantly higher value compared to the PRF + CAF group ($Z = 1.984$; $p = 0.0472$). The comparison of the change from baseline to 1 month in each of the two groups (SCTG + CAF vs. PRF + CAF) in relation to RD/VR did not indicate a significant difference ($Z = 0.313$; $p = 0.7540$) (Tables 1 and 2).

The comparison of the two groups (SCTG + CAF vs. PRF + CAF) with respect to the CAL parameter indicated that there was no statistically significant difference between the two groups preoperatively ($Z=-0.522$; $p=0.6015$) nor one month postoperatively ($Z=1.566$; $p=0.1172$). The comparison of the change from baseline to 1 month in each of the two groups (SCTG + CAF vs. PRF + CAF) with respect to CAL did not indicate a significant difference ($Z = -1.149$; $p = 0.2506$) (Tables 1 and 2).

The comparison of the groups (SCTG + CAF vs. PRF + CAF) with respect to the KAW parameter indicated that there was no statistically significant difference between the two groups preoperatively ($Z = 0.835$; $p = 0.4034$) nor one month postoperatively ($Z = -1.044$; $p = 0.2963$). The comparison of the change from baseline to 1 month in each of the two groups (SCTG + CAF vs. PRF + CAF) in relation to KAW also did not indicate a significant difference ($Z = 1.253$; $p = 0.2101$) (Tables 1 and 2).

Regarding the gingival thickness parameter, the comparison of the two groups (SCTG + CAF vs. PRF + CAF) indicated the absence of a significant difference preoperatively ($Z = 1.880$; $p = 0.0601$) as well as one month postoperatively ($Z = 0.0001$; $p = 1.000$). The comparison of the change from baseline to 1 month in each of the two groups (SCTG + CAF vs. PRF + CAF) in relation to gingival thickness indicated a significant difference ($Z=2.507$; $p=0.0122$) in favor of a significantly greater increase in gingival thickness in the PRF+CAF group (Tables 1 and 2).

Table 1. Comparison of SCTG + CAF and PRF + CAF groups at two time points (baseline and 1 month) according to selected parameters

Parameters		Parameters				p
		N	Mean±SD	Min Max	Median(IQR)	
PPD						
before	SCTG+CAF	5	1,60±0,65	1,0/ 2,5	1,5 (1,0-2,0)	Z=(-1,775); p=0,0758
	PRF+CAF	5	3,40±1,78	1,5/ 6,0	3,5 (2,0-4,0)	
1 month	SCTG+CAF	5	0,96±0,62	0,1/ 1,8	1,1 (0,7-1,1)	Z=(-0,940); p=0,3472
	PRF+CAF	5	0,80±0,97	0/ 2,5	0,5 (0,5-0,5)	
RD/VR						
before	SCTG+CAF	5	4,36±1,69	3,0/ 7,0	3,8 (3,0-5,0)	Z=1,358; p=0,1745
	PRF+CAF	5	3,00±1,54	1,5/ 55,5	3,0 (2,0-3,0)	
1 month	SCTG+CAF	5	2,48±0,63	1,8/ 3,2	2,2 (2,1-3,1)	Z=1,984; p=0,0472*
	PRF+CAF	5	1,00±1,06	0,0/ 2,5	1,0 (0,0-1,5)	
CAL						
before	SCTG+CAF	5	5,96±1,53	4,0/ 8,0	6,3 (5,0-6,5)	Z=(-0,522); p=0,6015
	PRF+CAF	5	6,40±1,43	4,5/ 8,0	6,5 (5,5 – 7,5)	
1 month	SCTG+CAF	5	3,44±0,67	2,8/ 4,3	3,2 (2,9-4,0)	Z=1,566; p=0,1172
	PRF+CAF	5	1,80±1,95	0,0/ 5,0	1,5 (0,5-2,0)	
KAW						
before	SCTG+CAF	5	2,18±0,97	0,8/3,0	2,8 (1,5-2,8)	Z=0,835; p=0,4034
	PRF+CAF	5	1,60±1,29	0,0/ 3,0	2,0 (0,5 – 2,5)	
1 month	SCTG+CAF	5	2,58±0,83	1,3/ 3,3	3,0 (2,2-3,1)	Z=(-1,044); p=0,2963
	PRF+CAF	5	4,20±2,77	0,0/ 7,0	5,0 (3,0-6,0)	
Gingival thickenss						
before	SCTG+CAF	5	1,76±1,20	0,5/ 3,1	1,2 (1,0-3,0)	Z=1,880; p=0,0601
	PRF+CAF	5	0,60±0,22	0,5/ 1,0	0,5 (0,5-0,5)	
1 month	SCTG+CAF	5	2,16±1,34	0,9/ 3,5	1,8 (1,4-3,2)	Z=0,0001; p=1,000
	PRF+CAF	5	1,90±0,41	1,5/ 2,6	1,8 (1,8-1,8)	

