The Effect of Regeneration Techniques on Periapical Surgery With Different Protocols for Different Lesion Types: A Meta-Analysis

Yang Deng, MS,* Xiaodan Zhu, MS,† Jun Yang, DDS,‡ Han Jiang, DDS,§ and Ping Yan, DDS∥

Purpose: To evaluate the effect of regeneration techniques (RTs) on the outcome of periapical surgery with different protocols for different lesion types.

Materials and Methods: PubMed, the Cochrane Library, and Embase were searched from the beginning of time until December 30, 2014. Studies that met the inclusion criteria were systematically evaluated, and a meta-analysis was performed.

Results: Eight randomized controlled trials met the inclusion criteria. A significantly better outcome was found in the combination group (membranes plus bone replacement analogues) (risk ratio [RR], 0.41; 95% confidence interval [CI], 0.22 to 0.77; \( P = .005 \)) and bone replacement analogue–only group (RR, 0.48; 95% CI, 0.23 to 0.98; \( P = .04 \)), whereas no significant beneficial effect was found in the membrane-only group (RR, 0.59; 95% CI, 0.29 to 1.17; \( P = .13 \)). The use of RTs favorably affected the outcome of periapical through-and-through lesions (RR, 0.38; 95% CI, 0.18 to 0.84; \( P = .02 \)) and large lesions (≥10 mm) (RR, 0.52; 95% CI, 0.28 to 0.97; \( P = .04 \)), whereas there was no significant benefit of using RTs for 4-wall lesions (RR, 0.54; 95% CI, 0.27 to 1.07; \( P = .08 \)).

Conclusions: Both the isolated use of bone replacement analogues and the combination of membranes and bone replacement analogues can improve the outcome of periapical surgery, whereas using membranes alone does not have significantly favorable effects. The use of RTs for through-and-through and large lesions should be recommended.

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Even when appropriate root canal treatment or retreatment is provided, periapical pathology persists in some cases. Therefore periapical surgery may be indicated, considering that it is the last therapeutic option before tooth extraction. The main objective of periapical surgery is to create an optimal environment for periapical tissue healing. Whether a successful outcome of periapical surgery is achieved can be affected by many factors, among which the size and location of the periapical bone loss are thought to be the most considerable factors except for control of bacterial egress. The periapical sites treated with conventional surgery alone, especially for large lesions, will often be filled with extensive fibrous connective tissues without complete healing. An ingrowth of non-osteogenic tissues into the bone loss site and down-growth of the epithelial tissue along the root surface can result in "repair" with new cells and structures that differ from the...
can act as space maintainers.12-14 With the introduction of regeneration techniques (RTs) (guided tissue or bone regeneration) to periodontology and implant dentistry, these have been proposed as an adjunct to periapical surgery. Regeneration is defined as reproduction or reconstruction of lost tissues and restoration of various functions of damaged human tissues and organs. The reasons for using RTs in periapical surgery are as follows: 1) to accelerate periapical healing and 2) to allow for healing in compromised clinical situations.2 RTs procedures for periapical surgery frequently include the use of barrier membranes, bone replacement analogues, cell signaling molecules, or growth factors to encourage growth of surrounding tissues and accelerate tissue healing.8 A barrier over an osseous defect can be used to improve the self-regenerative healing process by excluding the undesired proliferation of gingival connective tissue or oral epithelium into the defect, as well as maintaining an appropriate amount of space below the membrane to allow the cells of the periodontal ligament and trabecular bone to regenerate the lost tissue.9-11 The bone replacement analogues, most of which are bone grafts (autografts, allografts, xenografts, and alloplasts), have osteogenic and osteoinductive properties and also can act as space maintainers.12-14

Although RTs have great potential, they remain unpredictable in their ability to consistently produce acceptable outcomes in all situations.15 Some articles have already reviewed the effects of RTs on the outcome of periapical surgery,2,5,16 and most of them supported the use of RTs in periapical surgery. According to the membranes and bone replacement analogues—whether used or not—RTs mainly have 3 varied protocols: membranes only, membranes plus bone replacement analogues, and bone replacement analogues only. The previous published meta-analysis reported by Tsesis et al10 in 2011 only evaluated the effect of membranes, and no exact conclusions have been reached about which protocol is suited for which lesion type. Therefore the aim of this study was to formulate a reliable clinical guide for the use of membranes and bone replacement analogues in conjunction with periapical surgery by examining the relevant literature from recent years and performing a meta-analysis.

