



ELSEVIER

ORIGINAL ARTICLE

Systematic Review of the Clinical Performance of Connective Tissue Graft and Guided Tissue Regeneration in the Treatment of Gingival Recessions of Miller's Classification Grades I and II

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Background/Purpose: The objective of this meta-analysis was to assess and compare the effectiveness of connective tissue graft (CTG) and guided tissue regeneration (GTR) in treating patients with gingival recessions of Miller's classification grades I and II.

Methods: Nineteen clinical studies that met pre-stated inclusion criteria were screened from 250 initial articles for the systematic analysis of the clinical efficacies of CTG and GTR according to four clinical variables: recession depth reduction; clinical attachment gain; keratinized tissue gain; and probing depth reduction. The heterogeneity and weighted mean difference were calculated using a statistical package for meta-analysis.

Results: In the follow-up period shorter than 12 months, CTG resulted in more keratinized tissue than GTR ($p < 0.05$). In the follow-up period of 12 months or longer, CTG resulted in significantly greater reduction in recession depth, more keratinized tissue gain, and less probing depth reduction than GTR ($p < 0.05$).

Conclusion: With regard to recession depth reduction and keratinized tissue gain in the treatment of Miller's class I or II gingival recession, CTG was statistically significantly more effective than GTR.

1. Introduction

Gingival recession is defined as a shift of the gingival margin to a position apical to the level of the cemento-enamel junction.¹ Recession may be related to inappropriate tooth brushing or due to inflammatory destruction of the periodontium. Root hypersensitivity, esthetic problem, and abrasion may accompany gingival recession and spur patients to seek treatment. The main goal of treatment is to augment the width and height of the attached gingiva and create a harmonious soft tissue

appearance, as well as to obtain complete root coverage. Various methodologies have been used to treat gingival recession in the last decade, including many mucogingival graft techniques,^{2–6} or combined with guided tissue regeneration (GTR) procedures.⁷

The use of subepithelial connective tissue grafts (CTGs) and coronally positioned flaps (CPFs) for root coverage was developed by Langer and Langer,⁸ who reported an increase of 2–6 mm of root coverage over 4 years. A study selected paired defects and assessed the potential for root coverage with free gingival grafts (FGGs)

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and subepithelial CTGs.⁹ They found that root coverage averaged 43% for FGs and 80% for CTGs. Another study also indicated that CTGs had an 85% success rate, which was better than the 53% success rate with FGs.¹⁰

Polytetrafluoroethylene (ePTFE) was first used by Tinti and Vincenzi to cover roots.⁷ In the early days, non-bioabsorbable membranes such as Millipore filters (Millipore, Billerica, MA, USA) and ePTFE were used in the GTR technique; due to the inability to degrade, the clinical applications were limited.¹¹ The space-making concept is used with bioresorbable membranes adjunct to CPFs to avoid the need for a second surgical procedure to remove non-resorbable membrane. Bioabsorbable membranes are widely used nowadays, and include such materials as collagen, polyglycolic acid, polylactic acid, and polymers of the above-mentioned materials.¹² A study comparing the use of ePTFE and polyglycolic acid membranes for root coverage found no statistically significant differences in the mean root coverage between these two materials.¹³

Comparisons of the use of GTR and CTG combined with CPF to achieve complete root coverage are controversial. Factors that can influence outcomes of CTG and GTR when treating root coverage include the pre-treatment recession depth, the type of surgical modality used, histological features of the dentogingival junction after root coverage, root conditioning, type of GTR material chosen, and other confounding factors, such as smoking and bias caused by commercial interests.

