



Evaluating the Effectiveness and Stability of Regenerative Treatment and Orthodontic Tooth Movement in Stage IV Periodontitis: A Systematic Review and Meta-analysis

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ABSTRACT

Background and aim: The present systematic review and meta-analysis aimed to evaluate the effectiveness and stability of regenerative treatment and orthodontic tooth movement in stage IV periodontitis.

Material and methods: For the present systematic review and meta-analysis study, international databases such as MEDLINE (PubMed and Ovid), Web of Science, and Scopus were searched until October 2024 using keywords relevant to the study objectives. STATA/MP. v17 software was used to analyze data.

Results: The present study included ten studies. The present meta-analysis showed a mean reduction of 1.10 mm in probing depth (95% CI, -1.18mm, -1.03mm; $P < 0.001$), an attachment gain of 1.96 mm (95% CI, -2.13mm, 1.78mm; $P < 0.001$), and radiographic bone level of -1.44 mm (95% CI -1.65mm, -1.22mm; $p < 0.001$).

Conclusions: According to the one-year results of the present meta-analysis, an interdisciplinary approach can produce favorable and stable outcomes in motivated and cooperative patients with stage IV periodontitis who require orthodontic treatment.

1. Introduction

Stage IV periodontitis is comparable in severity and complexity to stage III regarding attachment loss, vertical bone loss, and periodontal inflammation. However, the presence of pathologic tooth migration (PTM), causing migration and spreading of the remaining teeth, hypermobility and secondary occlusal trauma, bite breakdown, and masticatory dysfunction, increases the severity and complexity of stage IV periodontitis and requires a complex Rehabilitation.^[1, 2] Because PTM causes functional and aesthetic changes, patients with this condition are interested in orthodontic treatment. Restoring and stabilizing function and esthetics for patients requires an interdisciplinary approach that includes comprehensive periodontal and orthodontic therapy to control periodontal infections, reconstruct the defects, and realign the migrated teeth.^[3] Both healthy patients and patients with successfully treated periodontitis do not appear to have clinically negative effects on their clinical bonding levels during orthodontic treatment with fixed appliances. Nevertheless, there is a lack of information regarding the

concurrent use of orthodontic treatment and periodontal therapy in patients with stage IV periodontitis.^[4, 5] In the long-term treatment of stage IV periodontitis, tooth preservation should be the first priority, as emphasized in the clinical practice guideline (CPG) EFP S3. Since regenerative procedures benefit intraosseous defects, the EFP S3 CPG advises patients with stage IV periodontitis who have intraosseous defects and require OT to receive both regenerative and consecutive OT. Based on two recent clinical studies, the EFP S3 CPG suggests initiating occupational therapy after periodontal regenerative therapy for four weeks to six months.^[6, 7] However, there is currently very little information about the long-term results of such combination therapy. Therefore, the present systematic review and meta-analysis aimed to evaluate the effectiveness and stability of regenerative treatment and orthodontic tooth movement in stage IV periodontitis.

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2. Material and methods

Search strategy and Information sources

The international databases Cochrane, Embase, and MEDLINE (PubMed and Ovid) were searched for relevant keywords until October 2024 to assess the effectiveness and stability of regenerative treatment and orthodontic tooth

movement in stage IV periodontitis (Table 1). Google Scholar was used with Web of Science, EBSCO, ISI, Elsevier, the Cochrane Central Register of Controlled Trials, and the Scopus Wiley Online Library. The present study is based on the 27-point checklist for PRISMA 2020.^[8]

Table 1. The search strategy used for each database.

NO.	Search Terms
The search strategy used in MEDLINE (via PubMed)	
1	"Regenerative Endodontics"[Mesh]
2	Entry Terms: Endodontic, Regenerative OR Endodontics, Regenerative OR Regenerative Endodontic
3	("Tooth Movement Techniques"[Mesh]) OR "Index of Orthodontic Treatment Need"[Mesh]
4	"stage IV periodontitis"[Mesh] OR "Periodontitis"[Mesh]
The search strategy used by Cochrane	
1	" Regenerative Endodontics " AND " orthodontic tooth movement" OR "Orthodontic treatment" AND " stage IV periodontitis"
2	Periodontitis
The search strategy used in Embase	
1	(Orthodontic treatment) OR (orthodontic tooth movement): ab, ti, kw.
2	Regenerative Endodontics: ab, ti, kw.
3	stage IV periodontitis: ab, ti, kw.
4	chapter' OR 'conference abstract' OR 'conference paper' OR 'conference review' OR 'editorial' OR 'erratum' OR 'letter' OR 'note' OR 'preprint' OR 'short survey'/it (Filter)

Selection criteria

English-language publications met the inclusion requirements for this study. The answers to the questions in the current study were based on the PICO strategy: Population (P): patients with stage IV periodontitis; Intervention (I): regenerative periodontal surgery and consecutive orthodontic tooth movement (C): baseline; Outcome (O): bone level, probing pocket depths, and probing pocket depths. Review studies and books; qualitative studies; animal studies; studies without comprehensive and relevant data.

