


# Periodontitis Phenotypes and Treatment Outcomes Following Combined Periodontal and Orthodontic Therapy: A Cohort Study

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**Background and Objectives:** Periodontitis is a heterogeneous condition, and patients may respond differently to combined periodontal and orthodontic treatment. This study aims to identify latent phenotypes of periodontitis and to evaluate their associations with recurrence and bone regeneration after combined periodontal–orthodontic treatment.

**Methods:** This single-centre observational cohort study included patients with periodontitis who completed combined periodontal and orthodontic treatment in 2023 and were followed for approximately two years, with re-evaluations conducted between January and July 2025. Latent class analysis was used to identify periodontitis phenotypes based on baseline periodontal characteristics. Outcomes included recurrence of periodontitis and bone regeneration. Associations between phenotypes and outcomes were examined using logistic regression models adjusted for age, sex, smoking status, and diabetes. Subgroup analyses were conducted by sex and age.

**Results:** Four distinct periodontitis phenotypes were identified: an inflammatory type, a high inflammation and structural damage type, a moderate and stable type, and a mild or minimal damage type. Compared with the mild or minimal damage phenotype, the high inflammation and structural damage phenotype was associated with a significantly higher risk of recurrence (OR 6.67, 95% CI 2.60–18.48). For bone regeneration, both the high inflammation and structural damage phenotype, and the moderate and stable phenotype showed a significantly lower likelihood of bone regeneration (OR 0.96, 95% CI 0.93–0.99, and OR 0.24, 95% CI 0.11–0.53, respectively). Subgroup analyses indicated that the association between the high inflammation and structural damage phenotype and recurrence was stronger among females and patients aged  $\geq 40$  years.

**Conclusion:** Periodontitis phenotypes differ in their risks of recurrence and bone regeneration following combined periodontal and orthodontic treatment. Baseline structural damage plays a key role in limiting regenerative potential, while severe structural damage combined with high inflammation substantially increases the risk of recurrence.

**Keywords:** periodontitis, orthodontic treatment, bone regeneration, recurrence, latent class analysis

## Introduction

Periodontitis is a chronic inflammatory disease that leads to progressive destruction of the supporting structures of the teeth, including alveolar bone, periodontal ligament, and cementum.<sup>1,2</sup> Its severity and progression vary widely among patients, reflecting differences in host response, baseline tissue conditions, and microbial composition.<sup>3</sup> This heterogeneity poses challenges for predicting treatment outcomes and tailoring individualized care.

Orthodontic treatment is increasingly applied in patients with periodontally compromised dentitions to correct malocclusion and improve function and aesthetics.<sup>4,5</sup> Evidence from systematic reviews suggests that combined periodontal and orthodontic therapy can stabilize periodontal conditions, reduce probing depth, and promote clinical attachment gains, particularly in teeth with pathological migration, flaring, or drifting.<sup>1,3</sup> The magnitude of these benefits is generally modest, however, and treatment outcomes are influenced by patient-specific factors such as baseline disease severity, periodontal phenotype, age, sex, timing of orthodontic intervention, and adjunctive procedures including bone augmentation or fiberotomy.<sup>2,6–8</sup> Potential risks remain,

particularly in teeth with thin biotypes, including gingival recession, alveolar bone dehiscence, and limited regenerative potential in structurally compromised sites.<sup>9,10</sup> Nonetheless, carefully planned interdisciplinary approaches, with appropriate force management and supportive periodontal therapy, have been shown to yield long-term stable outcomes even in severe cases.<sup>3,11,12</sup>

The current staging and grading system of classifying periodontitis offers a standardized framework, but it may not fully reflect the complex phenotypic heterogeneity that influences individual responses to combined periodontal and orthodontic treatment.<sup>2</sup> Latent class analysis (LCA) offers a data-driven approach to uncover unobserved subgroups of patients based on multiple periodontal parameters, enabling the identification of distinct phenotypes and potentially explaining variations in therapeutic outcomes.<sup>4</sup> Understanding periodontitis phenotypes, which integrate gingival morphology, alveolar bone characteristics, and microbial profiles, is increasingly recognized as crucial for predicting treatment outcomes and therapeutic success.<sup>13,14</sup> Cohort studies conducted in the United States and the Netherlands classified periodontitis patients based on clinical, radiographic, and microbiological characteristics, identifying at least three main patient subgroups with differential risks of disease progression and treatment response.<sup>15,16</sup> Despite increasing adoption of interdisciplinary periodontal-orthodontic treatment, there remains limited evidence linking baseline periodontitis phenotypes to clinical outcomes such as disease recurrence or alveolar bone regeneration. Understanding these associations could improve risk stratification, optimize individualized treatment planning, and enhance long-term prognosis.

