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TIME EFFECT ON THE PREDICTABILITY OF COLLAGEN MATRIX XENOGRAFT WITH MELATONIN GEL VERSUS CONNECTIVE TISSUE GRAFT IN TREATMENT OF GINGIVAL RECESSION RT1 IN THE ESTHETIC ZONE: A RANDOMIZED CLINICAL TRIAL

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ABSTRACT

Objectives: To achieve complete root coverage (CRC) in the most challenging scenario of multiple adjacent gingival recession (MAGR) Cairo et al. RTI (Miller's Class I and Class II). In this study, the efficacy of collagen matrix xenograft (XCM) with melatonin gel vs connective tissue graft was compared. Additionally, the study focused on the time impact on this clinical outcome.

Methods: Twenty-two systemically healthy patients with MAGR type RT1 were included in the study, and they were split into two groups at random. **Group I/Positive control**, treated by means of Modified Coronally Advanced Tunneling Technique MCAT technique and connective tissue graft CTG and Group **II/study** received collagen matrix xenograft with melatonin using MCAT technique. The complete root coverage and other clinical outcomes in terms of keratinized tissue width (KTW), clinical attachment level (CAL), periodontal pocket depth (PPD), Recession depth (RD), and percent of mean root coverage were evaluated at baseline, 6-, and 9-months post-intervention.

Results: Showed no statistical difference in terms of CRC & all of the before mentioned clinical parameters between the two groups in favor of CTG as being slightly superior in achieving CRC than XCM with melatonin to be after 6 months 16.67%& 0%. & at 9 months CRC was 41.67% & 60%.for XCM with melatonin & CTG respectively. Furthermore, the effect of time was highlighted at baseline, 6, and 9 months through all of the quantitative parameters in each group. CRC significantly increased from 9 % after 6 months to 50 % after 9 months.

Conclusion: (XCM) with melatonin gel may be submitted as a substitute for CTG in MAGR treatment due to the predictable results in CRC concurrent with a significant increase of all clinical parameters simultaneously with avoiding the second surgical site thus decreasing patient morbidity.

KEYWORDS: Gingival Recession, Connective Tissue Graft, Collagen matrix Xenograft, Melatonin gel

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INTRODUCTION

Gingival recession (GR) is defined as root surface exposure caused by an apical shift in the gingival margin's position with respect to the cemento-enamel junction (CEJ) [1], creating obstacles that are both practical and aesthetically pleasing. Males and females were equally distributed in the 50% mean prevalence of GR. The lower left canine and left first premolar were the teeth that went along with GR the most frequently [2]. Patients with either poor or adequate oral hygiene had a higher frequency of GR. GR is therefore thought to be multifactorial [3].

Plaque-induced gingival inflammation is considered a prime mover factor responsible for GR, next, vigorous tooth brushing is among the most common purposes [3]. Other contributing factors of GR are broadly categorized as anatomical, habits, iatrogenic, and physiologic factors. Among the anatomical ones are tooth malposition, presence of dehiscence, and fenestrations. High frenum attachment may be a barrier to getting rid of plaque and lead to a pull on the marginal gingiva [4]. In clinical practicality, it is almost observed that greater recession depth corresponds to minor keratinized tissue height remaining apical to the root exposure. Mucogingival problems are caused by deviations from the normal anatomic relation between the gingival margin and the muco-gingival junction [5]. Therefore, a lack of sufficient muco-gingival complex might cause localized inflammation, which increases the risk of GR formation [6].

In many cases, the exposed root surface coexists with aesthetic complaints, root hypersensitivity, mechanical root wear, and cervical root caries, and challenges in achieving ideal plaque control [7, 8]. These conditions incite patients to pursue corrective measures. The degree of symptoms will dictate the course of treatment, the patient's objective, and the corpus of information [8]. Pedicle grafts, connective tissue grafts, free gingival grafts, coronally advanced flaps, acellular dermal matrix, allografts, and guided tissue regeneration procedures with a membrane barrier are among the primary surgical fundamental categories that are now used for root covering [9]. Furthermore, a lot of clinical practices and literature studies also include combinations of various methods that are communistic [10].

According to Suclean et al. [11], modified coronally advanced tunnel technique has been suggested as a surgical treatment for multiple adjacent gingival recession because it can be utilized for incising the papillae without making vertical releasing incisions, which is crucial for enhancing the vascularization and supporting the soft tissue flap. Additionally, enhancing graft survival as a result of the flap's coronal displacement and full coverage of the soft tissue graft. The most predictable way to get CRC in Miller Class I and II (MAGR) is by the use of soft tissue grafting in the (MCAT) procedure, according to a systematic review assessing the predictability of several surgical approaches used for the treatment of (MAGR) [12].

Using (CTG) in both single and MAGR of RT1., could achieve predictable root coverage providing best outcomes. The increased availability of tissues, the second surgical site, the higher degree of complications, and the higher morbidity rate of the patient are factors that should be taken into account regarding the limitations of CTG. Thus, a biomaterial replacement that would surpass these constraints and offer clinical attachment level (CAL) gain, keratinized tissue augmentation, and root coverage is required for both MAGR and single recession treatment [13].

A recent systematic review by Panda et al. revealed a number of newly introduced CTG replacements. Acellular dermal matrix (ADM), enamel matrix derivate (EMD), platelet rich plasma (PRP) or platelet rich fibrin (PRF), and xenogeneic collagen matrix (XCM) are among the various biomaterials that can be used to mitigate the limitations of autogenous soft tissue transplants [14].

(XCM) has a significant fulfillment in a range of recession issues. Being bilayer, XCM is made up of an inner porous matrix that facilitates fast blood clot stabilization, encouraging swift vascularization and tissue integration, and an outer compacted layer that holds the suture and protects the defect. One of the criteria of XCM has been demonstrated to promote the replacement of keratinized gingiva in both width and thickness around dental implants as well as natural teeth [15].

A hormone primarily produced and secreted by the pineal gland is called melatonin (MT). Nocturnal messenger or hormone of darkness, as it is named, is released during the night by postsynaptic stimulation of the b-adrenergic receptors [16]. MT's capacity to function as a highly effective free radical scavenger is one of its key characteristics. It operates at both physiological and pharmaceutical concentrations on reactive compounds based on oxygen and nitrogen. It possesses immune-modulatory, protective, and anticancer qualities in addition to a strong antioxidant effect. It is utilized as a therapy for postsurgical wounds from tooth extractions and other oral lesions because it stimulates the synthesis of type I collagen fibers and the creation of bone [17]. Additionally, melatonin is in charge of raising the activities of cyclooxygenase-prostaglandin and nitric oxide synthase, which aid in boosting blood flow to the injured tissue [18].

