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Original Article

Regenerative Periodontal Therapy for Vital Teeth with Extensive Attachment Loss at the Root Apex: Two Cases with 5-Year Follow-Up

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ABSTRACT

Teeth exhibiting attachment loss that extends to the root apex are considered to have a severely compromised condition and an unfavorable periodontal outlook. When regeneration of periodontal structures is achievable, current protocols recommend performing endodontic therapy first. Nonetheless, root canal procedures may prolong treatment duration, elevate costs, introduce endodontic complications, and potentially weaken tooth structure mechanically. In this report, two individuals diagnosed with periodontitis stage III/IV grade C—without a smoking or diabetic history—presenting with apical attachment loss, were successfully managed through guided tissue regeneration. These two cases stand out as periodontal regeneration was achieved without prior endodontic therapy, and tooth vitality was preserved over time. The report outlines the management strategy that produced this clinical success and defines key factors for proper case selection. Within the scope of this study, vital teeth exhibiting radiographic bone loss involving the apex can be effectively treated with periodontal regenerative therapy and remain vital at least in the short to mid-term.

Keywords: Guided tissue regeneration, Periodontal prognosis, Tooth preservation, Cost-effectiveness, Clinical case

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Introduction

Regeneration of the periodontium represents the highest goal of periodontal care and is characterized as the restoration of lost periodontal tissues such as cementum, alveolar bone, and periodontal ligament [1]. Guided tissue regeneration (GTR) is a surgical method designed to achieve such outcomes through the use of membrane barriers that prevent epithelial invasion and maintain space for tissue regrowth [1, 2]. Clinically, GTR is particularly relevant for treating deep periodontal pockets linked with vertical bone defects—conditions once labeled as 'questionable' [3, 4] or even 'hopeless' [5–7]. Deep probing depths persisting after active therapy are known to correlate positively with an increased likelihood of tooth loss and disease relapse [8, 9]. Consequently, regenerative procedures focus on enhancing tooth prognosis by rebuilding support and reducing probing depth.

In the current periodontitis classification system, regeneration therapy remains the sole approach that can lead to a downgrade in disease stage [10, 11]. A recent meta-analysis forming part of the S3 clinical guidelines indicated that surgeries using either enamel matrix derivatives (EMD) or GTR result in significantly greater clinical attachment level (CAL) gains than open flap debridement alone. Thus, these are recommended for intrabony defects of ≥3 mm depth [12, 13]. Other comprehensive reviews have confirmed that such regenerative procedures improve long-term tooth survival, provided patients maintain proper supportive care [14–16].

When apical attachment loss is accompanied by altered pulp response, the condition is classified as an endo-periodontal lesion [17, 18]. The recommended therapy typically combines endodontic and periodontal regenerative procedures, with the root canal performed at least three months before surgical reassessment [19–21]. A previous review also proposed endodontic treatment for vital teeth if the bone defect extends to the root apex [22, 23]. However, endodontic therapy complicates treatment, increases procedural risks, and may influence the final prognosis [24]. Tooth preparation during canal access can also reduce structural strength, while diminished pulpal sensitivity may increase occlusal load, raising fracture risk [25, 26]. Long-term cohort data on periodontal patients with fixed prostheses have shown that teeth undergoing endodontic treatment and those with vertical fractures had the highest incidence of tooth loss [27]. Therefore, achieving regeneration without root canal therapy may offer advantages in cost, duration, treatment simplicity, and tooth longevity. The present case report demonstrates successful regeneration of apical defects in two patients without endodontic intervention, following the CARE reporting standards [28, 29].

Materials and Methods

Two individuals referred from general practice for periodontitis management underwent standard Step 1 and Step 2 therapy—behavioral modification, risk factor control, and professional mechanical plaque removal [30]. Following two review appointments within five to six months, persistent sites were evaluated for surgical therapy. Guided tissue regeneration was performed on tooth #46 (case 1) and #36 (case 2), both operated on by the same clinician (EN). Root canal therapy was omitted since both teeth consistently responded positively to pulp vitality tests (cold and electric) and displayed no clinical or radiographic signs of periapical disease.

Informed consent was obtained twice: first verbally after discussing the non-conventional nature of the procedure, associated risks, and alternatives, and again in written form prior to surgery, confirming the patients' full understanding and voluntary participation.

Post-surgery, both cases were reviewed periodically, documenting clinical and radiographic outcomes, including maintenance of tooth vitality, pocket depth reduction, CAL gain, bleeding on probing, gingival recession, and bone regeneration. Standardized digital periapical radiographs were taken using the long cone parallel technique with Rinn holders and analyzed according to Cortellini *et al*. [31, 32]. Assessments were performed by a blinded examiner (JRHT). Radiographic bone fill was calculated as the percentage ratio between filled intrabony component distance and the initial defect distance from the cemento-enamel junction to the bone crest.

