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Original Article

Treatment of multiple gingival recessions with concentrated growth factor membrane and coronally advanced tunnel technique via digital measurements: A randomized controlled clinical trial

Fei Xue [a†], Rui Zhang [b†], Yong Zhang [a], Jia Liu [c], Yu Cai [c], Pei Cao [c], Qingxian Luan [c*]

[a] *First Clinical Division, Peking University School and Hospital of Stomatology & National Clinical Research Center for Oral Diseases & National Engineering Laboratory for Digital and Material Technology of Stomatology & Beijing Key Laboratory of Digital Stomatology & Research Center of Engineering and Technology for Computerized Dentistry Ministry of Health, Beijing, PR China*

[b] *Third Clinical Division, Peking University School and Hospital of Stomatology & National Clinical Research Center for Oral Diseases & National Engineering Laboratory for Digital and Material Technology of Stomatology & Beijing Key Laboratory of Digital Stomatology & Research Center of Engineering and Technology for Computerized Dentistry Ministry of Health, Beijing, PR China*

[c] *Department of Periodontology, Peking University School and Hospital of Stomatology & National Clinical Research Center for Oral Diseases & National Engineering Laboratory for Digital and Material Technology of Stomatology & Beijing Key Laboratory of Digital Stomatology & Research Center of Engineering and Technology for Computerized Dentistry Ministry of Health, Beijing, PR China*

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KEYWORDS
Concentrated growth factor;
Connective tissue graft;
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Abstract *Background/purpose:* Research into biomaterial alternatives to connective tissue grafts (CTG) is a research hotspot. The purpose of this clinical trial was to compare the effectiveness of root coverage through tunnel technique with concentrated growth factor (CGF) vs CTG in treating multiple gingival recessions using digital measurements.
Materials and methods: Seventy Cairo Class I multiple gingival recessions (in 28 patients) were treated with either CGF or CTG combined with coronally advanced tunnel technique. Digital models were obtained at baseline, 2 weeks, 6 weeks, and 6 months post-op to compare the

* Corresponding author. Department of Periodontology, School and Hospital of Stomatology, Peking University, NO.22, Zhongguancun South Avenue, Haidian District, Beijing, 100081, PR China. Fax: +86 10 62173402.
E-mail address: kqluanqx@126.com (Q. Luan).
† These authors contributed equally to this work.

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Digital measurement;
Gingival recession

gain in gingival height, area, volume, and thickness. Tooth sensitivity, post-operative pain, and healing index were also recorded.
Results: Complete root coverage at 6 months post-op were 47.06% in the CGF group and 77.78% in the CTG groups. Mean root coverages were 80.55% and 96.18%, respectively. No statistical difference was demonstrated between the two groups in terms of gingival area gain at 2 weeks post-op, but the CTG group had greater increases in gingival height, area, volume, and thickness in the period after 2 weeks post-op. Pain scores were statistically significantly lower in the CGF group. At 6 months post-op, sensitivity scores decreased more significantly in the CTG group.
Conclusion: Digital measurements revealed post-operative gingival shrinkage was more pronounced in the CGF group than in the CTG group when combined with coronally advanced tunnel technique. Despite the ease-of-use and minimal post-operative discomfort, it is difficult to achieve similar root coverage outcomes to CTG when using CGF alone in treating multiple gingival recessions.

Introduction

Gingival recession (GR) is defined as apical shift of the gingival margin relative to the cemento-enamel junction (CEJ). The presence of GR may be associated with dentin hypersensitivity, root cavity, non-carious cervical lesions, and is often aesthetically unacceptable for patients.[1,2] Numerous techniques and biomaterials have been proposed for the treatment of single or multiple gingival recessions. The combination of connective tissue graft (CTG) and coronally advanced flap technique has been considered the gold standard for its high root coverage predictability and long-term stability. However, some limitations, such as the necessity of second surgical sites, inadequate palate tissue amount, potential post-operative bleeding, and pain may exist when using this technique. Consequently, alternative materials, such as autologous platelet concentrates, have been proposed.[3]

