Review

Guided Tissue Regeneration-Based Root Coverage: Meta-Analysis

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Background: *The goal of guided tissue regeneration-based root coverage (GTRC) is to repair gingival recession via new attachment formation. Numerous clinical trials have been conducted utilizing the concept of GTR to promote root coverage. Most GTRC studies have had relatively small sample sizes and have not utilized power calculations to determine appropriate sample size; therefore, it is difficult to draw strong conclusions from them. Hence, the purpose of this study is to combine data from currently available GTRC studies and to use meta-analysis to determine whether GTRC provides significantly improved clinical outcomes compared to conventional periodontal plastic surgical approaches for the treatment of marginal tissue recession.*

Methods: *Studies were identified that used GTR approaches to treat gingival recession from January 1990 to October 2001. Information from each study was entered into a database. Data were analyzed according to the following criteria: GTRC versus conventional mucogingival surgery (CMGS); membrane type; root conditioning; pretreatment recession depth; adjunctive use of bone replacement graft (BRG); and source of funding. Studies were ranked independently, and mean data from each were weighted accordingly. Meta-analysis was performed using the weighted means for each group. Paired* t *tests were used to determine statistical significance between each pair of groups.*

Results: *Forty papers were included for analysis. GTRC resulted in an average of 74% recession depth reduction, 41% complete root coverage, 3 mm AL gain, and 1 mm KG gain. Both GTRC and CMGS produced significant (*P *<0.05) improvement compared to baseline measurements. Compared to GTRC, CMGS resulted in significantly (*P *<0.05) increased KG (2.1 mm vs. 1.1 mm), root coverage (81% vs. 74%), and percentage of defects with complete root coverage (55% vs. 41%). Use of absorbable membranes, root conditioning, shallow pretreatment recession (<4 mm), and corporate sponsorship all resulted in significantly (*P *<0.05) improved percentages of sites with complete root coverage but had no effect on other parameters.*

Conclusions: *Based on this meta-analysis, guided tissue regeneration-based root coverage can be used successfully to repair gingival recession defects. Conventional mucogingival surgery, however, resulted in statistically better root coverage, width of keratinized gingiva, and complete root coverage.* J Periodontol 2003;74:1520-1533.

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KEY WORDS

Gingival recession/surgery; gingival recession/therapy; guided tissue regeneration; membranes, artificial; membranes, barrier; membranes, bioabsorbable; meta-analysis.

Gingival recession is defined as "the displacement of the marginal tissue apical to the cementoenamel junction (CEJ)."[1,2] Various periodontal plastic surgery techniques have been used for the treatment of gingival recession including pedicle soft tissue grafts, free soft tissue grafts, combination free/pedicle soft tissue grafts, and guided tissue regenerative procedures.[3-10] The goals of treatment are to restore the tissue margin to the CEJ and to create a normal gingival sulcus with a functional attachment.[11] Indications for root coverage include but are not limited to: esthetic concerns, root hypersensitivity, prevention or management of root caries and cervical abrasion, enhancement of restorative outcomes, and facilitation of plaque control.

Tinti and Vincenzi initially proposed using guided tissue regeneration-based root coverage (GTRC) as a mean to promote new attachment on denuded root surfaces.[10] Subsequent studies have assessed the effectiveness and predictability of GTRC using either non-absorbable or absorbable membranes.[12-18] Histologically, new bone and cementum with inserting fibers have been shown to form after GTRC.[19-22] Clinical results have also been promising. GTRC resulted in improved root coverage, gain of clinical attachment level and increased width of keratinized gingiva.[12-18,23-27] As an emerging new technique, GTRC had been compared to conventional mucogingival surgery (CMGS). The overall results of comparative studies indicated that GTRC produces comparable clinical outcomes to CMGS.[13-17,26] The

main advantages of GTRC as compared to CMGS include elimination of the morbidity and discomfort associated with a second site surgery for procuring graft material, and no limitations on the supply of graft material. Therefore, this technique may offer a promising alternative for the CMGS.

Factors that may influence the outcome of GTRC include but are not limited to: type of membrane (non-absorbable versus absorbable), pretreatment recession depth, root surface conditioning, adjunctive usage of bone replacement graft (BRG), smoking, and funding status, i.e., bias created by industry sponsorship.

In general, clinical trials have reported that absorbable and non-absorbable membranes achieved similar results.[12-18,23-27] Studies that have analyzed the influence of pretreatment recession depth on percentage of final root coverage have reported conflicting results. Pini Prato et al. reported better clinical results in deep recession (>5.0 mm) defects when GTRC was employed.[17] Müller et al. also suggested that shallow recession defects (1.5 to 3.5 mm) should not be treated with GTR.[28] However, Boltchi et al. indicated that initially shallow recession defects (<4.0 mm) achieved better clinical outcomes than deep recession defects (≥4.0 mm).[18] Therefore, further study is needed to determine whether pretreatment recession depth influences root coverage after GTRC.