We postulated that the utilization of MCAT in conjunction with xenogeneic collagen matrix and melatonin would yield better clinical results in terms of root coverage percentage when compared to CTG as a gold standard grafting material. This study attempted to investigate whether using melatonin will enhance blood follow in xenogeneic collagen matrix followed by proper healing and complete root coverage. Subsequently, if it could be a satisfactory substitute for the autogenous grafting material with the simultaneous avoidance of a secondary surgical intervention. Additionally, we also evaluated the effect of time in all clinical parameters (complete root coverage).

In this study, primary objective was evaluation of CRC and clinical soft tissue parameters improvement of (XCM) with melatonin gel versus (CTG) along time points 6 &9 months .Secondary objective was to evaluate time effect on the clinical predictability of different grafting material along the same time points 6 &9 months.

SUBJECT AND METHODS

Study design

A randomized, single-masked, controlled clinical trial was to be carried out as part of the investigation.22 patients were chosen from the outpatient clinic of the Department of Periodontology, Faculty of Dentistry, Ain Shams University, between January 2020 and January 2021, with the condition of gingival recession, in accordance with the World Workshop 2017 on the Classification of Periodontal and Peri-Implant Diseases and Conditions [19]. Patients who met the inclusion criteria and were demonstrating numerous adjacent GR at the maxillary or mandibular arch in the esthetic zone RT1 [20] were informed of the study's purpose and design after they were carefully reexamined. The following were the applied enrollment criteria: The patient's characteristics include not smoking, not reporting any immunological or systemic diseases, having gingival recession with no loss of interproximal attachment and GR depth ≥2 mm, full mouth bleeding on probing score [21] and plaque score[22] ≤20% after phase I therapy, only vital teeth involved, patients older than 18, not showing radiographic signs of periapical infection on the teeth to be treated or on the neighboring teeth, and h) having ≥2mm width of keratinized gingival tissue apically. Patients who did not cooperate, women who were nursing or pregnant, and people who had difficulty making decisions were excluded from the research. Individuals with para-functional habits, a history of occlusal trauma, furcation involvement,

periodontitis[19], and prior surgical treatment for GR were also disqualified. Each patient signed an informed consent form prior to enrollment. The study was filed in the ClinicalTrials.gov database with reference number NCT05976451 and authorized by the Research Ethics Committee of the Faculty of Dentistry, Ain Shams University (FDASU-REC IR102207).

Presurgical therapy and grouping.

A whole mouth non-surgical periodontal therapy was scheduled for the chosen patients. This involved manual instrumentation with supragingival scaling, subgingival debridement and curettage with ultrasonic instruments* and manual instrumentation with Gracey curettes**. For seven days, patients were instructed to brush their teeth twice a day and to use mouthwash contains chlorhexidine***. The patients received education on how to properly maintain full mechanical dental plaque control, which included using a roll-technique to brush with a soft toothbrush and waxed dental floss for interdental cleaning. Furthermore, patients received guidance on maintaining an ideal brushing technique to avoid any bad habits linked to the genesis or advancement of the GR. Patients were contacted again and talked about proper dental hygiene every other day. In certain cases, supragingival plaque removal was carried out. In order to confirm whether mucogingival surgery was necessary after starting treatment, patients were reexamined six weeks later (baseline data). Patients were randomized into Group I, which consisted of eleven patients with MAGR receiving treatment using a combination of CTG and MCAT method. Group II: Using XCM soaked in 0.1% melatonin gel, eleven patients with MAGR received treatment using the MCAT approach. The random block allocation method used by Random Allocation Software aims to provide random pairings of names together with extra flexibility in terms of output format and type.

Clinical assessments

Preoperative (baseline), 6, and 9 months after surgery, each patient's clinical parameters were evaluated by a covert clinical examiner. According to Dr. Mahetab AbdalWahab, MAW. To evaluate the reproducibility of the measurements, a calibration exercise was conducted on two separate interludes separated by 48 hours. Reproducing 90% of the recordings with a 1.0 mm variance was considered a good calibration. The initial periodontal condition of the selected sites was evaluated clinically using the following measures: Recession depth (RD) measures the distance between the cemento-enamel junction (CEJ) and the GM, Probing pocket depth (PPD) measures the distance from the gingival margin (GM) to the base of the sulcus or pocket [19], and Keratinized tissue width (KTW) measures the distance between the MGJ and the GM The distance between the CEJ and the mid-buccally bottom of the gingival sulcus is known as the clinical attachment level (CAL) [19]. After six and nine months, the CRC % of complete gingival recession coverage was determined. Gingival sulcus bleeding index (BI) [21] and plaque index (PI) [20]. A graduated periodontal probe**** was used for recording all clinical data, which was rounded to the nearest 0.5 mm.

Melatonin gel preparation

The Pharmacology and Toxicology Department of the Faculty of Pharmacy at Ain Shams University produced melatonin gel and supplied pure powder. To prepare methylcellulose solution (1 point 5 percent w/v), a third of the required amount (33mL out of 100mL) of freshly prepared distilled water

