A systematic review and meta-analysis of guided tissue regeneration/osseous grafting for the treatment of Class II furcation defects

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KEYWORDS
bone grafting; furcation defects; guided tissue regeneration; meta-analysis; systematic review

Abstract
Background/purpose: The purpose of this article was to conduct a systematic review of the clinical evidence on the efficacy of guide tissue regeneration (GTR) with/without osseous grafting (OG) in treating periodontal furcation Class II defects.

Materials and methods: Reports from randomized controlled clinical trials, with at least 6 months follow-up, comparing open flap debridement (OFD); GTR, and GTR + OG were located from various sources. Sources included the electronic databases of Cochrane Oral Health Group specialist trials register, MEDLINE, and PubMed; in addition, journal archives were hand-searched. Trials up to and including March 2012 were included. Using the PICO (Patient or Problem, Intervention, Comparison, and Outcome) question format, data from eligible articles were extracted and meta-analyzed. The outcomes measures were furcation closure rate, vertical/horizontal bone fill (re-entry), and vertical/horizontal attachment level gain.

Results: The meta-analysis showed that the GTR and GTR + OG groups obtained greater furcation closure rate, vertical/horizontal bone fill, and vertical/horizontal attachment level gain than the OFD group in mandibular molars. The GTR group obtained greater vertical/horizontal bone fill and vertical attachment level gain than the OFD group in maxillary molars. The GTR + OG group achieved better clinical outcomes than the GTR group did in all the comparing outcomes in mandibular molars.

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Introduction

Periodontal invasion of the furcation area in multirooted teeth causes a serious problem. It presents a great challenge to clinicians wishing to access adequate instrumentation to correct the unfavorable anatomic structure of teeth. Over the past two decades, several techniques have been proposed to improve the prognosis of furcation-involved teeth. Nonsurgical therapy is usually impossible to adequately clean the internal furcations. However, the traditional resective procedure results in complications, which negatively affect the long-term prognosis of the treated teeth. Thus, the technique of guided tissue regeneration (GTR) was introduced to overcome these limitations.

GTR is based on the placement of physical barriers, which protect against apical migrating epithelial cells and gingival connective tissue cells of the flap, thus allowing the inward migration of periodontal ligament cells and mesenchymal cells on the exposed root surface. GTR combined with the osseous grafting (OG) technique was invented for better clinical and histological outcomes. These techniques have been demonstrated successfully in previous research. Ideally, successful regeneration of periodontal furcation defects is the clinically complete elimination of horizontal and vertical defect components by bone fill. However, restoration of Class III furcation was not a predictable procedure, and varied outcomes were stated in previous studies.

Comprehensive review articles have been published on the outcomes of regenerative therapies for furcation defects. Some of the systematic reviews included literatures with lower evidence level, such as cohort or retrospective studies. Moreover, new clinical evidence has emerged over the past decade. Varying inclusion criteria may result in different studies having been included or excluded from meta-analysis. The current article systematically assessed the efficacy of open flap debridement (OFD), GTR, and the combined approach of GTR and OG in the treatment of Class II furcation defects, using clinical outcomes as the variables for comparison.

Materials and methods

Type of study

Randomized controlled clinical trials with at least 6 months follow-up were considered for this review. The study protocol followed the question format of PICO (Patient or Problem, Intervention, Comparison, and Outcome) presented by Needleman (2002), Counsell (1997), and Richardson et al (1995).

Conclusion: GTR technique seemed to be more effective than OFD for resolving Class II periodontal furcation defects, and the GTR + OG technique showed even better clinical results. The outcomes were better for mandibular molars than for maxillary molars.

Types of participants

The participants in the included studies had received a clinical diagnosis of chronic periodontitis, based on the international Classification of periodontal diseases. Their periodontal furcation destruction was categorized as Class II according to the classification of Hamp et al (1975). Data from studies on patients with aggressive periodontitis were excluded.

Types of interventions

After comprehensive oral hygiene instruction and through scaling and root planing, patients had received regenerative surgery performed with GTR or GTR + OG (with resorbable or nonresorbable membrane). We excluded studies of patients who had diabetes, cardiovascular disease, pregnancy, systemic diseases requiring prescription medications, or who smoked at the time of the study or who were taking antibiotics.

Types of outcome measures

The outcome measures were as follows: (1) furcation closure rate; (2) horizontal probing attachment level; (3) vertical probing attachment level; (4) horizontal bone fill (re-entry measure); and (5) vertical bone fill (re-entry measure).