The process of selection and data collection

Two researchers used a previously developed standard data collection form to reduce reporting, data collection errors, and omissions in individual subject data collection. The original form prepared by the research team included information such as the author's name, year of publication, study design, number of patients, mean age, gender, Smokers, intrabony defects, mean bone level, and observation period.

Heterogeneity and publication bias

The heterogeneity across studies was examined using the Chi-square (χ^2) test and quantified by the I^2 statistic. According to the I^2 value, heterogeneity was classified as low (less than 50%), between 50 and 74% means moderate heterogeneity, and above 75% is considered high heterogeneity.

Methodological quality

The quality of the included articles was assessed using the Newcastle-Ottawa Scale (NOS). As part of the NOS rating system, a maximum of nine (for prospective and cross-sectional studies) or ten (for case-control studies) stars can be awarded for each study. Two authors independently reviewed the quality assessment, and the third author resolved any discrepancies. High-quality studies were defined as those scoring six or more points.^[9]

The revised Cochrane method for assessing the risk of bias for randomized trials, RoB 2,^[10] is recommended for determining the likelihood of bias in studies used in Cochrane reviews. Rob 2 is based on a specific collection of bias domains and focuses on various study planning, implementation, and reporting aspects. Within each domain, a series of queries called "signaling questions" are presented to collect information about study characteristics that could potentially impact the risk of bias. Based on the answers to the signaling questions, an algorithm generates a bias risk score for each domain, which can be classified in terms of risk as Low, High, or Some Concerns.

Data analysis

Mean scores were calculated by examining mean differences with 95% confidence intervals. The results were reported using a fixed-effects model with the Inverse variance method. The data were analyzed at a significance level 0.05 using Stata software (version 17).

3. Results

Description of studies

A total of 251 results were retrieved from databases. The number of articles was reduced to 167 after eliminating duplicates, records marked as

ineligible by automation tools, and other reasons. After reviewing abstracts and titles, 54 articles were selected from the citations. As a result of the final search, ten studies were found suitable for inclusion in the current systematic review and meta-analysis.

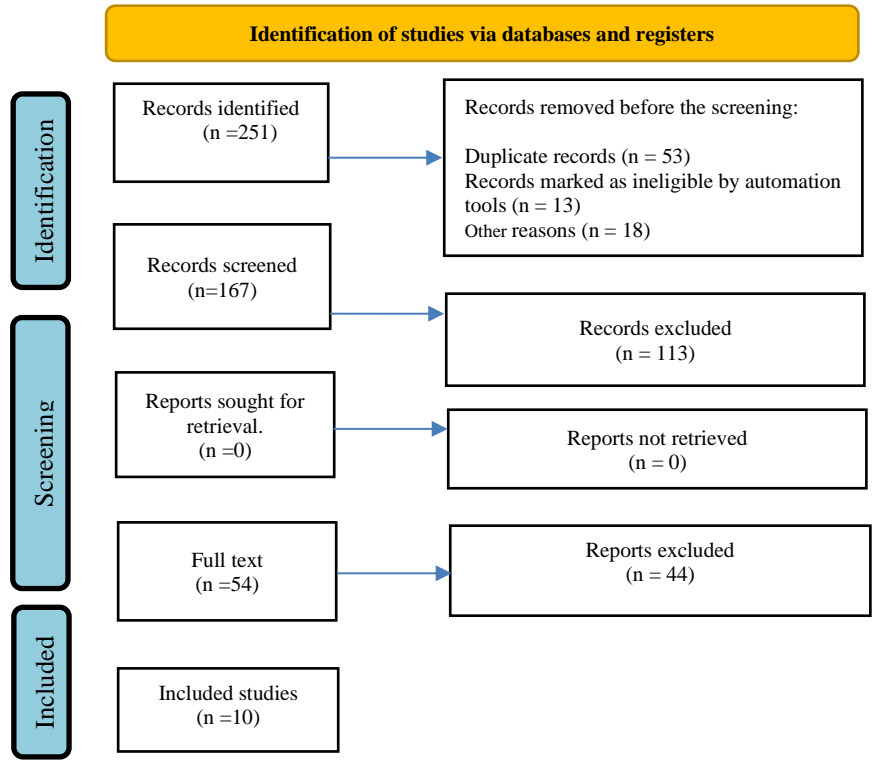


Fig. 1. PRISMA 2020 Checklist.