* Cavitron, 3000, Dentsply, York, PA

** Gracey curettes: Hu-Friedy, Chicago, IL

***Chlorhexidine Hcl 1.25 mg / 100 ml, Adco pharma Co, Cairo, Egypt

**** William's graduated periodontal probe, 10 mm, Hu-Friedy

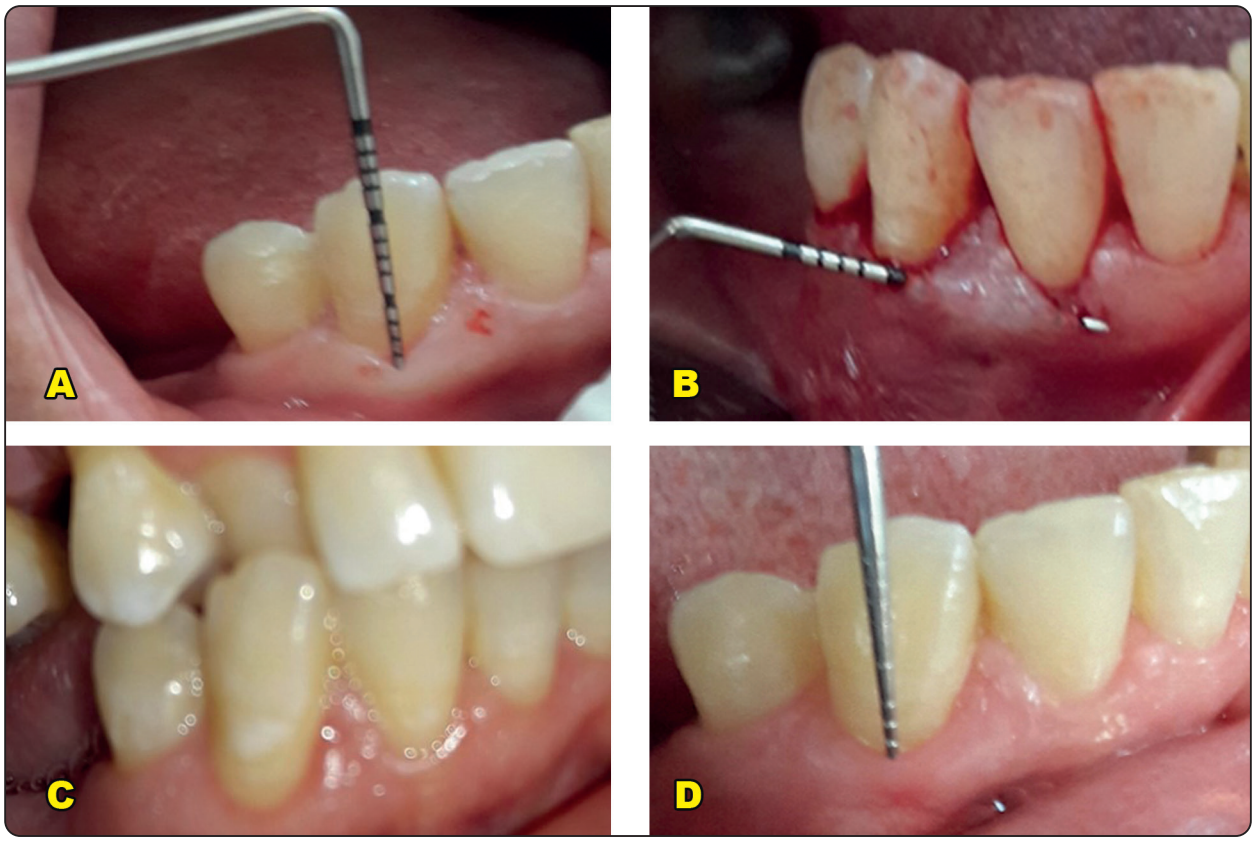

Fig (1) Clinical photos showing. (a) measurement of base line parameters. (b) tunneling preparation . (c) 6 months follow up. (d) 9 months follow up.

at 80°C (165) was gradually added while stirring to the calculated amounts of the polymer (1 point 5g methylcellulose, high viscosity 4000 CPS). The remaining water (roughly 67 mL), into which 150mg of melatonin had been dissolved while stirring, was added to create the final volume. Before being stored at 4°C until needed, the preparation was vacuum-sealed to release any trapped air. Melatonin gel 0 point 1 percent was then added.

Surgical protocol

All patients were treated with the MCAT technique by the same experienced clinician (DY). Under local anesthetic local infiltration (4% Articaine13 containing epinephrine at a concentration of 1:100 000). Intrasulcular incisions were made with micro-blade and a mucoperiosteal tunnel flap was raised beyond the level of the mucogingival junction while avoiding contact with the interdental papillae. The mucoperiosteal pouch was then carefully extended mesially and distally under the neighboring papillae until the adjacent sites were connected with the separation of any muscle attachment**,** thus tunneled flap could be advanced coronally without tension. Microsurgical blades and Gracey curettes were used to separate attaching fibers and muscles from the flap. In the control group, a palatal CTG of a thickness of 1 to 1.5 mm was harvested by using the single incision technique. Immediately after harvesting, the autogenous graft was placed in saline solution and kept moist to prevent desiccation until it is inserted into the recipient site. The palatal donor site was closed with a modified mattress suture. In test group bioresorbable collagen matrix (Mucograft®, Geistlich, Wolhusen, Switzerland) XCM trimmed and soaked with melatonin gel for

5 mints. Then, the grafting materials were inserted into the tunnel in both groups and facilitated with the help of the support suture. The entire gingiva-papillary complex was moved coronally and stabilized using sling sutures attempting to completely cover the graft. All patients were provided one gram of amoxicillinclavulanate potassium twice a day for one week [23], five hundred milligrams of metronidazole twice a day for one week [24], and a total of two days of 600 mg of ibuprofen twice a day.[25] Patients were told to clean their mouths twice a day with a 0.12% chlorhexidine digluconate mouthwash [26]. Ten days following surgery, sutures were removed. The surgical area was off-limits to brushing and flossing for two and four weeks, respectively. Patients were instructed to resume utilizing the toothbrush roller technique for their regular oral hygiene measurements after 15 days. In order to ensure patient compliance, recall sessions were planned every week for the first six weeks following surgery. After that, they were scheduled every month until the trial's nine-month mark, at which point clinical parameters were recorded.

Ethical approval of studies and informed consent

The research was authorized by the Ain Shams University Faculty of Dentistry Research Ethics Committee (FDASU-REC IR102207) and registered under the reference number NCT05976451 in the ClinicalTrials.gov database. Each patient signed an informed consent form prior to being enrolled in the trial.

Statistical analysis

Next, a commercially accessible software package (SPSS 18; SPSS, Chicago, IL, USA) was used to do statistical analysis. The mean, standard deviation (SD), median, and range of the values were displayed. The Kolmogorov-Smirnov test of normalcy was used to examine the data for normalcy. For parametric data, the independent t test was used to compare the two groups; for non-parametric data, the Mann Whitney U test was employed. In order to compare various observations, many measurements for parametric data, the ANOVA test was employed; for non-parametric data, the Freedman test was used; and for multiple pairwise comparisons, Tukey's post hoc test was utilized. A significant threshold of $P \leq 0.05$ was applied.

A power analysis for multiple adjacent gingival recession therapy was conducted in compliance with a study by Ramachandran L et al., [27]. Using a two-sided two-sample t-test, the mean percentage RC for groups 1 and 2 was 67.1% and 35.5%, respectively, with estimated group standard deviations of 22.9% and 16.1%. Consequently, the sample size computation showed that eight participants in each group would yield 80% power to detect a real difference of 5% between the test and control groups. Nevertheless, twenty-four patients were enrolled (12 in each group), considering the possibility that some patients would disappear during follow-up.

RESULTS

Following surgery, every patient recovered without any complications and showed an excellent soft tissue response to both therapy regimes. Allergic reactions, abscesses, or infections were not observed during the trial. 24 patients initiated the research. Over the course of the nine-month study period, 11 patients in each group adhered to the guidelines for appointments and dismissals. One patient from group II lost after six months, while another from group I lost after surgery (Figure 3). In order to perform this study, twenty-one patients—ten men and eleven women—between the ages of 20 and 45—with a mean age of 29.95 ± 6.4 years and MAGR RT1 were involved (Table.1).