Since different studies are carried out using different populations, different designs, and a wide range of specific factors for each study, it was suggested that combining them may produce an evaluation that has broader ability to be generalized than any single study by itself.¹⁴ The objective of this systematic review was to assess the effectiveness of CTG and GTR in treating patients with gingival recessions and to compare the efficacy of CTG with GTR for root coverage. The study procedures in our review process followed the PICO format [which stands for patient (or disease), intervention (a drug or test), comparison (another drug, placebo or test), and outcome].¹⁵

2. Material and Methods

2.1. Search strategy

The search was conducted using the Ovid MEDLINE database, from 1950 to and including March 2009. No hand searching was conducted. The search used the following descriptors: gingival recession/therapy, gingival recession/surgery, tooth root/surgery, guided tissue regeneration, or connective tissue/transplantation. Afterwards, the operator "and" was used at the end of the process to narrow the search and select articles that contained all of the PICO terms.

2.2. Criteria for screening and selection of references

To be eligible for inclusion in this review, studies had to be human clinical trials conducted on patients with a diagnosis of gingival recession of Miller's classification grade I or II, used CTG or GTR as the treatment modalities for gingival recession, and have a follow-up period of at least 6 months. All reviewed articles were confined to journals published in English only. Exclusion criteria for the root coverage procedures were studies that included furcation-involved teeth, or that had subjects who smoked, or that had follow-up periods shorter than 6 months, or the treated recessions were other than Miller's classification grade I or II.

2.3. Screening procedure

Titles and abstracts were initially screened for possible inclusion by viewing them according to the following criteria: they had to be human trials; they had to use GTR or CTG for gingival recession treatment; and they had to include clinical outcomes. Reports that clearly did not meet the inclusion criteria were excluded; otherwise, the articles were included for a secondary review. The full text of possibly relevant studies was then secondarily screened according to the inclusion criteria. Any disagreement in the selection process was resolved by discussion between two reviewers. The screening process is illustrated in Figure 1, and the characteristics of the 18 included studies are reported in Table 1.^{13,16-32} There were only three articles included for 12-month follow-up for each CTG and GTR subgroup. Forty-two articles were excluded; they are listed in Table 2 with the reason for exclusion.^{7,11,33-72} The outcome measures assessed were recession depth reduction, clinical attachment gain, keratinized tissue gain, and probing depth reduction.

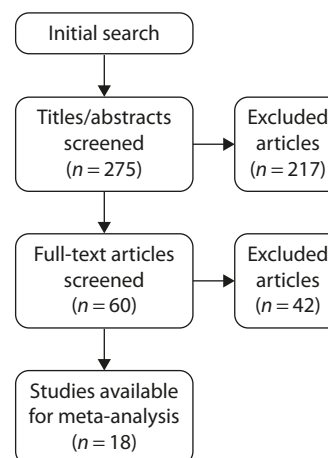


Figure 1 Flow chart of article-screening procedure.