Search methods for identification of studies

We searched the Cochrane Oral Health Group specialist trials register as well as MEDLINE and PubMed up to March 2012 using the searching keywords: “guided tissue regeneration” OR “guidied-tissue-regeneration” OR “GTR” OR “osseous graft” OR “bone graft” OR “bone replacement graft” OR “bone substitute” OR “periodontal regeneration” OR “periodontal-regeneration” OR “regenerative therapy” OR “regenerative-therapy” OR “furcation defects” OR “furcation involvement”. Furthermore, we hand-searched the complete archives of the Journal of Periodontology, Journal of Clinical Periodontology, and Journal of Periodontal Research up to March 2012, as well as the reference lists of all relevant papers and review articles.

Selection of studies

Titles and abstracts were managed by downloading EndNote 13 software (ENDNOTE X3; Thomson Reuters, New York, U.S.A.). The selection of papers, the decision about eligibility, and data extraction were carried out by two reviewers (T.-H. Chen and C.-C. Yen). Any disagreements
were resolved by further discussion with a third reviewer (H.-K. Lu). Studies meeting the inclusion criteria underwent validity criteria assessment and data extraction.

Data extraction

The following data were extracted. General study characteristics, included year of the study, country of origin, authors, age of participants, severity of periodontal disease, methods for implementing randomization, surgical techniques used, length of time at follow-up, defect site, and measurement technique. The outcome measures included vertical and horizontal probing attachment level (vPAL and hPAL), vertical and horizontal bone fill of the defects (vBF and hBF), and furcation closure rate.

Data synthesis

Data of the outcomes were extracted from each study. Parallel group and split-mouth studies were combined in the meta-analysis of treatment effects. For binary outcomes such as furcation closure, the effect size measure was odds ratios with 95% confidence intervals (CI). For continuous outcomes such as probing attachment level gain, mean differences and 95% CI were used to summarize the results for each study. The meta-analysis was conducted using the fixed- or random-effects methods. Fixed-effects meta-analysis was used when the heterogeneity was small (I-square < 60%, P > 0.05). When the heterogeneity was large (I-square > 60%, P < 0.05), a random-effects model analysis was undertaken. All statistical analysis was conducted using statistical software package Stata version 11 (Stata Corporation, College Station, TX, USA).

Results

Study characteristics

After duplicate studies was removed, 344 articles were identified; independent screening of titles and abstracts led to the rejection of 287 articles (Fig. 1). The full text of the remaining 57 publications was then obtained. Out of these, 37 articles were excluded for reasons indicated in Tables 1 and 2. The characteristics of the final 20 included studies are reported in Table 1 (kappa value for inter-reviewer agreement is 0.89). Thirteen studies reported comparison of OFD and GTR, four studies reported comparison of OFD and GTR + OG, and another six studies reported comparison of GTR and GTR + OG. The results from these studies were separated into maxillary and mandibular data for meta-analysis. The risk of bias in individual studies were assessed and listed in Table 3.

Vertical bone fill

Maxillary Class II furcation

The results of the fixed-effect meta-analysis of the three included studies that had addressed this outcome showed a statistically significant greater vertical bone fill for GTR groups compared with OFD (Fig. 2A). The weighted mean difference between GTR/OFD was 0.71 mm (favors GTR; 95% CI: 0.53, 0.9; I-square = 0%; P = 0.799).

Mandibular Class II furcation

The results of the meta-analysis of the 10 included studies that had addressed this outcome showed statistically significant greater vertical bone fill for GTR groups compared with OFD, GTR + OG with OFD, and GTR + OG compared with GTR (Fig. 2B–D). The weighted mean difference between GTR/OFD was 1.46 mm (favors GTR; 95% CI: 0.66, 2.27; I-square = 90%; P < 0.001). GTR + OG/OFD was 1.77 mm (favors GTR + OG; 95% CI: 0.9, 2.63; I-square = 0%; P = 0.392), and GTR + OG/GTR was 0.87 mm (favors GTR + OG; 95% CI: 0.43, 1.3; I-square = 0%; P = 0.57).