Therefore, this study aimed to identify distinct periodontitis phenotypes using latent class analysis and to examine their associations with recurrence and bone regeneration following combined periodontal and orthodontic therapy.

## Methods

### Study Design and Population

This was an observational cohort study conducted at Dalian Medical University School and Hospital of Stomatology. Patients with periodontitis who completed orthodontic treatment in 2023 were screened for eligibility. Baseline demographic and periodontal characteristics were collected at the start of orthodontic treatment. All included patients received standard non-surgical periodontal therapy, including scaling and root planing, prior to and during orthodontic treatment. Orthodontic treatment consisted of fixed or removable appliances according to standard clinical protocols. No orthognathic or periodontal surgical procedures were performed during the study period. After completion of orthodontic treatment, patients entered a retention phase and were followed for approximately two years. Periodontal re-evaluations were performed between January 2025 and July 2025. Patients were excluded if they were pregnant or breastfeeding during the study period, or if they had a history of malignant disease. Patients requiring additional surgical interventions were also excluded.

### Ethical Approval

This study was approved by the Biomedical Ethics Committee of Dalian Stomatological Hospital (Ethical approval number: DLKQLL20250402). All procedures were conducted in accordance with the ethical standards of the institutional research committee and in line with the Declaration of Helsinki. Informed consent was obtained from all participants.

### Variables

Baseline data included age, sex, smoking status, and history of diabetes. Baseline data included age, sex, smoking status, and history of diabetes. Periodontal clinical parameters were recorded by trained clinicians. All clinical measurements were standardized based on consensus among three experienced periodontists who jointly reviewed and agreed on the assessment criteria prior to the study. Bleeding on probing was measured as the proportion of sites showing bleeding. Probing depth and alveolar bone loss were measured in millimeters. Tooth mobility was assessed for each tooth and classified as Grade I, II, or III. Furcation involvement, calculus, and suppuration were recorded as present or absent at each site. Alveolar bone loss was evaluated radiographically using standardized periapical and panoramic radiographs, with follow-up images compared using identical projection angles and exposure settings to assess bone regeneration.

## Outcomes

Two outcomes were assessed at follow-up. The primary outcome was recurrence, defined as the presence of clinical signs indicating reactivation or progression of periodontitis after treatment. The secondary outcome was bone regeneration, defined as radiographic or clinical evidence of alveolar bone improvement following combined periodontal and orthodontic treatment. During the two-year observational period, no additional periodontal or orthodontic treatment was provided apart from routine retention maintenance visits.

## Statistical Analysis

Latent class analysis was conducted to identify unobserved periodontitis phenotypes based on baseline periodontal variables, including bleeding on probing, probing depth, alveolar bone loss, tooth mobility, furcation involvement, calculus, and suppuration.<sup>17</sup> Models specifying two to five latent classes were fitted sequentially. To determine the optimal number of classes, model fit was evaluated using the Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), and G-squared (Gsq) statistics.<sup>18</sup> Lower values of these indices indicated better model fit. The final model was selected based on a combination of statistical fit, parsimony, and clinical interpretability of the derived classes.<sup>19</sup> After phenotype classification, baseline characteristics were summarized across phenotypes.

Logistic regression models were used to evaluate the associations between periodontitis phenotypes and treatment outcomes, including recurrence and bone regeneration. Model 1 included phenotype as the independent variable only. Model 2 was adjusted for age, sex, smoking status, and diabetes. Results were presented as odds ratios with 95% confidence intervals. Prespecified subgroup analyses were performed to explore potential effect modification by sex and age. Sex-stratified analyses were conducted separately for males and females. Age-stratified analyses were performed using a cutoff of 40 years. Within each subgroup, logistic regression models were fitted using the same modelling strategy as in the main analysis.

All statistical analyses were performed using R software. A two-sided *P* value of less than 0.05 was considered statistically significant.

## Results

### Latent Class Model Fit and Selection

Latent class models with two to five classes were fitted to baseline periodontal variables. Model fit indices are shown in Table 1. The two-class model showed an AIC of 4624, a BIC of 4746, and a G-squared value of 460. The three-class model improved model fit, with a lower AIC of 4477, BIC of 4663, and G-squared of 284. The four-class model provided the best overall fit, with the lowest AIC (4402) and G-squared value (179), and a lower BIC (4651) compared with the two- and three-class models. In contrast, the five-class model showed worse fit across all indices (AIC 4703, BIC 4703, G-squared 4703).