Table 1 Characteristics of included articles

Reference	Year	Study description*	Defects	Participants	Interventions		Duration
					Control	Test	
Aichelmann-Reidy et al ¹⁶	2001	Controlled clinical trial, split-mouth	Miller's class I or II	22	ADM allograft	CTG	6 mo
Borghetti et al ¹⁷	1999	RCT, comparative study, split-mouth	Miller's class I	14	GTR with Guidor Matrix barrier	CTG	6 mo
Caffesse et al ¹⁸	2000	RCT, comparative study	Miller's class I or II No pocket > 4 mm	36	CTG (with citric acid for root demineralization)	CTG	6 mo
Ito et al ¹⁹	2000	Comparative study	Miller's class I or II Pocket depth ≥ 4 mm	6	FGG	GTR with ePTFE	6/12 mo
Jepsen et al ²⁰	1998	RCT, comparative study, split-mouth	Miller's class I or II	15	GTR with ePTFE	CTG	12 mo
Lins et al ²¹	2003	RCT, split-mouth	Miller's class I or II Pocket depth ≥ 2 mm	10	CRF	GTR with ePTFE + CRF	6 mo
Matarasso et al ²²	1998	RCT, comparative study	Miller's class I or II	20	GTR with PLA membrane + double papilla flap	GTR + CRF	12 mo
Müller et al ²³	2001	Comparative study	Miller's class I or II	22	GTR with PLA	CTG	6/12 mo
Novaes et al ²⁴	2001	RCT, comparative study, split-mouth	Miller's class I or II	9	ADM allograft	CTG + CPF	3/6 mo
Paolantonio ²⁵	2002	RCT, comparative study, split-mouth	Miller's class I or II	45	GTR with PLA membrane CPRT	CTG	12 mo
Rocuzzo et al ¹³	1996	RCT, comparative study, split-mouth	Miller's I or II Pocket depth ≥ 4 mm	12	GTR with ePTFE	GTR with Guidor	6 mo
Romagna-Genon ²⁶	2001	RCT, comparative study, split-mouth	Miller's class I or II Pocket depth ≥ 3 mm	21	GTR with collagen membrane	CTG	3/6 mo
Tatakis & Trombelli ²⁷	2000	RCT, comparative study	Miller's class I or II	12	GTR with Guidor Matrix barrier	CTG	6 mo
Tözüm & Dinç ²⁸	2003	Clinical trial	Miller's class II	14		CTG	8 mo
Trombelli et al ²⁹	1998	Case report	Miller's class I or II	6		GTR with Guidor Matrix barrier	6 mo
Trombelli et al ³⁰	1998	Clinical trial, split-mouth	Miller's class I or II	12	GTR with Resolut membrane	CTG	6 mo
Wang et al ³¹	2001	RCT, comparative study, split-mouth	Miller's class I or II Pocket depth ≥ 3 mm	16	GTR with collagen membrane	CTG	6 mo
Zahedi et al ³²	1998	Clinical trial	Miller's class I	15		GTR with collagen	2 yr

*According to Ovid MEDLINE. RCT = randomized controlled trial; ADM = acellular dermal matrix; GTR = guided tissue regeneration; CTG = connective tissue graft; FGG = free gingival graft; ePTFE = extended polytetrafluoroethylene; CRF = coronally repositioned flap; PLA = polylactic acid; CPRT = combined periodontal regenerative treatment; CPF = coronally positioned flap.

Table 2 List of full-text articles excluded

Reason for exclusion	Study
Minimum of 6 months of follow-up data not presented	Al-Zahrani et al (2004), ³³ Christgau et al (1995), ³⁴ Harris (1992), ³⁵ Harris (2001), ³⁶ Harris (2003) ³⁷
Smokers included	Amarante et al (2000), ³⁸ Boltchi et al (2000), ³⁹ Cetiner et al (2003), ⁴⁰ Harris (1997), ⁴¹ Harris (2000), ⁴² Harris (2002), ⁴³ Harris (2002), ⁴⁴ Hirsch et al (2001), ⁴⁵ Jepsen et al (2000), ⁴⁶ Leknes et al (2005), ⁴⁷ Müller et al (1998), ⁴⁸ Müller et al (1999), ⁴⁹ Silvestri et al (2003), ⁵⁰ Trombelli et al (2005) ⁵¹
Treatment on recession other than Miller's classification grade I or II	Borghetti & Louise (1994), ⁵² Harris (1997), ⁵³ Harris (1998), ⁵⁴ Harris (2002), ⁵⁵ Lee et al (2002), ⁵⁶ Müller et al (2000), ⁵⁷ Pini Prato et al (1992), ⁵⁸ Pini Prato et al (1996), ⁵⁹ Tinti et al (1992), ¹¹ Trombelli et al (1994), ⁶⁰ Trombelli et al (1995), ⁶¹ Waterman (1997), ⁶² Weigel et al (1995), ⁶³ Wennström & Zucchelli (1996) ⁶⁴
CTG techniques other than coronally positioned flap	Tözüm et al (2005), ⁶⁵ Dembowska & Drozdzik (2007) ⁶⁶
Statistics unavailable	Bouchard et al (1994), ⁶⁷ Ricci et al (1996), ⁶⁸ Rosetti et al (2000), ⁶⁹ Tinti & Vincenzi (1994), ⁷ Trombelli et al (1995), ⁷⁰ Wang & Al-Shammari (2002), ⁷¹ Zucchelli et al (2003) ⁷²

CTG=connective tissue graft.