**Materials and Methods**

To specifically evaluate the effect of RTs, we conducted a subgroup analysis based on different methods and different lesion types in periapical diseases.

**Inclusion Criteria**

Studies were selected based on the following inclusion criteria: 1) The study design was a controlled clinical trial. 2) Regarding participants, the patient had to have a tooth for which orthograde root canal therapy had failed and in which periapical radiolucency was present. 3) Regarding intervention, the use of RTs was the only treatment difference between the 2 groups, regardless of the whether there was combined therapy. 4) The follow-up time was at least 1 year. 5) Success and failure were evaluated using clinical assessment and radiographic parameters.

**Exclusion Criteria**

Studies were excluded if the inclusion criteria were not met or if they presented any of the following exclusion criteria: 1) Patients had undergone prior periapical surgery. 2) The rate of loss to follow-up was greater than 20%. 3) Data for the outcomes of interest were unable to be extracted. 4) Root fracture or root perforation occurred.

**Search Strategy**

The search covered 3 databases (PubMed, the Cochrane Library, and Embase), without restrictions on language, from the beginning of time until December 30, 2014. The structured search strategies used the following format for search terms: (periapical surgery OR surgical endodontic treatment OR apicoectomy OR periradicular surgery OR endodontic surgery OR root-end surgery OR root-end resection) AND (guided tissue regeneration OR bone regeneration OR bone grafts OR barrier membranes). A manual search of the reference articles was conducted to identify additional studies.

**Selection of Studies**

The articles were initially evaluated for relevance based on their titles and abstracts. Then, the full texts of the possibly relevant studies were obtained. Studies that fulfilled the inclusion and exclusion criteria regarding eligibility were included. If full-text versions of the relevant studies were not available, we contacted the first author or corresponding author. To minimize the potential for reviewer bias, 2 reviewers independently performed the article selection. For any disagreements that could not be resolved by discussion, a third reviewer was consulted to achieve consensus.

**Data Extraction**

Two independent reviewers extracted information after reading the full text of the included articles. The following parameters were extracted from each
study: first author’s name, year of publication, methods and study design, number of patients in each group, characteristics of the study population, follow-up period, dropout rate and reasons for dropout, lesion types, therapy protocols, and success and failure rates. For publications reporting on the same population, the article with the most comprehensive data was included in this meta-analysis. If the data were unavailable, the authors were contacted via e-mail for additional information.

Success was defined as the absence of clinical signs or symptoms (pain, swelling, percussion sensitivity, or sinus tracts) and a radiographic classification of complete healing. Failure was defined as the presence of any clinical signs or symptoms mentioned previously. Radiographic failure included unsatisfactory, doubtful, or incomplete healing (reduction or same lesion size) or complete failure (increase in lesion size).

ASSESSMENT OF RISK OF BIAS AND QUALITY OF EVIDENCE

All of the included studies were evaluated based on the Cochrane Risk of Bias Tool recommended by the Cochrane Handbook for Systematic Reviews of Interventions, version 5.1.0 (http://www.cochrane-handbook.org/). Two reviewers independently assessed the study quality using the following 7 criteria: random sequence generation, allocation concealment, blinding of participants, blinding of outcome assessment, incomplete outcome data, selective reporting, and other bias. If there was disagreement, consensus was reached through discussion or consultation with a third reviewer. A high quality of evidence was estimated when all domains were at low risk of bias, a moderate quality of evidence was estimated when 1 or more key domains were at an unclear risk of bias and none were at a high risk of bias, and a low quality of evidence was estimated when 1 or more domains were at a high risk of bias.

STATISTICAL ANALYSIS

RevMan, version 5.1, provided by The Cochrane Collaboration, was used to perform the meta-analysis, and the tooth was used as the analysis unit. The risk ratio and 95% confidence interval were used as measurable statistics and calculated with fixed- and random-effects meta-analysis using the Mantel-Haenszel method for dichotomized data, and \( P < .05 \) was considered to indicate a significant difference.

The statistical heterogeneity among studies was evaluated with the \( \chi^2 \) test, with significance set at \( P < .10 \). The \( I^2 \) statistic was used to assess the percentage of heterogeneity. If \( I^2 \) ranges from 0 to 40%, the heterogeneity is mild. If \( I^2 \) ranges from 40 to 60%, the heterogeneity may be moderate. If \( I^2 \) ranges from 50 to 90%, the heterogeneity may be significant. If \( I^2 \) ranges from 75 to 100%, it indicates extreme heterogeneity. In general, if \( P > .10 \) and \( I^2 \) is less than 50%, all included studies are considered homogeneous, and the fixed-effects model can be chosen for analysis. If not, the source of heterogeneity should be analyzed. Evaluation of publication bias was not conducted because of the limited number of included studies in the final analysis.

