International Journal for Multidisciplinary Research (IJFMR)
E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

Influence of Early Versus Delayed Timing Orthodontic Intrusion on Clinical Parameters of Pathological Tooth Migration in Periodontitis Patient: A Systematic Review Meta-Analysis

Dr. Noor Asyikin Saad[1], Dr. Farha Ariffin[2], Dr. Maryati Md Dasor[3], Dr. Fara Azwin Adam[4]

[1]Periodontist, Unit Periodontologi, Klinik Pergigian Baling, Malaysia Ministry of Health
[2]Periodontist, Center of Periodontology Studies, Faculty of Dentistry, Universiti Teknologi MARA
[3]Orthodontist, Center of Peadiatric Dentistry and Orthodontics Studies, Faculty of Dentistry, Universiti Teknologi MARA
[4]Periodontist, Center of Periodontology Studies, Faculty of Dentistry, Universiti Teknologi MARA

Abstract

Orthodontic intervention vital aim is restoring physiological normal masticatory function, occlusal contacts and aesthetic. This systematic review and meta-analysis evaluated the effect of orthodontic intrusion timing on clinical attachment level (CAL) and probing pocket depth (PPD) in periodontitis patient with pathological tooth migration (PTM) compared with baseline.

This review was conducted in adherence to Cochrane Handbook, PRISMA guidelines and registered with PROSPERO. Fourteen studies were included after screened and analyzed 2932 articles from six different related databases. The pooled data of 14 studies (17 subgroups) showed significant PPD reduction following orthodontic intrusion with MD was 1.36mm (95% CI: 0.60 to 2.13; Z= 3.49; p=0.0005), with high heterogeneity (I^2= 98%). Analysis based on timing revealed a significant greater PPD reduction in the simultaneous/ immediate group (MD=2.02 mm; 95% CI: 0.79 to 3.25; I^2= 98%) compared to delayed intrusion (MD=0.16 mm; 95% CI: -0.08 to 0.39; I^2=55%), although high heterogeneity for groups differences observed (I^2=88.1%).

In conclusion, orthodontic intrusion may improve clinical parameters in periodontally compromised teeth with PTM, especially in early intervention. However, the additional benefit of incorporate orthodontic intervention remain uncertain, and further controlled studies are necessary to draw a definitive conclusion.

Keywords: Orthod*, Intrusion, Periodontitis, Periodontal disease*, Tooth migration.

1. INTRODUCTION

Periodontitis, known as chronic inflammatory disease, affecting majority of the adult population, including in Malaysia, where it had been reported in 9 out of 10 adult patients [1]. The disease arises from a complex relationship between an imbalance of oral microbiota and host's immune response [2]. The accumulation of periodontopathogen, such as *Porphyromonas gingivalis* [3], may trigger host's inflammatory response

[4], leading to immune cell infiltration into surrounding periodontal tissues [5], and subsequent destruction of the supporting periodontal structures of the teeth [2], [6].

Pathological tooth migration (PTM) is a critical consequence of an advance stage of periodontal disease, which affecting 30 to 56 percent of the periodontitis patients [7]. PTM in periodontitis patient predominantly involved combination type of displacement. The main displacement of PTM in periodontally compromised patient included facial flaring (proclination), diastema, rotation, extrusion and tipping [8]. The PTM may lead to other complication including exacerbate the periodontal condition, impair oral function, impair aesthetic, affecting long-term prognosis of the related tooth, tooth loss, and then lead to the affecting patient's quality of life.

Orthodontic intervention aims not only to attain aesthetic but also restoring normal masticatory function and occlusal contacts [9]. Ideal orthodontic intervention achieves maximum tooth movement without damaging periodontal status. Studies showed that orthodontic intervention in periodontally compromised patients with PTM may help in relieving occlusal trauma, stabilize the dentition and improve periodontal status [11]. However, special measures are essential when performing orthodontic movement in periodontally compromised teeth [13, 14] including in performing intrusion movement to correct extruded tooth due to periodontitis. There was limited evidence on appropriate timing for orthodontic intrusion in periodontally compromised patient, some evidence suggests starting orthodontic intervention after achieving periodontal stability [13], while some evidence recommended for early orthodontic intervention following periodontal therapy [14]. Therefore, this review aimed to evaluate the effect of timing of orthodontic intrusion on clinical parameters of periodontally compromised patients.

2. METHODS

The protocol of this review was registered with PROSPERO (CRD42022352346) before the initiation of this review. The conduct of this review adhered to the latest updated Cochrane Handbook for Systematic Review of Interventions [15] and reporting was according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guideline and extension for abstract [16], [17].