Table 3 Comparison of connective tissue graft (CTG) and guided tissue regeneration (GTR) in studies with follow-up periods < 12 months

Outcome	Study type	No. of studies	Weighted mean difference (mm)	95% confidence interval	Heterogeneity	
					χ^2	<i>p</i>
Recession depth reduction	CTG	10	2.5806	2.2621, 2.8910	26.7992	<0.05
	GTR	11	2.1772	1.8374, 2.5170	78.4538	<0.05
Clinical attachment gain	CTG	9	1.7408	1.4462, 2.0353	40.1455	<0.05
	GTR	11	2.1867	1.8430, 2.5304	87.4348	<0.05
Keratinized tissue gain	CTG	7	1.2797*	0.9771, 1.5823	11.2156	<0.0819
	GTR	9	0.4938*	0.2133, 0.7774	9.0238	0.3403
Probing depth reduction	CTG	9	0.4670	0.2246, 0.7093	23.0840	<0.05
	GTR	10	0.6656	0.4087, 0.9226	30.5473	<0.05

**p*<0.05 between groups.

2.4. Quantitative data synthesis

The analysis was conducted using COMPREHENSIVE META-ANALYSIS version 1 (Biostat Inc., Englewood, NJ, USA, 1999). A weighted treatment effect was calculated using Cochran's test for heterogeneity, and the results expressed as weighted mean differences with 95% confidence interval. Intergroup discrepancies of treatment outcomes were accessed by analysis of variance (ANOVA). Statistical significance was accepted for *p* values <0.05. Although some intragroup variances reached statistical significance, random-effect models do not "adjust for", "account for", or "explain" heterogeneity. Thus, fixed effects were used to interpret the estimates in this study.

3. Results

The studies included in the meta-analysis were divided into two aspects for data analysis according to the following period: in one group of studies, patients were observed for < 12 months; in the other group, patients were followed-up for 12 months or longer.

The weighted mean differences for CTG and GTR between the baseline and post-treatment results, and χ^2 for heterogeneity of the outcomes of various parameters < 12 months are presented in Table 3. The CTG group showed significantly greater gain in keratinized tissue compared to the GTR group when the follow-up period of the included studies was < 12 months (*p*<0.05; Figure 2).^{13,16-19,21,24,27,29-31}