SD - standard deviation; IQR - Interquartile range
*significant for p<0,05

Table 2. Comparison of the two SCTG+CAF and PRF+CAF RMDQ groups according to the difference in selected-parameters between two times zero/ 1 month

Parameters		Parameters			p
		N	Mean±SD	Median(IQR)	
PPD					
SCTG+CAF	before	5	0,64±0,28	0,70 (0,40-0,90)	Z=(-1,567); p=0,1172
	1 month	5			
PRF+CAF	before	5	2,60±2,38	3,00 (2,00-3,50)	
	1 month	5			
RD/VR					
SCTG+CAF	before	5	1,88±1,18	1,60 (1,29-1,80)	Z=0,313; p=0,7540
	1 month	5			
PRF+CAF	before	5	2,00±2,06	1,50 (0,50-2,00)	
	1 month	5			
CAL					
SCTG+CAF	before	5	2,52±1,35	2,20 (2,10-2,30)	Z=(-1,149); p=0,2506
	1 month	5			
PRF+CAF	before	5	4,60±3,29	4,50 (4,00-7,50)	
	1 month	5			
KAW					
SCTG+CAF	before	5	-0,40±0,20	-0,30 [-0,50-(-0,30)]	Z=1,253; p=0,2101
	1 month	5			
PRF+CAF	before	5	-2,60±2,58	-1,30 [-1,30-(-1,00)]	
	1 month	5			
Gingival thickenss					
SCTG+CAF	before	5	-0,40±0,27	-0,40 [-0,50-(-0,20)]	Z=2,507; p=0,0122*
	1 month	5			
PRF+CAF	before	5	-1,30±0,49	-1,30 [-1,30-(-1,00)]	
	1 month	5			

SD - standard deviation; IQR - Interquartile range
*significant for p<0,05

Regarding the gingival biotype, it was observed that at baseline, the gingival biotype was thin in all subjects in both groups. One month after the intervention, it was observed that in all subjects in the SCTG + CAF group, the gingival biotype remained thin, whereas in the PRF + CAF group, a change from thin to thick biotype was observed in 2 (40%) subjects.

Discussion

A narrow keratinized attached gingiva (KTW < 2 mm) is one of the main contributing factors to gingival recession[9]. The principles of modern aesthetic mucogingival surgery are based on complete and predictable coverage of exposed root surfaces[10,3], the establishment of homeostasis of the mucogingival complex, and regeneration of the lost attachment, including the formation of new cementum, as well as regeneration of the alveolar bone[11]. The goal of periodontal plastic surgery is to develop a minimally invasive surgical technique that promotes and accelerates rapid regeneration, causes minimal postoperative discomfort, and allows maximum aesthetic and functional patient satisfaction[28]. The most commonly used grafts are free gingival graft (FGG) and subepithelial connective tissue graft (SCTG), which are currently recognized as the gold standard in the treatment of this condition, while the most widely accepted and frequently used surgical technique worldwide and in our country is the coronally advanced flap (CAF).

The SCTG harvesting technique is more time-consuming, increasing the risk of morbidity as it involves a second surgical site (donor site) and thus increases patient discomfort in the form of postoperative pain and the risk of bleeding, dehiscence, or flap necrosis[14]. Limitations in the quantity and quality of donor tissue are also disadvantages of SCTG[3]. SCTG (subepithelial connective tissue graft) and PRF (platelet-rich fibrin) share a common autologous origin, representing different therapeutic concepts and strategies; however, the analyzed studies suggest similar clinical outcomes.