2.1 Eligible Criteria

The criteria for studies to be included in this review was based on the PICOS below:

1. Population/ patient (P): Adult patient aged 18 years old and more diagnosed with periodontitis in accordance with the previous [18] and current [19] classification, presented with any type of pathological tooth migration (PTM) which needed for orthodontic intervention [7].
2. Intervention (I): The timing of orthodontic intervention incorporated intrusion movement defined as bodily movement along the long axis in an axial (apical direction towards the gingiva (Marcotte, 1990)) as main movement to correct the PTM.
3. Comparator/ control (C): Baseline clinical data on probing pocket depth (PPD).
4. Outcome (O): Mean PPD reduction which was defined as the distance from the marginal of gingival to the base of periodontal pocket in millimeter (mm).
5. Studies (S): Clinical studies including randomized controlled clinical trial, non-randomized clinical trial, cohort prospective and case series. Reviews and case reports were excluded.

2.2. Study Identification and Selection

The systematic electronic search was conducted by two reviewers (NAS and FAA) independently from October 2022 up to November 2024 across 6 databases included PubMed, Scopus, Cochrane, Wiley, Web of Sciences and Google Scholar. The manual search of all potentially relevant articles was performed from

the references, similar and cited lists of included papers. This review was limited to the articles published in English.

A preliminary search was performed using the same databases with the search term ((“orthodon*” OR “intrusion”) AND (“periodontal disease*” OR “periodontitis”)) to check either the key articles were able to retrieve or not. The search terms were refined by adding or removing terms, checked terms frequency and adjusted the field tags. The main search terms for this review were showed in the Table 1 via the ‘copy-paste’ method to eliminate any discrepancy.

Table 1 Full Search Strategies for Each Databases.

Database	Search Strategy
MedLine via PubMed	("periodontitis" OR "periodontal disease*" OR "periodontally compromised") AND ("orthodon*" OR "intrusion" OR "intrud*" OR "intrusive") select clinical studies
Scopus	("periodontitis" OR "periodontal disease*" OR "periodontally compromised*") AND ("orthodon* intrusion" OR "intrusi*" OR "intrude*") limit to article and english
Central	"periodontitis" OR "periodontal disease*" OR "periodontally compromi*" in Title Abstract Keyword AND "orthodon*" OR "intrus*" OR "intrud*" OR "orthodontic intrusi*" in All Text limit to English
Web of Sciences	periodontitis AND orthodontic intrusion
Wiley	("periodontitis" OR "periodontal disease*" OR "periodontally compromised*") AND ("orthodon* intrusion" OR "intrusi*" OR "intrude*") journal
Google Scholar	periodontitis AND “orthodontic intrusion” clinical study

There were two stages of identification and selection for studies to be included in this review. First was initial screening of articles titles and abstracts, followed by assessment of fulltext articles against eligible criteria. Those articles that do not meet the standard were excluded and documented with justification. In case of disagreement, the third reviewer (FRA) was interrogated to verified and resolve it.

2.3. Data Extraction

Two primary reviewers (NAS and FAA) performed data extraction from selected studies independently by utilizing the standard Cochrane Data Collection Form. Two additional reviewers verified the extracted data to resolved discrepancies. Information retrieved upon data extraction included author’s names, publication year, country, sample characteristic (age, gender, systemic condition, PTM and periodontal classification), orthodontic intervention timing, and clinical conditions (before and after treatment, changes, primary parameter measured was PPD).

2.4. Risk-of-bias and Quality Assessment

The risk-of-bias and quality assessment of selected studies was conducted by one reviewer (NAS) and discussed with others reviewer. Four different tools were utilized based on the four different study designs included in this review: the Cochrane Risk of Bias Version 2.0 (RoB 2.0) for randomized controlled clinical trials or controlled clinical trials [20], Risk of Bias in Non-randomized Studies of Intervention

(ROBINS-I) for non-randomized studies [21], Newcastle-Ottawa Scale (NOS) for cohort studies [22], and National Institute of Health's quality assessment tools (NIH) for case series studies [23].

The quality of included studies was assessed using the Grading of Recommendation, Assessment, Development, and Evaluation (GRADE) system [24] with four grades of evidence quality. The GRADE level of outcomes was presented in summary of findings (SoF) table for clearer, concise and transparent results [25].

2.5. Meta-Analyses and Publication Bias

Meta-analyses and assessment publication bias were performed using RevMan software version 5.4 and Stata 18.0. In this review, PPD was assessed as a continuous outcome, with the changes calculated between baseline (pre-) and after (post-) orthodontic intervention. Data extraction included the mean difference (MD) and standard deviation (SD) for each included study. A random-effect model was employed to account the potential clinical and methodological heterogeneity among studies. The analyses comprised the generation of forest plot to display effect sizes which was expressed as MD with corresponding 95% confidence interval (CI) and calculation of the I^2 value to assess heterogeneity. Funnel plot, complemented with Egger's and Begg's test was utilized to evaluate potential of publication bias.

3. RESULTS

3.1. Included Studies

The electronic and manual search across six databases identified 2932 articles, following initial screening 51 articles were selected for full-text assessment. Only fourteen articles (17 subgroups; 259 participants) were included for further analyses (Figure 1).

