

Regenerative Periodontal Therapy in Intrabony Defects and Long-Term Tooth Prognosis



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KEYWORDS

- Periodontal regeneration • Bone grafts • Bone substitutes • GTR
- Enamel matrix proteins • EMD • Long term

KEY POINTS

- Periodontal regenerative procedures yield significantly better clinical outcomes in intrabony defects compared with open flap debridement, on the medium- to long-term.
- Combination approaches, including the use of a bone graft seem to be more efficacious compared with monotherapy.
- Periodontal regenerative procedures result in higher rates of tooth preservation compared with open flap debridement on the medium- to long-term.

WHY PERIODONTAL REGENERATIVE PROCEDURES?

To arrest progressive attachment loss and/or prevent further disease progression, control of the infection caused by the oral bacterial biofilm remains the primary aim of periodontal treatment. For most patients and teeth/sites, this goal can be commonly achieved through proper and adequate self-performed oral hygiene and professionally performed nonsurgical and/or conventional surgical periodontal treatment. In the clinic, this translates into reduced probing pocket depths (PD) and gain in clinical attachment level (CAL), reduced tendency to bleeding on probing (BoP), and stable/increased bone

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levels, compared with pretreatment levels. Nevertheless, residual (deep) PD can still be present following nonsurgical and/or conventional surgical periodontal therapy, commonly in teeth/sites with deep intrabony defects and/or deep furcation involvements. Deep PD after periodontal therapy is indeed associated with an increased risk for disease progression and tooth loss. In a long-term study,¹ deep residual PD or a deep furcation involvement (ie, class II and III) after treatment has been associated with an exponential higher risk for periodontitis progression and tooth loss. Specifically, a greater than 10 times higher risk for tooth loss has been reported for teeth with a residual PD greater than or equal to 6 mm compared with teeth with a residual PD of less than or equal to 3 mm, whereas teeth with a class II or III furcation involvement showed about 5 to 13 times higher risk for tooth loss compared with teeth with no furcation involvement.¹ Deep defects can be managed efficiently with either resective or regenerative approaches. Resective approaches, however, have the drawback of extensive soft tissue recession and often further loss of attachment.²⁻⁴ Thus, a variety of surgical regenerative treatment protocols have been developed and refined during the last 3 to 4 decades, with the aim to enhance treatment outcomes and at the same time to evade/reduce the aforementioned shortcomings of conventional and/or resective approaches. Indeed, significantly better clinical (ie, larger CAL gains, shallower residual PD, and less recession) and radiographic results (ie, larger bone level gain and reduced residual intrabony defects) have been collectively reported after regenerative periodontal procedures compared with conventional surgical procedures. Periodontal regenerative procedures—as the term coins—result also in significantly better histologic outcomes compared with conventional surgery (ie, larger amounts of new cementum, periodontal ligament, and alveolar bone) if correct case selection, appropriate execution of treatment, and undisturbed healing are provided (for review see^{5,6}).

LONGEVITY OF TREATMENT

The overall goal of periodontal therapy is to reestablish periodontal health and contribute to the overall oral well-being, that is, having only a few sites with bleeding on probing and no teeth with deep PD, the teeth are capable of functioning trouble-free, and preferably there is a satisfactory esthetic appearance. This goal should be achieved by preserving as many teeth as possible, for as long as possible. It is well established that the clinical conditions obtained after conventional periodontal therapy, nonsurgical or surgical, can be maintained for several decades, provided that the patient is keeping an adequate oral hygiene level.^{7,8} Thus, if one treatment should be considered better than conventional periodontal therapy, the results of this treatment should also be maintainable for a long period. In this context, the histologic outcomes obtained after periodontal regenerative procedures show variability in terms of the relative tissue composition of the various constituents of the periodontium, mainly depending on the use and/or the type of biomaterial and/or bone substitute.^{6,9} For example, the use of deproteinized bovine bone—a barely resorbable material—results in a regenerated periodontium, where the new bone tissue contains a substantial number of the grafted particles after completed healing^{10,11} (Fig. 1). It is thus relevant to assess the long-term outcome of the various periodontal regenerative procedures and the possible impact of presence of graft substitute particles within the tissues. In the following section, results from a relatively recently performed systematic appraisal of the literature on the long-term outcome of regenerative periodontal treatment in intrabony defects are shortly discussed.¹² In the recent systematic literature search, only publications from randomized clinical trials on regenerative periodontal treatment with an average follow-up greater than or equal to 3 years, but with a