**Table 1** Model Fit Indices for Latent Class Analysis Identifying Periodontitis phenotypes

Classes	AIC	BIC	Gsq
2	4624	4746	460
3	4477	4663	284
4	4402	4651	179
5	4703	4703	4703

**Note:** Fit Statistics for Models with One to Five Latent Classes are Presented, Including Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), and G-Squared (Gsq). The Optimal Number of Classes Was Determined Based on Model Fit Indices, Parsimony, and Interpretability.

G-squared 4703), indicating overfitting. Based on these quantitative criteria and the clinical interpretability of the derived classes, the four-class solution was selected for subsequent analyses.

## Baseline Characteristics by Periodontitis Phenotypes

Latent class analysis identified four distinct periodontitis phenotypes among patients receiving combined periodontal and orthodontic treatment. Radar plot visualization showed clear separation of these phenotypes across multiple periodontal dimensions, including inflammatory burden, probing depth, structural damage, and tooth stability (Figure 1). The four phenotypes were labelled as Inflammatory type, High inflammation and structural damage type, Mild or minimal damage type, and Moderate and stable type.

The Inflammatory type was characterized by high bleeding on probing and increased probing depth, with moderate alveolar bone loss. Tooth mobility and furcation involvement were modest. The High inflammation and structural damage type showed the highest bleeding on probing and the greatest probing depth, accompanied by the highest tooth mobility and the greatest frequency of furcation involvement (17.1%). In contrast, the Mild or minimal damage type, which represented the largest subgroup, showed lower bleeding on probing, the shallowest probing depth, and the lowest tooth mobility, indicating good periodontal stability. The Moderate and stable type showed intermediate bleeding on probing and probing depth, with moderate bone loss and tooth mobility, suggesting controlled inflammation and relatively stable structural conditions. Baseline demographic and clinical characteristics across phenotypes are presented in Table 2. Age differed significantly among phenotypes, with younger patients more commonly observed in the inflammatory and high inflammation and structural damage phenotypes ( $P = 0.003$ ). Sex distribution also varied, with a lower proportion of males in the inflammatory phenotype ( $P = 0.041$ ).

Key periodontal parameters, including bleeding on probing, probing depth, and tooth mobility, differed significantly across phenotypes (all  $P < 0.05$ ), supporting clear differentiation in inflammatory activity and periodontal stability. In contrast, smoking status, diabetes prevalence, alveolar bone loss, calculus, suppuration, and furcation involvement did not differ significantly across groups.

## Influence of Phenotypes on Recurrence and Bone Regeneration

Table 3 shows the associations between periodontitis phenotypes and treatment outcomes, using the mild or minimal damage phenotype as the reference group. For recurrence, the unadjusted model (Model 1) showed that the high inflammation and structural damage phenotype had a markedly increased risk ( $OR\ 4.55$ , 95%  $CI\ 1.96$  to  $10.97$ ). This association strengthened after adjusting for age, sex, smoking, and diabetes (Model 2), with an odds ratio of  $6.67$  (95%  $CI\ 2.60$  to  $18.48$ ). In contrast, the inflammatory and moderate and stable phenotypes showed no significant association with recurrence in either model. For bone regeneration, phenotype-specific differences were also observed. In the adjusted analysis (Model 2), the moderate and stable phenotype was associated with a significantly lower likelihood of bone regeneration compared with the reference group ( $OR\ 0.24$ , 95%  $CI\ 0.11$  to  $0.53$ ). The high inflammation and structural damage phenotype also showed reduced odds of bone regeneration in the unadjusted model ( $OR\ 0.25$ , 95%  $CI$

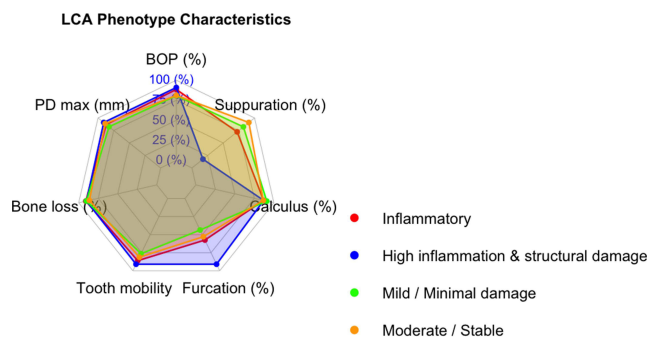


Figure 1 Radar plot of periodontitis phenotypes identified by latent class analysis.