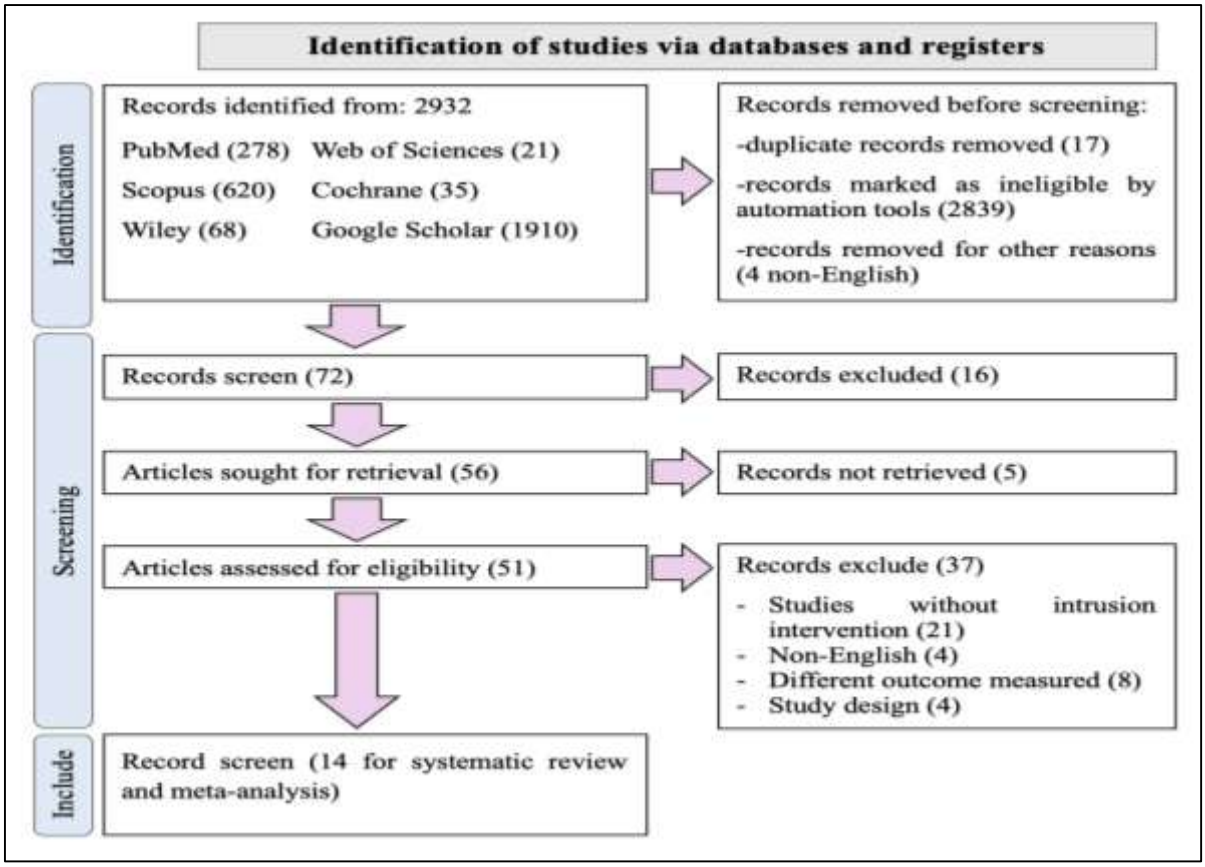

Figure 1 PRISMA 2020 flow diagram summarized the studies identification and justification for exclusion with final 14 included studies.

3.2. Study Characteristics

The fourteen included studies consisted of three randomized controlled trials (RCT) [26], [27], [28], one non-randomized controlled trial (NRCT) [29], four prospective cohort (PC) studies [30], [31], [32], [33], and six prospective case series (PCS) studies [34], [35], [36], [37], [38], [39].

Table 2 Characteristics of included studies.

Authors **Year of publication** **Country** **Study design**	**Participants:** Number Gender: M/F Age: mean ± SD (range)	**Condition** Systemic Group	**Periodontitis** Classification Type of PTM	**Orthodontic Therapy (OI)** Movement Timing
Ghouraba et al. **2024** **Egypt** **RCT (split mouth)**	10 NR (20-35)	Excluded patient with systemic disease GTR-OI (Ghouraba A) versus OI-GTR (Ghauraba B)	NS Over-erupted	Intrusion, levelling and alignment Delayed versus simultaneous
Attia et al. **2019** **Egypt** **RCT (split mouth)**	15 4/11 (25-37)	Excluded patient with systemic disease With (Attia A) versus without (Attia B) diode laser	Chronic Crowding, elongation and migration	Intrusion and alignment Immediate
Zhang et al. **2017** **China** **RCT**	59 38/21 36.5 ± 5.8 (22-46)	Excluded patient with systemic disease including DM Perio with PTM versus Perio without PTM (excluded) versus healthy (excluded)	Mild/ moderate/ severe Elongation and displacement	Intrusion and alignment Simultaneous
El-Attar et al. **2019** **Egypt** **NRCT**	14 NR 31.9 (20-40)	NR GTR (El-Attar A) versus OFD (El-Attar B)	Aggressive Extruded/ migrated	Intrusion and alignment Simultaneous
Navarrete et al. **2023** **Chile** **PC**	42 16/26 42 (25-55)	Excluded patient with systemic disease	Generalized (stage III or IV) Protruded	Intrusion, levelling and alignment Delayed
Carvalho et al. **2018** **Brazil**	10 1/9 25 ± 5.22	Excluded patient with systemic disease	Aggressive NS	Intrusion and alignment Delayed