Case 1

A 41-year-old male of Chinese origin was referred from a general dentist for specialized periodontal management. At the time of evaluation, the patient reported no symptoms or discomfort. He had no history of smoking or diabetes and his hypertension was effectively managed using atenolol and losartan. Dental history revealed annual checkups at a private clinic and prior extractions of teeth #17, #16, #47, and #27 due to pain and mobility. Clinical and radiographic findings supported a diagnosis of localized stage III, grade C periodontitis **(Figures 1 and 2)**. Tooth #46 showed apical bone loss but remained vital, symptom-free, and firm.

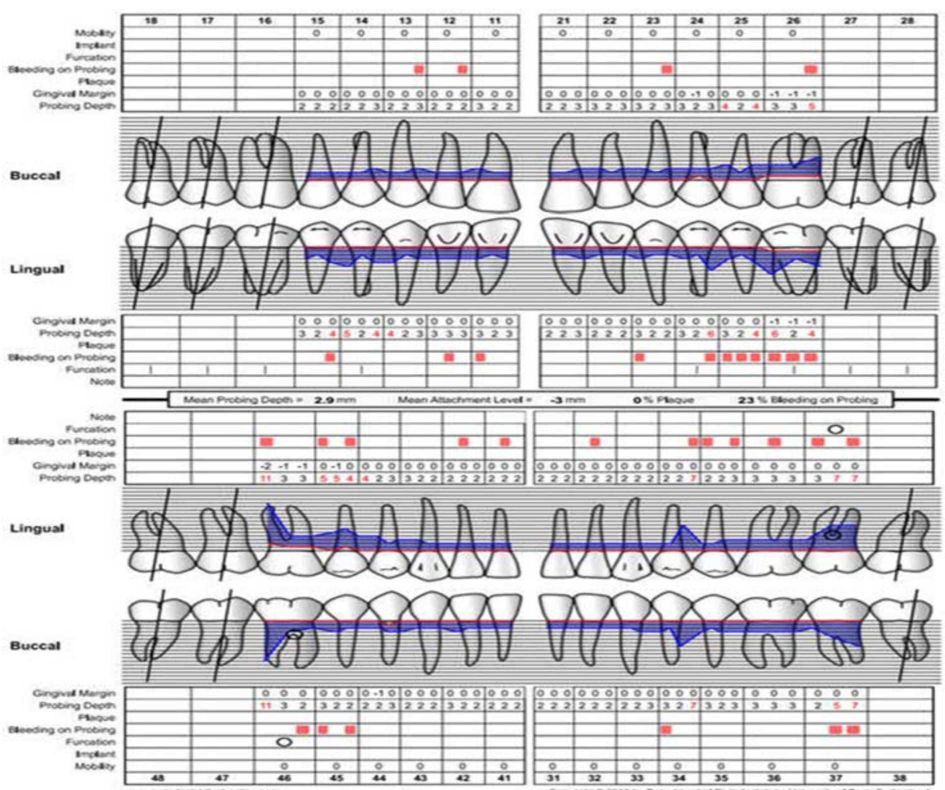
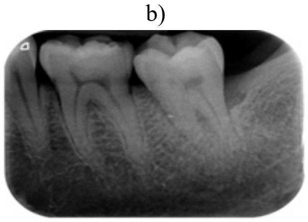


Figure 1. Periodontal chart at initial assessment—Case 1.

a)

b)



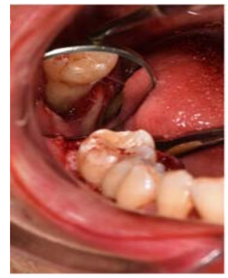
c)

Figure 2. Radiographs before treatment—Case 1. Orthopantomogram captured in August 2018, and periapical images obtained in October 2018 at the referring clinic.

After local anesthesia with 2% mepivacaine containing 1:100,000 epinephrine, a modified double papilla preservation flap was designed [33] **(Figure 3a)**. A full-thickness flap was reflected; inflammatory tissue was meticulously eliminated, and the root surface was scaled to the apex. The defect, which was contained, measured 8 mm vertically and 6 mm horizontally **(Figure 3b)**. The cavity was packed with collagen-enriched deproteinized bovine bone (Bio-Oss® Collagen) and sealed with a resorbable collagen barrier (Bio-Gide®). The flap was secured with monofilament absorbable sutures to achieve complete closure **(Figures 3c and 3d)**.