**Table 2** Baseline Demographic and Clinical Characteristics of Patients Undergoing Combined Periodontal and Orthodontic Treatment by Periodontitis Phenotype (N=499)

	Mild/Minimal Damage	Inflammatory	Moderate/Stable	High Inflammation & Structural Damage	p value
n	195	37	191	76	
Age, mean (SD)	39.64 (9.45)	36.73 (8.70)	40.88 (9.18)	36.88 (7.85)	0.003
Male, n (%)	75 (38.5)	7 (18.9)	53 (27.7)	24 (31.6)	0.041
Smoke, n (%)	55 (28.2)	9 (24.3)	50 (26.2)	22 (28.9)	0.925
Diabetes, n (%)	11 (5.6)	2 (5.4)	4 (2.1)	3 (3.9)	0.340
Bleeding on probing (%), mean (SD)	0.50 (0.16)	0.54 (0.19)	0.50 (0.19)	0.56 (0.22)	0.038
Periodontal probing depth (mm), mean (SD)	4.31 (0.96)	4.54 (1.04)	4.63 (0.95)	4.75 (1.50)	0.004
Alveolar bone loss (mm), mean (SD)	3.65 (0.83)	3.68 (1.13)	3.49 (1.11)	3.64 (1.28)	0.440
Tooth mobility <sup>1</sup> , mean (SD)	1.13 (0.36)	1.27 (0.56)	1.20 (0.41)	1.34 (0.50)	0.002
Furcation, n (%)	16 (8.2)	4 (10.8)	19 (9.9)	13 (17.1)	0.194
Calculus, n (%)	193 (99.0)	35 (94.6)	180 (94.2)	72 (94.7)	0.078
Suppuration, n (%)	12 (6.2)	2 (5.4)	13 (6.8)	1 (1.3)	0.351

**Note:** <sup>1</sup>Tooth mobility was assessed for each tooth and classified as Grade I, II, or III according to standard clinical criteria.

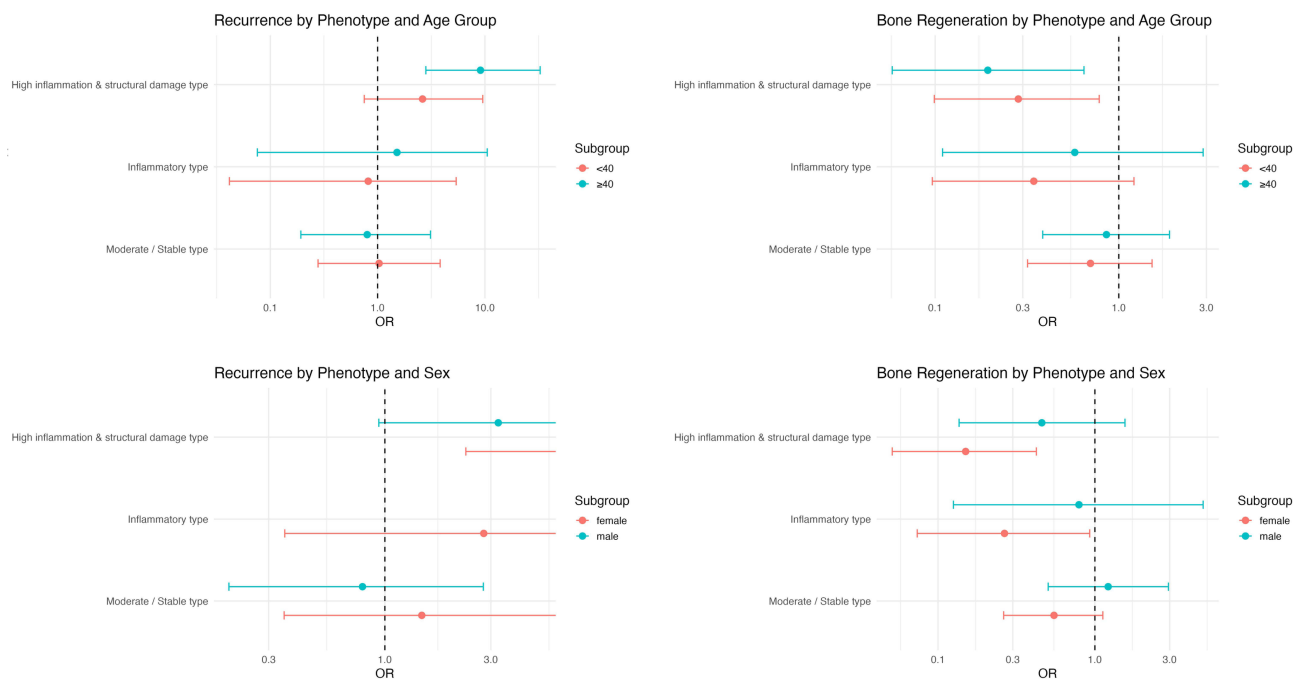
**Table 3** Associations Between Periodontitis Phenotypes and Outcomes of Combined Periodontal and Orthodontic Treatment