PC	(NR)			
Khorsand et al. 2013 **Iran** **PC**	8 1/7 30 (NR)	Excluded patient with systemic disease	Aggressive Extruded ≥1mm & diastema	Intrusion and alignment Delayed
Gawish et al. 2005 **Egypt** **PC**	15 4/10 38-55	NR	Severe Extrusion ≥1mm	Intrusion and alignment Immediate
Cao et al. 2015 **China** **PCS**	14 3/11 (22-41)	Excluded patient with systemic disease	Chronic Proclined, migration and extruded	Intrusion and alignment Simultaneous
Bayani et al. 2015 **Iran** **PCS**	10 0/10 43.6 (25-57)	NR	NS Over-erupted	Intrusion Delayed
Ghezzi et al. 2013 **Italy** **PCS**	10 4/6 (31-59)	Excluded patient with systemic disease	Generalized severe (2 aggressive 8 chronic) Diastema	Intrusion and alignment (body) Immediate
Ghezzi et al. 2008 **Italy** **PCS**	14 NR NR (>20)	Excluded patient with systemic disease	Severe Migration and diastema	Intrusion and alignment (body) Delayed
Re et al. 2004 **Italy** **PCS**	28 6/22 44.79 ± 7.76 (29-60)	Excluded patient with systemic disease	Chronic severe Migration, extrusion and diastema	Intrusion and alignment Immediate
Corrento et al. 2003 **Italy** **PCS**	10 2/8 (33-53)	Excluded patient with systemic disease	Severe Migration and extrusion	Intrusion and alignment Immediate

RCT- randomized controlled trial, NRCT- non-randomized controlled trial; PC- prospective cohort; PCS- prospective case series; M- male; F- female; SD- standard deviation; NR- not reported; NS- not specify; OI- orthodontic intrusion; PTM- pathological tooth migration.

Geographically, four studies were conducted in Italy, four studies in Egypt, two in Iran, two in China, one in Brazil and one in Chile. A total of 259 patients were evaluated, mostly without systemic disease, with aged ranged 20 to 60 years old. Participants were diagnosed with different forms of periodontal disease, with ten out of 14 studies included over-erupted, elongated, and extruded type of PTM, which almost half

of the participants involved anterior teeth. All included studies involved orthodontic intrusion and alignment movement. Majority of studies employed simultaneous/ immediate timing for initiation of orthodontic intervention. The details of characteristic of included studies are presented in Table 2.

3.3. Risk of Bias

All RCTs showed high-risk of overall risk-of-bias due to the randomization process (Zhang 2017) and outcomes measured (Attia 2019 and Ghouraba 2024), which reflected moderate quality of studies. Other studies showed low risk-of-bias with good quality of studies except for Carvalho (2018) with fair study's quality due to the comparator group was drawn from different source (non-periodontitis patients) and the was no clear demonstration that the outcomes of interest were absent at the start of study due to the different source of population.

Figure 2 Risk-of-bias of all included studies (2a) RoB 2.0 (2b) Robin-I (2c) NOS (2d) NIH tool.

3.4. Results Synthesis

3.4.1. Meta-Analyses

The pooled effect for simultaneous/ immediate timing group showed a statistically significant higher PPD reduction with MD of 2.02 mm (95% CI: 0.79 to 3.25; Z= 3.21; $P<0.05$) compared to delayed timing group with MD of 0.16 mm (95% CI: -0.08 to 0.39; Z= 1.33; $P>0.05$). Simultaneous/ immediate timing presented with high heterogeneity (I^2= 98%), while delayed group showed moderate heterogeneity (I^2= 55%). The overall pooled estimate across all included studies in this review showed a significant PPD reduction following orthodontic intrusion MD of 1.36 mm (95% CI: 0.60 to 2.13; Z= 3.49; $P<0.05$), although there was high heterogeneity observed between timing (I^2= 88.1%).

In accordance with the funnel plot, the simultaneous/ immediate timing group appears to result in a more pronounced and significant reduction of PPD compared to delayed timing group. The studies in the delayed timing groups tend to cluster at one side and centrally suggesting more consistent effect size among group, less variability but smaller effect sizes. The studies within the simultaneous/ immediate group were widely dispersed and positioned far from vertical line which indicating variability in reported effect sizes. The asymmetrical distribution and wide scatter especially in less precise studies (studies with larger standard error, SE) may indicate publication bias. Begg's test showed a Kendall's score of 42.00 (p=0.091) showed no significant correlation, while Egger's regression test showed an intercept of 4.44 (p=0.62) demonstrated no significant asymmetry which interpreted as no statistical evidence of publication bias.