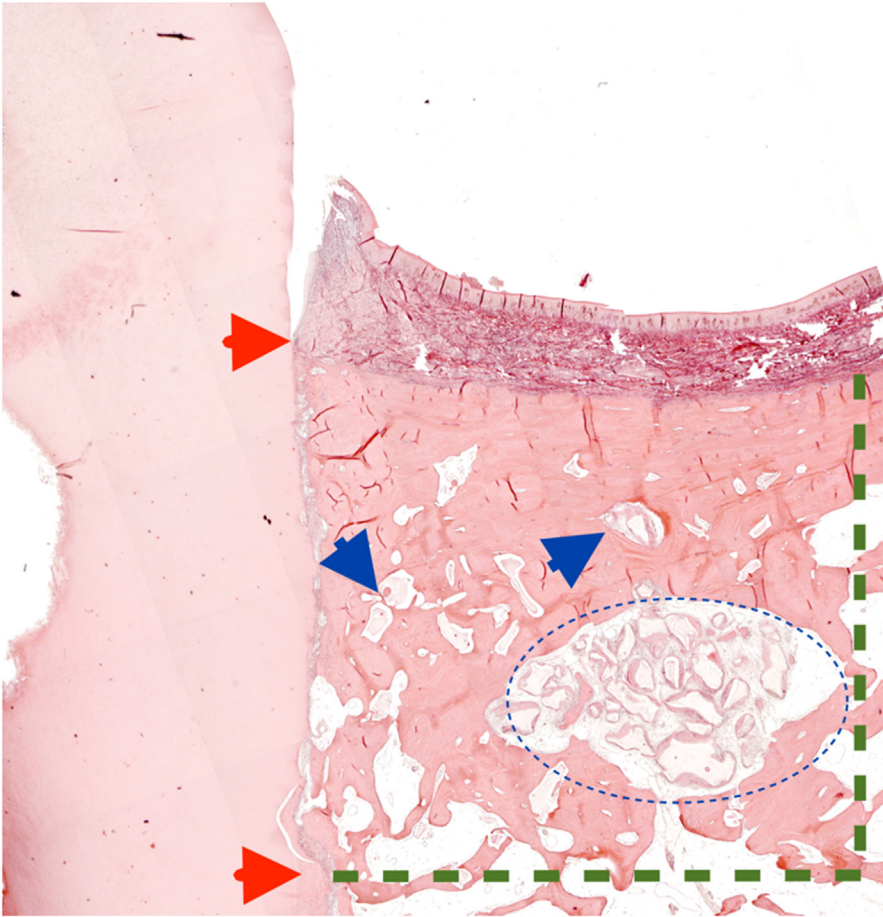


Fig. 1. Histologic image from the molar of a dog, where a large box-type defect (outlined by the dotted *green line*) was grafted with a deproteinized bovine bone/collagen construct and covered with a collagen membrane, 1.5 years after treatment. Complete regeneration of the periodontium was observed (*red arrows* indicate the bottom of the original defect and the coronal extension of new cementum formation), whereas graft particles (*blue arrowheads*) could be observed completely engulfed within the new bone. Occasionally, large numbers of particles were aggregated in dense connective tissue within bone cavities (outlined by the *dotted blue line*).

minimum follow-up greater than or equal to 2 years, were identified, which is already setting the bar high for the decision-making for the success of regenerative procedures. In perspective, what is appropriate longevity of treatment may be a matter of debate, and aspects of professional effort and cost-effectiveness, as well as patient-related outcomes including suffering should be taken into account. However, the success of any treatment modality should be tested and established over time.