Horizontal bone fill

Maxillary Class II furcation

The results of the meta-analysis of the four included studies that had addressed this outcome showed greater horizontal bone fill for GTR groups compared with OFD, but the result failed to reach statistical significance (Fig. 3A). The weighted mean difference between GTR/OFD was 0.72 mm (favors GTR; 95% CI: −0.07, 1.51; I-square = 92.8%; P < 0.001).

Mandibular Class II furcation

The results of the meta-analysis of the 11 included studies that had addressed this outcome showed a statistically significant greater horizontal bone fill for GTR groups compared with OFD, GTR + OG with OFD, and GTR + OG compared with GTR (Fig. 3B–D). The weighted mean difference between GTR/OFD was 1.55 mm (favors GTR; 95% CI: 0.72, 2.39; I-square = 92.9%; P < 0.001). GTR + OG/OFD was 1.34 mm (favors GTR + OG; 95% CI: 0.68, 2.0; I-square = 65.9%; P = 0.087), and GTR + OG/GTR was 0.86 mm (favors GTR + OG; 95% CI: 0.25, 1.11; I-square = 34.6%; P = 0.204).

Vertical probing attachment level gain

Maxillary Class II furcation

The results of the meta-analysis of the four included studies that had addressed this outcome showed a statistically significant greater vertical probing attachment level gain for GTR groups compared with OFD (Fig. 4A). The weighted mean difference between GTR/OFD was 1.02 mm (favors GTR; 95% CI: 0.75, 1.3; I-square = 22.4%; P = 0.265).

Mandibular Class II furcation

The results of the meta-analysis of the 17 included studies that had addressed this outcome showed a statistically significant greater vertical probing attachment level gain for GTR groups compared with OFD, GTR + OG compared with OFD, and GTR + OG compared with GTR (Fig. 4B–D). The weighted mean difference between GTR/OFD was 1.53 mm (favors GTR; 95% CI: 0.86, 2.19; I-square = 90.7%; P < 0.001). GTR + OG/OFD was 1.53 mm (favors GTR + OG; 95% CI: 0.53, 0.9; I-square = 0%; P = 0.799).
0.63, 2.44; I-square = 76.4%; P = 0.005), and GTR + OG/GTR was 0.47 mm (favors GTR + OG; 95% CI: 0.13, 0.82; I-square = 24.4%; P = 0.251). The difference between GTR + OG/GTR reaches P < 0.001.

Horizontal probing attachment level gain

Maxillary Class II furcation

Among the four studies included in the maxillary group, no data were available regarding horizontal probing attachment level gain.

Mandibular Class II furcation

The results of the meta-analysis of the 10 included studies that had addressed this outcome showed a statistically significant greater horizontal probing attachment level gain for GTR groups compared with OFD, GTR + OG compared with OFD, and GTR + OG compared with GTR (Fig. 5A–C).14,33,70,72,74,75,78–81 The weighted mean difference between GTR/OFD was 1.15 mm (favors GTR; 95% CI: 0.68, 1.62; I-square = 33.3%; P = 0.2), GTR + OG/OFD was 1.76 mm (favors GTR + OG; 95% CI: 0.55, 2.97; I-square = 85.1%; P < 0.001), and GTR + OG/GTR was 0.66 mm (favors GTR + OG; 95% CI: 0.25, 1.07; I-square = 0%; P = 0.937). The statistical difference in P value between GTR + OG/GTR is less than 0.001.

Furcation closure

Because of some ambiguity and wide heterogeneity in the reported results of the included studies, we were unable to conduct meta-analysis of complete versus partial closure.

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<tr>
<th>Rationale for exclusion</th>
<th>References</th>
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<tr>
<td>Similar or repetitive studies</td>
<td>Cury et al77 2003; Tsao et al34 2006; Casarin et al35,36 2009, 2010</td>
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<tr>
<td>Coronally positioned flap as control group</td>
<td>Garrett et al56 1990; Andersson et al57 1994; Lekovic et al58 1998; de Santana et al59 1999; Kerdvongbundit et al60 1999</td>
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<tr>
<td>Effects on antibiotics</td>
<td>Vest et al61 1999; Lyons et al62 2008</td>
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</table>
We therefore pooled the data and classified it according to a binary outcome, namely "improved" or "not improved." "Improved" meant that Class II furcation defects had become Class I or had completely closed up after surgical intervention; "not improved" meant that Class II furcation defects did not improve or had worsened after surgical intervention.

Maxillary Class II furcation
Only one study reported the closure rate; thus, no meta-analysis could be conducted.