There was no comparison with control group without orthodontic intrusion intervention could be performed regarding the timing of orthodontic intrusion on periodontally compromised patient due to the absence of relevant RCTs and comparative studies addressing the specific variable.

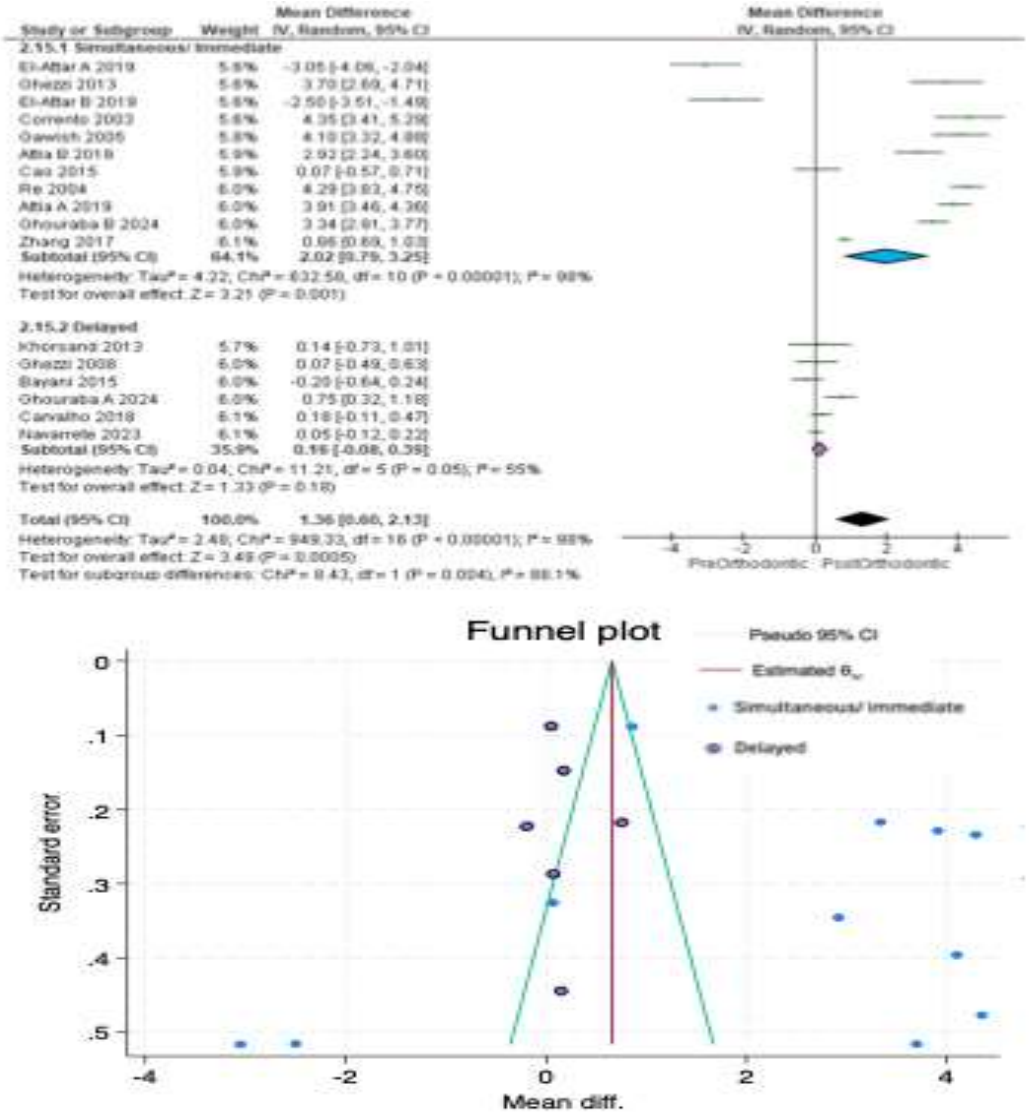

Figure 3 Forest and funnel plot illustrated the impact of orthodontic intrusion timing on PPD changes in periodontally compromised teeth with PTM.

3.4.2. Quality Assessment

The simultaneous/ immediate timing group was rated as moderate-GRADE certainty of evidence due to the high and clinical meaningful effect, while in contrast, the delayed group was rated as low-GRADE certainty of evidence. Although high variability and potential publication bias, the finding showed direct and moderately precise and moderate-good quality evidence favoring early intervention of orthodontic intrusion following periodontal therapy. However, more studies are still necessary to draw a definitive conclusion of this matter.

Table 3 Summary of finding: Changes of PPD following orthodontic intrusion based on timing in periodontally compromised patients with PTM

Outcome	Estimate Level	Relative Difference	No of participants (studies/ sub-studies)	GRADE	Comments
PPD	Delayed: 0.16 (-0.08, 0.39) Simultaneous/ immediate: 2.02 (0.79, 3.25)	Simultaneous/ immediate timing achieved higher (twelve times) PPD reduction compared to delayed	259 (14/17)	⊕⊕⊖⊖ Low	Large magnitude of effect Moderate-high precision, moderate to good quality, serious risk of bias and inconsistency (I^2= 98%), possible publication bias.