Root conditioning agents have been used in combination with root coverage procedures for their ability to decontaminate root surfaces, remove endotoxins/bacterial by-products, eliminate the smear layer, expose collagen fibrils and dentinal tubules, and further promote new attachment formation.[29] Nevertheless, studies have also reported that these agents may compromise blood supply, leading to delayed wound healing, increased root hypersensitivity and impaired cell migration,[30,31] which may compromise final clinical results. Adding bone replacement grafts (BRG) during GTR treatment has resulted in better fill of intrabony defects.[32] This is attributed to the ability of BRG to create and maintain space under the membranes as well as its osteoinductive and/or osteoconductive capacity.[33-36] However, use of BRG in conjunction with GTRC procedures has yielded conflicting results.[37,38] Another factor that may affect GTRC is smoking, which has been shown to be a major risk factor for the development and progression of periodontal disease.[39-42] In addition, smoking has been reported to impair periodontal wound healing,[43-46] especially GTR procedures.[47] One study showed smokers had less than 50% attachment gain when compared to non-smokers.[47] Finally, financial support from a sponsoring company presents a conflict of interest that may influence how data are reported. No study has looked at the effect this potential bias might have on results.

Meta-analysis is a statistical method that combines and summarizes the results of several studies.[48] Meta-analysis, therefore, could be a useful tool in decision-making and health technology assessment. Studies have used meta-analysis to determine the effect of GTR for the treatment of intrabony/furcation defects but similar studies have not been done to determine the usefulness of GTR for treatment of recession defects.[32,49] Cortellini and Bowers, in an evidence-based study, concluded that GTR, GTR combined with the use of demineralized freeze-dried bone allograft (DFDBA), and freeze-dried bone allograft (FDBA) alone are the most predictable regenerative procedures for achieving probing depth reduction, bone fill, and attachment level gain in infrabony defects.[32] Laurell et al. also utilized the meta-analysis approach to evaluate GTR studies spanning 20 years for the treatment of intrabony defects and reported that intrabony defects should be equal to or deeper than 4.0 mm to benefit from GTR procedures.[49] As a result of these studies, it seems that meta-analysis may be a useful resource for clinicians to guide their decision making before utilizing GTRC procedures. Therefore, the purposes of this meta-analysis study were to: 1) define the clinical outcomes of GTRC; 2) quantify the mean overall expected improvement; 3) evaluate the differences between GTRC and CMGS; and 4) examine factors (membrane type, pretreatment recession depth, root conditioning, adjunctive usage of BRG, smoking, and funding status) that may affect GTRC.

MATERIALS AND METHODS

A literature survey was conducted by using the National Library of Medicine computerized bibliographic database, MEDLINE, to identify studies that evaluated the use of GTR for the treatment of gingival recession defects. The search was supplemented by reviewing the bibliographies of these papers and scanning the review articles for potential data sources. No attempt was made to contact researchers in this field to obtain original data or unpublished studies.

Key words for the data search included: GTR, GTR-based root coverage (GTRC), non-absorbable/non-resorbable membrane(s)/barrier(s), absorbable/bioabsorbable membrane(s)/barrier(s), gingival recession/therapy, and gingival recession/surgery. The

search then was limited to English language and to the period of January 1, 1990 to October 31, 2001.

The following inclusion criteria were applied: 1) published in English; 2) randomized controlled human clinical trials; 3) comparative studies (prospective and retrospective studies); 4) case control studies; 5) case reports; 6) 6 months or greater duration; and 7) studies from January 1, 1990 to October 31, 2001. In addition, when multiple reports utilizing the same subjects were identified, only data from the most recent report were used. The following exclusion criteria were applied: 1) animal studies; 2) abstracts; 3) descriptive studies; 4) histological studies; and 5) studies with insufficient data. Then, studies were ranked, with the most important at the top of the list (Table 1).

Statistical Analysis

Meta-analysis was performed by utilizing a statistical package.‡ Weighted means and standard deviations were computed for each group (as defined by the treatment category), considering the sample size for each study. Overall means were computed for all clinical parameters (recession depth [RD], probing depth [PD], clinical attachment level [CAL], and width of keratinized gingiva [KG]) and for clinical attachment level gain, increase in width of keratinized gingiva, percentage root coverage, and percentage of cases with complete root coverage. Paired *t* tests were used to test for differences between treatments at 95% confidence intervals. The effective sample size for the meta-analysis was the number of studies that were analyzed at any one timepoint. Overall combined results for each variable were considered significant at or below the 0.05 probability level.

Formula I was used to calculate the weighted mean,§ and formula II was used to calculate the weighted standard deviation.‖

Table 1.