Study characteristics

Two included studies used RCT design, two case series, and six retrospective studies. The sample size was variable among studies, but the number of patients was 285; all were diagnosed with stage IV periodontitis. The characteristics of the studies are reported in Table 2.

Bias Assessments

The risk of bias in all studies was classified as low risk of bias.

Table 2. Summary of characteristics of the included studies.

Study. Years	Study Design	Number of Patients		Mean Age	Smokers %	Intrabony Defects	Mean Bone Level All	Observation Period (Years)
		Male	Female					
Tietmann et al., 2021 ^[6]	Retrospective	20	28	45.3	12.5	526	8.31 ± 1.51 mm	4
Jepsen et al., 2021 ^[7]	RCT	17	26	45.4	12.5	43	NR	1
Dung et al., 2024 ^[11]	Case series	3	14	43	NR	17	NR	12
Tietmann et al., 2024 ^[12]	Case series		10	42	9	103	8.32 ± 2.45 mm	1
Jepsen et al., 2023 ^[13]	RCT	17	26	45.4	NR	NR	NR	2
Tietmann et al., 2023 ^[14]	Retrospective	9	13	43.9	9.1	266	8.33 ± 2.45 mm	10
Tu et al., 2022 ^[15]	Retrospective	10	11	43.44	0	41	8.05 ± 1.64 mm	10
Aimetti et al., 2020 ^[16]	Retrospective	11	32	52.6	14.3	NR	NR	11

Jiao et al., 2019 ^[17]	Retrospective	8	16	NR	NR	NR	NR	12
Cao et al., 2015 ^[18]	Retrospective	3	11	38.9	0	56	NR	1

NPs: nanoparticles; NR: not reported.

Mean radiographic bone level

The mean differences in radiographic bone level between after 1 year and baseline was -1.44 mm (MD: -1.44mm 95% CI -1.65mm, -1.22mm; p<0.001) with high heterogeneity (I² =99.16; p<0.001). The radiographic bone level gain was significant after 1 year.(Fig. 2)

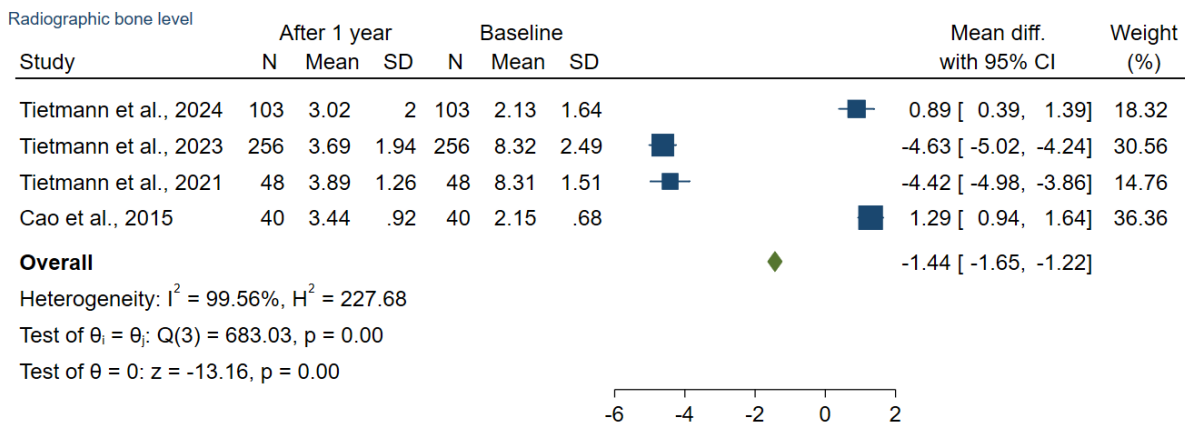
Probing pocket depth

The mean differences in Probing pocket depth between after 1 year and baseline was -1.10 mm (MD: -1.10mm 95% CI -1.18mm, -1.03mm; p<0.001)

with high heterogeneity (I² =98.75%; p<0.001). Mean probing pocket depth was significantly reduced after 1 year.(Fig. 3)