After surgery, the patient was prescribed ibuprofen 400 mg three times daily as needed for five days, amoxicillin 500 mg three times daily for five days, and instructed to use chlorhexidine mouth rinse for plaque control. Reviews took place at 10 days (suture removal), three months (maintenance cleaning), and subsequently at six-month intervals for supportive care.

a)



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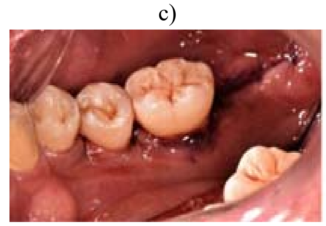

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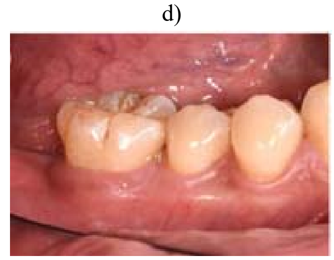

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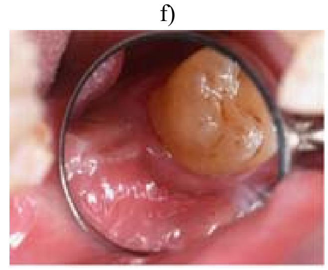


g)

Figure 3. Surgical steps for #46: a) incision outline; b) three-wall intrabony defect; c) buccal closure; d) lingual closure; e) five-year review—buccal view; f) five-year review—lingual view; g) five-year review—distal aspect.

Case 2

A 40-year-old Chinese male was referred for evaluation of severe periodontal destruction. His chief complaint was gingival deterioration. The individual had no smoking or diabetic history, took no medications, and reported family susceptibility to gum disease. He visited a private practitioner approximately every two years. Previous tooth loss included #16, #12, #26, #28, #31, and #42, all due to periodontal breakdown. Based on the clinical and radiographic findings, a diagnosis of generalized stage IV, grade C periodontitis was established **(Figures 4 and 5)**. Tooth #36 showed apical bone involvement yet retained vitality, stability, and absence of symptoms.

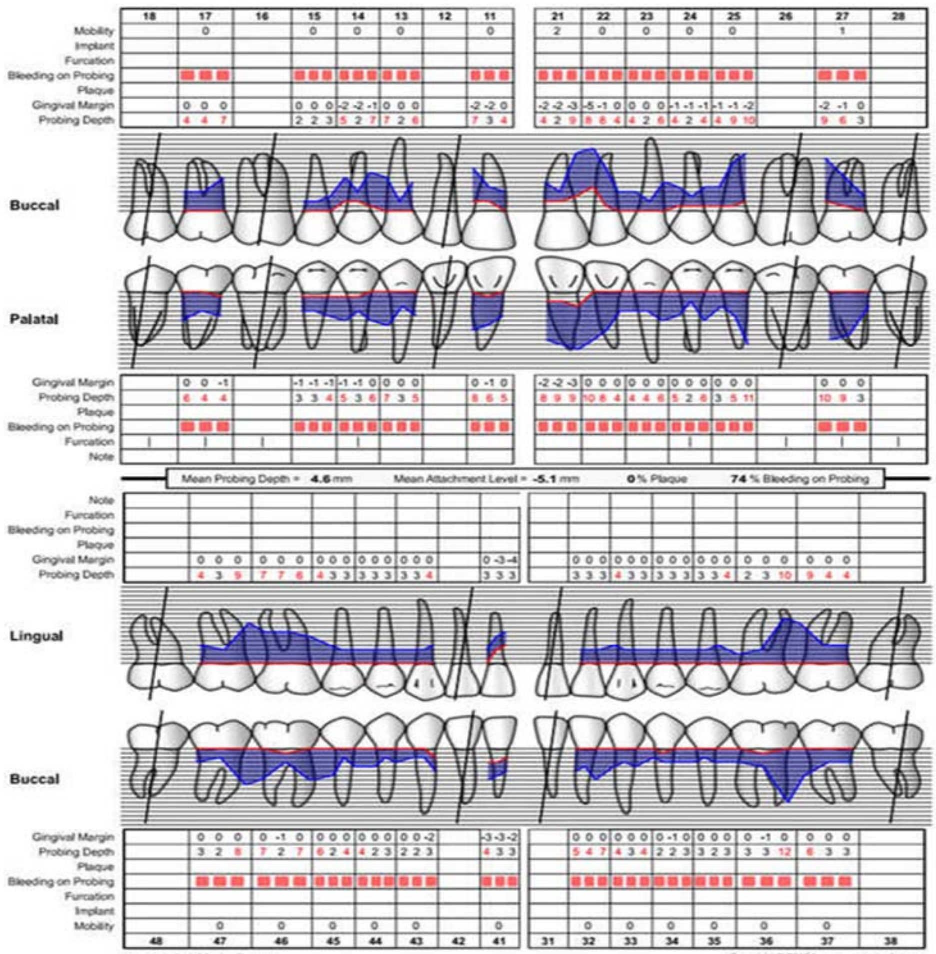


Figure 4. Baseline periodontal chart—Case 2.