Study Distribution and Point Assigned

Study Design	Point Assigned*	Percentage
Randomized, longitudinal controlled clinical trial	7	30.0%
Cohort study	6	0%
Case-controlled study	5	5.0%
Retrospective comparative study	4	8.3%
Non-controlled case study	3	21.7%
Case report	2	18.3%
Descriptive study	1	16.7%

* Adapted from Newman and McGuire.[50]

Table 2.

Clinical Outcomes After GTR-Based Root Coverage (40 studies, 693 defects)

Clinical Parameter	Initial	Final	Difference
Recession depth	4.2 ± 1.0	1.1 ± 0.9*	3.1 ± 0.9
Probing depth	1.5 ± 0.4	1.2 ± 0.5	0.3 ± 0.5
Clinical attachment level	5.5 ± 1.1	2.4 ± 1.1*	3.1 ± 1.2
Keratinized gingiva	2.1 ± 1.1	3.1 ± 0.9*	1.0 ± 0.9
Percentage root coverage		75.0 ± 11.0	
Complete root coverage (%)		42.0 ± 19.8	

Data reported as weighted mean ± SD in mm and % for root coverage and complete root coverage.
* Statistical difference at $P<0.05$ level from baseline.

RESULTS

GTR-Based Root Coverage

Table 1 shows the distribution of studies according to study design. The MEDLINE search and the review of bibliographies of appropriate papers identified 60 papers that evaluated GTR in the treatment of gingival recession defects. Of these 60 papers, 20 papers were eliminated because they did not meet the set inclusion criteria (Appendix).

Table 2 shows the clinical outcomes after GTRC treatment. GTRC resulted in significant gain of CAL equal to 3.1 ± 1.2 mm ($P<0.05$). In addition, keratinized gingiva was significantly increased by 1.0 ± 0.9 mm. On average, GTRC resulted in 75.0 ± 11.0% root coverage and complete root coverage in 42.0 ± 19.8% of the cases.

GTR-Based Root Coverage Versus Conventional Mucogingival Surgery

Table 3 summarizes the results of 18 studies that compared GTRC with CMGS. The CMGS group comprised 271 sites, and the GTRC group comprised 272 sites. There were no statistically significant differ-

‡ SPSS Inc., Chicago, IL.
§ Formula I: Weighted mean (WM) = Σ [(Mean$_1$.n$_1$/n$_1$ + n$_2$ + .. + n$_f$) + (Mean$_2$.n$_2$/n$_1$ + n$_2$ + .. + n$_f$) + ... + (Mean$_f$.n$_f$/n$_1$ + n$_2$ + .. + n$_f$)].
‖ Formula II: Weighted standard deviation (WSD) = Σ[(SD$_1$.n$_1$/n$_1$ + n$_2$ + .. + n$_f$) + ... + (SD$_2$.n$_2$/n$_1$ + n$_2$ + .. + n$_f$) + (SD$_f$.n$_f$/n$_1$ + n$_2$ + .. + n$_f$)].

Table 3.

GTR-Based Root Coverage Versus Conventional Mucogingival Surgery

	CMGS (18 studies, 271 defects)			GTRC (18 studies, 272 defects)		
Clinical Parameter	Baseline	Final	Difference	Baseline	Final	Difference
Recession depth	4.0 ± 0.9	0.8 ± 0.7*	3.2 ± 0.7	4.2 ± 0.9	1.1 ± 0.9*	3.1 ± 0.9
Probing depth	1.5 ± 0.5	1.4 ± 0.6	0.1 ± 0.6	1.6 ± 0.6	1.2 ± 0.5	0.4 ± 0.6
Clinical attachment level	5.5 ± 1.1	2.8 ± 1.0*	2.7 ± 1.2	5.8 ± 1.0	2.7 ± 1.1*	3.1 ± 1.3
Keratinized gingiva	1.8 ± 0.7	3.9 ± 1.0*	2.1 ± 1.1	1.8 ± 0.9	2.9 ± 0.8*	1.1 ± 0.8†
Percentage root coverage		81.0 ± 6.7			74.1 ± 9.1†	
Complete root coverage (%)		55.3 ± 17.8			41.3 ± 19.4†	

Data reported as weighted mean ± SD in mm and % for root coverage and complete root coverage.
* Statistical difference at $P<0.05$ level from baseline.
† Statistical difference at $P<0.05$ level between groups.

Table 4.