TABLE (1) Gender and age distribution in both groups

CHARACTERISTICS	GROUP I (N= 10)	GROUP II (N=12)
AGE GROUP (Y)		
20-25	3	3
26-30	2	3
31- 35	3	4
36-40	0	1
41-45	2	1
MEAN AGE	30.2±7	29.75±6.1
GENDER		
MALE	5	5
FEMALE	5	7

There were statistically non-significant variations between the two groups and observation periods with regard to gingival bleeding and plaque indices, with a score of 0 recorded in all instances at the start of the trial and at 6, 9 months of follow-up. Regarding CAL, PD, RD, and KTW, no statistically significant differences were seen between treatment groups at baseline (P >0.05). Following surgery, neither group's mean PD changed, and there were no statistically significant differences between the treatment groups (P >0.05). In reference to CAL, group I recorded a higher mean value (2.95±0.8 mm) at 6 months compared to group II (2.86±1.16 mm), with no significant difference between groups (p=0.846). However, at base time, there were no statistically significant variations in CAL between group II and group I (p=0.620). Group II recorded a mean value of 1.95±0.91 mm at 9 months, which was greater than the study group's 1.65±0.67 mm. However, there was no significant difference between the groups (p=0.396). However, the RD decrease in group I and II at 6 month (1.5±0.53mm; 1.23±0.72mm) respectively. Group I recorded a decrease in RD (-1.05±0.44), compared to a decrease (-1.23±0.47) in group II, with no significant between groups (p=0.382). In the interval from 6 to 9 months, group I recorded a decrease (-1.1±0.74mm), compared to (-0.55±0.72mm) in group II, with no significant between groups (p=0.098). Regarding KTW, Overall in the interval from baseline to 9 months, group I recorded an increase (0.55±0.5), compared to (0.18±0.4) group II, with no significant between groups (p=0.069), with no significant between groups (p=0.069). table (2). Regarding the effect of time, within each group, the value of CAL and RD showed a gradual significant decrease by time. The difference by time was statistically significant in group I (p=0.000) and group II (p=0.000). While, the value of KTW showed a significant increase at 9 months (p=0.002) in group I, whereas group II showed no statistical significant difference by time (p=0.135) table (3). Percentage of CRC was 41.67% in the group I and 60% in the group II at 9 months after surgery, but the difference was insignificant (Figure. 2).

TABLE (2) Clinical parameter at baseline and after 6 and 9 months

Parameter	Baseline			Postoperative (6 months)			Postoperative (9months)		
	Group I control	Group II study	p- value	Group I control	Group II study	p- value	Group I control	Group II study	p- value
PI	0	0	1^{ns}	0	0	1^{ns}	0	0	1^{ns}
GI	0	0	1^{ns}	0	0	1^{ns}	0	0	1^{ns}
CAL (mm)	4.05±0.90	4.27±1.10	0.620^{ns}	2.95±0.80	2.86±1.16	0.846^{ns}	1.65±0.67	1.95±0.91	0.396^{ns}
VPD (mm)	1.5±0.53	1.8±0.87	0.441^{ns}	1.55±0.50	1.64±0.81	0.969^{ns}	1.25±0.54	1.27±0.47	0.093^{ns}
RD (mm)	2.55±0.5	2.45±0.69	0.722^{ns}	1.5±0.53	1.23±0.72	0.339^{ns}	0.40±0.52	0.68±0.78	0.384^{ns}
KTW (mm)	3.5±1.27	3.36±1.36	0.823^{ns}	3.50±1.3	3.4 ±1.4	0.805^{ns}	4.05±1.06	3.55±1.44	0.355^{ns}

C.I.L.= 95%confidence interval lower, C.I.U.= 95%confidence interval upper. Significance level p≤0.05, ns=non-significant

TABLE (3) Effect of time at baseline, 6, and 9 months on the study parameters.

Variables	Baseline	After 6 months	After 9 months	Friedmann test	p
	Median(min-max)	Median(min-max)	Median(min-max)		
Recession depth	2.75(1-3)	1.5(0-2)	0.25(0-2)	40.68	<0.001*
Percent of root coverage [a*]	36.67(0-100)	29.17(0-75	91.67(33.33-100)	27.59	<0.001*
Clinical attachment level	3(1-5)	4(3-6)	2(1-4)	41.95	<0.001*
Periodontal pocket depth	1.75(1-3)	1(0.5-3)	2(1-3)	14.39	<0.001*
Keratinized tissue width	3(2-5)	3(2-6)	3(2-5)	18	<0.001*

: significant p-value, a* : the time of percent root coverage is measured after 6 months, from 6-9 month, and after 9 months.

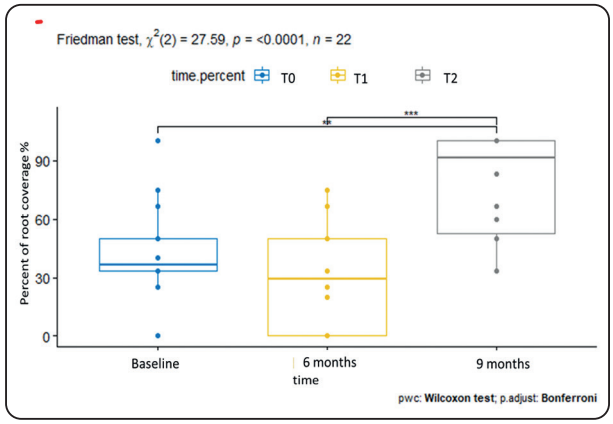

Fig (2). percent of root coverage at baseline, 6 months and 9 months.