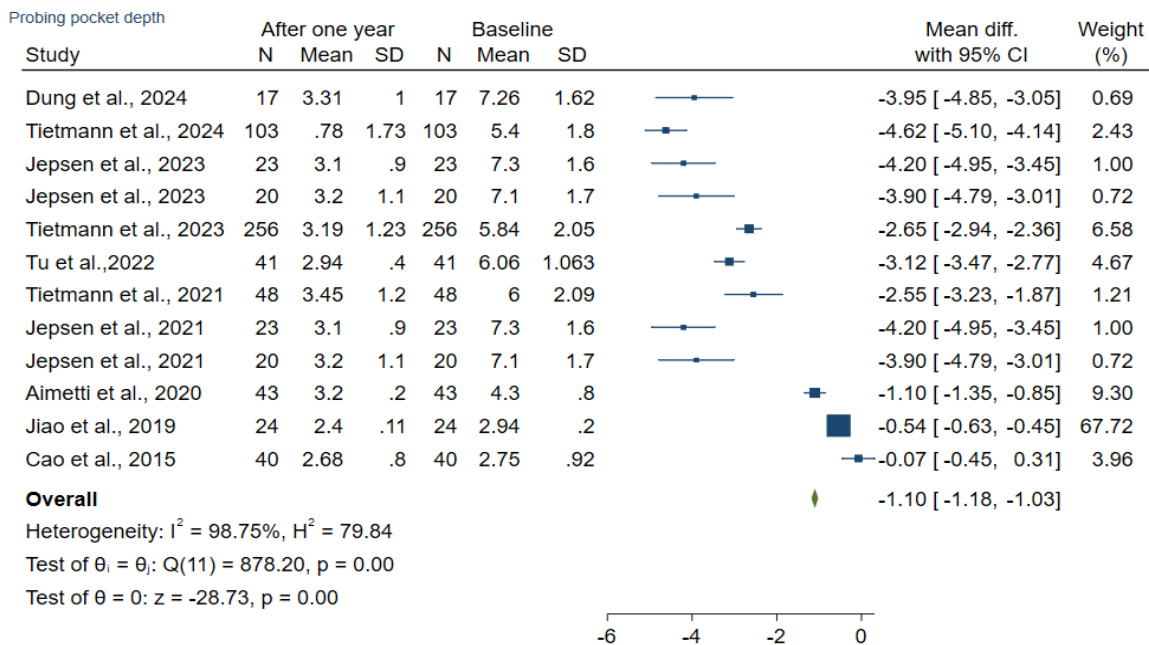
Clinical attachment level

The mean differences in clinical attachment level between after 1 year and baseline was -1.96 mm (MD: -1.96mm 95% CI -2.13mm, -1.78mm; p<0.001) with high heterogeneity (I² =96.45%; p<0.001). Mean clinical attachment level decreased from baseline to after 1 year.(Fig. 4)



Fixed-effects inverse-variance model

Fig. 2. The forest plot showed mean radiographic bone level after 1 year and baseline.



Fixed-effects inverse-variance model

Fig. 3. The forest plot showed probing pocket depth between the 1 year and baseline.