Non-Absorbable Versus Absorbable Membranes for GTRC

	Non-Absorbable (19 studies, 223 defects)			Absorbable (28 studies, 470 defects)		
Clinical Parameter	Baseline	Final	Difference	Baseline	Final	Difference
Recession depth	4.9 ± 0.8	1.3 ± 0.6*	3.6 ± 0.6	3.7 ± 0.9†	0.9 ± 0.8*	2.8 ± 0.9†
Probing depth	1.5 ± 0.6	1.1 ± 0.5	0.4 ± 0.5	1.4 ± 0.5	1.3 ± 0.5	0.1 ± 0.4
Clinical attachment level	5.6 ± 0.7	2.4 ± 1.0*	3.2 ± 1.6	5.1 ± 1.1	2.0 ± 1.0*	3.1 ± 1.0
Keratinized gingiva	1.5 ± 0.9	2.7 ± 1.0*	1.2 ± 1.0	2.0 ± 0.9	2.9 ± 0.8*	0.9 ± 0.9
Percentage root coverage		74.3 ± 5.7			76.3 ± 13.2	
Complete root coverage (%)		35.0 ± 17.2			45.0 ± 20.9	

Data reported as weighted mean ± SD in mm and % for root coverage and complete root coverage. No statistical analysis was done on the complete root coverage (%) due to lack of original raw data to adjust the initial recession depth difference.
* Statistical difference at $P<0.05$ level from baseline.
† Statistical difference at $P<0.05$ level between groups.

ences between groups for clinical parameters (RD, PD, CAL, and KG) prior to treatment. Both procedures produced statistically significant ($P<0.05$) decreases in recession depth. CMGS reduced recession depth from a pretreatment average of 4.0 ± 0.9 mm to 0.8 ± 0.7 mm post-treatment, corresponding to 81.0 ± 6.7% root coverage. With GTRC, average pretreatment recession of 4.2 ± 1.0 mm was reduced to 1.2 ± 0.9 mm, corresponding to 72.0 ± 9.1% root coverage. CMGS yielded complete root coverage in 55.3 ± 17.8% of treated cases, while GTRC resulted in complete root coverage in only 41.3 ± 19.4% of treated cases. These differences were statistically significant ($P<0.05$).

There were no statistically significant differences in probing depth changes between treatments. Both CMGS and GTRC resulted in significant gains of clinical attachment (2.7 ± 1.2 mm and 3.1 ± 1.3 mm, respectively, $P<0.05$), but there was no difference between the two groups. CMGS increased width of keratinized gingiva by 2.1 ± 1.1 mm, while GTRC increased KG width by only 1.1 ± 0.8 mm. This difference was statistically significant ($P<0.05$).

Non-Absorbable Membranes Versus Absorbable Membranes

Non-absorbable membranes were used in 19 studies to treat 223 recession defects. Absorbable membranes were used in 28 studies to treat 470 recession defects (Table 4). Use of both non-absorbable and absorbable membranes significantly reduced recession depth when compared to baseline measurements ($P<0.05$). The type of membrane used (non-absorbable vs. absorbable) did not affect PD reduction (0.4 ± 0.5 mm vs. 0.1 ± 0.4 mm), gain in CAL (3.2 ± 1.6 mm vs. 3.1 ± 1.0 mm), KG gain (1.2 ± 1.0 mm vs. 0.9 ± 0.9 mm), or percentage of root coverage (74.3 ± 5.7% vs. 76.3 ± 13.2%). Cases treated with absorbable membranes had a higher percentage of complete root coverage compared to non-absorbable membranes (45.0 ± 20.9% vs. 35.0 ± 17.2%, respectively).

Effect of Root Surface Conditioning on GTRC

Root surface conditioning was used in 16 studies with 281 recession defects compared to 31 studies with 412 recession defects that did not (Table 5). There was no significant difference between sites treated with and without root surface conditioning agents with regard to all clinical parameters measured except percentage of sites with complete root coverage. The root surface conditioning treated group had a higher percentage of complete root coverage than sites treated without root conditioning agents (51.7 ± 22.4% vs. 32.1 ± 15.1%, respectively).

Table 5.

Effect of Root Conditioning on GTRC

	Non-Conditioning (31 studies, 412 defects)			Conditioning (16 studies, 281 defects)		
Clinical Parameter	Baseline	Final	Difference	Baseline	Final	Difference
Recession depth	4.5 ± 1.0	1.2 ± 1.0*	3.3 ± 1.0	3.6 ± 0.8†	0.9 ± 0.8*	2.7 ± 0.8
Probing depth	1.4 ± 0.6	1.3 ± 0.5	0.1 ± 0.5	1.5 ± 0.5	1.1 ± 0.5	0.4 ± 0.4
Clinical attachment level	6.1 ± 1.0	2.9 ± 1.2*	3.2 ± 1.4	5.2 ± 0.9	2.0 ± 0.8*	3.2 ± 0.9
Keratinized gingiva	1.9 ± 0.9	2.8 ± 0.8*	0.9 ± 0.9	1.8 ± 1.0	2.8 ± 1.0*	1.0 ± 0.9
Percentage root coverage		73.5 ± 11.0			75.5 ± 9.2	
Complete root coverage (%)		32.1 ± 15.1			51.7 ± 22.4	

Data reported as weighted mean ± SD in mm and % for root coverage and complete root coverage. No statistical analysis was done on the complete root coverage (%) due to lack of original raw data to adjust the initial recession depth difference.
* Statistical difference at $P<0.05$ level from baseline.
† Statistical difference at $P<0.05$ level between groups.