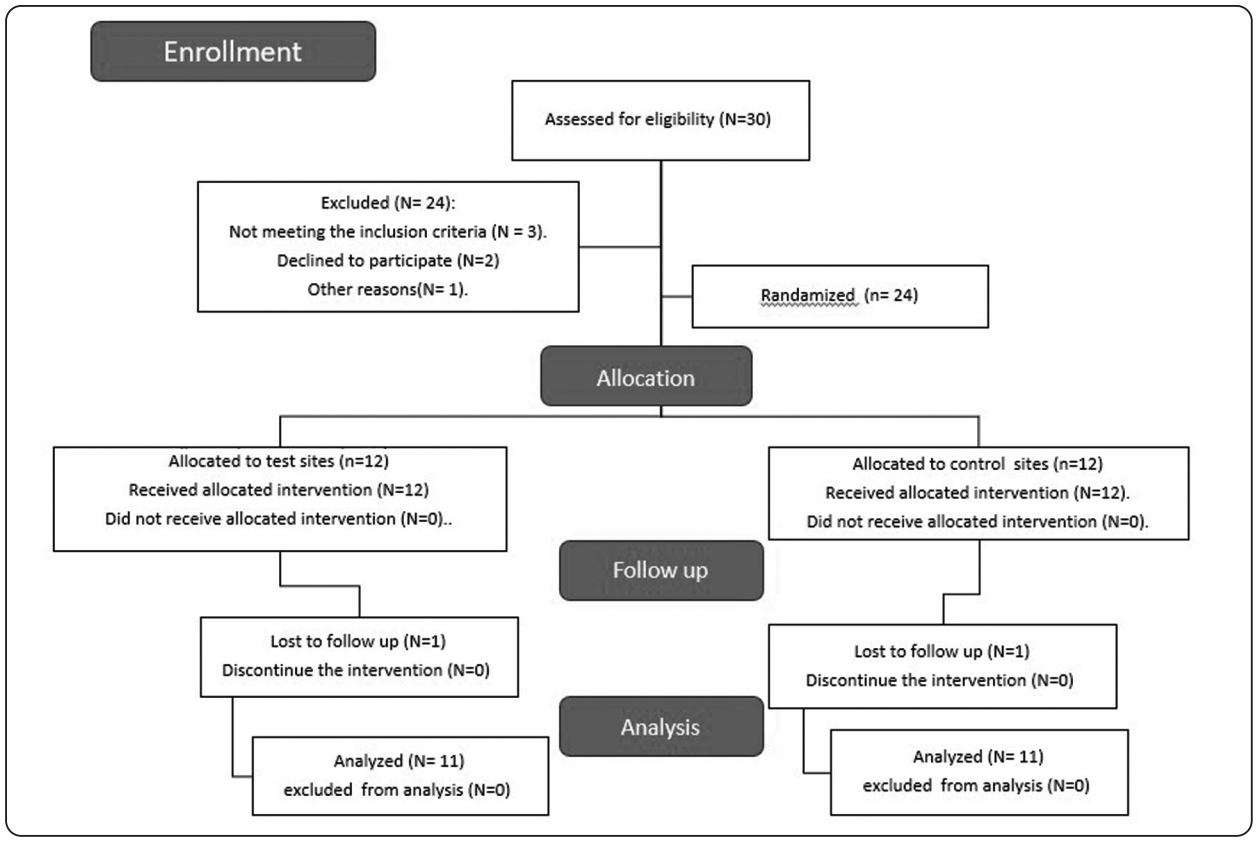

Fig (3). Consort diagram showing the study design.

DISCUSSION

As far as the authors are aware, this is the first trial to use XCM in conjunction with melatonin (ML) gel as an adjuvant for the treatment of GR. The use of extracellular collagen (XCM) as a procedure adjunct may be pertinent for a number of reasons. Firstly, the outer layer of dense collagen fibers has the ability to protect cells against bacterial invasion and to provide elasticity, which facilitates the suturing process. Secondly, the inner layer of collagen is porous and spongy, which facilitates the formation of a coagulum and promotes tissue integration and angiogenesis [28], The absence of the second site's morbidity and pain following an autogenous connective tissue graft is the final component. Melatonin has several positive characteristics that enhance our findings, such as a notable decrease in the production of TNF-α, IL-6, and IL-1β, and an early anti-inflammatory effect mediated by the TLR4/MyD88 signaling pathway. Melatonin also promotes healing [29]. Moreover, ML controls the differentiation and proliferation of fibroblasts by upregulating collagen III alpha mRNA, decorin (DCN), tissue inhibitor of metalloproteinases 1 (TIMP1), and interleukin 10 (IL-10), while downregulating matrix metalloproteinase-1 (MMP1). These cytokines all aid in maintaining and restoring the integrity of gingival tissues, which is essential for controlling the healing process during gingival recession treatment) [30].

According to our findings, after 6 and 9 months, both groups' CAL and PPD improved with each surgical method and remained stable throughout time, similar to baseline values. These results were due to Jepsen et al., 2013[31], who compared coronal advancement flap CAF mixed with the xenogeneic collagen matrix with CAF alone and found no significant difference between them regarding CAL and PPD. There was also no statistically significant difference between groups.

With regard to RD, there was no significant difference between group I and II, but there were statistically significant differences in both groups between baseline and 6 months ($p < 0.001$), baseline and 9 months ($p < 0.001$), and between 6 months and 9 months ($p < 0.001$). Due to the combined effects of ML's antibacterial and anti-inflammatory properties and XCM's fibroblast migration to its scaffold, these results confirmed that both ML and XCM were equally effective in treating GR as CTG grafting. This enhances the grafting material's predictability and does away with the disadvantage of autogenous grafting.

In our study there is a statistically significant variations in RC% between 6 months and after 9 months ($p < 0.001$) in both groups, baseline and after 9 months ($p < 0.001$). Root covering treatments, periodontal regeneration, and the impact of time on the stability of postsurgical outcomes are also areas of study [32, 33, 34]. Although some researchers have demonstrated that 6-month data can already be used to predict the 3-year outcomes of root coverage treatments [35, 36], other researchers have noted a potential shift in the gingival level between flap alone and CTG. Specifically, it has been hypothesized that the inclusion of CTG may aid in the gingival margin's progressive coronal migration, also referred to as the "creeping attachment" [37]. This was consistent with our time effect results, which showed statistical significance from the study's baseline to its conclusion. In both groups, the median percent of root coverage was 29.17% at six months and increased to 91% at nine months. There is no statistically significant difference between these outcomes.

At nine months, CTG also had a greater CRC percentage than group XCM (60% vs. 41.66%), however this difference was not statistically significant (p-value of 0.06). While this result is consistent with a systematic review by Cairo et al. who concluded that using CTG as a grafting material unquestionably offers the best opportunity to accomplish CRC with the best aesthetic

results[38, 39], on the other hand, patient morbidity, surgical time, and the risk of complications, along with other limitations, led researchers to look for alternatives to CTG. As mentioned in a very interesting systematic review by Tavelli et al. 2018[40], they applied XCM mixed with melatonin gel.

Following six months of MAGR therapy, Cieślik-Wegemund et al. [41], who submitted a coronally advanced tunnel technique, determined that there was a lower percentage of RC in the group xenograft dermal matrix (XDM) than in the group CTG, which is consistent with our data. In contrast, Pietruska et al. [42], who also used a tunnel approach, demonstrated a statistically significant difference in mean root coverage for the treatment of mandible recessions after 12 months between group XDM (53.20%) and group CTG (83.10%). According to Discepoli et al.'s systematic review and meta-analysis [43], According to type and location of recession ,variations in the effectiveness of surgical methods and the predictability of recession coverage could account for discrepancies among studies. The mandible's structure is less conducive to root coverage. Maxillary teeth had higher mean root coverage than mandibular teeth, according to a recent multicenter re-analysis research [44]. According to a meta-analysis, CTG plus CAF together led to a considerably larger proportion of CRC and mean reduction in GR when treating GRs, compared to CAF plus xenogeneic collagen matrices [15]. These results are consistent with that finding.