Concentrated growth factor (CGF), which was first introduced by Sacco, has emerged as a potential regenerative material.[4] Rather than being obtained by constant speed centrifugation as in platelet-rich fibrin (PRF), CGF is acquired using a special device at varying speed. Some studies have reported higher tensile strength and higher growth factors for CGF when compared to PRF.[5] In addition, CGF has also been characterized as less enzymatically degradable than PRF and as having a longer growth factor release time.[6] Currently, CGF is widely applied in a variety of dental surgeries, including the sinus lifts, peri-implantitis, periodontal regeneration, and root coverage.[7–9] CGF can not only significantly promote the proliferation and osteo-induction of periodontal ligament stem cells but has also resulted in better bone formation than PRF in treatments for femur defects in adult dogs.[10,11]

Compared to coronally advanced flap technique, coronally advanced tunnel technique allows flap elevation without detachment of the papillary or vertical releasing incisions. It is believed that coronally advanced tunnel technique can provide better blood supply, less post-operative morbidity, faster and earlier wound healing, and improved aesthetic results by avoiding any kind of visible incisions. Studies have also shown that coronally advanced tunnel technique has relatively wider applications and satisfactory aesthetic results in the treatment of teeth with narrow keratinized gingival width.[12]

Intraoral scanning equipment and software applications have rapidly advanced.[13] Recent surveys have revealed that digital models obtained via intraoral scanning have achieved clinically satisfactory accuracy for capturing gingival contour in anterior maxilla, with a comparable or superior precision to conventional plaster models.[14] Therefore, there is a tendency toward utilization of digital modelling techniques as an alternative to plaster modelling, due to the advantages of greater patient comfort, easier storage requirements, and more comprehensive data gathering.[15,16]

The purpose of this study was to compare the effectiveness of root coverage through coronally advanced tunnel technique using CGF or CTG in treating multiple gingival recessions as observed using digital measurements.

Materials and methods

This clinical investigation was designed as a single center, randomized prospective clinical comparative study. The study protocol was approved by the Ethics Committee of Peking University Stomatology Hospital (PKUSSIRB-201947089) and registered in the Chinese Clinical Trial Registry (ChiCTR1900026768). All procedures performed in the present study involving human participants were in accordance with the standards of the declaration of Helsinki 1975, which was amended in 2000. Written informed consent for participation was obtained from each subject recruited in this study.

Study population

A total of 28 patients were selected among individuals who attended the First Clinical Division, Peking University

Hospital and School of Stomatology from October 2019 to June 2022. A total of 70 gingival sites were randomly divided into two groups using to a random number table method. 34 sites were treated using coronally advanced tunnel technique combined with CGF membrane while the remaining 36 sites were treated using coronally advanced tunnel technique combined with CTG.

All participants met the inclusion criteria: (1) aged 18–65; (2) presented $\geq$2 adjacent teeth with $\geq$1.5 mm Cairo class I gingival recession with identifiable CEJ at incisors, canines, and premolars;[17] (3) good oral hygiene with bleeding index $\leq$1. The exclusion criteria were: (1) patient taking medication that could affect the gingival health; (2) smoker; (3) thin gingival biotype; (4) received other oral surgery.

Concentrated growth factor membranes preparation

Before the surgical procedure, 2 tubes of 10 mL peripheral venous blood were collected from the patient and immediately centrifuged in a CGF centrifuge machine (Silfradent, Sofia, Italy) according to CGF protocols (30 s acceleration, 2 min 2700 rpm, 4 min 2400 rpm, 4 min 2700 rpm, 3 min 3000 rpm, 36 s deceleration and stop). Two CGF clots were removed from the tubes and compressed to obtain an overlapping CGF membrane at a constant thickness of 1 mm. The CGF membranes were applied to recipient sites immediately.