Mandibular Class II furcation
The results of the meta-analysis of the six included studies that had addressed this outcome showed a statistically significant difference for "improved" sites for GTR groups compared with OFD, GTR + OG compared with OFD, and GTR + OG compared with GTR (Fig. 6A–C). The odds ratios between GTR/OFD was 4.31 (favors GTR; 95% CI: 1.35, 13.77; I-square = 0%; P = 0.394), GTR + OG/OFD was 6.94 (favors GTR + OG; 95% CI: 1.36, 35.42; I-square = 20.4%; P = 0.262), and GTR + OG/GTR was 5.12 (favors GTR + OG; 95% CI: 1.18, 22.21; I-square = 0%; P = 0.365).

Discussion
In this systematic review, we showed that GTR and GTR + OG for furcation II defects achieved greater probing attachment level gain and bone fill (vertical/horizontal) than did the conventional OFD procedure. The closure rate of Class II furcation defects were also higher in the GTR and GTR + OG group than in the OFD group. The GTR + OG obtained even better clinical outcomes than GTR did.

Defect morphology may influence the surgical outcome. Our previous study shows that most furcal involvement of mandibular molars possessed wide furcal entrances (>0.75 mm). The anatomy of furcal entrances may or may not influence the prevalence and long-term prognosis of furcal destruction of molars. However, another dry laboratory study shows that the developmental grooves over the short root trunk above the furcal entrance may hamper the result of the subgingival GTR technique using a teflon membrane. The present study excludes the synthetic analysis of the influence of defect morphology over GTR results because most of the included literature missed the data and description of defect anatomy. The great heterogeneity of defect morphology in included articles is another concern.

Murphy and Gunsolley collected cohort or retrospective studies and reviewed the efficiency of GTR therapy in furcation defects in 2003. According to Oxford CEBM (Centre for Evidence-based Medicine, March 2009), this article is classified as level 2b evidence. A higher level and contemporary systemic review is required. In the present review, we focus on the articles that are randomized clinical trials and more comprehensive data up to the year 2012 are included in this study.

In a study of GTR using resorbable and nonresorbable membranes in dogs, the histological results showed no significant differences in new bone growth of both experimental groups. In a clinical split-mouth study, clinical and radiographical data showed that resorbable membranes provided attachment gains comparable to nonresorbable expanded polytetrafluoroethylene (e-PTFE) membranes. In the present study, the comparison of the clinical results of GTR by using resorbable and nonresorbable membranes was not included in Table 3 in order to avoid distraction.

In a concurrent Cochrane Summaries study of guided tissue regeneration for periodontal infra-bony defects, it was concluded that there is marked variability between studies of GTR. However, GTR plus bone grafts showed a greater amount of hard tissue sounding with a mean difference of 3.37 mm. In a systemic review of guided tissue regeneration for the treatment of periodontal intrabony and furcation defects, the augmentation of GTR membranes with a particulate graft enhanced vertical pocket depth reduction and horizontal open probing attachment gain. Six studies were examined for the effect of the use of grafting materials under GTR barriers using the outcome variable vertical probing attachment level (VPAL). VPAL was significantly gained by the addition of variable particulate bone grafts. The heterogeneity was not significant. In the present study, three articles were included for the evaluation of the combination effect of membranes and demineralized freeze-dried bone Allograft (DFDBA) on furcation treatment. The results are in accordance with the result of a Cochrane review that GTR technique plus bone grafts may achieve greater hard tissue as compared to that of GTR alone.

A long-term study observed the stability of initial clinical attachment level gains as evident 6 months post-surgically by comparing these results with measurements obtained 1 year and 5 years post-surgically. They demonstrated that the new attachment level gain could be maintained over

<table>
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<th>Table 2 Inclusion and exclusion criteria.</th>
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<tr>
<td><strong>Inclusion criteria</strong></td>
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<td>Randomized clinical trials</td>
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<tr>
<td>Intervention of Class II furcation defect</td>
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<tr>
<td>caused by chronic periodontitis</td>
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<tr>
<td>OFD compared with GTR(BG)</td>
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<td>At least 6 mo follow-up</td>
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</table>