Several attempts were exerted by number of systematic reviews to evaluate the efficacy of RC procedures [45,46]. Even though, the promising selection of a particular flap design remains controversial [47], the current study adopted the MCAT surgical technique creating full-thickness pouch by avoiding vertical releasing incisions synchronous with attaching muscles and the inserting collagen fibers abstraction from the inner part of the flap, thus a tension-free coronal mobilization flap can be created, allowing root coverage. That is in accordance with Pini Prato et al and Hwang et al [48,49] who have been previously clarified that flap thickness with tension-free flap management and adaptation were among the pivotal factors for achieving predictable root coverage.

The gingival phenotype's KTW component is another crucial topic of discussion. This component may help prevent recessions from happening again in the future (secondary prevention). A statistically significant difference in KTW was found in both the test and control groups between 6 and 9 months ($p < 0.001$), baseline and 9 months ($p < 0.001$), and after 6 and 9 months. Substantially, the mean increase in KTW did not differ substantially between XDM (0.63 mm) and CTG (0.9 mm), in agreement with Mauricio et al [50, 51].

Other clinical trials have also produced positive results supporting XCM's non-inferiority. Consequently, even though it was not as effective as the CTG, it appears that the xenogeneic collagen matrix utilized in this study was able to alter the gingival phenotype in some way, with the added benefit of saving time and avoiding the need for a second surgical site. The long-term stability of the gingival margin depends on two important factors: gingival thickness and KTW [52].

At nine months, the control group had a considerably higher frequency of teeth demonstrating CRC than the test group ($p<0.05$); at that time, 60% of the control group's patients (6 out of 10) had achieved CRC, compared to 41.66% of the test group's patients (5 out of 12).

Conclusion: the predictable results achieved with (XCM) &melatonin gel in terms of CRC concurrent with a significant increase of all clinical parameters simultaneously while avoiding the second surgical site, so decreasing patient morbidity, it could be submitted as a good substitute for CTG in MAGR treatment

Limitations

Numerous medical professionals have shared the percentage of sites that kept all of their root coverage as well as the amount of the mRC that declines throughout time. While there are still disagreements regarding the various methods in the literature, CTG-based procedures show the least amount of gingival margin level changes over time [53, 54].

Leknes et al. [55] disproved our hypothesis of a time effect by failing to find differences in root coverage between CAF and GTR at different time points. This finding highlights the influence of other factors, such as patient maintenance and motivation, on non-traumatic brushing habits and the long-term stability of the outcomes. A strict maintenance protocol has recommended that patients' hygiene practices be examined for traumatic teeth brushing at every consultation, which has a substantial impact on the durability of the outcomes acquired after RC surgery [56].

Abbreviations

XCM: xenogeneic collagen matrix; CRC: complete root coverage ; MAGR: multiple adjacent gingival recession; KTW: keratinized tissue width; CAL: clinical attachment level; PPD: periodontal pocket depth; RD: Recession depth; GR: Gingival recession; CEJ: Cemento-enamel junction; MCAT: Modified Coronally Advanced Tunneling Technique; CTG: connective tissue graft; PRP: Platelet rich plasma; PRF: Platelet rich fibrin; ADM: acellular dermal matrix; EMD: enamel matrix derivate; MT: Melatonin; CRC: complete root coverage; PI: Plaque index; BI: Gingival sulcus bleeding index; CAF: coronal advancement flap.

CONFLICT OF INTEREST

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REFERENCES

1. Prato GP. Mucogingival deformities. Annals of periodontology. 1999 Dec;4(1):98-100.
2. Fragkioudakis I, Tassou D, Sideri M, Vouros I. Prevalence and clinical characteristics of gingival recession in Greek young adults: A cross-sectional study. Clinical and Experimental Dental Research. 2021 Oct; 7(5):672-8.
3. Kassab MM, Cohen RE. The etiology and prevalence of gingival recession. The journal of the American Dental association. 2003 Feb 1; 134(2):220-5.
4. Matthew B M Thomas. Free gingival grafts to manage recession – when and how? DENTAL HEALTH. 2014; 53(1-6).
5. Zucchelli G. Mucogingival Esthetic Surgery, 1st edition 2013 Book. Title-No.: 19881 Quintessence Publishing, Italy.
6. Ravipudi, S., Appukuttan, D., Prakash, P., & Victor, D. (2017). Gingival Recession: Short Literature Review on Etiology, Classifications and Various Treatment Options. Journal of Pharmaceutical Sciences and Research, 9(2), 215.
7. Tonetti MS, Jepsen S. Clinical efficacy of periodontal plastic surgery procedures:Consensus Report of Group 2 of the 10th European Workshop on Periodontology.J Clin Periodontol 2014; 41 (Suppl. 15): S36–S43. doi: 10.1111/jcpe.12219.
8. Dr. J Leake,Dr. J. Mayhall Treatment of Gingival Recession: An Analysis of Current Literature.
9. Haim Tal, Ofer Moses, Ron Zohar, Haya Meir, Carlos Nemcovsky. Root coverage of advanced gingival recession: a comparative study between acellular dermal matrix allograft and subepithelial connective tissue grafts. J Periodontol. 2002 Dec;73(12):1405-11. doi: 10.1902/jop.2002.73.12.1405.
10. Hou LT, Yan JJ, Liu CM, Huang JF, Jehing SM, Wong MY, et al. Treatment of gingival recession- literature review of current progress. China Dental Journal. 2005;24(2):71-78.
11. Sculean A, Cosgarea R, Stähli A, et al. Treatment of multiple adjacent Miller class I and II gingival recessions with

a Modified Coronally Advanced Tunnel (MCAT). J Clin Periodontol. 2013; 40(7): 713–72.