	Recurrence		Bone Regeneration	
	Model 1	Model 2	Model 1	Model 2
(Intercept)	0.05 (0.03–0.1)	0.03 (0–0.18)	0.51 (0.39–1.33)	0.44 (0.16–1.2)
Age		1 (0.95–1.04)		1.72 (0.9–3.27)
Male		1.33 (0.52–3.24)		0.37 (0.18–0.74)
Smoke		1.57 (0.63–3.86)		0.14 (0.05–0.46)
Diabetes		15.41 (5.18–46.24)		0.02 (0.39–0.79)
Phenotype				
Inflammatory	1.06 (0.16–4.23)	1.2 (0.16–5.62)	0.42 (0.16–1.15)	0.75 (0.43–1.32)
Moderate/Stable	0.91 (0.36–2.32)	1.34 (0.48–3.76)	0.77 (0.44–1.34)	0.24 (0.11–0.53)
High inflammation and structural damage	4.55 (1.96–10.97)	6.67 (2.6–18.48)	0.25 (0.11–0.55)	0.96 (0.93–0.99)

0.11 to 0.55); however, this association was substantially attenuated and became marginal after adjustment for covariates (*OR* 0.96, 95% *CI* 0.93 to 0.99). The inflammatory phenotype showed no significant association with bone regeneration.

### Subgroup Analyses by Sex and Age

Subgroup analyses by sex and age are shown in [Figure 2](#). Among female patients, the high inflammation and structural damage phenotype was strongly associated with recurrence (*OR* 8.16, 95% *CI* 2.31 to 38.09). A similar but weaker association was observed in males. Age-stratified analyses showed that the association between the high inflammation and structural damage phenotype and recurrence was stronger in patients aged 40 years or older (*OR* 9.10, 95% *CI* 2.82 to 32.73) than in younger patients. No consistent phenotype-specific differences were observed for recurrence in the inflammatory or moderate and stable phenotypes across subgroups. For bone regeneration, subgroup analyses showed generally consistent trends across sex and age strata, with lower regenerative potential observed in phenotypes with greater baseline structural damage.



**Figure 2** Subgroup analyses of the effects of periodontitis phenotypes on outcomes of combined periodontal and orthodontic treatment by age and sex.

## Discussion

This study investigated the effects of combined periodontal and orthodontic treatment across different periodontitis phenotypes. Using latent class analysis, we identified four distinct phenotypes that varied in inflammation, structural damage, and tooth stability. We found that patients with high inflammation combined with severe structural damage had an increased risk of disease recurrence and poorer bone regeneration, while patients with moderate structural damage, even with controlled inflammation, also showed reduced bone regenerative potential. These findings highlight the heterogeneity of periodontitis and suggest that stratifying patients based on baseline periodontal characteristics can guide more personalized treatment planning.

Our findings emphasize that baseline structural integrity is a key determinant of treatment outcomes. Patients with moderate structural damage, despite well-controlled inflammation, demonstrated reduced bone regeneration.<sup>20</sup> Structural compromise likely limits the spatial and biological support necessary for new bone formation, restricts vascularization, and impairs cellular function within the periodontal ligament and alveolar bone.<sup>21,22</sup> These observations align with mechanistic studies showing that osteogenic differentiation and periodontal regeneration are highly dependent on both cellular activity and the extracellular matrix microenvironment, which are disrupted in structurally compromised sites.<sup>11,23</sup> Recent preclinical studies further support that concurrent inflammation and orthodontic forces can increase local osteoclast activity, root resorption, and bone loss, highlighting the importance of controlled mechanical loading during treatment.<sup>24</sup> In patients with severe structural damage, the presence of active inflammation further amplified the risk of recurrence, suggesting a synergistic effect of inflammation and tissue loss on treatment outcomes.<sup>25</sup> High inflammatory burden can perpetuate osteoclast activation, release pro-inflammatory cytokines, and induce tissue catabolism, creating a local microenvironment that hinders healing and promotes disease progression.<sup>22</sup> This is consistent with evidence that persistent inflammation, even after periodontal stabilization, is a major driver of recurrence, while severe baseline tissue loss predicts poorer regenerative outcomes.<sup>9,26</sup> Clinical studies demonstrate that periodontal regeneration combined with orthodontics can significantly reduce inflammatory markers and improve functional and aesthetic outcomes compared with periodontal regeneration alone.<sup>27,28</sup>