LONG-TERM OUTCOMES IN INTRABONY DEFECTS

Thirty publications from a medium timeframe of 3 to 5 years (19 studies) and long-term of greater than 5 years (11 studies) were identified up to 04/2020, reporting on the

following 6 regenerative/reconstructive approaches: (1) grafting, (2) guided tissue regeneration (GTR), (3) enamel matrix derivatives (EMD), (4) GTR + grafting, (5) EMD + grafting, and (6) various combinations, including those using different type of blood-derived growth factor constructs (BC). The treatments mostly reported on were GTR and EMD, without any adjunct use of a bone graft/substitute (14 and 9 different groups, respectively), and GTR was mostly performed with resorbable membranes (only 5 groups out of 24 used nonresorbable membranes). The most used grafting materials were alloplasts (11 groups) and xenografts (8 groups), whereas 5 groups combined BC with GTR, EMD, and/or bone grafts. Nine studies provided information on the long-term outcome of conventional periodontal surgery (ie, open flap debridement [OFD]).

On average, residual PD ranged from 3.9 ± 1.5 mm to 5.6 ± 1.1 mm and from 4.5 ± 1.8 mm to 7.6 ± 2.1 mm at the medium and long term, respectively, in teeth treated with OFD. The corresponding values from teeth treated with a regenerative approach ranged from 2.1 ± 0.4 mm (in a group treated with EMD + BC) to 4.7 ± 1.2 mm (in a group treated with GTR) at the medium term and from 2.9 ± 0.9 mm to 5.8 ± 1.9 mm (both in GTR groups) in the long term. Collectively, residual PD after regenerative/reconstructive approaches was on average at a level that is considered maintainable by regular maintenance treatment, that is, less than 5 mm, in most of the included groups (47 out of 50 groups reporting on residual PD; 94%), whereas this was the case in only 4 out of 9 groups treated with OFD (Fig. 2). As mentioned earlier, presence of deep pockets greater than or equal to 6 mm showed a greater than 10 times higher risk for tooth loss compared with teeth with no pockets.¹

In regard with CAL, the range was 0.8 ± 1.4 mm to 1.7 ± 1.3 mm and -1.2 ± 2.4 mm to 3.7 ± 3.4 mm at the medium and long term, respectively, in teeth treated with OFD. The corresponding values in teeth treated with a regenerative approach ranged from 1.6 ± 1.5 (GTR) mm to 5.4 ± 1.2 mm (grafting + BC) at the medium term and from 1.5 ± 1.2 mm to 5.2 ± 2.6 mm (both in GTR groups) in the long term. Collectively, CAL gain after regenerative/reconstructive approaches was on average greater than or equal to 3 mm in more than half of the groups (29 out of 54 groups; 54%), whereas this was the case in only 1 out of 9 groups treated with OFD.

Furthermore, by means of a network meta-analysis, it was attempted to provide a hierarchy of treatment, that is, which treatment was superior in terms of residual PD and CAL gain. The more efficacious treatments were found to be combination approaches including the use of a bone graft/substitute (eg, GTR + grafting, EMD + grafting), which means that monotherapies presented with relatively deeper residual PD and less CAL gain, compared with combination approaches. Indeed, in recent systematic reviews of preclinical¹³ and human histologic studies⁶ on regenerative periodontal therapy, sole implantation of bone grafts and/or substitutes in periodontal defects does not predictably lead to substantial amounts of periodontal regeneration. Rather, a portion of the bone graft/substitute particles often remains encapsulated within connective tissue. In contrast, grafting in combination with another regenerative approach (eg, GTR or EMD) gives larger and more predictable outcomes. In this context, it must be mentioned that grafting, in combination with a BC, does not necessarily enhance the outcome of treatment significantly compared with only grafting. Specifically, as reported in other recent systematic reviews, use of platelet-rich plasma¹⁴ or platelet-derived growth factor¹⁵ failed to provide any significant additional benefit in terms of clinical results, whereas use of platelet-rich fibrin (PRF) seems to result in significantly better clinical improvements compared with only grafting.¹⁶ Nevertheless, there is scarce information regarding the medium- or long-term outcome of treatment with adjunct use of PRF.