12. Hofmänner P, Alessandri R, Laugisch O, et al. Predictability of surgical techniques used for coverage of multiple adjacent gingival recessions a systematic review. Quintessence Int. 2012; 43(7):545–554.
13. Dragana L Rakasevic, Iva Z Milinkovic, Sasa M Jankovic, Ivan A Soldatovic, Zoran M Aleksic, Natasa S Nikolic-Jakoba. The use of collagen porcine dermal matrix and connective tissue graft with modified coronally advanced tunnel technique in the treatment of multiple adjacent type I gingival recessions: A randomized, controlled clinical trial. J Esthet Restor Dent. 2020 Oct;32(7):681-690. doi: 10.1111/jerd.12624. Epub 2020 Jul 24.
14. Sourav Panda, Shahnawaz Khijmatgar, corresponding author, Heber Arbildo-Vega, Abhaya Chandra Das, Manoj Kumar, Mohit Das, Leonardo Mancini, and Massimo Del Fabbro. Stability of biomaterials used in adjunct to coronally advanced flap: A systematic review and network meta-analysis. Clin Exp Dent Res. 2022 Feb; 8(1): 421–438. Published online 2021 Nov 29.
15. Mohammed A AlSarhan, Reham Al Jasser, Mohammad Abdullah Tarish, Anas AlHuzaimi, Hamad Alzoman. Xenogeneic collagen matrix versus connective tissue graft for the treatment of multiple gingival recessions: A systematic review and meta-analysis. Meta-Analysis Clin Exp Dent Res,2019 Jun 30;5(5):566-579. doi: 10.1002/cre2.210.
16. Alina Masters, Seithikurippu R Pandi-Perumal, Azizi Seixas, Jean-Louis Girardin, and Samy I. McFarlane1Melatonin, the Hormone of Darkness: From Sleep Promotion to Ebola Treatment. Brain Disord Ther. 2014; 4(1): 1000151.
17. Mohammad taghi Chitsazi, 1 Masoumeh Faramarzie, ,Mehrnoosh Sadighi, Adileh Shirmohammadi, and Arash Hashemzadeh. Effects of adjective use of melatonin and vitamin C in the treatment of chronic periodontitis: A randomized clinical trial. J Dent Res Dent Clin Dent Prospects. 2017 Autumn; 11(4): 236–240.
18. Korkmaz A, Reiter RJ, Topal T, Manchester LC, Oter S and Tan DX. "Melatonin: an established antioxidant worthy of use in clinical trials,"MolecularMedicine, 2009; 15(1-2): 43–50.
19. Papapanou PN, Sanz M, Buduneli N, et al. Periodontitis: Consensus report of workgroup 2 of the 2017 World Workshopon the Classification of Periodontal and Peri-Implant Diseases and Conditions. J Periodontol. 2018;89:S173-S182.
20. Cortellini P, Bissada NF. Mucogingival conditions in the natural dentition: Narrative review, case definitions, and diagnostic considerations. Journal of periodontology. 2018 Jun;89:S204-13.
21. Muhlemann HR. Gingival sulcus bleeding-a leading symptom in initial gingivitis. Helv Odontol Acta. 1971; 15:107-113.
22. Marks IM. Components and correlates of psychiatric questionnaires: Observations on the Cornell Medical Index, Eysenck Personality Inventory and Tavistock Self-Assessment Inventory in phobic patients. Br J Med Psychol. 1967;40(3):261-272.
23. Yin X, Li Y, Li J, et al. Generation and periodontal differentiation of human gingival fibroblasts-derived integrationfree induced pluripotent stem cells. Biochem Biophys Res Commun. 2016;473:726-732.
24. Fournier BP, Larjava H, Hakkinen L. Gingiva as a source of stem cells with therapeutic potential. Stem Cells Dev. 2013;22:3157-3177.
25. McGuire MK, Scheyer ET. A randomized, double-blind, placebo-controlled study to determine the safety and efficacy of cultured and expanded autologous fibroblast injections for the treatment of interdental papillary insufficiency associated with the papilla priming procedure. J Periodontol. 2007;78:4-17.
26. Papapanou PN, Sanz M, Buduneli N, et al. Periodontitis: Consensus report of workgroup 2 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. J Periodontol. 2018;89:S173-S182.
27. Ramachandran L, Parthasarathy H, Tadepalli A. Long term evaluation of modified mucogingival flap technique with novel fish derived collagen matrix and connective tissue graft in treatment of multiple mandibular class iii gingival recession defectsa retrospective study. Int J Dentistry Oral Sci. 2021;8(10):4892-96. Doi: dx.doi. org/10.19070/2377-8075-21000989.
28. Dominiak, M.; Mierzwa, D.; Puzio, M.; Gedrange, T. Clinical evaluation of the effectiveness of using a collagen matrix in gingival recession coverage-pilot study. J. Stoma 2012, 65, 184–197.
29. Renn TY, Huang YK, Feng SW, Wang HW, Lee WF, Lin CT, Burnouf T, Chen LY, Kao PF, Chang HM. Prophylactic supplement with melatonin successfully suppresses the pathogenesis of periodontitis through normalizing RANKL/OPG ratio and depressing the TLR 4/MyD88 signaling pathway. Journal of pineal research. 2018 Apr;64(3):e12464.

30. Gómez-Florit M, Ramis JM, Monjo M. Anti-fibrotic and anti-inflammatory properties of melatonin on human gingival fibroblasts in vitro. Biochemical pharmacology. 2013 Dec 15;86(12):1784-90.

31. Jepsen K, Jepsen S, Zucchelli G, Stefanini M, de Sanctis M, Baldini N, Greven B, Heinz B, Wennström J, Cassel B, Vignoletti F. Treatment of gingival recession defects with a coronally advanced flap and a xenogeneic collagen matrix: a multicenter randomized clinical trial. Journal of clinical periodontology. 2013 Jan;40(1):82-9.

32. Giovan Paolo Pini Prato, Cristina Magnani, Leandro Chambrone. Long-term evaluation (20 years) of the outcomes of coronally advanced flap in the treatment of single recession-type defects. J Periodontol.2018 Mar;89(3):265-274. doi: 10.1002/JPER.17-0379 .

33. Pierpaolo Cortellini, Jacopo Buti, Giovanpaolo Pini Prato, Maurizio S Tonetti. Periodontal regeneration compared with access flap surgery in human intra-bony defects 20-year follow-up of a randomized clinical trial: tooth retention, periodontitis recurrence and costs. J Clin Periodontol. 2017 Jan;44(1):58-66. doi: 10.1111/jcpe.12638.

34. Lorenzo Tavelli, Shayan Baroot, Francesco Cairo and Giulio Rasperini. The Effect of Time on Root Coverage Outcomes. 2019:J Dent Res 98 (Spec Iss A):Abstract No. 1679.

35. Francesco Cairo, Pierpaolo Cortellini, Maurizio Tonetti and Michele Nieri. Stability of root coverage outcomes at single maxillary gingival recession with loss of interdental attachment: 3-year extension results from a randomized, controlled, clinical trial,April 2015Journal Of Clinical Periodontology 42(6).

36. Karin Jepsen ,Martina Stefanini, Mariano Sanz and Giovanni Zucchelli. Long-Term Stability of Root Coverage by Coronally Advanced Flap Procedure, March 2017Journal of Periodontology 88(7):1-15.

37. Giovanpaolo Pini-Prato, Debora Franceschi, Francesco Cairo, Michele Nieri, and Roberto Rotundo. Classification of Dental Surface Defectsin Areas of Gingival Recession. J Periodontol Volume81, Issue6.,Pages 885-890 June 2010.