Results

SCREENING RESULTS

An overview of the selection process is shown in Figure 1. Full-text versions of a total of 17 studies were obtained for detailed evaluation, and 9 studies were excluded for various reasons: 2 did not have a sufficient follow-up time, 1 had a dropout rate greater than 20%, 1 included patients with perforations, 1 failed to report success and failure rates, 3 were not randomized controlled trials, 2 were animal trials, and 1 had no control group (Table 1). Finally, 8 studies (7 in English and 1 in French) were included in this meta-analysis and were subjected to data extraction, risk-of-bias assessment, and data synthesis and analysis. The main characteristics of the included studies are summarized in Table 2.

RISK OF BIAS AND QUALITY OF EVIDENCE

The risk-of-bias assessment for each included study is shown in Figure 2. All of the included studies met the inclusion and exclusion criteria, but some of them did not adequately describe their methods in detail. Because the outcome was not likely to be influenced by the lack of participant blinding, we considered performance bias as low risk. Two studies were at high risk of bias for incomplete outcome data because they did not analyze the causes of failure in the follow-up period, and the rate of loss to follow-up was not even between the test and control groups. Two included studies were of low quality, and six were moderate (Table 3).

RESULTS OF META-ANALYSIS

Figure 3 shows the results of our meta-analysis. All data from the included studies were used to calculate the overall effect of RTs on the outcome of periapical surgery. Because a heterogeneity test showed that there was low heterogeneity among these studies (\( \chi^2 = 2.81, P = 0.9, I^2 = 0% \)), the fixed-effects model for meta-analysis was used. On the basis of the results, a trend toward better outcomes was found when RTs were used compared with the control group. The results from subgroup analysis showed that 2 of the
protocols—bone replacement analogue–only group and combination group—had significantly better outcomes than the control group; however, the membrane-only group showed no significant differences. Regarding lesion type, there was a trend for better outcomes using RTs for all 3 lesion types:

- Through and through
- 4 wall
- Large (\( \geq 10 \text{ mm} \))

However, statistically significant differences were only found in the through-and-through group and large lesion group. Because of the limited data extracted from the included studies, we did not perform an analysis of the effect of RTs for apico-marginal lesions and small lesions and we could not directly compare the effect of membranes and bone replacement analogues.

**Discussion**

Because effective results have been achieved when using RTs for periodontology and implant dentistry, RTs have been recommended as an adjunct treatment to periapical surgery with the goal of improving the quality of healing in terms of replacing damaged or lost tissue by cells, tissues, and structures that are the same as the original ones. Although a range of studies reported considerable outcomes of periapical surgery using RTs, there has been no consensus about the gold standard. There is a lack of consistency among reported articles on periapical surgery regarding contemporary methodology, in particular the use of RTs. In this meta-analysis, the effects of RTs on

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**Table 1. EXCLUDED STUDIES AND REASONS FOR EXCLUSION**

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stassen et al., 1994</td>
<td>Included patients with perforations</td>
</tr>
<tr>
<td>Yoshikawa et al., 2002</td>
<td>Animal trial</td>
</tr>
<tr>
<td>Garrett et al., 2002</td>
<td>Loss to follow-up &gt;20%</td>
</tr>
<tr>
<td>Dietrich et al., 2003</td>
<td>Not a randomized controlled clinical trial</td>
</tr>
<tr>
<td>Marín-Botero et al., 2006</td>
<td>No control group</td>
</tr>
<tr>
<td>Pantchev et al., 2009</td>
<td>Retrospective study</td>
</tr>
<tr>
<td>Taschieri et al., 2011</td>
<td>Retrospective study</td>
</tr>
<tr>
<td>Artzi et al., 2012</td>
<td>Animal trial</td>
</tr>
<tr>
<td>Vaishnavi et al., 2011</td>
<td>No measurable results</td>
</tr>
</tbody>
</table>

periapical surgery with different methods were compared for different lesions. Clinical evidence indicates that most of the repair or regeneration of the bone defect takes place during the first year after the procedure and that very few changes occur later. Therefore our study only extracted data collected at 1 year after periapical surgery.