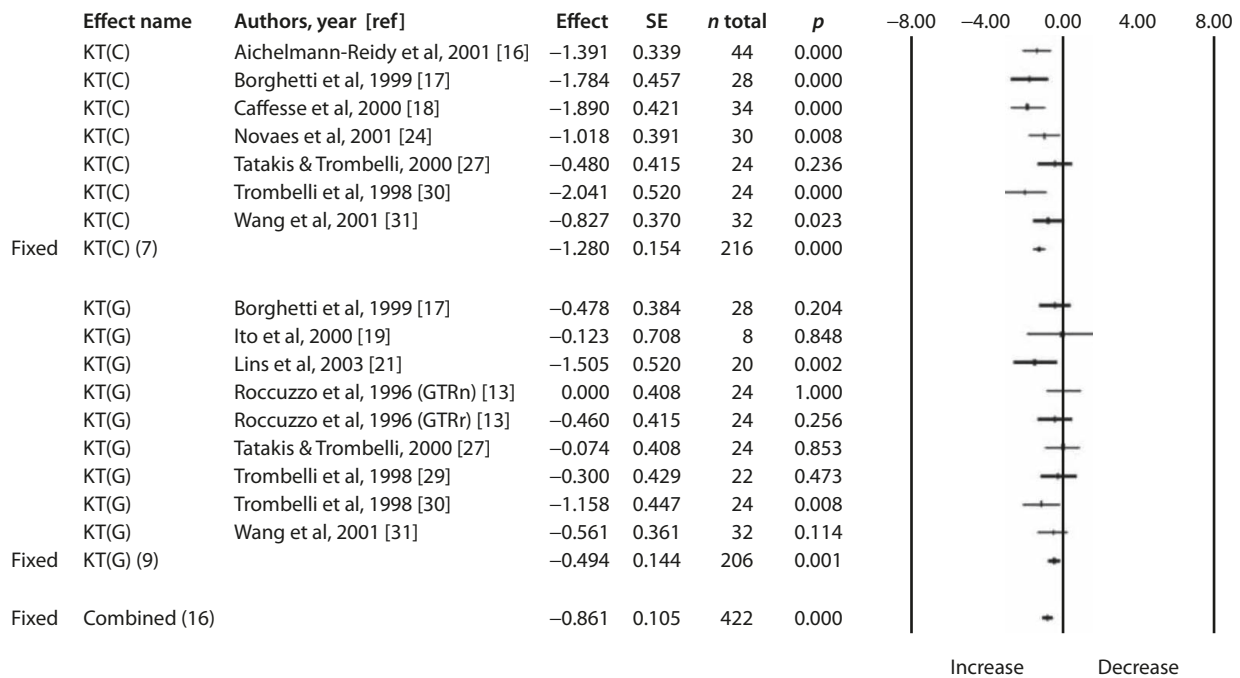


Figure 2 Comparative results of fixed effects for connective tissue graft (C) and guided tissue regeneration (G) for keratinized tissue gain (KT) in studies with follow-up period < 12 months. SE=standard error; GTRn=guided tissue regeneration with non-resorbable membrane; GTRr=guided tissue regeneration with resorbable membrane.

Table 4 Comparison of connective tissue graft (CTG) and guided tissue regeneration (GTR) in studies with follow-up periods ≥ 12 months

Outcome	Study type	No. of studies	Weighted mean difference (mm)	95% confidence interval	Heterogeneity	
					χ^2	p
Recession depth reduction	CTG	4	3.2289*	2.6254, 3.8323	17.6602	<0.05
	GTR	6	2.4444*	1.7914, 2.6973	43.1889	<0.05
Clinical attachment gain	CTG	4	2.7047	2.1589, 3.2545	17.0271	<0.05
	GTR	6	2.0842	1.6137, 2.5548	48.8968	<0.05
Keratinized tissue gain	CTG	3	1.7860*	1.2748, 2.2972	3.1317	0.2089
	GTR	5	0.5614*	0.1806, 0.9422	7.5551	0.1093
Probing depth reduction	CTG	4	0.2880*	0.0792, 0.6552	0.4051	0.9392
	GTR	4	0.8548*	0.4370, 1.2726	13.5710	<0.05

*p < 0.05 between groups.

Table 4 delineates the significant weighted mean differences in the categories of recession depth reduction (Figure 3A),^{19,20,22,23,25,32,73} keratinized tissue gain (Figure 3B),^{19,20,22,25,32,73} and probing depth reduction (Figure 3C)^{20,22,23,25,73} when comparing the results of studies with CTG and GTR procedures followed-up for ≥ 12 months.

4. Discussion

In a systematic review that assessed the literature on a variety of soft tissue augmentation procedures directed

at root coverage, the reviewers concluded that there was greater gain in root coverage with CTG than with GTR.⁷⁴ In the study of Al-Hamdan et al, conventional mucogingival surgery also resulted in statistically better root coverage than did GTR.⁷⁵ The results of this analysis are in accordance with the above studies, i.e., that CTG results in significantly greater reduction in recession depth compared to GTR in studies followed-up for ≥ 12 months. However, comparing the intergroup results in the present study, there was no significant difference between the CTG and GTR groups in studies followed-up for < 12 months, although the CTG data implied a slightly larger weighted mean difference in recession