38. Francesco Cairo, Umberto Pagliaro, Jacopo Buti, Michela Baccini, Filippo Graziani, Paolo Tonelli 7, Gabriella Pagavino 8, Maurizio S Tonetti. Root coverage procedures improve patient aesthetics. A systematic review and Bayesian network meta-analysis 2016 J Clin Periodontol ,Nov;43(11):965-975.

39. Zucchelli G, Tavelli L, McGuire MK, Rasperini G, Feinberg SE, Wang HL, Giannobile WV. Autogenous soft tissue grafting for periodontal and peri-implant plastic surgical reconstruction. Journal of Periodontology. 2020 Jan;91(1):9-16.

40. Lorenzo Tavelli, Shayan Barootchi, Andrea Ravidà, Tae-Ju Oh, Hom-Lay Wang. What Is the Safety Zone for Palatal Soft Tissue Graft Harvesting Based on the Locations of the Greater Palatine Artery and Foramen? A Systematic Review J Oral Maxillofac Surg. 2019 Feb;77(2):271.e1-271.e9

41. Marta Cieślik-Wegemund, Beata Wierucka-Młynarczyk, Marta Tanasiewicz, Łukasz Gilowski . Tunnel Technique With Collagen Matrix Compared With Connective Tissue Graft for Treatment of Periodontal Recession: A Randomized Clinical Trial. J Periodontol. 2016 Dec;87(12):1436-1443.

42. Pietruska, M., Skurska, A., Podlewski, L., Milewski, R., & Pietruski, J. .Clinical evaluation of Miller class I and II recessions treatment with the use of modified coronally advanced tunnel technique with either collagen matrix or subepithelial connective tissue graft: A randomized clinical study. Journal of Clinical Periodontology, 2019, 46(1), 86– 95.

43. Discepoli N, Mirra R, Ferrari M. Efficacy of enamel derivatives to improve keratinized tissue as adjunct to coverage of gingival recessions: a systematic review and meta-analysis. Materials. 2019 Aug 30;12(17):2790.

44. Giovanni Zucchelli, Lorenzo Tavelli, Shayan Barootchi, Martina Stefanini, Giulio Rasperini, Cristina Valles, José Nart, Hom-Lay Wang.The influence of tooth location on the outcomes of multiple adjacent gingival recessions treated with coronally advanced flap: A multicenter reanalysis study. J Periodontol, 2019 Nov;90(11):1244-1251.

45. Francesco Cairo 1, Michele Nieri, Umberto Pagliaro. Efficacy of periodontal plastic surgery procedures in the treatment of localized facial gingival recessions. A systematic review, J Clin Periodontol, 2014 Apr;41 Suppl 15:S44-62

46. Lorenzo Tavelli, Shayan Barootchi, Trang V N Nguyen, Mustafa Tattan, Andrea Ravidà, Hom-Lay Wang. Efficacy of tunnel technique in the treatment of localized and multiple gingival recessions: A systematic review and meta-analysis. J Periodontol. 2018 Sep;89(9):1075-1090.

47. Mauro Pedrine Santamaria, Felipe Lucas da Silva Neves, Camila Augusto Silveira, Ingrid Fernandes Mathias, Stephanie Botti Fernandes-Dias, Maria Aparecida Neves Jardini, Dimitris N Tatakis. Connective tissue graft and tunnel or trapezoidal flap for the treatment of single maxillary gingival recessions: a randomized clinical trial. J Clin Periodontol. 2017 May;44(5):540-547.

48. G Pini Prato 1, U Pagliaro, C Baldi, M Nieri, D Saletta, F Cairo, P Cortellini. oronally advanced flap procedure for root coverage. Flap with tension versus flap without tension: a randomized controlled clinical study. J Periodontol 2000 Feb;71(2):188-201.

49. Debby Hwang and Hom-Lay Wang Flap Thickness as a Predictor of Root Coverage: A Systematic Review Journal of Periodontology, November 2006 ,77(10):1625-34.

50. Dominiak, M.; Mierzwa, D.; Puzio, M.; Gedrange, T. Clinical evaluation of the effectiveness of using a collagen matrix in gingival recession coverage-pilot study. J. Stoma 2012, 65, 184–197.

51. Jonathan Meza-Mauricio 1, Jônatas Cortez-Gianezzi 1, Poliana Mendes Duarte 2, Lorenzo Tavelli 3, Giulio Rasperini 3 4, Marcelo de Faveri. Comparison between a xenogeneic dermal matrix and connective tissue graft for the treatment of multiple adjacent gingival recessions: a randomized controlled clinical trial. Clin Oral Investig. 2021 Dec;25(12):6919-6929.

52. Shayan Barootchi,corresponding Lorenzo Tavelli, Riccardo Di Gianfilippo, Kerby Shedden, Tae-Ju Oh, 1 Giulio Rasperini, Rodrigo Neiva, William V. Giannobile, and Hom-Lay Wang Soft tissue phenotype modification predicts gingival margin long-term (10-year) stability: Longitudinal analysis of six randomized clinical trials. J Clin Periodontol. 2022 Jul; 49(7): 672–683.

53. Giovan Paolo Pini Prato, Debora Franceschi, Pierpaolo Cortellini, Leandro Chambrone. Long-term evaluation (20 years) of the outcomes of subepithelial connective tissue graft plus coronally advanced flap in the treatment of maxillary single recession-type defects. J Periodontol, 2018 Nov; 89(11):1290-1299.

54. Giulio Rasperini, Raffaele Acunzo, Gaia Pellegrini 1, Giorgio Pagni, Maurizio Tonetti, Giovan Paolo Pini Prato, Pierpaolo Cortellini. Predictor factors for long-term outcomes stability of coronally advanced flap with or without connective tissue graft in the treatment of single maxillary gingival recessions: 9 years results of a randomized controlled clinical trial J Clin Periodontol. 2018 Sep; 45(9):1107-1117..

55. Knut N Leknes 1, Evandro S Amarante, Daniel E Price, Olav E Bøe, Ragnfrid J Skavland, Tryggve Lie. Coronally positioned flap procedures with or without a biodegradable membrane in the treatment of human gingival recession. A 6-year follow-up study. J Clin Periodontol, 2005 May; 32(5):518-29.

56. Giulio Rasperini, Raffaele Acunzo, Gaia Pellegrini, Giorgio Pagni, Maurizio Tonetti, Giovan Paolo Pini Prato, Pierpaolo Cortellini.Predictor factors for long-term outcomes stability of coronally advanced flap with or without connective tissue graft in the treatment of single maxillary gingival recessions: 9 years results of a randomized controlled clinical trial. J Clin Periodontol. 2018;45:1107–1117.