Connective tissue graft preparation

A CTG of 1 mm thickness and 5 mm width was harvested from the palate using a de-epithelialized graft method. Then, the CTG was trimmed to fit the dimension of the surgical area. The donor site was re-covered with a collagen membrane (Yierkang, Beijing, China) and sutured using 5-0 polypropylene absorbable sutures (Johnson & Johnson, New Brunswick, NJ, USA).

Surgical procedures

All subjects were treated using coronally advanced tunnel technique in combination with CGF or CTG by the same surgeon (Figs. 1 and 2). Prior to the surgical procedure, the exposed root was planed using Gracey curettes (Hu-Friedy, Chicago, IL, USA) and conditioned using 17% ethylenediaminetetraacetic acid (Pulpdent Corp, Watertown, MA, USA) for 3 min. After application of local anesthesia, crevicular incisions were made around the compromised teeth and one adjacent tooth on each side. The split thickness tunnel was extended apically above the mucogingival junction and horizontally beyond one adjacent tooth using tunnel instruments (Hu-Friedy, Chicago, IL, USA) without disrupting the interdental papilla. Thereafter, the tunnel flap could be coronally positioned beyond the CEJ without excessive tension. Subsequently, a CGF or CTG was carefully inserted into the tunnel. 5-0 polypropylene absorbable sutures were used in sling sutures along with vertical mattress sutures to coronally reposition the tissue. Compression was applied to the recipient area using sterile gauze pads for 1 min.

Post-operative care

All patients were prescribed amoxicillin 500 mg (twice a day for 3 days) and instructed to rinse their mouth using 0.2% chlorhexidine solution (twice a day for 2 weeks). Fenbid (ibuprofen) was given for post-operative pain (every 8 hours as needed). The sutures were removed at 2 weeks post-op. Patients were then instructed to perform the rolling brushing technique with a soft toothbrush. Re-examinations were conducted at 1, 2, 6 weeks and 6 months after surgery. Supragingival plaque was removed when necessary.

Clinical measurement parameters

Probing depth, keratinized tissue width and tooth sensitivity score were recorded at baseline and 6 months post-surgery while post-operative pain scores were recorded at 1, 2, 3, 5, 7,10, and 14 days after surgery. Both post-operative pain and tooth sensitivity were assessed using a visual analog scale questionnaire on a scale of 1–10. An assessment of soft tissue healing was performed at 2 weeks post-surgery using the healing index system described by Landry et al.[18] All clinical measurements were carried out by a single examiner.

Digital measurement parameters

A Trios color intraoral scanner (3 shape, Copenhagen, Denmark) was used to obtain digital models at baseline, 2 weeks, 6 weeks and 6 months after surgery. All digital measurements were performed using Geomagic Studio 2013 (3D Systems, Rock Hill, SC, USA) adhering to the method described in our previous study (Fig. 3).[19] The gingival recession height, width, and area were measured according to the baseline digital models while the gain of gingival height, area, and volume were measured using the superimposition of digital models between baseline and corresponding post-operative digital models. The gingival mean thickness was calculated by dividing the gingival volume gain at the site of interest by the corresponding gingival area gain. The mean root coverage was considered to be the percentage calculated by dividing post-operative gingival height gain by pre-operative gingival recession height. Notably, all values greater than 100% were calculated as 100% because post-operative gingival area gain greater than or equal to the pre-operative gingival recession area was considered to be complete root coverage. All digital measurements were performed by a single examiner.

Statistical analysis

According to the results of power analysis ($\alpha = 0.05$, 80% power which is equal $\beta = 0.20$), 14 participants in every group were needed in each group.[20] Normality was checked using the Shapiro–Wilk test. Comparison of the means of all parameters in each study group was