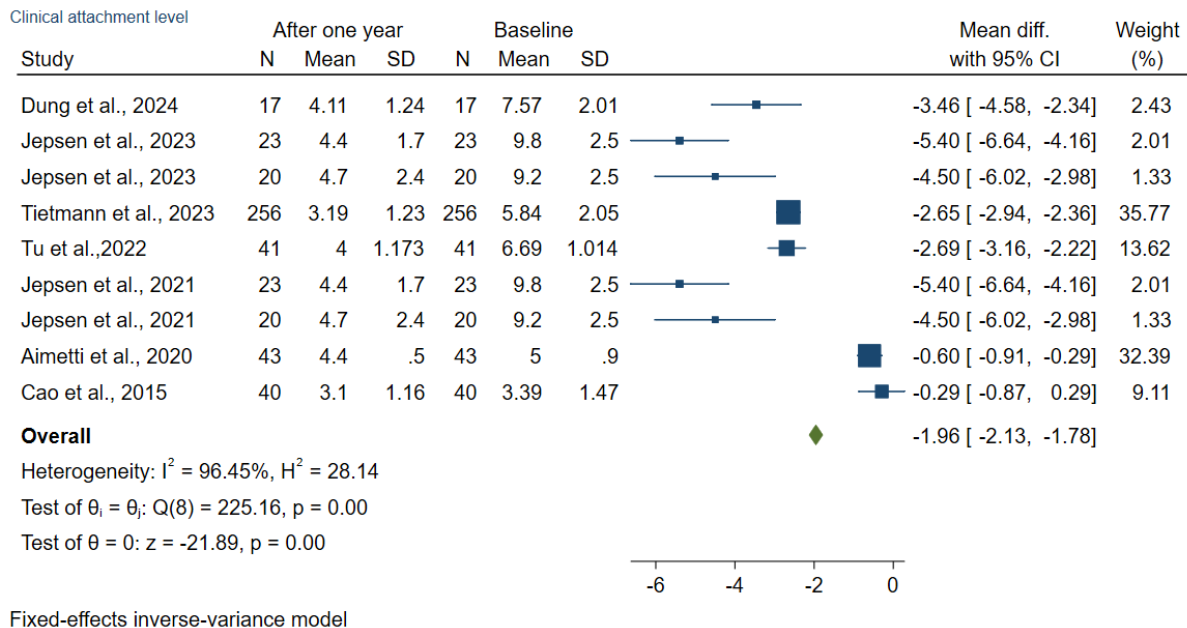


Fig. 4. The forest plot showed clinical attachment level after 1 year and baseline.

4. Discussion

The present meta-analysis study reveals the on-year effectiveness of a combined regenerative and orthodontic treatment in patients with stage IV periodontitis. The advantage of combining periodontal regenerative surgery and orthodontic treatment simultaneously is that the overall treatment time can be shortened.^[19] Poor plaque control and maintenance care increase the risk of treatment failure and subsequent periodontal tissue destruction, which should be highlighted. For this reason, careful plaque control and maintenance therapy are necessary to ensure the effectiveness and durability of treatment results.^[6, 20] For patients with compromised periodontal health, periodontal regenerative surgery may be performed before, concurrently with, or after orthodontic treatment, depending on individual needs and circumstances. Regenerative therapy for deep and narrow intrabony defects is generally more reliable and successful than for wide and shallow defects, which have a worse prognosis.^[21] The present meta-analysis showed a mean reduction of 1.10 mm in probing depth (95% CI, -1.18mm, -1.03mm; $P < 0.001$), an attachment gain of 1.96 mm (95% CI, -2.13mm, 1.78mm; $P < 0.001$), and radiographic bone level of -1.44 mm (95% CI -1.65mm, -1.22mm; $p < 0.001$). High heterogeneity was observed between studies, which could be due to variations in initial PD, CAL, defect morphology, tooth type, and restorative materials. While some studies have shown positive treatment outcomes for both anterior and posterior intraosseous defects, others have primarily examined the outcomes of intraosseous defects on anterior teeth with pathologic tooth migration. Other reasons for heterogeneity between studies include the difference in study protocols regarding restorative methods, patient and defect selection, outcome criteria selection, time points between reconstruction and orthodontic treatment, and follow-up duration. The inflammatory phase of the wound associated with intrabony periodontal defects persists in periodontal disease [Stage III or IV], and the inflammatory environment prevents fibroblasts from fulfilling their functions. Mechanical forces are known to deform the space between the periodontal ligament and the alveolar bone in the early stages of tooth movement.^[22] Injured microdeformations can promote periodontal regeneration and tissue remodeling by applying micromechanical forces shortly after regenerative surgery and stimulating cell

proliferation and migration.^[23, 24] However, understanding the biological processes underlying orthodontic tooth movement is still incomplete.^[25] More carefully planned preclinical research is required to clarify the relationship between biomechanical force application and regenerative medicine in periodontal defects and explain the positive clinical results of this study.

According to several recognized scoring systems, previous research has shown that periodontal therapy improves Oral Health-Related Quality of Life (OHRQoL) for patients with periodontitis.^[25, 26] Most of these side effects were documented one week to twelve months after non-surgical periodontal therapy. In the first post-operative week, patients who underwent periodontal surgery reported a lower OHRQoL.^[27] Some studies found that periodontal surgery had minimal effects compared to non-surgical treatment,^[28] while others found that the additional improvements were more noticeable after surgery.^[29] In addition, orthodontic treatment has been proven to improve the OHRQoL of patients with misaligned or maloccluded teeth. However, most of these studies were conducted on children and adolescents.^[29] Periodontology and orthodontics should work closely together in future interdisciplinary research. Given that many adult patients with severe periodontitis are interested in orthodontic treatment for oral rehabilitation due to the aesthetic and functional changes caused by pathological tooth migration, further exploration of the synergy between regenerative periodontal medicine and biomechanical orthodontic forces and their effects is of great importance from a clinical perspective.

5. Conclusion

The current meta-analysis suggests that regenerative therapy combined with orthodontic tooth movement in patients with stage IV periodontitis can lead to positive and stable results after one year while offering promising prospects.

Conflict of Interest

The authors declared that there is no conflict of interest.

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