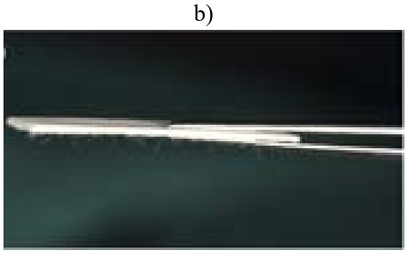
Figure 5. Pre-treatment radiographs—Case 2. Orthopantomogram acquired in August 2020 from the referring practice.

Following administration of 2% mepivacaine with 1:100,000 epinephrine, access to the lesion around #36 was obtained using a modified papilla preservation double flap approach **(Figure 6a)**. After debridement and root planing to the apex, a contained three-wall defect measuring 6 mm in width and 5–8 mm in depth was noted **(Figure 6b)**. Owing to religious restrictions against animal products, the grafting material consisted of freeze-dried bone allograft (SureOss®) and acellular dermal matrix (SureDerm®) **(Figures 6c and 6d)**. Primary closure was secured with absorbable monofilament sutures **(Figures 6e and 6f)**.

Postoperative medications mirrored those of the first case: ibuprofen 400 mg three times daily as required for five days, amoxicillin 500 mg three times daily for five days, and chlorhexidine mouthwash for oral hygiene. The patient was reviewed after 10 days for suture removal, followed by 3-month intervals during the first six months, and then routine six-month maintenance visits thereafter.

a)

b)



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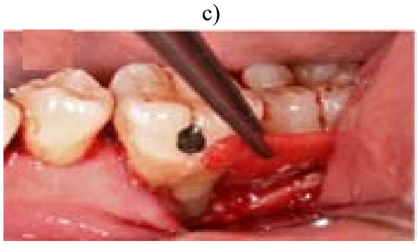

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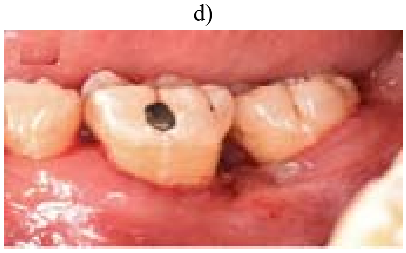

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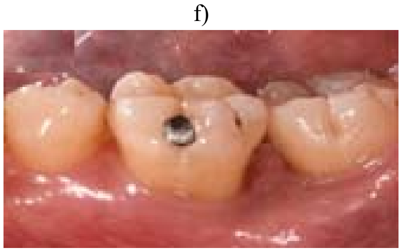


g)

h)

Figure 6. Surgical sequence for #36: a) incision outline; b) three-wall intrabony defect; c) alloderm membrane; d) regenerative materials placed; e) buccal closure; f) lingual closure; g) three-year review—buccal view; h) three-year review—lingual view.

Results and Discussion

At the five-year follow-up for Case 1, the treated tooth demonstrated continued vitality and absence of symptoms **(Figures 3e–3g)**. A 7 mm improvement in the clinical attachment level was sustained throughout the observation period **(Table 1)**. Radiographic assessment revealed approximately 71% bone regeneration and a normal periapical appearance after five years **(Figure 7)**.

a)

b)

c)

d)

e)

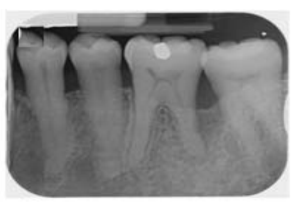
Figure 7. Serial radiographs of tooth #46 taken at a) baseline, b) 1 year, c) 2 years, d) 3.5 years, and e) 5 years.

Table 1. Comparison of site-specific post-surgical parameters for #46 between baseline and follow-up.