GTR = guided tissue regeneration; OFD = open flap debridement; RCT = randomized controlled trial.
<table>
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<tr>
<th>Author/yr</th>
<th>Study type/method</th>
<th>Follow-up period</th>
<th>Patients</th>
<th>Defects</th>
<th>Surgical treatment</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pontoriero et al 14 1988</td>
<td>Split mouth 2 treatment groups, no re-entry, standardized probing pressure</td>
<td>6 mo</td>
<td>21 individuals</td>
<td>Age 22–26 yr</td>
<td>23 buccal and 19 lingual Class II furcation defects of mandibular molar</td>
<td>Control: OFD Test: e-PTFE barrier removed at 1–2 mo</td>
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<tr>
<td>Lekovic et al 63 1989</td>
<td>Split mouth 2 treatment groups, re-entry, acrylic stent</td>
<td>6 mo</td>
<td>12 individuals</td>
<td>Age 29–47 yr</td>
<td>24 buccal Class II furcation defects of mandibular molar</td>
<td>Control: OFD Test: e-PTFE barrier removed at 2 mo</td>
</tr>
<tr>
<td>Lekovic et al 64 1991</td>
<td>Split mouth 2 treatment groups, re-entry, acrylic stent</td>
<td>6 mo</td>
<td>15 individuals</td>
<td>Mean age 39.67 yr</td>
<td>30 buccal Class II furcation defects of mandibular molar</td>
<td>Control: OFD Test: periosteal graft as barrier membrane</td>
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<tr>
<td>Metzler et al 65 1991</td>
<td>Split mouth 2 treatment groups, re-entry</td>
<td>6 mo</td>
<td>17 individuals</td>
<td>Age 29–64 yr</td>
<td>12 buccal pairs and 5 interproximal pairs of Class II furcation defects in maxillary molar</td>
<td>Control: OFD Test: e-PTFE barrier removed at 4–6 wk</td>
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<tr>
<td>Mellonig et al 66 1994</td>
<td>Split mouth 2 treatment groups, re-entry</td>
<td>6 mo</td>
<td>13 individuals</td>
<td>Age 29–90 yr</td>
<td>22 mandibular and 16 maxillary molars with Class II furcation defects</td>
<td>Control: OFD Test: e-PTFE barrier with DFDBA removed at 6 wk</td>
</tr>
<tr>
<td>Wallace et al 67 1994</td>
<td>Split mouth 2 treatment groups, re-entry, standardized probing pressure</td>
<td>6 mo</td>
<td>6 individuals</td>
<td>Age 30–55 yr</td>
<td>17 buccal Class II furcation defects of mandibular molars</td>
<td>Control: OFD Test: e-PTFE barrier removed at 4–6 wk</td>
</tr>
<tr>
<td>Wang et al 68 1994</td>
<td>Split mouth 2 treatment groups, re-entry, acrylic stent</td>
<td>12 mo</td>
<td>12 individuals</td>
<td>Age 32–68 yr</td>
<td>24 buccal Class II furcation defects of mandibular molar</td>
<td>Control: OFD Test: collagen membrane alone</td>
</tr>
<tr>
<td>Pontoriero and Lindhe 69 1995</td>
<td>Split mouth 2 treatment groups, re-entry, standard periodontal probe</td>
<td>6 mo</td>
<td>28 individuals</td>
<td>Age 21–59 yr</td>
<td>56 Class II furcation defects on buccal (20), mesial (20), and distal (16) aspect of maxillary molar</td>
<td>Control: OFD Test: e-PTFE barrier removed at 6 wk</td>
</tr>
<tr>
<td>Luepke et al 70 1999</td>
<td>Split mouth 2 treatment groups, re-entry, standardized probing pressure</td>
<td>6 mo</td>
<td>14 individuals</td>
<td>Age 36–74 yr</td>
<td>30 buccal Class II furcation defects of mandibular molars</td>
<td>Control: polyactic acid membrane alone</td>
</tr>
<tr>
<td>Avera et al 71 1999</td>
<td>Split mouth 2 treatment groups, re-entry, acrylic stent</td>
<td>9 mo</td>
<td>8 individuals</td>
<td>Mean age 42 ± 6.5 yr</td>
<td>16 mesial Class II furcation defects of maxillary molars</td>
<td>Control: OFD Test: e-PTFE barrier removed at 6 wk</td>
</tr>
<tr>
<td>De Leonardis et al 72 1999</td>
<td>Split mouth 2 treatment groups, no re-entry, standardized probing pressure</td>
<td>6 mo</td>
<td>12 individuals</td>
<td>Age 32–67 yr</td>
<td>24 Class II furcation defects of mandibular molars</td>
<td>Control: polyactic acid membrane alone</td>
</tr>
<tr>
<td>Simonpietri et al 73 2000</td>
<td>Split mouth 2 treatment groups, re-entry, acrylic stent</td>
<td>6 mo</td>
<td>14 individuals</td>
<td>Age 33–62 yr</td>
<td>30 Class II furcation defects of mandibular molars</td>
<td>Control: cellulose membrane alone</td>
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<tr>
<td>Study authors</td>
<td>Design</td>
<td>Treatment</td>
<td>Subjects</td>
<td>Results</td>
<td>Control</td>
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<tr>
<td>Houser et al.2001</td>
<td>Split mouth (8) and parallel group (13) 2 treatment groups, re-entry, standardized probing pressure</td>