Table 6.

Effect of Bone Replacement Graft on GTRC

	Non-Grafting (2 studies, 21 defects)			Grafting (2 studies, 20 defects)		
Clinical Parameter	Baseline	Final	Difference	Baseline	Final	Difference
Recession depth	3.7 ± 0.8	0.8 ± 0.9*	2.9 ± 0.9	3.6 ± 0.6	0.7 ± 0.8*	2.9 ± 0.8
Keratinized gingiva	1.7 ± 1.0	3.0 ± 1.0*	1.3 ± 1.2	1.8 ± 0.8	3.6 ± 1.0*	1.8 ± 1.2
Percentage root coverage		78.5 ± 14.1			79.6 ± 16.0	

Data reported as weighted mean ± SD in mm and % for root coverage and complete root coverage.
* Statistical difference at $P<0.05$ level from baseline.

Effect of Bone Replacement Graft on GTRC

Only two studies with a total of 41 sites met the criteria for inclusion in this database (Table 6). BRG was utilized in 21 of these sites, while 20 sites were treated without BRG. The addition of bone BRG did not improve the percentage of root coverage (79.6 ± 16% vs. 78.5 ± 14.1% with no BRG). Use of BRG also had no effect on post-treatment increase in width of keratinized gingiva. The percentage of sites with complete root coverage was not reported in these two articles.

Effect of Pretreatment Recession Depth on GTRC

Twenty-one studies with 363 recession defects had a mean pretreatment recession depth of <4.0 mm, while 26 studies with 330 recession defects had a mean of ≥4.0 mm pretreatment recession depth (Table 7). No difference was noted between initially shallow (<4.0 mm) and initially deep (≥4.0 mm) recession defects in terms of post-treatment recession depth reduction, percentage of root coverage, PD changes, and gain of KG. Gain of CAL was significantly greater for deep recession defects compared to shallow recession defects (3.9 ± 1.4 mm vs. 2.2 ± 0.9 mm, $P<0.05$). In contrast, shallow recession defects exhibited higher percentage of complete root coverage than deep defects (51.2 ± 22.1% vs. 32.0 ± 13.0%, respectively, $P<0.05$).

The Impact of Study Sponsor on GTRC

Nine studies were company funded and 31 were not (Table 8). Generally, better root coverage was reported in company-sponsored versus non-sponsored studies; however, this difference did not reach the level of statistical significance (76.6 ± 10.8% vs. 73.1 ± 10.6%, respectively, $P\geq0.05$). There was no difference between the two groups in term of KG gain (0.9 ± 0.9 mm vs. 1.1 ± 0.9 mm, respectively). Interestingly, the non-

Table 7.

Influence of Pretreatment Recession Depth on GTRC

	Recession Depth <4 mm (21 studies, 363 defects)			Recession Depth ≥4 mm (26 studies, 330 defects)		
Clinical Parameter	Baseline	Final	Difference	Baseline	Final	Difference
Recession depth	3.4 ± 0.9	0.8 ± 0.8*	2.6 ± 0.8	4.8 ± 1.0†	1.3 ± 0.8*	3.5 ± 0.8
Probing depth	1.5 ± 0.5	1.3 ± 0.5	0.2 ± 0.5	1.4 ± 0.6	1.1 ± 0.5	0.3 ± 0.5
Clinical attachment level	4.7 ± 1.1	2.5 ± 1.0*	2.2 ± 0.9	6.4 ± 0.9†	2.5 ± 1.1*	3.9 ± 1.4†
Keratinized gingiva	2.0 ± 1.1	2.8 ± 1.0*	0.8 ± 1.0	1.8 ± 0.8	2.9 ± 0.9*	1.1 ± 0.9
Percentage root coverage		76.1 ± 16.1			73.5 ± 6.0	
Complete root coverage (%)		51.2 ± 22.1			32.0 ± 13.0†	

Data reported as weighted mean ± SD in mm and % for root coverage and complete root coverage.
* Statistical difference at $P<0.05$ level from baseline.
† Statistical difference at $P<0.05$ level between groups.

Table 8.