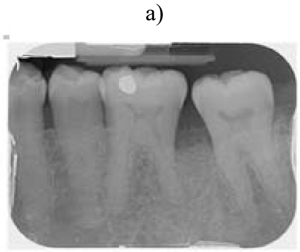
Parameter	Initial	3 Months	6 Months	1 Year	1.5 Years	2 Years	3 Years	3.5 Years	5 Years
Tooth Vitality	+	+	+	+	+	+	+	+	+
Probing Pocket Depth (mm)	11	N/A	4	4	3	3	3	3	4
PPD Reduction from Baseline (mm)	N/A	N/A	−7	−7	−8	−8	−8	−8	−7
Clinical Attachment Level (mm)	13	N/A	6	6	5	5	5	5	6
CAL Gain from Baseline	N/A	N/A	+7	+7	+8	+8	+8	+8	+7
Bleeding on Probing	+	N/A	−	+	−	−	+	−	+
Gingival Recession (mm)	2	N/A	2	2	2	2	2	2	2
Percentage Bone Fill	N/A	N/A	N/A	73	N/A	73	N/A	73	71

Abbreviations: PPD – probing pocket depth; CAL – clinical attachment level; BOP – bleeding on probing; GR – gingival recession; N/A – not applicable.

For Case 2, the final evaluation occurred three years after surgery **(Figures 6g and 6h)**. The treated tooth remained vital and symptom-free, showing a persistent 8 mm gain in attachment **(Table 2)**. Radiographically, complete bone fill (100%) was observed and maintained until the last recall **(Figure 8)**.



a)



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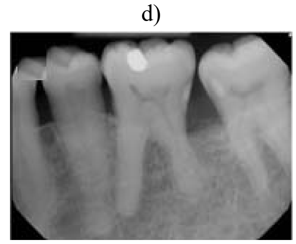

e)

Figure 8. Radiographic progression for #36 captured at a) preoperative stage, b) 6 months, c) 1 year, d) 1.5 years, and e) 3 years.

Table 2. Comparison of site-specific post-surgical clinical measures for #36 relative to baseline.

Parameter	Initial	3 Months	6 Months	1 Year	1.5 Years	3 Years
Tooth Vitality	+	+	+	+	+	+
Probing Pocket Depth (mm)	14	N/A	5	5	5	5
PPD Reduction from Baseline (mm)	N/A	N/A	−9	−9	−9	−9
Clinical Attachment Level (mm)	16	N/A	8	8	8	8
CAL Gain from Baseline	N/A	N/A	+8	+8	+8	+8
Bleeding on Probing	+	N/A	+	+	+	+
Gingival Recession (mm)	2	N/A	3	3	3	3
Percentage Bone Fill	N/A	N/A	100	100	100	100

Abbreviations: PPD – probing pocket depth; CAL – clinical attachment level; BOP – bleeding on probing; GR – gingival recession; N/A – not applicable.

These two clinical cases illustrate the successful regeneration of periodontal support and improved prognosis of key teeth using a regenerative approach. In contrast to options such as root resection, extraction, or implant therapy, guided tissue regeneration offers a less invasive and more economical solution with preservation of natural dentition [34, 35].

In both cases, no root canal treatment was undertaken despite the radiographic evidence of apical bone loss—diverging from established protocols, which advocate endodontic intervention for non-vital teeth, inadequate prior endodontic therapy, or vital teeth with apical extension of defects [31, 36–38]. The rationale for omitting endodontic therapy included several considerations.

First, clinical and radiographic evaluations prior to surgery showed no evidence of pulpal or periapical pathology, and long-term monitoring confirmed absence of endodontic complications or symptoms such as discomfort or infection. Second, pulp vitality tests consistently yielded positive results, suggesting a healthy pulp. Literature reports indicate that pulp tissue may remain viable even when the bacterial front is near the apical foramina [39, 40], allowing the tooth to sustain vitality following regenerative therapy. Third, it has been demonstrated that guided tissue regeneration in deep osseous defects does not compromise pulpal health, nor does root canal therapy negatively affect regenerative healing [41, 42]. Finally, after being fully informed of the potential risks, benefits, and costs, both patients chose to proceed without root canal therapy, accepting the possibility of future endodontic treatment or extraction should devitalization occur.

The clinical attachment gains and radiographic outcomes observed align closely with findings from a multicenter randomized clinical trial on the management of both shallow and deep intrabony defects [43]. Comparable outcomes have also been reported in previous studies showing that regeneration in root canal–treated teeth can successfully alter the prognosis of teeth previously considered hopeless, even when bone loss extended to or beyond the apex [31, 44]. Long-term monitoring in that trial recorded tooth survival rates of 92% at five years and 88% at ten years [36, 45]. Similarly, another investigation documented a five-year survival rate of 92% in endo-periodontal lesions successfully managed by regenerative periodontal therapy [20]. In that study, endodontic intervention was only undertaken in 15% of cases, specifically when sensibility testing indicated pulpal necrosis. Evidence from more recent literature further supports that combined endodontic and periodontal regenerative procedures can also achieve predictable long-term retention in teeth affected by both pathologies [19, 46, 47].