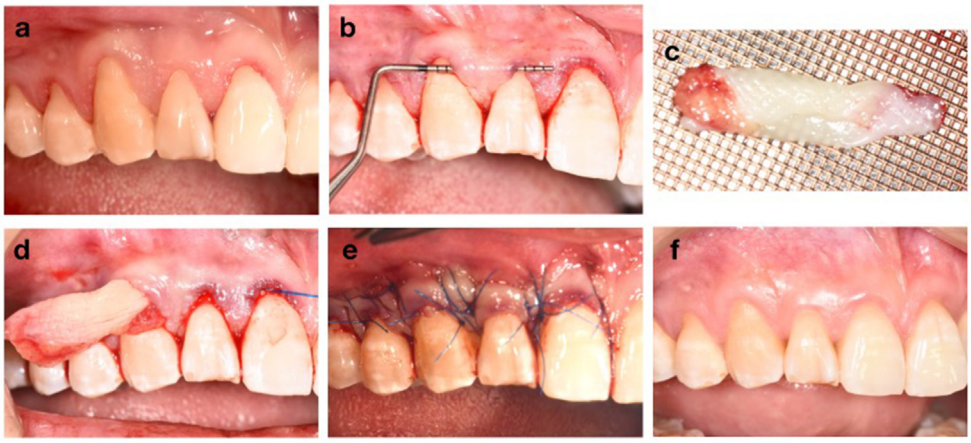

Figure 1 Surgical protocol of gingival recession defects treated by coronally advanced tunnel with CGF. Baseline (a); prepared tunnel (b); prepared CGF membrane (c); inserted CGF membrane into the tunnel (d); sutured (e); 6 months post-op (f).

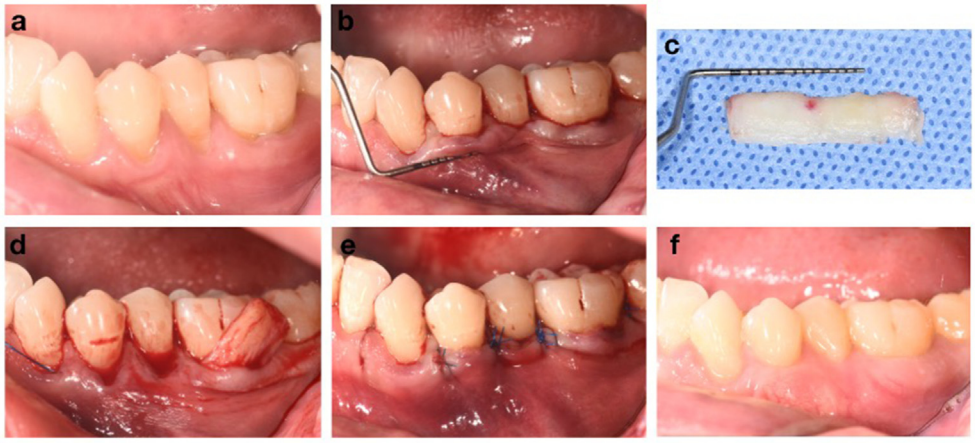

Figure 2 Surgical protocol of gingival recession defects treated by coronally advanced tunnel with CTG. Baseline (a); prepared tunnel (b); harvested CTG from palate (c); inserted CTG into the tunnel (d); sutured (e); 6 months post-op (f).

performed using the Mann—Whitney U-test (p_1). The Wilcoxon signed-rank test was used to determine the difference in parameters between baseline and 6-months after surgery (p_2). Friedman's test with Dunn's multiple comparison correction was used to evaluate the difference in parameters over time (p_3). $p < 0.05$ was considered to indicate statistically significance.

Results

A total of 70 Cairo Class I multiple gingival recessions (43 in maxillary and 27 in mandible) across 28 patients (17 men and 11 women, aged 38.56 ± 9.28 years) were included in this study. 36 defects (12 incisors, 10 canines and 14 premolars) were treated using coronally advanced tunnel technique with CTG, while 34 defects (15 incisors, 9 canines and 10 premolars) were treated with CGF. All patients completed a 6-month follow-up period.

Table 1 shows that the CGF and CTG groups were not different at baseline. The probing depth did not show any marked change between baseline and 6 months post-surgery for either group. However, a significant increase in keratinized tissue width was observed in both groups at 6 months compared with the baseline, with no differences were observed between the groups (Table 2).