The results of this meta-analysis showed that use of RTs in periapical surgery yielded better outcomes than traditional periapical surgery, which was inconsistent with the previous meta-analysis. Analysis was performed isolating the use of barrier membranes, bone replacement analogues, or the combination of both. There were no significant differences for the group that only used membranes in periapical surgery, which is consistent with some previous studies: von Arx and Cochran suggested that good long-term results have been achieved with traditional periapical surgery and that membrane application was unnecessary. Some other studies also reported that placement of a membrane over the bony defect during periapical surgery does not significantly affect the rate of healing. The different materials used for the membranes might influence the present results. Many studies have reported that nonabsorbable membranes might be stiffer than resorbable membranes in terms of maintaining the defect space, and the process of membrane resorption might adversely affect tissue regeneration. Because it is beyond the scope of this article to review the effect of different membrane materials on surgical outcomes, readers are encouraged to consult the relevant literature to obtain more definitive conclusions.

Our meta-analysis showed that the isolated use of bone replacement analogues and the simultaneous use of membranes and bone replacement analogues both achieved more satisfactory outcomes than traditional surgery. Considering the results of these 3 comparisons (bone replacement analogues, membranes, and combination), the bone replacement analogues seem to have played the most important role in the healing process in periapical surgery. We speculate that the reason may be that buccally and lingually placed membranes may collapse toward the defect for a large defect; therefore, placing resorbable bone replacement analogues in the bone defects not only can conduct or induct bone regeneration, but also can support nonrigid membranes. However, the difficulty of radiographic healing interpretation must be stressed because the radiopacity of most filling substitutes compounds the radiographic differentiation between incomplete (“scar tissue”) and uncertain healing categories.

A series of studies indicated that defect morphology is an important factor in the clinical outcome of periapical surgery. According to most clinical

<table>
<thead>
<tr>
<th>Author, Publication Year</th>
<th>Age, yr</th>
<th>Sample Size</th>
<th>Lesion</th>
<th>Lesion Diameter</th>
<th>Protocol</th>
<th>Dropouts, n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pecora et al, 1995</td>
<td>27-50</td>
<td>20</td>
<td>—</td>
<td>≥10 mm</td>
<td>e-PTFE membrane vs control</td>
<td>0</td>
</tr>
<tr>
<td>Pecora et al, 2001</td>
<td>30-60</td>
<td>20</td>
<td>Tunnel</td>
<td>≥10 mm</td>
<td>Calcium sulphate vs control</td>
<td>2</td>
</tr>
<tr>
<td>Tobón et al, 2002</td>
<td>14-74</td>
<td>28</td>
<td>—</td>
<td>—</td>
<td>e-PTFE membrane + hydroxyapatite OsteoGen (Impladent Ltd, Holliswood, NY) vs control</td>
<td>2</td>
</tr>
<tr>
<td>Taschieri et al, 2007</td>
<td>Mean, 38.2</td>
<td>62</td>
<td>Tunnel/4 wall</td>
<td>≥10 mm</td>
<td>Collagen membrane + bovine bone mineral vs control</td>
<td>3</td>
</tr>
<tr>
<td>Taschieri et al, 2008</td>
<td>Mean, 38</td>
<td>33</td>
<td>Tunnel</td>
<td>—</td>
<td>Collagen membrane + bovine bone mineral vs control</td>
<td>2</td>
</tr>
<tr>
<td>Taschieri et al, 2008</td>
<td>Unclear</td>
<td>73</td>
<td>—</td>
<td>≥10 mm</td>
<td>Collagen membrane + bovine bone mineral vs control</td>
<td>4</td>
</tr>
<tr>
<td>Dominiak et al, 2009</td>
<td>9-60</td>
<td>106</td>
<td>4 wall</td>
<td>—</td>
<td>Collagen membrane vs bovine bone mineral vs bovine bone mineral + PRP vs control</td>
<td>1</td>
</tr>
<tr>
<td>Goyal et al, 2011</td>
<td>17-45</td>
<td>30</td>
<td>Apico-marginal</td>
<td>—</td>
<td>Collagen membrane vs collagen sponge + PRP vs PRP</td>
<td>5</td>
</tr>
</tbody>
</table>

Abbreviation: e-PTFE, nonresorbable expanded polytetrafluoroethylene; PRP, platelet-rich plasma.