Periodontal regeneration offers the potential to alter the prognosis of teeth once deemed ‘hopeless,’ providing a more economical substitute for extraction and prosthetic restoration, thereby yielding cost-efficient results for patients [48]. As demonstrated in this report, reliable and clinically significant improvements can be achieved in the management of deep intrabony lesions while sustaining pulp vitality.

Several key aspects contributed to the favorable results observed in these cases. These included precise diagnosis, timely intervention before endodontic compromise, meticulous periodontal cleaning, and maintenance of apical vascular integrity during surgery. Crucially, selecting suitable cases was essential—specifically, teeth that were unquestionably vital, symptom-free, non-mobile, and located within three-walled, well-contained defects suitable for regenerative therapy.

A notable advantage of this report lies in its uniqueness, as no prior studies have directly evaluated regenerative outcomes with and without root canal procedures in teeth presenting with apical involvement. Another strength is the extended follow-up period, which confirmed that tooth vitality was preserved following treatment. Comparable outcomes were achieved regardless of the biomaterials utilized.

However, the primary limitation is the small sample size, comprising only two cases. Additionally, the long-term stability of the clinical attachment gained is influenced by the patient’s oral hygiene practices and compliance with maintenance visits [49]. While these initial findings are encouraging, larger-scale investigations are required to confirm reproducibility and validate the long-term effectiveness of this treatment approach.

Conclusion

With careful case selection, vital teeth exhibiting radiographic bone loss extending to the root apex can be successfully managed using periodontal regenerative techniques, maintaining vitality over the short- to mid-term. The clinical and radiographic improvements achieved in this study were sustained for up to 5 years.

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Conflict of Interest: None

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Ethics Statement: None

References

1. American Academy of Periodontology. Glossary of Periodontal Terms [Internet]. Chicago (IL): American Academy of Periodontology; [cited 2021 Jan 8]. Available from: https://members.perio.org/libraries/glossary?ssopc=1
2. Egwunatum AE, Uyovbisere E, Umeh LC. Effect of forest-incubated composts on crude-oil soils for *Zea mays, L.* cultivation in Delta State, Nigeria. World J Environ Biosci. 2022;11(3):14-20. doi:10.51847/j5Pyls0seh
3. Alharthi NS. Endocannabinoid system components: A crucial role in regulation of disease. J Adv Pharm Educ Res. 2022;12(3):72-81. doi:10.51847/FIVP7AOddG
4. Kwok V, Caton JG. Commentary: Prognosis revisited: A system for assigning periodontal prognosis. J Periodontol. 2007;78(11):2063–71.
5. Machtei EE, Hirsch I. Retention of hopeless teeth: The effect on the adjacent proximal bone following periodontal surgery. J Periodontol. 2007;78(12):2246–52.
6. Graetz C, Dorfer CE, Kahl M, Kocher T, Fawzy El-Sayed K, Wiebe JF, et al. Retention of questionable and hopeless teeth in compliant patients treated for aggressive periodontitis. J Clin Periodontol. 2011;38(8):707–14.
7. Alshammari E. Efficacy of Generic vs. branded Isotretinoin for Acne treatment: a case report. J Adv Pharm Educ Res. 2021;11(1):125-7. doi:10.51847/UvTeFaq1oI
8. Satushieva L, Isakov A, Maremkulova R, Tekueva M, Zalikhanova L. Some peculiarities of administrative penalties system and the order of their imposition in Russia. J Organ Behav Res. 2021;6(2):100-8. doi:10.51847/DnsGazKwqt
9. Siow DSF, Goh EXJ, Ong MMA, Preshaw PM. Risk factors for tooth loss and progression of periodontitis in patients undergoing periodontal maintenance therapy. J Clin Periodontol. 2023;50(1):61–70.
10. Tonetti MS, Greenwell H, Kornman KS. Staging and grading of periodontitis: Framework and proposal of a new classification and case definition. J Periodontol. 2018;89(Suppl 1):S159–S172.
11. Petronis Z, Pliatkute I, Janovskiene A, Leketas M. The Relationship between cervical spine abnormalities and temporomandibular joint internal disorders: a systematic review of literature. Ann Dent Spec. 2023;11(4):20-8. doi:10.51847/sGUN5P9OQA
12. Maiti S, Rai N, Appanna P, Jessy P. Digital telescopic denture- a viable treatment modality of preventive prosthodontics: clinical report. Ann Dent Spec. 2022;10(4):1-4. doi:10.51847/eEgUl0vYgd
13. Nibali L, Koidou VP, Nieri M, Barbato L, Pagliaro U, Cairo F. Regenerative surgery versus access flap for the treatment of intra-bony periodontal defects: A systematic review and meta-analysis. J Clin Periodontol. 2020;47(Suppl 22):320–51.
14. Stavropoulos A, Bertl K, Spineli LM, Sculean A, Cortellini P, Tonetti M. Medium- and long-term clinical benefits of periodontal regenerative/reconstructive procedures in intrabony defects: Systematic review and network meta-analysis of randomized controlled clinical studies. J Clin Periodontol. 2021;48(3):410–30.
15. Kao RT, Nares S, Reynolds MA. Periodontal regeneration – intrabony defects: A systematic review from the AAP Regeneration Workshop. J Periodontol. 2015;86(Suppl 2):S77–104.
16. Karpov VY, Medvedev IN, Komarov MN, Puchkova NG, Sharagin VI, Petina ES. The influence of regular physical activity on the functional parameters of the youthful organism. J Biochem Technol. 2023;14(2):18-23. doi:10.51847/QB2dBXs8ij
17. Nguyen DT, Hoang TH. The influence of organizational capabilities on operational efficiency: a study of vietnamese businesses. Asian J Indiv Organ Behav. 2022;2:15-20. doi:10.51847/PapKxH2ZYU
18. Herrera D, Retamal-Valdes B, Alonso B, Feres M. Acute periodontal lesions (periodontal abscesses and necrotizing periodontal diseases) and endo-periodontal lesions. J Periodontol. 2018;89(Suppl 1):S85–102.
19. Tietmann C, Tezer I, Youssef E, Jepsen S, Jepsen K. Management of teeth with grade 3 endo-periodontal