Post-operative gingival augmentation was encountered distinctly at 2 weeks post-surgery in both groups, then gradually decreased (Table 3). While gingival area gain showed no significant difference between the groups at 2 weeks post-surgery, the CTG group displayed a higher gain of gingival height, volume, and thickness in the subsequent period. Augmentation of gingiva remained largely stable in the CTG group beyond 6 weeks post-surgery. In the CGF group, only gingival height gain was observed to have no significant difference between 6 weeks and 6 months post-surgery.

During intergroup comparisons, post-operative pain scores were statistically significantly higher in the CTG group than in the CGF group. It was not until 3 days after surgery that the pain scores had declined significantly in both groups. Significantly higher values of tooth sensitivity were recorded in the test group when compared with

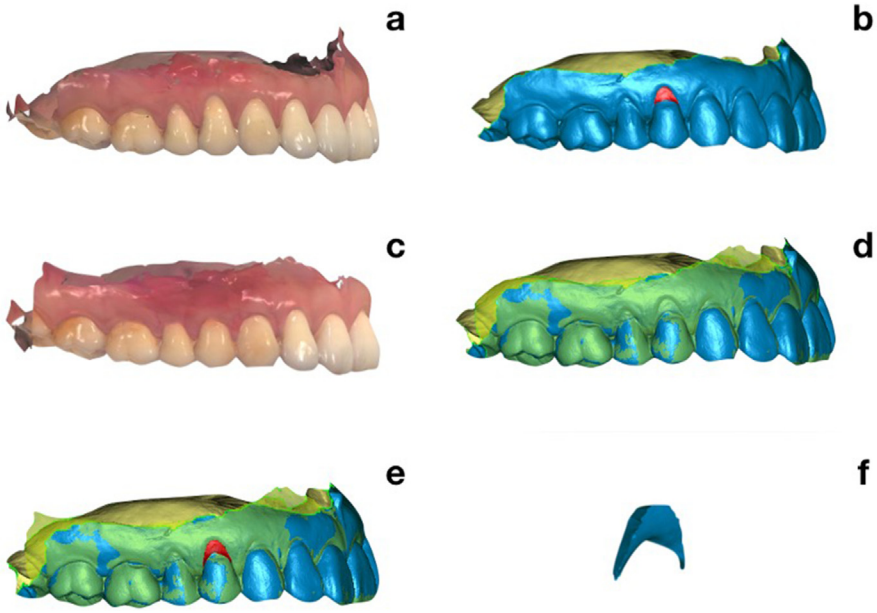

Figure 3 Digital measurements of the right upper first premolar between Baseline and 2 weeks after surgery. Pre-operative intraoral scan (a); measurement of gingival recession height, width, and area on the Baseline model (b); post-operative intraoral scan (c); superimposition of two digital models (d); measurement of gingival height and area gain (e); measurement of gingival volume gain on reconstructed region of interest (f).

Table 1 Comparisons of gingival recession height, width, and area at baseline.

	Control group	Test group	p_1
Gingival recession height (mm)	2.092 ± 0.720	1.912 ± 0.829	0.193
Gingival recession width (mm)	3.063 ± 0.547	3.637 ± 0.959	0.061
Gingival recession area (mm^2)	6.139 ± 2.005	7.374 ± 5.277	0.842

controls at 6 months post-surgery. Despite the fact that the healing index was slightly lower in the test group, no significantly difference was observed between two groups (Table 4).

The mean root coverage at 6 months post-op was 80.55 ± 22.03% in the CGF group and 96.18 ± 7.66% in the CTG group ($p = 0.004$). Meanwhile, 47.06% (16/34) of defects in the CGF group and 77.78% (28/36) of defects in the CTG group were achieved complete root coverage after treatment ($p < 0.001$).