* The sample size indicates the number of patients finally included in the study.
† We only extracted the data from the collagen membrane group, bovine bone mineral group, and control group.
‡ We only extracted the data from the collagen sponge–plus–PRP group and the PRP group, which was considered the control group.
and experimental studies, periapical lesions have been classified into the following 3 main types: 1) 4-wall lesion, 2) through-and-through (tunnel) lesion, and 3) apico-marginal lesion. Our study showed that the use of RTs is beneficial for through-and-through defects, whereas there was no significant advantage with the use of RTs for 4-wall defects, which was consistent with previous systematic reviews and meta-analysis. The most credible explanation may be that a 4-wall lesion only misses the bone around the root and the facial cortex removed during the surgical procedure, and therefore the risk of proliferation of gingival connective tissue or migration of oral epithelium into the defect is low; in contrast, the through-and-through lesion has a high risk of repair with scar tissue, and therefore it can benefit the most from the use of RTs, which prevent the soft tissue from proliferating into the bone defect.

With respect to lesion size, we observed that there is benefit to the use of RTs for a large periapical lesion (≥10 mm), irrespective of the type of lesion. This is because the osseous regeneration of a large wound does not occur spontaneously, and the defect will otherwise heal with soft tissue. Therefore large lesions need regeneration technology to recruit and differentiate progenitor cells into osteoblasts, cementoblasts, and periodontal ligament cells. Given the paucity of data about the effect of RTs for small lesions and apico-marginal lesions, we did not conduct a meta-analysis for small lesions and apico-marginal lesions.

Many of our included studies had small sample sizes, and therefore their overall veracity is questionable and their results should be interpreted with caution. In addition, more well-designed randomized controlled trials with large sample sizes are needed to draw more definitive conclusions.

The findings of our study mirror those of other studies and confirm, but do not add to, the currently available body of evidence:

- Both the isolated use of bone replacement analogues and the combined use of membranes with bone replacement analogues could improve the outcome of periapical surgery, whereas using barrier membranes alone does not have a more favorable effect on the rate of healing compared with conventional surgery.
- The use of RTs in periapical surgery for through-and-through and large (≥10 mm) lesions should be recommended, whereas RTs are not warranted for 4-wall lesions.
**FIGURE 3.** Forest plots of meta-analysis for different methods and different lesion types. Events indicates the number of failures. CI, confidence interval; M-H, Mantel Haenszel test; RR, risk ratio; RT, regeneration techniques.


<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental</th>
<th>Control</th>
<th>Weight</th>
<th>Risk Ratio M-H, Fixed 95% CI</th>
<th>Risk Ratio M-H, Fixed 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A</strong> Dominiai 2009</td>
<td>5 26 9 25</td>
<td>60.5%</td>
<td>0.53 [0.21, 1.37]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pecora 1995</td>
<td>1 10 1 10</td>
<td>8.6%</td>
<td>1.30 [0.07, 13.87]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tobon 2002</td>
<td>3 9 5 9</td>
<td>32.5%</td>
<td>0.60 [0.20, 1.79]</td>
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<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>45</td>
<td>44</td>
<td>100.0%</td>
<td>0.59 [0.29, 1.17]</td>
<td></td>
</tr>
<tr>
<td><strong>Total events</strong></td>
<td>9 15</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Heterogeneity:</strong> Ch² = 0.20, df = 2 (P = 0.91); I² = 0%</td>
<td></td>
<td></td>
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<tr>
<td><strong>Test for overall effect:</strong> Z = 1.51 (P = 0.13)</td>
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</table>

**B** Membrane only vs Control

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental</th>
<th>Control</th>
<th>Weight</th>
<th>Risk Ratio M-H, Fixed 95% CI</th>
<th>Risk Ratio M-H, Fixed 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dominiai 2009</td>
<td>5 30 9 25</td>
<td>57.7%</td>
<td>0.94 [0.18, 1.28]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Goyal 2011</td>
<td>2 9 1 6</td>
<td>7.1%</td>
<td>1.33 [0.15, 11.64]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pecora 2001</td>
<td>2 9 6 9</td>
<td>35.3%</td>
<td>0.33 [0.09, 1.23]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>48</td>
<td>40</td>
<td>100.0%</td>
<td>0.48 [0.23, 0.98]</td>
<td></td>
</tr>
<tr>
<td><strong>Total events</strong></td>
<td>9 16</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Heterogeneity:</strong> Ch² = 1.16, df = 2 (P = 0.55); I² = 0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Test for overall effect:</strong> Z = 2.03 (P = 0.04)</td>
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</tbody>
</table>