The development of platelet concentrates (biological agents) traces its origins to the concept of fibrin adhesives[25]. Their emergence revolutionized the concept of tissue repair and regeneration[29]. Wound healing is a central concept in regenerative surgical science. Healing occurs as a result of a complex interaction between different types of cells (fibroblasts, epithelial cells, osteoblasts) and signaling molecules, which are released from thrombocytes in the form of cytokines and growth factors (GFs)[30].

Since no anticoagulant is required in the A-PRF preparation procedure, and due to the concentration of platelets (up to 97%) and leukocytes (up to 50%) from the original blood volume[31,32], PRF is also defined as an autologous platelet- and leukocyte-rich fibrin biomaterial[20,31]. The advantages of PRF over PRP include a shorter preparation time, absence of biochemical modification or exogenous anticoagulants (resulting in a more cost-effective procedure without the risk of blood-borne diseases or immune reactions), and the ability to allow natural polymerization similar to a physiological blood clot[33].

PRF membranes possess mechanical adhesive properties and a biological function similar to fibrin glue, thereby maintaining the flap in a stable position and enhancing angiogenesis[34]. These biological properties correspond to the findings of Al Jasser R et al.[35], as well as the studies by Anton Sculean et al.[36] and Madi M and Ahmed M. Elakel[37], and are further supported by the study by Rucha Sh et al.[25].

Regarding the statistically significant decrease in the RD/VR value in the (PRF + CAF) group, i.e., a significant increase in the value of vertical recession in the (SCTG + CAF) group ($Z = 1.984$; $p = 0.0472$) observed in our subjects and compared between the two groups one month postoperatively, these findings indicate concordance with the results of Eren G. & Atilla G. (14), Mijiritsky E. et al.[21], and the randomized controlled clinical study by Sonam Mufti et al.[38], in which a significant decrease in VGR/GR/VR values was reported in the (PRF + CAF) group and a comparative increase in the (SCTG + CAF) group. However, these findings are contrary to those reported by Macedo Iunes, C. T. et al.[39] in their split-mouth randomized clinical study, where significantly lower GR/RD/VR values were observed in the control (SCTG + CAF) group, with values progressively decreasing in the postoperative period.

There is also agreement with the significant reduction in RD values reported by Ucak T. Ö. et al. (40), where GR/RD values significantly decreased in the test group (CAF + CTG + PRF), as well as in the randomized parallel-controlled clinical study by Keceli G. H. et al. (41), where a significant intragroup reduction in VR/RD values was observed at 1 month postoperatively.

Panda S. et al.[42], as well as the studies by Madi M. and Ahmed M. Elakel[37], reported a non-significant reduction in RD values. Similarly, Al Jasser R. et al.[35] and Kumar A. et al.[28] conducted comparative analyses, and their results indicated a non-significant reduction in VGR/GR values, most pronounced in the (PRF + CAF) group.

A discrepancy between our results and those reported by Moraschini V. et al.[30], Hernan S. Garzon et al.[43], Collins R. J. et al.[44], as well as Culhaoglu R. et al.[45], was observed. The systematic review by Amine K. et al.[46], based on multiple randomized clinical trials, reported that the obtained values of complete root coverage (CRC) and recession reduction (RecRed) in the (PRF + CAF) modality were comparable to those observed in CAF + SCTG surgical treatment.

A reduction in PPD values was reported in the studies by Madi M. and Ahmed M. Elakel[37], Mijiritsky E. et al.[21], and Miron R. J. and Zucchelli G. et al.[47], while a significant reduction was also observed in the study by Kumar A. et al.[28], who conducted a comparative analysis and reported significant decreases in this parameter during the first 3 months postoperatively, specifically in the group treated with the (PRF + CAF) modality.

The non-significant changes in PPD values between the two compared groups (baseline to 1 month postoperatively), as well as the comparison of changes within the same group over time, observed in our study, correspond with the unchanged PPD values reported by Keceli G. H. et al.[41], Macedo Lunes C. T. et al.[39], Culhaoglu R. et al.[45], Collins R. J. et al.[44] in their randomized split-mouth study, Miron J. R. and Sculean A. et al.4[8], as well as Eren G. and Atilla G.[14].

The CAL values showed a tendency to decrease in the studies by Eren G. and Atilla G.[14], Madi M. and Ahmed M. Elakel[37], and Mijiritsky E. et al.[21], but a significant decrease was reported in Panda S. et al.[42], as well as in the randomized parallel-controlled clinical study by Keceli G. H. et al.[41]. CAL values remained unchanged in the studies by Moraschini V. et al.[30] and in the randomized controlled clinical studies by Culhaoglu R. et al.[45] and Macedo Lunes C. et al.[39].