Impact of Study Sponsor on GTRC

	Company Funded (10 studies, 222 defects)			Non-Company Funded (20 studies, 471 defects)		
Clinical Parameter	Baseline	Final	Difference	Baseline	Final	Difference
Recession depth	3.4 ± 0.9	0.8 ± 0.8*	2.6 ± 0.8	4.5 ± 0.9†	1.2 ± 0.8*	3.3 ± 0.9
Probing depth	1.5 ± 0.5	1.2 ± 0.4	0.3 ± 0.4	1.4 ± 0.5	1.2 ± 0.5	0.2 ± 0.4
Clinical attachment level	4.4 ± 1.1	2.0 ± 1.0*	2.4 ± 0.9	5.6 ± 0.9†	2.2 ± 1.1*	3.4 ± 1.3†
Keratinized gingiva	2.1 ± 1.0	3.0 ± 0.9*	0.9 ± 0.9	1.8 ± 0.9	2.9 ± 0.9*	1.1 ± 0.9
Percentage root coverage		76.6 ± 10.8			73.1 ± 10.6	
Complete root coverage (%)		55.8 ± 23.9			33.2 ± 16.5	

Data reported as weighted mean ± SD in mm and % for root coverage and complete root coverage. No statistical analysis was done on the complete root coverage (%) due to lack of original raw data to adjust the initial recession depth difference.
* Statistical difference at $P<0.05$ level from baseline.
† Statistical difference at $P<0.05$ level between groups.

sponsored studies reported significantly greater gain of CAL than sponsored studies (3.4 ± 1.3 mm vs. 2.4 ± 0.9 mm, respectively, $P<0.05$). However, the company-sponsored studies had significantly less pretreatment recession depth than non-sponsored studies (4.4 ± 1.1 mm vs. 5.6 ± 0.9 mm, respectively, $P<0.05$). The company-funded projects also reported a higher percentage of complete root coverage than non-company funded projects (55.8 ± 23.9% vs. 33.2 ± 16.5%).

DISCUSSION

Various periodontal plastic surgical procedures have been developed to treat gingival recession defects. GTRC was introduced because of its ability to promote new attachment, new bone, and new periodontal ligament formation.[19-22] Because there have been a limited number of studies with relatively small sample size and short study duration, it is difficult to determine the true benefits of this new approach. Meta-analysis provides a systematic reviewing strategy where results from similar studies can be combined and analyzed.[32,49,50-58] At the time of this study, there were no published articles in which meta-analysis had be used for GTRC procedures.

Our meta-analysis indicated that GTRC could be successfully used to treat gingival recession defects. Overall, GTRC resulted in significant improvement in recession depth (3.1 mm), CAL gain (3.1 mm), increase of keratinized gingiva (1.0 mm), and percentage of root coverage (75.0%).

When studies that directly compared GTRC and CMGS were analyzed, the results indicated that both GTRC and CMGS achieved significant root coverage (74% vs. 81%, respectively). This is consistent with findings reported by Wennström[2] and Greenwell et al.[58] Recently, Wang et al. reported similar findings (73% root coverage) after treating recession defects with collagen membranes.[59] CMGS resulted in a slightly higher percentage of root coverage (84%); however, there was no statistically significant difference between treatments. The authors attributed the difference to variations in

pretreatment tissue thickness. Similarly, Harris, using GTRC, found that treatment of recession defects with thin marginal tissue (<0.5 mm) resulted in only 26.7% root coverage, while 95.5% root coverage was achieved in areas with thick tissue (≥0.5 mm).[14] Other possible factors that may explain the difference between the two procedures are incidence of membrane exposure with GTRC and size and/or shape of the defects.

The results of this analysis show that both CMGS and GTRC can produce similar CAL gain. This agrees with most randomized controlled clinical trials.[13,16,59-62] One cannot draw conclusions regarding the type of attachment that was gained based on clinical measurements; however, histological reports have shown new connective tissue attachment with new cementum formation following GTRC procedures in humans.[21] In addition, Gottlow et al. observed an extensive amount of new connective tissue attachment and bone at 6, 12, and 24 months following repair of buccal recession defects in monkeys.[63]

CMGS increased the width of keratinized gingiva significantly more than GTRC. CMGS often involves grafting of connective tissue from keratinized mucosa while GTRC does not. Karring et al. found that the phenotypic expression of the epithelial surface was determined by the underlying connective tissue.[64]

In the present study, non-absorbable and absorbable membranes both resulted in significant root coverage (74% vs. 76%, respectively). Roccuzzo et al.[25] and Zucchelli et al.[26] found similar results in randomized controlled clinical studies. Our analysis revealed that the percentage of sites with complete root coverage was greater with absorbable membranes (45%) than with non-absorbable membranes (35%) (P <0.05). This agrees with Zucchelli et al., who concluded connective tissue grafts and GTR with absorbable membranes provided more predictable complete root coverage than GTR with non-absorbable membranes.[26] The slight difference may be attributed to the membrane retrieval procedure in the non-absorbable membrane group, which might have compromised the final outcome.