The underlying biological mechanisms are multifactorial. Structural compromise reduces vascular supply, limits recruitment of mesenchymal stem cells, and alters the organization of the periodontal extracellular matrix, all of which are essential for successful tissue regeneration.<sup>23</sup> In addition, adjunctive therapies such as photothermal composite hydrogels or antibiotic-loaded scaffolds can sequentially control inflammation and promote bone regeneration in severe periodontitis.<sup>29</sup> Orthodontic

forces applied to compromised sites may exacerbate local inflammation if not carefully controlled.<sup>30</sup> However, previous clinical and narrative reviews indicate that orthodontic treatment following active periodontal therapy, with supportive periodontal care (SPC), does not adversely affect long-term periodontal stability.<sup>31,32</sup> These findings underscore the importance of balancing mechanical forces with inflammation control to optimize regenerative outcomes.<sup>33</sup>

Patient-specific factors such as age and sex may further modulate these effects. Older patients and females with high-risk phenotypes exhibited higher recurrence rates, consistent with prior studies showing that age-related declines in immune function, hormonal influences, and reduced regenerative capacity can impair healing.<sup>12</sup> Moreover, patients' subjective perception of dental aesthetics was a strong predictor of interest in orthodontic treatment, independent of periodontal severity or demographic factors,<sup>31,32</sup> emphasizing the importance of integrating patient-reported outcomes into treatment planning.

Clinically, our results support a phenotype-based approach to combined periodontal and orthodontic therapy. Assessing both structural integrity and inflammatory status prior to treatment can help identify high-risk patients who may benefit from more intensive monitoring, adjunctive regenerative therapies, or modified orthodontic force application.<sup>34,35</sup> This strategy allows clinicians to better predict bone regenerative potential, tailor individualized interventions, and optimize long-term outcomes in patients with complex periodontal conditions.

This study has some limitations. First, this study was conducted at a single-centre observational cohort study, which may limit generalizability. Second, bone regeneration was evaluated using clinical and radiographic measures, which may not fully capture subtle microstructural changes in alveolar bone, but these measures reflect routine clinical practice and are widely accepted in periodontal research. Third, although we adjusted for major confounders (including age, sex, smoking status, diabetes, and clinical periodontal parameters), residual confounding from unmeasured factors cannot be completely excluded. Future studies incorporating additional behavioural and biological factors may further clarify phenotype-specific treatment responses.

## Conclusions

In conclusion, this study identified four distinct periodontitis phenotypes among patients undergoing combined periodontal and orthodontic treatment using latent class analysis. These phenotypes differed not only in baseline inflammatory activity and structural damage but also in their subsequent risks of disease recurrence and bone regeneration. Patients characterized by high inflammation combined with severe structural damage exhibited the highest risk of recurrence, while those with moderate structural damage, even in the presence of relatively controlled inflammation, demonstrated reduced bone regenerative potential. These findings underscore the heterogeneity of periodontitis and suggest that baseline periodontal phenotype, particularly structural status, plays an important role in shaping treatment outcomes. Incorporating phenotype-based stratification into clinical assessment may help clinicians better identify high-risk patients, optimize treatment planning, and improve long-term management following combined periodontal and orthodontic therapy.

## Author Contributions

Hongtao Jiang contributed to the conception and design of the study, performed data analysis, and interpreted the results. Qi Zhao, Zhaoxin Dong, and Tianhao Li were responsible for data acquisition, including clinical and radiographic assessments, and contributed to data verification. Jiang Sun supervised the study, critically reviewed and revised the manuscript, and provided overall guidance. All authors contributed to drafting, revising, and critically reviewing the manuscript; gave final approval of the version to be published; agreed on the journal to which the article was submitted; and agree to be accountable for all aspects of the work.

## Funding

There is no funding to report.

## Disclosure

The authors declare no conflicts of interest in this work.

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