4. DISCUSSION

The optimal timing of orthodontic intervention including intrusion movement remains debated. A successful clinical outcome depends highly on close interdisciplinary collaboration and patient compliance on oral hygiene and treatment or maintenance protocol [13]. In order to optimize clinical outcomes and minimize risks, a comprehensive tailored approach is essential. Most studies recommended to initiate orthodontic intervention after achieving periodontal stability, in order to reduce the risks or complication following orthodontic movement [13], [40]. In severe bone loss cases, an extended healing period is necessary to allow for adequate healing, maturation and stabilization of the periodontal tissue to provide a stable foundation prior orthodontic movement [13], [40]. Therefore, delayed approach is recommended to help in achieving desired outcomes without compromising the newly formed attachment following periodontal therapy.

However, Zasciurinskiene (2018) reported that simultaneous orthodontic intervention with periodontal therapy may be effective in selected patients particularly in compliance patients with moderate type of periodontitis, strict periodontal maintenance protocol and light continuous orthodontic force employed [14], [41]. Early approach has been suggested due to the mitotic activity of periodontal cells and active bone remodelling during periodontal healing, which later may enhance the regeneration of periodontal tissues and improve treatment outcomes [14]. Thus, the timing of orthodontic movement during this active biological phase may help in optimizing the periodontal healing and regeneration.

Future research should focus on more robust, standardized protocol, well-designed and high-quality RCT studies that comparing different timing of orthodontic intrusion in periodontally compromised patients with PTM. They should focus on evaluating the effect on both clinical and radiological periodontal parameters, comparing the impact of utilizing different biomechanics for orthodontic intrusion, and incorporating longer follow-ups period to help in determining the longterm stability of the outcomes. Additionally, future research also should evaluate the risks and complications that associated with orthodontic intrusion movement systematically to ensure the long-term safety and efficacy of the treatment approach.

5. CONCLUSION

Considering the limitation in our review, we can conclude that simultaneous/ immediate timing initiating orthodontic intrusion was associated with pronounced clinical outcome (PPD reduction) which indicating the significant positive impact on periodontal conditions in periodontally compromised patients. Close interdisciplinary collaboration between periodontists and orthodontist is crucial in ensuring comprehensive and coordinated treatment planning and management. However, given the high heterogeneity among studies and potential publication bias, this review findings should be interpreted with caution and more comprehensive and high-quality evidence is required to draw definitive conclusion.

REFERENCES

1. R. B. Saub, “National Oral Health Surveys of Adults 2010 (NOHSA 2010): Initial Findings (Unweighted data).,” 2013.
2. R. P. Darveau, “Periodontitis: a polymicrobial disruption of host homeostasis,” *Nat Rev Microbiol*, vol. 8, no. 7, pp. 481–490, Jul. 2010, doi: 10.1038/nrmicro2337.
3. S. C. Holt and J. L. Ebersole, “Porphyromonas gingivalis, Treponema denticola, and Tannerella forsythia: the ‘red complex’, a prototype polybacterial pathogenic consortium in periodontitis,” *Periodontol 2000*, vol. 38, no. 1, pp. 72–122, Jun. 2005, doi: 10.1111/j.1600-0757.2005.00113.x.
4. N. S. Jakubovics, S. D. Goodman, L. Mashburn-Warren, G. P. Stafford, and F. Cieplik, “The dental plaque biofilm matrix,” *Periodontol 2000*, vol. 86, no. 1, pp. 32–56, Jun. 2021, doi: 10.1111/prd.12361.
5. R. C. Page and H. E. Schroeder, “Pathogenesis of inflammatory periodontal disease. A summary of current work.,” *Lab Invest*, vol. 34, no. 3, pp. 235–249, 1976.
6. R. J. Genco, “Host Responses in Periodontal Diseases: Current Concepts,” *J Periodontol*, vol. 63, no. 4S, pp. 338–355, Apr. 1992, doi: 10.1902/jop.1992.63.4s.338.
7. M. A. Brunsvold, P. Nair, and T. W. Oates, “Chief complaints of patients seeking treatment for periodontitis.,” *The Journal of the American Dental Association*, vol. 130, no. 3, pp. 359–364, Mar. 1999, doi: 10.14219/jada.archive.1999.0205.
8. P. P. Towfighi, M. A. Brunsvold, A. T. Storey, R. M. Arnold, D. E. Willman, and C. A. McMahan, “Pathologic Migration of Anterior Teeth in Patients With Moderate to Severe Periodontitis,” *J Periodontol*, vol. 68, no. 10, pp. 967–972, Oct. 1997, doi: 10.1902/jop.1997.68.10.967.
9. G. H. Gameiro, I. B. Magalhães, M. M. Szymanski, and A. S. Andrade, “Is the main goal of mastication achieved after orthodontic treatment? A prospective longitudinal study,” *Dental Press J Orthod*, vol. 22, no. 3, pp. 72–78, Jun. 2017, doi: 10.1590/2177-6709.22.3.072-078.oar.