<td>21 individuals Mean age 46 yr</td>
<td>31 Class II furcation defects of mandibular molars</td>
<td>Control: OFD Test: collagen membrane with bovine bone&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Group 1: calcium sulfate, Group 2: calcium sulfate + calcium sulfate and doxycycline (2:1), Group 3: calcium sulfate + calcium sulfate and DFDBA (2:1)</td>
<td>PD, REC, ΔvPAL, ΔhPAL vBF and hBF</td>
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<tr>
<td>Maragos et al.2002</td>
<td>Split mouth 3 treatment groups, re-entry, acrylic stent</td>
<td>17 individuals Age 40–72 yr Mean age 55.8 yr</td>
<td>36 Class II furcation defects of mandibular molars</td>
<td>Control: OFD Test: collagen membrane</td>
<td>Group 1: OFD, Group 2: FDBA, Group 3: collagen membrane&lt;sup&gt;b&lt;/sup&gt; + FDBA</td>
<td>PD, REC, ΔvPAL, ΔhPAL, furcation closure</td>
</tr>
<tr>
<td>Prathibha et al.2002</td>
<td>Split mouth 2 treatment groups, re-entry, acrylic stent</td>
<td>10 individuals Age 20–50 yr Mean age 45 yr</td>
<td>20 buccal Class II furcation defects of mandibular molar</td>
<td>Control: OFD Test: e-PTFE&lt;sup&gt;a&lt;/sup&gt; barrier removed at 6 wk</td>
<td>Control: OFD Test: polylactic acid membrane&lt;sup&gt;c&lt;/sup&gt;</td>
<td>PD, REC, ΔvPAL vBF, hBF, GI, PI, ΔvPAL, ΔhPAL, radiography examination</td>
</tr>
<tr>
<td>Cury et al.2003</td>
<td>Split mouth 2 treatment groups, no re-entry, acrylic stent and manual probe</td>
<td>9 individuals Mean age 45 yr</td>
<td>18 buccal Class II furcation defects of mandibular molars</td>
<td>Control: OFD Test: polylactic acid membrane&lt;sup&gt;c&lt;/sup&gt;</td>
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<tr>
<td>Bremm et al.2004</td>
<td>Split mouth 2 treatment groups, no re-entry, acrylic stent and manual probe</td>
<td>10 individuals Mean age 44 yr</td>
<td>20 Class II furcation defects of mandibular molars</td>
<td>Control: OFD Test: resorbable membrane&lt;sup&gt;f&lt;/sup&gt;</td>
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<tr>
<td>Belal et al.2005</td>
<td>Parallel group 5 treatment groups, re-entry, standardized probing pressure</td>
<td>20 individuals Age 35–55 yr</td>
<td>50 Class II furcation defects of mandibular molars</td>
<td>Group 1: PGA/PLA membrane&lt;sup&gt;g&lt;/sup&gt; alone, Group 2: PGA/PLA membrane&lt;sup&gt;g&lt;/sup&gt; + HA, Group 3: CTG as a barrier, Group 4: CTG + HA, Group 5: OFD</td>
<td></td>
<td>PD, REC, ΔvPAL, ΔhPAL, furcation closure</td>
</tr>
<tr>
<td>Tsao et al.2006</td>
<td>Parallel group 3 treatment groups, re-entry, acrylic stent</td>
<td>27 individuals Age 30–77 yr</td>
<td>27 Class II furcation defects of mandibular molars</td>
<td>Group 1: OFD, Group 2: FDBA, Group 3: collagen membrane&lt;sup&gt;b&lt;/sup&gt; + FDBA</td>
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<tr>
<td>Santana et al.2009</td>
<td>Parallel group 2 treatment groups, no re-entry (measure at 4th week), standardized probing pressure</td>
<td>60 individuals Age 41–63 yr Mean age 48.3 yr</td>
<td>60 buccal Class II furcation defects of mandibular molars</td>
<td>Control: OFD Test: PTFE barrier&lt;sup&gt;h&lt;/sup&gt; + HA removed at 4 wk</td>
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**Notes:**
- **BI** = bleeding index; **e-PTFE** = expanded polytetrafluoroethylene; **hBF** = horizontal bone fill; **MWF** = modified Widman flap; **OFD** = open flap debridement; **PD** = probing depth; **PI** = plaque index; **REC** = gingiva recession; **vBF** = vertical bone fill; **ΔhPAL** = horizontal probing attachment level gain; **ΔvPAL** = vertical probing attachment level gain.
- <sup>a</sup> Gore-Tex, W.L. Gore & Assoc. Inc., Flagstaff, AZ, USA.
- <sup>b</sup> BioMend (formerly Periobarrier), Calcitek Inc., Carlsbad, CA, USA.
- <sup>c</sup> Guidor Matrix Barrier, Guidor AB, Huddinge, Sweden.
- <sup>d</sup> Gengiflex, Biofill Produtos Biotecnológicos, Curitiba, PR, Brazil.
- <sup>e</sup> Geistlich Bio-Gide and Geistlich Bio-Oss, Geistlich Pharma AG, Wolhusen, Switzerland.
- <sup>f</sup> ATRISORB FreeFlow, TOLMAR Inc., Fort Collins, CO, USA.
- <sup>g</sup> Gore RESOLUT ADAPT, W.L. Gore & Assoc. Inc., Flagstaff, AZ, USA.
- <sup>h</sup> Bionnovation, São Paulo, SP, Brazil.
periods up to 5 years. Similarly, another study approached furcal defects using an ePTFE membrane, citric acid root conditioning, and composite osseous grafting. The gains in probing attachment levels showed stability after 5 years.