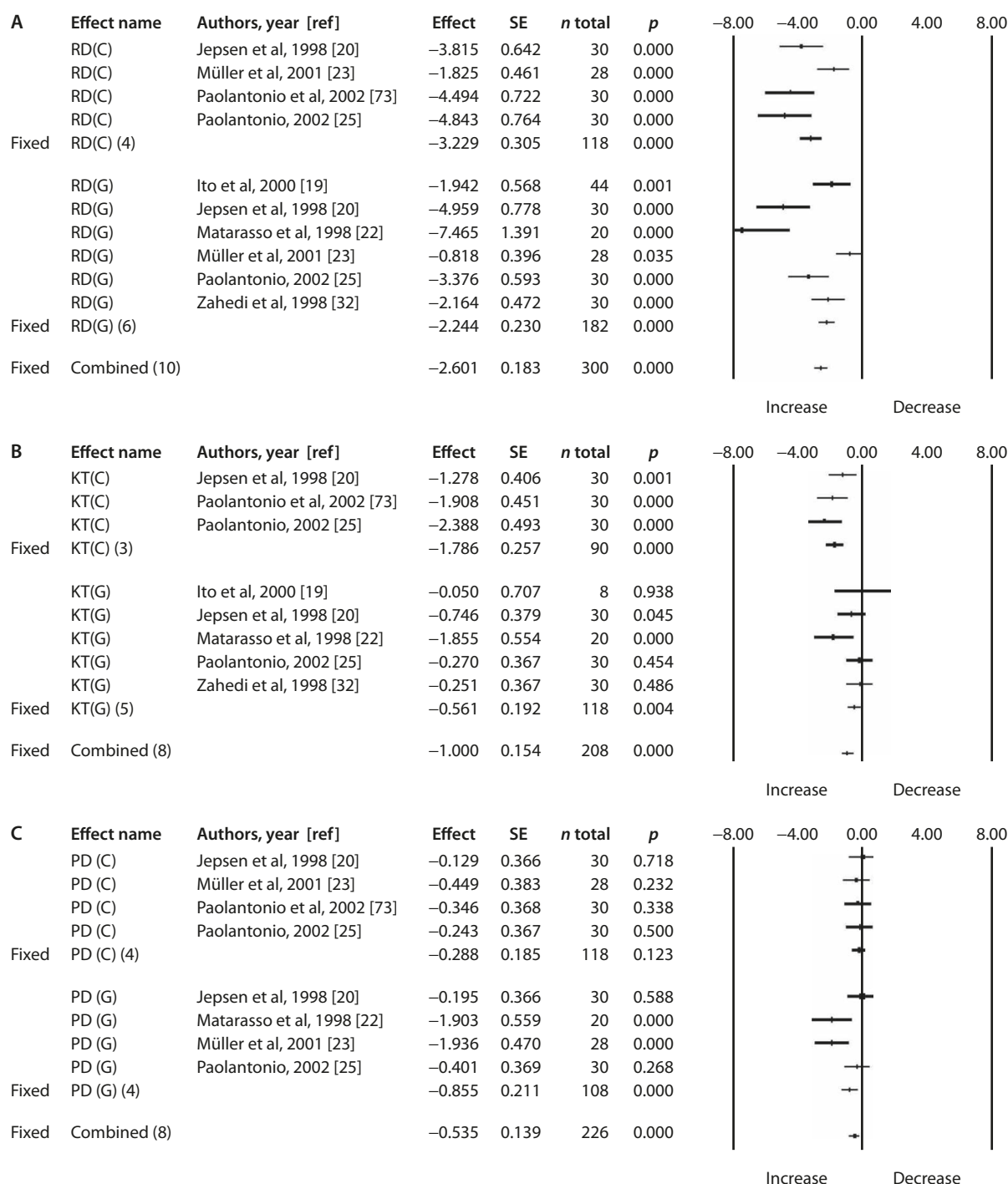


Figure 3 Forest plots presenting the fixed effects of connective tissue graft (C) and guided tissue regeneration (G) in: (A) reduction of recession depth (RD); (B) keratinized tissue gain (KT); and (C) pocket depth reduction (PD) in studies with follow-up period ≥ 12 months. SE=standard error.