10. N. GKANTIDIS, P. CHRISTOU, and N. TOPOUZELIS, "The orthodontic-periodontic interrelationship in integrated treatment challenges: a systematic review," *J Oral Rehabil*, vol. 37, no. 5, pp. 377–390, May 2010, doi: 10.1111/j.1365-2842.2010.02068.x.
11. S. Gurkeerat, A. Izhar, M. Dahaiya, V. Goyal, R. Singh, and N. Gupta, "Orthodontic Management of Periodontally Compromised Adult Patients-A Case Series.," *Journal of Contemporary Orthodontics*, vol. 3, no. 1, pp. 1–5, 2018.
12. C. Navarrete *et al.*, "Levels of Pro-Inflammatory and Bone-Resorptive Mediators in Periodontally Compromised Patients under Orthodontic Treatment Involving Intermittent Forces of Low Intensities," *Int J Mol Sci*, vol. 24, no. 5, p. 4807, Mar. 2023, doi: 10.3390/ijms24054807.
13. G. P. Pini Prato and L. Chambrone, "Orthodontic treatment in periodontal patients: The use of periodontal gold standards to overcome the 'grey zone,'" Apr. 01, 2020, *Wiley-Blackwell*. doi: 10.1002/JPER.19-0306.
14. K. Jepsen *et al.*, "The effect of timing of orthodontic therapy on the outcomes of regenerative periodontal surgery in patients with stage <scp>IV</scp> periodontitis: A multicenter randomized trial," *J Clin Periodontol*, vol. 48, no. 10, pp. 1282–1292, Oct. 2021, doi: 10.1111/jcpe.13528.
15. M. Cumpston *et al.*, "Updated guidance for trusted systematic reviews: a new edition of the Cochrane Handbook for Systematic Reviews of Interventions," *Cochrane Database of Systematic Reviews*, Oct. 2019, doi: 10.1002/14651858.ED000142.
16. E. M. Beller *et al.*, "PRISMA for Abstracts: Reporting Systematic Reviews in Journal and Conference Abstracts," *PLoS Med*, vol. 10, no. 4, p. e1001419, Apr. 2013, doi: 10.1371/journal.pmed.1001419.
17. M. J. Page *et al.*, "The PRISMA 2020 statement: an updated guideline for reporting systematic reviews," *BMJ*, p. n71, Mar. 2021, doi: 10.1136/bmj.n71.
18. G. C. Armitage, "Development of a Classification System for Periodontal Diseases and Conditions," *Ann Periodontol*, vol. 4, no. 1, pp. 1–6, Dec. 1999, doi: 10.1902/annals.1999.4.1.1.
19. M. S. Tonetti, H. Greenwell, and K. S. Kornman, "Staging and grading of periodontitis: Framework and proposal of a new classification and case definition," *J Clin Periodontol*, vol. 45, no. S20, Jun. 2018, doi: 10.1111/jcpe.12945.
20. J. P. Higgins, J. Savović, M. J. Page, R. G. Elbers, and J. A. Sterne, "Assessing risk of bias in a randomized trial," in *Cochrane Handbook for Systematic Reviews of Interventions*, Wiley, 2019, pp. 205–228. doi: 10.1002/9781119536604.ch8.
21. J. A. Sterne *et al.*, "ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions," *BMJ*, p. i4919, Oct. 2016, doi: 10.1136/bmj.i4919.
22. G. Wells *et al.*, "Newcastle-Ottawa quality assessment scale cohort studies," *University of Ottawa*, 2014.
23. NHLBI, "Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies.," *National Heart, Lung, and Blood Institute. Https://Www.Nhlbi.Nih.Gov/Health-Topics/Study-Quality-Assessment-Tools. Last Update: July 2021.*.
24. G. H. Guyatt *et al.*, "GRADE guidelines: 4. Rating the quality of evidence—study limitations (risk of bias)," *J Clin Epidemiol*, vol. 64, no. 4, pp. 407–415, Apr. 2011, doi: 10.1016/j.jclinepi.2010.07.017.
25. A. Carrasco-Labra *et al.*, "Improving GRADE evidence tables part 1: a randomized trial shows improved understanding of content in summary of findings tables with a new format," *J Clin Epidemiol*, vol. 74, pp. 7–18, Jun. 2016, doi: 10.1016/j.jclinepi.2015.12.007.