The use of root surface demineralization agents has been advocated as an adjunct to root coverage procedures, particularly in conjunction with soft tissue grafting.[65,66] Smear layer removal, exposure of dentinal tubules, exposure of collagen fibrils, removal of endotoxins, and promotion of new attachment formation are all reasons that have been used to justify use of root surface conditioning.[67,68] In the present study, recession defects treated with or without root surface conditioning during GTRC had similar improvements in clinical parameters and reductions in recession; however, the sites treated with conditioning agents were more likely to attain complete root coverage (52%) than sites treated without conditioning (32%). However, controlled clinical trials failed to show any beneficial effect when root conditioning agents (i.e., citric acid) were used during free gingival grafts or laterally displaced flaps.[2,69-71] This is further supported by a meta-analysis that evaluated GTR treatment with or without root surface demineralization in mandibular Class II furcation defects.[72]

Studies have suggested that space creation and maintenance are essential for periodontal regeneration.[73,74] Bone replacement grafts (BRG) have been advocated for maintaining space under membranes and providing osteoinductive and osteoconductive capacity. Data from this meta-analysis showed that addition of BRG during GTRC procedures provided no additional benefit; however, it should be noted that only a small number of studies were analyzed. Therefore, the effect of BRG on GTRC remains to be determined.

This meta-analysis revealed no significant difference in percentage root coverage for sites that were initially ≥4.0 mm and sites that were initially <4.0 mm (73% and 76%, respectively). Boltchi et al., on the other hand, reported that sites with <4.0 mm were positively correlated with root coverage gain but the difference was not significant.[18] Contrary to this, Pini Prato et al. reported better root coverage with initially deep recession defects (≥5.0 mm).[17] Similarly, Müller et al. reported only 50% root coverage when GTRC procedures were used to treat shallow (1.5 to 3.5 mm) gingival recession defects.[28] They also reported that membrane exposure was a common observation, which may have affected the final clinical outcomes in their study. Our meta-analysis showed that sites with initial recession depth ≥4.0 mm had significantly better CAL gains than sites that were initially <4.0 mm (3.9 mm vs. 2.2 mm). It should however be obvious that the initial CAL places a limit on the potential for attachment gain; e.g., a site with 2.0 mm of attachment loss could not achieve 4.0 mm of attachment gain. This is also a consistent finding among other GTRC studies that reported the raw data.[23,25] For instance, Jepsen et al. observed that deep recession defects (≥4.0 mm) had greater CAL gain (1 to 3 mm) compared to shallow recession defects (<4.0 mm).[23] However, the nature of new attachment remains to be investigated in human histological studies.

An often-raised question is, does corporate sponsorship of a study influence the reporting of findings by investigators? Our data indicated studies with

industry sponsorship reported significantly less clinical attachment gain (2.4 mm vs. 3.4 mm) and a better rate of complete root coverage (55% vs. 33%) than non-sponsored studies. This may be attributed to the fact that sponsored studies also had significantly shallower initial recession depth (3.4 mm vs. 4.5 mm) and attachment level (4.4 mm vs. 5.6 mm) at baseline than non-sponsored studies.

Data based on meta-analyses that summarize data from many similar studies remain controversial and may be challenged. The attempt to calculate a single summary measure of treatment efficacy may not be valid because the individual trials assess different patient groups and may measure different responses to therapy. Publication bias and English language bias are problems that need to be addressed in this present meta-analysis. Certainly, if a larger number of studies, with increased numbers of subjects, were available, the results of this meta-analysis would be more reliable. Unfortunately, we could not include non-English papers or unpublished data. The criteria for judging studies are not always consistent, and eliminating some studies may bias the results. Therefore, the best approach would be to include all studies in the analysis. This is less a problem than eliminating certain studies.[75] Finally, some authors caution that meta-analysis may be appropriate for hypothesis generation, but not for determining which new treatment modality to use on patients.[76] While it is possible that the results from the present meta-analysis are biased by the selection of studies, the varied treatment regimens used in these studies, the choice of outcome measures, the diversity of data presentation within the studies, and small number of trials in each stratum, the results of the present analysis will serve to complement a qualitative overview of the literature on the subject of GTR as an alternative treatment for recession defects. In addition, no covariance analysis was performed to adjust the effect of initial recession depth difference noted for percentage of complete root coverage due to lack of original raw data from each study.

The effect of mobility, pretreatment tooth vitality, membrane exposure, and pretreatment tissue thickness could not be evaluated because of the limited data available. In addition, we only found five clinical trials that evaluated the correlation between smoking and GTRC. It was not possible to incorporate this data into the analyses. Trombelli and Scabbia reported that smokers obtained less root coverage compared to non-smokers (57% vs. 78%, respectively).[77] Müller et al. also reported 55% root coverage in one light smoker (2 pack-years) and 100% root coverage in a moderate smoker (7.5 pack-years).[78] In one report, it was found that smoking decreased the expected root coverage to 0.52 mm.[25] Finally, Boltchi et al.[18] and Amarante et al.[79] could not determine the effect of smoking in their studies because the study period was too short and the sample size was limited. Further studies are needed to determine how these factors may influence GTRC procedure.