depth reduction. We propose that creeping attachment may be an important event in making the difference with regard to the time frame of the relevant studies of root coverage. According to a longitudinal study, 72.7% of sites treated by CTG exhibited creeping attachment, with an average increase of 0.55 mm of coverage. Creeping attachment was highest at 12 months.⁵⁶ At the present time, there is no evidence that the method of

GTR using a membrane technique for root coverage promotes creeping attachment 1 year after treatment.

The data in our analysis show limited but greater gain in keratinized tissue width with CTG than with GTR in both follow-up periods. This difference was also evident in the meta-analysis of some systematic studies that favored CTG in terms of gains in keratinized tissue.⁷⁴ CTG generally involves the grafting of connective tissue

harvested from keratinized oral mucosa. Karring et al proved that the clinical and structural features of keratinized tissues are genetically controlled by the underlying connective tissue rather than functionally determined by mechanical factors.^{76,77} At least in part, the grafting of CTGs may play a role in regulating the keratinization of new oral epithelium at the recipient site.

A meta-analysis of GTR-based root coverage showed that both conventional mucogingival surgery and GTR can produce similar clinical attachment gains.⁷⁵ No differences were found in another study comparing gain in attachment for GTR, FGGs, CTGs, and CPFs.⁷⁸ Our meta-analysis found that there was no significant weighted mean difference between CTG and GTR in clinical attachment gain.

Clinically, little information is available regarding the nature of the histological interface between CTGs and root surfaces. Most case reports present a long junctional epithelium, true regeneration of the periodontal unit, or unpredictable root resorption at the graft-root surface interface.⁷⁹ On the other hand, there are also few histological reports derived from randomized controlled trials of GTR-based root coverage. GTR-based root coverage using collagen membranes in mongrel dogs showed a statistically significant increase in new attachment and newly formed connective tissue compared to CPFs at 16 weeks.⁸⁰ However, in one clinical study with recession defects of four teeth treated with GTR using polylactic acid, the root coverage obtained was a long junctional epithelial attachment in three defects. The results of that study showed no regeneration in any of the four defects.⁸¹ In a split-mouth study that focused on the biologic success of GTR and CTG procedures for root coverage, no differences in terms of biologic rehabilitation (including coverage height, bone, cementum and connective tissue attachment regeneration, length of the epithelium, resorption, and ankylosis) between the recessions treated with ePTFE membranes and those treated with CTG were found.⁸² Obviously, the final decision point that makes the difference in the interface between the root and grafting materials for root coverage depends on the skill and concept of the surgeon, the various methodologies, the prerequisite for root conditioning, and even the individual variability of subjects who undergo the surgery.

In the present study, there was no difference in the weighted mean comparison of recession depth reduction for both follow-up periods between GTR with non-resorbable membranes and GTR with resorbable membranes. The biocharacter of the membrane materials does not seem to cause any difference in the holding of the recession margin of the gingiva and keratinized tissue gain, but does cause a difference in clinical attachment gain and probing depth reduction. We surmise that in the majority of cases, the studies in both GTRn and GTRr groups were conducted on single root teeth with Miller's classification grade I or II recession, and

which were deeply submerged beneath thick mucoperiosteal flaps. The convex topographical characteristics of root morphology, unlike the root trunk over multiple root teeth, can ensure complete adaptation of the membrane on root surfaces in both procedures.⁸³

5. Conclusion

When considering recession depth reduction and keratinized tissue gain in treating gingival recessions of Miller's classification grade I or II, our systematic review indicated that CTG was statistically significantly more effective than GTR with follow-up periods longer than 12 months.

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