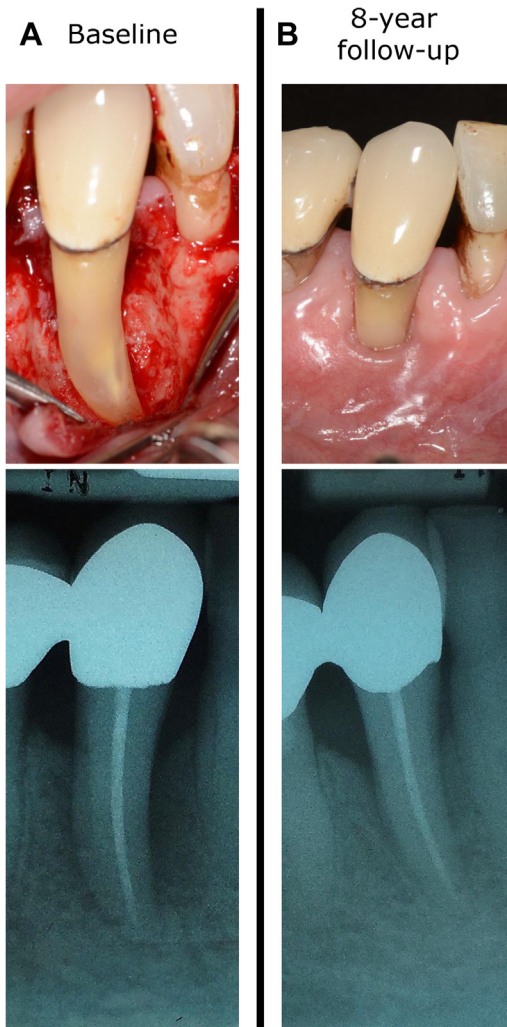


Fig. 2. (A). Pre-operative radiograph and intra-surgical photograph of a tooth harboring deep intrabony defect at its mesial and distal aspect, which was treated with EMD, as monotherapy. (B) Radiograph and clinical photograph of the tooth 8, years post-operatively.

LONG-TERM TOOTH SURVIVAL

As discussed earlier, periodontal treatment aims to preserve as many teeth as possible, for as long as possible. Among the studies included in the aforementioned review,¹² 25 publications reported on tooth loss. In general, tooth loss was scarce, with only a fraction of studies reporting loss of greater than or equal to 1 tooth; specifically, only 0.4% of the teeth treated with a regenerative/reconstructive approach were lost due to recurrent periodontitis, whereas the corresponding number of lost teeth, previously treated with OFD, was 2.8%. Thus, the better clinical improvements observed after regenerative/reconstructive treatment on the medium to long term can be translated into increased tooth retention/survival. Importantly, most teeth were lost

only from 5 years after treatment; thus, regenerative/reconstructive treatment supported survival of teeth that were rather compromised at baseline.

The low rate of tooth loss after regenerative periodontal therapy is related to the observation that only a fraction of the treated teeth experienced some limited extent loss of the CAL gain obtained postoperatively. Further, these findings imply that the mere presence of bone graft/substitute particles within the regenerated/reconstructed periodontal tissues does not have per se any negative consequence on periodontal homeostasis over the years. In perspective, disease recurrence and tooth loss following periodontal therapy are largely dependent on patient compliance, including maintenance therapy and/or general dental care,^{7,8,17} as well as smoking habits, and should not solely be attributed to a treatment delivered several years earlier.

SUMMARY

Periodontal regenerative procedures, in particular combination approaches including grafting, result in significantly better clinical outcomes in intrabony defects, compared with OFD, on a medium to long term. This, in turn, translates into higher tooth retention in the long term, and therefore, periodontal regenerative/reconstructive therapy is strongly recommended for the treatment of intrabony defects.

CLINICS CARE POINTS

- Periodontal regeneration is a predictable and successful treatment for intrabony defects.
- Successful regeneration of periodontal defects will enable the clinicians and patients to retain natural teeth.
- Compliance and elimination of risk factors (eg. smoking) are critical for the long-term success of periodontal regenerative procedures.

DISCLOSURE

The authors declare no conflict of interest in regard with the present work.

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