lesions by combined endodontic and regenerative periodontal therapy. J Clin Med. 2023;13(1):93.

20. Oh S, Chung SH, Han JY. Periodontal regenerative therapy in endo-periodontal lesions: A retrospective study over 5 years. J Periodontal Implant Sci. 2019;49(2):90–104.
21. Elgendy TYAAA. Evaluating internal auditor selection through analytical network process: a case study approach. Ann Organ Cult Leadersh Extern Engagem J. 2023;4:35-44. doi:10.51847/K4wmaJTGng
22. Nasr AMA, Ahmed YAM, Gafar AAM, Ahmed SAD, Barri BKA, Meshref ET, et al. A Systematic review of the prevalence and risk factors associated with choriocarcinoma in Saudi Arabia. Asian J Curr Res Clin Cancer. 2022;2(1):18-24. doi:10.51847/YkmsatQnNJ
23. Cortellini P, Tonetti MS. Clinical concepts for regenerative therapy in intrabony defects. Periodontol 2000. 2015;68(1):282–307.
24. Bhuva B, Ikram O. Complications in endodontics. Prim Dent J. 2020;9(2):52–58.
25. Zeb-un-Nisa Z, Ali SI, Shahnaz S, Mumtaz T, Swaleh MM. Quality evaluation of sustained-release domperidone formulations. Pharm Sci Drug Des. 2021;1:32-40. doi:10.51847/aYTknOi1Xe
26. Awawdeh L, Hemaidat K, Al-Omari W. Higher maximal occlusal bite force in endodontically treated teeth versus vital contralateral counterparts. J Endod. 2017;43(6):871–5.
27. Di Febo G, Bedendo A, Romano F, Cairo F, Carnevale G. Fixed prosthodontic treatment outcomes in the long-term management of patients with periodontal disease: A 20-year follow-up report. Int J Prosthodont. 2015;28(3):246–51.
28. Drobotova AN, Filippova VV, Ovechko OY, Leshchenko YY, Belova PS, Tabukhova AZ. Postpartum bleeding: definition, diagnostic approaches, and management protocols in contemporary research. Interdiscip Res Med Sci Spec. 2023;3(2):31-5. doi:10.51847/ShO1maIzLU
29. Riley DS, Barber MS, Kienle GS, Aronson JK, von Schoen-Angerer T, Tugwell P, et al. CARE guidelines for case reports: Explanation and elaboration document. J Clin Epidemiol. 2017;89(1):218–35.
30. Sanz M, Herrera D, Kebschull M, Chapple I, Jepsen S, Beglundh T, et al. Treatment of stage I–III periodontitis: The EFP S3 level clinical practice guideline. J Clin Periodontol. 2020;47(Suppl 22):4–60.
31. Cortellini P, Stalpers G, Mollo A, Tonetti MS. Periodontal regeneration versus extraction and prosthetic replacement of teeth severely compromised by attachment loss to the apex: 5-year results of an ongoing randomized clinical trial. J Clin Periodontol. 2011;38(10):915–24.
32. Yang J, Tang Z, Shan Z, Leung YY. Integrating rapid maxillary expansion and le fort osteotomy for esthetic rehabilitation: a clinical case report. J Curr Res Oral Surg. 2023;3:22-6. doi:10.51847/E0OEwI52jo
33. Cortellini P, Prato GP, Tonetti MS. The modified papilla preservation technique: A new surgical approach for interproximal regenerative procedures. J Periodontol. 1995;66(4):261–6.
34. Ng E, Tay JRH, Ong MMA. Minimally invasive periodontology: A treatment philosophy and suggested approach. Int J Dent. 2021;2021(1):2810264.
35. Hassan F, Hatah E. An analytical exploration of various non-pharmacological approaches utilized in managing diabetes among patients in Malaysia. Int J Soc Psychol Asp Healthc. 2022;2:27-37. doi:10.51847/JmKuHOeBQX
36. Rahman AAU, Khoso MH, Shaikh Z, Malik E, Siyal FJ, Rahoojo A, et al. Misconceptions and facts: a unique investigation into COVID-19 among medical students at a Rural University in Sindh. Ann Pharm Educ Saf Public Health Advocacy. 2021;1:25-31. doi:10.51847/ZBLMqB8Vf1
37. Cortellini P, Stalpers G, Mollo A, Tonetti MS. Periodontal regeneration versus extraction and dental implant or prosthetic replacement of teeth severely compromised by attachment loss to the apex: 10-year outcomes, survival analysis and mean cumulative cost of recurrence. J Clin Periodontol. 2020;47(7):768–76.
38. Cortellini P, Cortellini S, Tonetti MS. Papilla preservation flaps for periodontal regeneration of molars severely compromised by combined furcation and intrabony defects: Retrospective analysis of a registry-based cohort. J Periodontol. 2020;91(2):165–73.
39. Langeland K, Rodrigues H, Dowden W. Periodontal disease, bacteria, and pulpal histopathology. Oral Surg Oral Med Oral Pathol. 1974;37(2):257–70.
40. Grin NA, Platova EG, Dukaev MV, Magomedovic AM, Gairbekov MK, Sulimanova KI, et al. Evaluating the effectiveness of silver nanoparticle-modified dental fillings on enhancing hard tissue durability. Int J Dent Res Allied Sci. 2023;3(2):29-35. doi:10.51847/XdLVg7zuuq
41. Duangthip D, Gao SS, Chen KJ, Lo ECM, Chu CH. Investigating the relationship between oral health related life quality and the severity of dental caries in children. Turk J Dent Hyg. 2023;3:22-8. doi:10.51847/hRLJbKoNZM
42. Cortellini P, Tonetti MS. Evaluation of the effect of tooth vitality on regenerative outcomes in infrabony defects. J Clin Periodontol. 2001;28(7):672–9.