In the present review, we divided furcation closing condition into two groups, “improved” and “not improved”, to assess the improvement in clinical parameters during 6–12 months follow-up in the majority of cases. Meta-analysis of six studies that included data on mandibular closure rate found a significantly higher proportion of “improved” sites for GTR and GTR + OG groups compared with OFD (OR = 4.31 and 6.94). Because the heterogeneity between the included studies was not significant (P = 0.394 and 0.262), GTR appeared to be a more promising therapy than OFD for mandibular Class II furcation defects. As compared to included studies of GTR and GTR + OG groups, the result of meta-analysis showed that GTR + OG could significantly achieve higher proportion of “improved” sites with low heterogeneity. The conjuction of osseous grafting assisted the GTR procedure in treating Class II furcation defects. The data indicated that complete resolution of mandible furcation still did not occur consistently though.

We could not collect enough clinically controlled maxillary studies to meta-analyze the furcation closure rate. Most of these studies did not describe the closure rate. One study showed that one of 10 sites of mesial furcation and two of 10 sites of buccal furcation were completely closed by the GTR technique. Another study did not report any data on complete closure of maxillary molar furcation. We could not draw a clear conclusion from these studies.

The results of the meta-analysis of the 12 mandibular studies showed a statistically significant greater vertical clinical probing attachment level gain for GTR and GTR + OG groups compared with OFD (weighted mean difference = 1.53 mm and 1.53 mm). The difference between maxillary and mandibular molar results may be due to topographical differences, which included furcation anatomy, root trunk length, and biotype of adjacent alveolar bone. Metzler (1991) reported that GTR offered limited application as a therapeutic modality for Class II furcations of maxillary molars. Even if the outcomes were different in buccal of interproximal furcation (significant hPAL only in buccal furcation), Pontoriero and Lindhe (1995) still concluded that “the reason for the different outcome of GTR therapy in maxillary and mandibular furcation defects is most likely related to the anatomy of the defects, the presence of deep grooves in the root surface of the maxillary furcation, the limited access for root surface debridement, and the amount of remaining periodontium facing the defect.” Jepsen et al also systemically reviewed the outcomes of GTR for furcation defects and calculated the outcomes for studies that reported mixed maxillary and mandibular data. The weighted mean difference of all the outcomes showed less improvement in the maxillary group than the mandibular group, for both vertical and horizontal attachment level gain.