**C** Bone replacement analogues only vs Control

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental</th>
<th>Control</th>
<th>Weight</th>
<th>Risk Ratio M-H, Fixed 95% CI</th>
<th>Risk Ratio M-H, Fixed 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tatschier 2007</td>
<td>4 24 9 35</td>
<td>28.4%</td>
<td>0.85 [0.23, 1.87]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tatschier 2008 (30)</td>
<td>4 23 9 36</td>
<td>31.1%</td>
<td>0.48 [0.16, 1.43]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tatschier 2008 (31)</td>
<td>2 17 6 14</td>
<td>23.7%</td>
<td>0.79 [0.07, 1.55]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tobon 2002</td>
<td>0 8 5 9</td>
<td>18.6%</td>
<td>0.10 [0.01, 1.56]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>82</td>
<td>94</td>
<td>100.0%</td>
<td>0.41 [0.22, 0.77]</td>
<td></td>
</tr>
<tr>
<td><strong>Total events</strong></td>
<td>10 20</td>
<td></td>
<td></td>
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<tr>
<td><strong>Heterogeneity:</strong> Ch² = 2.12, df = 3 (P = 0.55); I² = 0%</td>
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<tr>
<td><strong>Test for overall effect:</strong> Z = 2.78 (P = 0.005)</td>
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**D** Combination vs Control

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental</th>
<th>Control</th>
<th>Weight</th>
<th>Risk Ratio M-H, Fixed 95% CI</th>
<th>Risk Ratio M-H, Fixed 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pecora 2001</td>
<td>2 9 6 9</td>
<td>36.6%</td>
<td>0.33 [0.09, 1.23]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tatschier 2007</td>
<td>2 8 5 13</td>
<td>22.3%</td>
<td>0.85 [0.16, 2.59]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tatschier 2008 (31)</td>
<td>2 17 6 14</td>
<td>40.1%</td>
<td>0.27 [0.07, 1.15]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>34</td>
<td>36</td>
<td>100.0%</td>
<td>0.38 [0.18, 0.84]</td>
<td></td>
</tr>
<tr>
<td><strong>Total events</strong></td>
<td>6 17</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Heterogeneity:</strong> Ch² = 0.81, df = 2 (P = 0.67); I² = 0%</td>
<td></td>
<td></td>
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<tr>
<td><strong>Test for overall effect:</strong> Z = 2.40 (P = 0.02)</td>
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<td></td>
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</tbody>
</table>

**E** Through and through lesion: RT VS Control

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental</th>
<th>Control</th>
<th>Weight</th>
<th>Risk Ratio M-H, Fixed 95% CI</th>
<th>Risk Ratio M-H, Fixed 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dominiai 2009</td>
<td>10 56 9 25</td>
<td>78.7%</td>
<td>0.56 [0.23, 1.07]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tatschier 2007</td>
<td>2 16 4 22</td>
<td>21.3%</td>
<td>0.69 [0.14, 3.31]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>72</td>
<td>47</td>
<td>100.0%</td>
<td>0.54 [0.27, 1.07]</td>
<td></td>
</tr>
<tr>
<td><strong>Total events</strong></td>
<td>12 13</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Heterogeneity:</strong> Ch² = 0.14, df = 1 (P = 0.71); I² = 0%</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td><strong>Test for overall effect:</strong> Z = 1.75 (P = 0.08)</td>
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</tr>
</tbody>
</table>

**F** 4-wall lesion: RT VS Control

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental</th>
<th>Control</th>
<th>Weight</th>
<th>Risk Ratio M-H, Fixed 95% CI</th>
<th>Risk Ratio M-H, Fixed 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pecora 1995</td>
<td>1 10 1 10</td>
<td>4.4%</td>
<td>1.00 [0.07, 13.87]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pecora 2001</td>
<td>2 9 6 9</td>
<td>26.2%</td>
<td>0.33 [0.09, 1.23]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tatschier 2007</td>
<td>4 24 9 35</td>
<td>31.9%</td>
<td>0.65 [0.23, 1.87]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tatschier 2008 (30)</td>
<td>4 33 9 36</td>
<td>37.5%</td>
<td>0.48 [0.16, 1.43]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>76</td>
<td>90</td>
<td>100.0%</td>
<td>0.52 [0.28, 0.97]</td>
<td></td>
</tr>
<tr>
<td><strong>Total events</strong></td>
<td>11 25</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Heterogeneity:</strong> Ch² = 0.97, df = 3 (P = 0.93); I² = 0%</td>
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<td></td>
</tr>
<tr>
<td><strong>Test for overall effect:</strong> Z = 2.04 (P = 0.04)</td>
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</tr>
</tbody>
</table>
References