26. R. F. Ghouraba, N. F. Abotaha, and S. M. A. Sagha, "Comparative evaluation of treatment of angular bone defect related to over-erupted tooth using guided tissue regeneration (GTR) followed by orthodontic intrusion (OI) versus OI followed by GTR: a controlled clinical trial," *BMC Oral Health*, vol. 24, no. 1, p. 273, Feb. 2024, doi: 10.1186/s12903-024-04036-9.
27. M. S. Attia, H. Hazzaa, F. A. Al-Aziz, and G. M. Elewa, "Evaluation of adjunctive use of low-level diode laser biostimulation with combined orthodontic regenerative therapy.," *J Int Acad Periodontol*, vol. 21, no. 2, pp. 63–73, 2019.
28. J. Zhang *et al.*, "Efficacy of combined orthodontic-periodontic treatment for patients with periodontitis and its effect on inflammatory cytokines: A comparative study," *American Journal of Orthodontics and Dentofacial Orthopedics*, vol. 152, no. 4, pp. 494–500, Oct. 2017, doi: 10.1016/j.ajodo.2017.01.028.
29. El-Attar H, El-Kadi A, Rabie A, Ezz-el-Arab A, Salah N, and Bedair T, "Evaluation of the Combined Orthodontic- Periodontal Therapy in the Management of Extruded Anterior Teeth in Patients with Aggressive Periodontitis," *Int J Health Sci Res*, vol. 9, no. 12, pp. 25–38, Dec. 2019.
30. C. V. Carvalho *et al.*, "Orthodontic treatment in patients with aggressive periodontitis," *American Journal of Orthodontics and Dentofacial Orthopedics*, vol. 153, no. 4, pp. 550–557, Apr. 2018, doi: 10.1016/j.ajodo.2017.08.018.
31. A. S. Gawish, A. E. Salama, and H. S. Sadek, "Egyptian Orthodontic Journal CLINICAL EVALUATION OF PERIODONTAL REGENERATIVE TECHNIQUE AND ORTHODONTIC THERAPY IN MANAGEMENT OF PATHOLOGICALLY MIGRATED TOOTH," 2005.
32. A. Khorsand *et al.*, "Periodontal parameters following orthodontic treatment in patients with aggressive periodontitis: A before-after clinical study. ," *Dent Res J (Isfahan)*, vol. 10, no. 6, p. 744, 2013.
33. C. Navarrete *et al.*, "Levels of Pro-Inflammatory and Bone-Resorptive Mediators in Periodontally Compromised Patients under Orthodontic Treatment Involving Intermittent Forces of Low Intensities," *Int J Mol Sci*, vol. 24, no. 5, p. 4807, Mar. 2023, doi: 10.3390/ijms24054807.
34. S. Bayani, F. Heravi, M. Radvar, N. Anbiaee, and A. S. Madani, "Periodontal changes following molar intrusion with miniscrews.," *Dent Res J (Isfahan)*, vol. 12, no. 4, pp. 379–385, 2015.
35. T. Cao, L. Xu, J. Shi, and Y. Zhou, "Combined orthodontic-periodontal treatment in periodontal patients with anteriorly displaced incisors," *American Journal of Orthodontics and Dentofacial Orthopedics*, vol. 148, no. 5, pp. 805–813, Nov. 2015, doi: 10.1016/j.ajodo.2015.05.026.
36. C. , Ghezzi, S. Masiero, M. Silvestri, G. Zanotti, and G. Rasperini, "Orthodontic Treatment of Periodontally Involved Teeth After Tissue Regeneration.," *Int J Periodontics Restorative Dent*, vol. 28, no. 6, pp. 559–567, 2008.
37. C. Ghezzi, V. M. Viganò, P. Francinetti, G. Zanotti, and S. Masiero, "Orthodontic Treatment After Induced Periodontal Regeneration in Deep Infrabony Defects," *Clin Adv Periodontics*, vol. 3, no. 1, pp. 24–31, Feb. 2013, doi: 10.1902/cap.2012.110085.
38. S. Re, D. Cardaropoli, R. Abundo, and G. Corrente, "Reduction of gingival recession following orthodontic intrusion in periodontally compromised patients," *Orthod Craniofac Res*, vol. 7, no. 1, pp. 35–39, Feb. 2004, doi: 10.1111/j.1601-6343.2004.00277.x.
39. G. Corrente, R. Abundo, S. Re, D. Cardaropoli, and G. Cardaropoli, "Orthodontic Movement into Infrabony Defects in Patients with Advanced Periodontal Disease: A Clinical and Radiological Study," *J Periodontol*, vol. 74, no. 8, pp. 1104–1109, Aug. 2003, doi: 10.1902/jop.2003.74.8.1104.

40. P. Fleming, “Timing orthodontic treatment: early or late?,” *Aust Dent J*, vol. 62, no. S1, pp. 11–19, Mar. 2017, doi: 10.1111/adj.12474.
41. E. Zasčiurinskienė, N. Basevičienė, R. Lindsten, C. Slotte, H. Jansson, and K. Bjerklin, “Orthodontic treatment simultaneous to or after periodontal cause-related treatment in periodontitis susceptible patients. Part I: Clinical outcome. A randomized clinical trial,” *J Clin Periodontol*, vol. 45, no. 2, pp. 213–224, Feb. 2018, doi: 10.1111/jcpe.12835.