Within limitations of this study, it can be concluded that:

1. Both conventional mucogingival surgery and guided tissue regeneration-based root coverage can be used to repair gingival recession defects with good success.

2. Guided tissue regeneration-based root coverage resulted in 75% root coverage, with a complete coverage of 42%, 3.1 mm gain of attachment level, and 1.0 mm increase in the amount of keratinized gingiva.

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APPENDIX: CITATIONS, SAMPLE SIZE, LENGTH OF FOLLOW-UP, RANKING (BASED UPON TABLE 1 CRITERIA), AND EXCLUSION REASONS

Study	Sample Size		Treatment Length (months)	Rank	Exclusion Reasons
	N	Sites (GTR)			
Cortellini et al 1991[20]	-	-	-	6	Not enough data
Tinti et al 1992[12]	12	12	6	5	+
Pini Prato et al 1992[13]	25	25	18	1	+
Pini Prato et al 1992[80]	-	-	15	-	Not enough data
Tinti et al 1993[81]	-	-	12	-	No data
Cortellini et al 1991[21]	-	-	5	-	Histologic report
Pini Prato et al 1993[82]	-	-	-	-	Not enough data
Shanaman 1993[83]	2	3	24	6	+
Shih & Allen 1994[84]	-	-	8	-	Not enough data
Trombelli et al 1994[85]	15	15	6	5	+
Tinti & Vincenzi 1994[86]	12	12	15	5	+
Pini Prato et al 1995[87]	9	9	6	5	+
Trombelli et al 1995[27]	16	24	12	4	+
Trombelli et al 1995[88]	8	16	6	1	+
De Sanctis et al 1996[89]	-	-	-	-	Not enough data
Ito & Mural 1996[90]	2	4	6	6	+
Pini Prato et al 1996[17]	25	25	48	1	+
Rachlin et al 1996[91]	10	10	12	5	+
Ricci et al 1996[92]	18	18	12	1	+
Roccuzzo & Buser 1996[24]	12	12	9	5	+
Roccuzzo et al 1996[25]	12	12	6	1	+
Pini Prato 1996[93]	-	-	-	-	Review article
Urbani et al 1992[94]	-	-	-	-	Not enough data
Wang et al 1996[95]	-	-	-	-	Descriptive
Saadoun et al 1996[96]	-	-	-	-	Not enough data
Abitbol et al 1997[97]	-	-	-	-	Descriptive
Harris 1997[14]	10	10	6	4	+
Ozcan et al 1997[98]	5	14	6	1	+
Shieh et al 1997[99]	10	10	6	3	+
Trombelli et al 1997[77]	22	22	6	4	+
Trombelli et al 1997[100]	8	10	12	4	+

APPENDIX: CONTINUED

Study	Sample Size		Treatment Length (months)	Rank	Exclusion Reasons
	N	Sites (GTR)			
Vanden Bogaerde et al 1997[101]	-	-	-	-	Not enough data
Waterman 1997[102]	13	17	12	5	+
Harris 1998[15]	24	37	6	4	+
Trombelli et al 1998[103]	6	11	6	6	+
Hirsch & Brayer 1998[104]	-	-	-	-	Descriptive
Jepsen et al 1998[23]	15	15	12	1	+
Parma-Benfenati et al 1998[105]	-	-	-	-	Histologic report
Scabbia et al 1997[106]	20	20	48	5	No baseline data
Trombelli et al 1998[16]	12	12	6	1	+
Vincenzi et al 1998[107]	-	-	-	-	Histologic report
Zahedi et al 1998[108]	15	15	24	5	+
Zucchelli et al 1998[26]	18	18	12	1	+
Matarsso et al 1998[60]	10	10	12	1	+
Trombelli 1998[109]	-	-	-	-	Review article
Tatakis & Trombelli 1999[110]	-	-	5	-	Histologic report
Borghetti et al 1999[61]	14	14	6	1	+
Harris 1999[111]	-	-	6	-	Histologic report
Muller et al 1999[78]	9	14	6	3	+
Duval et al 2000[37]	14	17	6	1	+
Muller et al 2000[112]	14	31	12	5	+
Tatakis & Trombelli 2000[62]	12	12	6	1	+
Amarante et al 2000[79]	20	20	6	1	+
Rosetti et al 2000[113]	12	12	18	1	+
Boltchi et al 2000[18]	41	100	6	5	+
Dodge et al 2000[38]	12	12	12	1	+
Tinti et al 2001[114]	10	10	12	5	+
Romagna-Genon 2001[115]	12	12	6	1	+
Muller et al 2001[28]	9	14	12	3	+
Wang et al 2001[59]	16	16	6	1	+