43. Cortellini P, Carnevale G, Sanz M, Tonetti MS. Treatment of deep and shallow intrabony defects: A multicenter randomized controlled clinical trial. J Clin Periodontol. 1998;25(12):981–7.
44. Mashhour K, Saad E, Abdelghany H, Hashem W. Acute Toxicity Comparison between 3DCRT and SIB-IMRT in Preoperative concurrent chemo-radiotherapy for locally advanced rectal cancer. Arch Int J Cancer Allied Sci. 2023;3(2):16-24. doi:10.51847/PVlZaAgP9c
45. Uneno Y, Todayama N. Immersive roleplay and intensive training: advancing clinical ethics consultation in Japan. Asian J Ethics Health Med. 2023;3:40-53. doi:10.51847/4N6jGjIXgl
46. AlJasser R, Bukhary S, AlSarhan M, Alotaibi D, AlOraini S, Habib SR. Regenerative therapy modality for treatment of true combined endodontic-periodontal lesions: A randomized controlled clinical trial. Int J Environ Res Public Health. 2021;18(11):6220.
47. Covello F, Ruoppolo G, Carissimo C, Zumbo G, Ferrara C, Polimeni A, et al. Study of quality of life associated with oral health in patients with MS (Multiple Sclerosis). Ann J Dent Med Assist. 2021;1(2):17-23. doi:10.51847/JddDeasVKr
48. Tay JRH, Ng E, Nair R, Tan ZS, Tan SHX. Economic evaluations in the treatment and evaluation of patients with periodontal disease: A critical review. J Clin Periodontol. 2021;48(5):679–94.
49. Cortellini P, Pini-Prato G, Tonetti M. Periodontal regeneration of human infrabony defects (V): Effect of oral hygiene on long-term stability. J Clin Periodontol. 1994;21(9):606–10.