Discussion

Research for alternative biomaterials to CTG in root coverage surgery has been a hot topic. Since the acquisition of CTG inevitably requires creation of a second instance of tissue damage, at the donor site, among other drawbacks.[21] The purpose of this study was to evaluate the effectiveness of CGF as an alternative biomaterial to CTG for management of gingival recession in combination with coronally advanced tunnel technique within 6 months, as assessed by digital measurement. Three-dimensional quantitative measurements taken via intraoral scanning enabled the study to obtain more accurate and more abundant data. Recent surveys revealed that digital models created via intraoral scanning have achieved clinically satisfying accuracy for capturing gingival contour, with a comparable or superior precision to conventional plaster models.[15,22]

Table 2 Comparisons of probing depth and keratinized tissue width.

		Control group	Test group	p_1
Probing depth (mm)	Baseline	1.120 ± 0.332	1.143 ± 0.427	0.589
	6 months	1.280 ± 0.458	1.214 ± 0.418	0.773
	p_2	0.063	0.125	
Keratinized tissue width (mm)	Baseline	2.820 ± 0.852	2.500 ± 0.793	0.067
	6 months	3.440 ± 0.712	3.464 ± 0.932	0.792
	p_2	0.000***	0.002**	

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

Table 3 Comparisons of the gain of gingival height, area, volume, and mean thickness by digital measurements.

		Control group	Test group	p_1
Gingival height gain (mm)	2 weeks	2.932 ± 0.839	2.300 ± 1.255	0.029*
	6 weeks	2.599 ± 0.881**	1.555 ± 0.522***	0.000***
	6 months	2.532 ± 0.921##	1.332 ± 0.457###	0.000***
	p_3	0.000***	0.000***	
Gingival area gain (mm^2)	2 weeks	10.277 ± 3.658	10.031 ± 4.810	0.215
	6 weeks	9.023 ± 3.408***	6.719 ± 3.835***	0.001**
	6 months	9.115 ± 3.902###	5.867 ± 3.087### , &	0.001**
	p_3	0.000***	0.000***	
Gingival volume gain (mm^3)	2 weeks	11.973 ± 6.987	7.385 ± 5.220	0.013*
	6 weeks	9.443 ± 6.776***	3.487 ± 2.785***	0.000***
	6 months	9.216 ± 6.454###	2.377 ± 2.073###, &&	0.000***
	p_3	0.000***	0.000***	
Gingival mean thickness (mm)	2 weeks	1.100 ± 0.417	0.659 ± 0.275	0.000***
	6 weeks	0.962 ± 0.398	0.467 ± 0.200*	0.000***
	6 months	0.918 ± 0.399##	0.361 ± 0.190###, &&	0.000***
	p_3	0.005**	0.000***	

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$ indicate statistical significance between 2 weeks and 6 weeks.
#$p < 0.05$, ##$p < 0.01$, ###$p < 0.001$ indicate statistical significance between 2 weeks and 6 months.
& $p < 0.05$, && $p < 0.01$ indicate statistical significance between 6 weeks and 6 months.

Autologous platelet concentrates have gained attention for the treatment of gingival recession in the last several decades.[3] CGF, a the third-generation platelet concentrate derived from autologous blood, contains a variety of autologous growth factors such as transforming growth factor-β (TGF-β), platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), and insulin-like growth factor-1 (IGF-1) which are of crucial importance in tissue regeneration.[23] The proliferation of osteoblast and gingival fibroblast was significantly greater than that of PRF when CGF was added into the medium.[5] A recent study by Qi et al. demonstrated that CGF not only promotes the proliferation and migration of gingival mesenchymal stem cells but also enhances the expression of pro-angiogenic and collagen-related proteins *in vitro*, making it a prerequisite for gingival tissue repair and regeneration.[24]

In the present study, the mean root coverages, after 6 months, were 80.55% for the CGF group and 96.18% for the CTG group. Additionally, the percentages of complete root coverage achieved were 47.06% in the CGF group and 77.78% in the CTG group. Both groups showed significantly improved clinical outcomes at 6 months post-surgery when compared with baseline, but the CTG group displayed superior results. Similar mean root coverage results were achieved by Korkmaz et al. using the tunnel technique.[25] However, split-mouth trials that used CGF in combination with coronally advanced flap technique showed varying mean root coverages from 52.45% to 86.67%.[26,27] It may be difficult to draw conclusions from the insufficient clinical evidence available. Both the coronally advanced flap and the tunnel techniques resulted in excellent clinical and patient-centered outcomes when combined with CTG.[28] Nevertheless, the coronally advanced tunnel technique may lead to better color blend and aesthetic marginal morphology by retaining the intactness of the papillary region and because of its lack of vertical releasing incisions, which allows for better vascular supply and less trauma.