The findings of our study, in which there was no statistically significant change in CAL values between the groups (baseline to 1 month postoperatively), as well as within the same group over time, correspond with the non-significant changes in CAL reported in the meta-analysis by Miron J. R. and Sculean A. et al.[48]. In contrast, significant increases in CAL values were reported in the studies by Oncu E. et al.[49], Miron R. J. and Zucchelli G. et al.[47], and Sonam Mufti et al.[38]. Similar findings were also reported by Kumar A. et al.[28].

A positive trend in KTW values, although not statistically significant, was reported in the study by Panda S. et al.[42]. A similar pattern was observed in the study by Eren G. and Atilla G.[14], whose results remained stable up to three months postoperatively.

A statistically significant increase in KTW values was reported by Culhaoglu R. et al.[45] in the control group of subjects treated with (SCTG + CAF), as well as by Sonam Mufti et al.[38]. Similar results were also demonstrated by Miron J. R. and Sculean A. et al.[48] in their meta-analysis and review, as well as by Mancini L. et al.[50], Mijiritsky E. et al.[21], Miron R. J. et al.[47], and Oncu E. et al.[49].

In the study by Macedo Lunes C. et al.[39], a split-mouth randomized clinical trial, a significant increase in KTW values was observed in the (PRF + CAF) group, as was also reported in the study by Ucak T. Ö. et al.[40], where a significant increase in KTW values was detected in the test group treated with PRF.

In the randomized parallel-controlled clinical study by Keceli G. H. et al.[41], a significant increase in KTW values was observed after intra-group comparison in both groups at one month postoperatively. Borderline statistical significance of increased KTW values was reported in the study by Al Jasser R. et al.[35].

Our findings correspond to those reported by Moraschini V. et al.[30] and the split-mouth randomized clinical study by Hernan S. Garzon et al.[43], in terms of the absence of statistically significant changes in KTW values in both within-group and between-group comparisons.

The results of Eren G. and Atilla G.[14] tend toward a moderate increase in GT values, whereas a significant increase in GT/VSTT/TKT (keratinized tissue thickness) was reported by Sonam Mufti et al.[38], Oncu E. et al.[49], Mancini L. et al.[50], Mijiritsky E. et al.[21], Panda S. et al.[42], and Shivakumar et al.[51], which correspond with our findings in this study, where a statistically significant difference in gingival thickness (GT) was observed, with the (PRF + CAF) group showing ($Z = 2.507$; $p = 0.0122$) compared to the change within the same group (baseline to 1 month postoperatively).

A statistically significant increase in tissue thickness (TT) was observed intra- and inter-group in the postoperative period, as documented in the randomized parallel-controlled clinical study by Keceli G. H. et al.[41]. A significant increase in TT/VSTT was also demonstrated by Kumar A. et al.[28], but in favor of the therapeutic procedure (SCTG + CAF).

Non-significant changes in GT/VSTT values were reported by Collins R. J. et al.[44] in their randomized split-mouth study, as well as in the randomized controlled clinical study by Culhaoglu R. et al.[45], and also by Macedo Lunes C. et al.[39].

The findings obtained in our study regarding gingival biotype (thin/thick) indicate a clear shift in gingival phenotype in 40% of subjects in the PRF + CAF group one month postoperatively.

Conclusion

The second generation of platelet-rich fibrin (PRF; A-PRF and I-PRF), as an adjunct to the widely accepted CAF surgical method in the treatment of localized Miller Class I and II gingival recessions, is not only a substitute for the established "gold standard" for the treatment of this type of gingival defects (SCTG), but also an equally effective alternative, considering the wide spectrum of advantages which unequivocally demonstrate the influence of this 3D matrix as a promoter of early neoangiogenesis, an initiator of rapid soft tissue regeneration and repair, and an accelerator of overall wound healing, which is a central concept in mucogingival surgery.

Autologous biological membranes (PRF) are cost-effective, available in optimal quantities unlike SCTG, easy to handle from a surgical perspective, and associated with superior patient comfort due to the elimination of postoperative discomfort and the absence of donor site morbidity.

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