### Table 4: Quality assessment of the included clinical articles.

<table>
<thead>
<tr>
<th>Study</th>
<th>Sequence generation</th>
<th>Allocation concealment</th>
<th>Blinding of participants, personnel, and outcome assessors</th>
<th>Incomplete outcome data</th>
<th>Selective outcome reporting</th>
<th>Other sources of bias</th>
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<tr>
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Figure 2  (A–D) Forest plots for randomized controlled trials that evaluated change in vBF (mm) for mandibular and maxillary Class II furcations. GTR = guided tissue regeneration; OFD = open flap debridement; OG = osseous grafting; vBF = vertical bone fill.
Figure 3  (A–D) Forest plots for randomized controlled trials that evaluated change in hBF (mm) for mandibular and maxillary Class II furcations. GTR = guided tissue regeneration; hBF = horizontal bone fill; OFD = open flap debridement; OG = osseous grafting.
Figure 4  (A–D) Forest plots for randomized controlled trials that evaluated change in vPAL (mm) for mandibular and maxillary Class II furcations. GTR = guided tissue regeneration; OFD = open flap debridement; OG = osseous grafting; vPAL = vertical probing attachment level gain.
Figure 5  (A–D) Forest plots for randomized controlled trials that evaluated change in hPAL (mm) for mandibular Class II furcations. GTR = guided tissue regeneration; hPAL = horizontal probing attachment level gain; OFD = open flap debridement; OG = osseous grafting.
Figure 6  (A–C) Forest plots for randomized controlled trials that evaluated odds ratios for the improvement of mandibular Class II furcations. GTR = guided tissue regeneration; OFD = open flap debridement; OG = osseous grafting.
For re-entry bone filling measurement, the outcomes of our meta-analysis of mandibular studies showed 1.46 mm greater vBF for GTR groups compared with OFD and 1.77 mm greater for GTR + OG groups compared with OFD. The GTR and GTR + OG groups had better hBF outcomes than OFD groups (1.55 mm and 1.43 mm). The outcome of the meta-analysis of the maxillary studies showed 0.71 mm greater vBF for GTR than OFD (P < 0.001) and 0.72 mm greater hBF in GTR than OFD (P = 0.073). These findings demonstrated that GTR obtained better results in mandibular molars than in maxillary molars. A systemic review by Needelman et al.86 showed that for intrabony defects, GTR was associated with greater attachment gain than OFD, with a mean difference of 1.22 mm (P < 0.001). This result was more similar to the outcomes of mandibular studies than maxillary studies, and may imply that the outcomes of GTR therapy are clinically significant only for intrabony and mandibular Class II furcation defects. In the present study, data for maxillary and mandibular procedures were compared because of the differences in topographical condition of teeth and outcomes of GTR.

All the meta-analysis outcomes in this review demonstrated that GTR + OG significantly achieved better clinical results than GTR in treatment of mandibular molar Class II furcation defect (vBF = 0.87 mm; hBF = 0.68; vPAL = 0.47 mm; hPAL = 0.66 mm). Murphy and Gunsolley22 reviewed the efficiency of GTR therapy in intrabony and furcation defects. They concluded that the use of augmentation materials in addition to the physical barrier enhanced the regeneration outcome in the treatment of furcation defects with GTR. However, studies of the same comparison of maxillary molars are scarce, and comparison between the GTR and GTR + OG groups through meta-analysis of randomized controlled trials cannot be made.

In the current study, the GTR + OG group achieved better clinical outcomes than the GTR group in all compared parameters; nevertheless, the type of membrane material used for GTR was not analyzed. Kinaia et al.69 reviewed randomized controlled trials for treating molar furcation Class II involvement. It was concluded that there were no significant weight mean differences between resorbable and nonresorbable membranes with regard to reducing vertical probing depths and gaining vertical attachment levels and horizontal bone. However, the use of resorbable membrane was superior to nonresorbable membrane in vertical bone fill.

Our meta-analysis showed that GTR therapy is more effective in treating Class II furcation defects than OFD. The treatment outcome is more consistent in the mandibular molars than maxillary molars. The conjunctive osseous grafting enhanced clinical outcomes of GTR in treatment of mandibular molars. New techniques with comprehensive clinical trials and more promising results should be developed to achieve the goal of solving maxillary furcation problems.

References