Table 4 Comparisons of post-operative pain, tooth sensitivity, and healing index.

		Control group	Test group	p_1
Post-operative pain	1 day	4.917 ± 0.669	4.143 ± 0.663	0.008**
	2 days	4.083 ± 0.669	3.429 ± 0.514	0.006**
	3 days	3.583 ± 0.669	2.786 ± 0.579	0.001**
	5 days	2.750 ± 0.622***	2.214 ± 0.426**	0.042*
	7 days	2.167 ± 0.577***	1.500 ± 0.519***	0.006**
	10 days	1.500 ± 0.674***	0.714 ± 0.469***	0.002**
	14 days	1.000 ± 0.603***	0.429 ± 0.514***	0.022*
	p_3	0.000***	0.000***	
Tooth sensitivity	Baseline	0.857 ± 0.848	0.880 ± 0.666	0.668
	6 months	0.143 ± 0.356	0.400 ± 0.577	0.041*
	p_2	0.000***	0.033*	
Healing index	2 weeks	4.720 ± 0.458	4.500 ± 0.577	0.233

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

Based on the results of this study, though there was no difference in terms of gingival area gain at 2 weeks post-surgery between the two groups, more significant contraction of gingival tissue could be observed in the CGF group. In addition, there was no significant difference in any gingival parameters between 6 weeks and 6 months post-operative in the CTG group. However, in the CGF group, the same situation was observed only for gingival height change. All of these results indicate that the augmented gingiva was sustained with greater stability when using CTG compared to CGF alone.

Unlike previous studies that mostly used endodontic spreaders and calipers to measure gingival thickness changes, this study utilized a digital method to measure the dynamic change of gingival thickness within 6 months post-surgery in regions of interest. The results of this study showed that the gingival mean thickness in the CGF group at 6 months post-surgery was 0.357 $\pm$ 0.208 mm, which is comparable or slightly higher than in the previous study. This may be attributed, at least partially, to the two layers of CGF membranes used in this study. The previous study indicated that multilayered PRF was recommended to provide a higher mean root coverage percentage.[29]

In this study, the keratinized tissue width increased significantly in both groups at 6 months post-op compared to baseline. Although some studies have suggested that platelet concentrates are more favorable for the increase of keratinized tissue width, there was no significant intergroup difference in this study.[27,30] The increased amount of keratinized tissue width in the test groups could be attributed to the favorable effect of growth factors, which are released from CGF, on gingival and fibroblast proliferation.

Post-operative pain scores in the CGF group in this study were significantly lower than those in the CTG group. This is probably because of the absence of an additional donor area in the CGF group, thus avoiding the discomfort caused by sutures or eating during while the donor site was still healing. Though recent studies have shown that the abundant growth factors released from platelet concentrates may be beneficial to the healing of the wound, due to its promotion to endothelial tube formation, the healing index in this study did not differ significantly between the two groups.[31]

The present study had several limitations. Firstly, more reliable results could be achieved with the split-mouth design to minimize interpatient influence on wound healing. In addition, this study only investigated post-operative gingival thickness changes and did not consider the potential effect of original gingival thickness on post-operative outcomes. Future studies with larger sample sizes and longer follow-up periods are anticipated.

Within the limitations of this study, our results suggest that CTG is more spatially sustainable and has better long-term stability than CGF when combined with coronally advanced tunnel technique in treating multiple gingival recessions.

Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

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