Article

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Systemic Immune-Inflammation Index as a Novel Biomarker for Differentiating Stage III and IV Periodontitis: A Propensity Score-Matched Retrospective Study

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Background: According to the 2017 classification of periodontal and peri-implant diseases, Stage III and IV periodontitis are defined as severe and advanced forms, respectively. However, current diagnostic differentiation relies largely on clinical probing and lacks objective biomarkers that reflect the systemic inflammatory burden. The Systemic Immune-Inflammation Index (SII)—integrating neutrophil, lymphocyte, and platelet counts—comprehensively reflects the balance of the host "inflammation-immunity-thrombosis" network. Previous studies, however, often failed to adequately control for systemic confounders such as age, smoking status, and metabolic syndrome. Therefore, this study aims to apply Propensity Score Matching (PSM) to rigorously adjust for confounding variables and to evaluate the clinical utility of SII as a novel biomarker for differentiating Stage IV from Stage III periodontitis.

Methods: This retrospective case-control study enrolled patients diagnosed with Stage III and IV periodontitis. To mitigate selection bias, a 1:1 PSM analysis was performed to balance baseline covariates, including age, gender, smoking status, diabetes mellitus, hypertension, body mass index (BMI), and educational level. Differences in SII levels between groups were analyzed using the Mann-Whitney U test. A multivariate logistic regression model was constructed to assess the association between SII and the risk of Stage IV periodontitis. Additionally, Restricted Cubic Spline (RCS) modeling was employed to explore potential non-linear dose-response relationships.

Results: After PSM, a total of 212 patients with balanced baseline characteristics were included (106 each for Stage III and IV). Analysis revealed that SII levels were significantly higher in patients with Stage IV periodontitis compared to those with Stage III [Median: 577.23 vs. 529.06, $p = 0.003$]. Multivariate logistic regression confirmed that, even after adjusting for all confounding factors, elevated SII levels remained an independent risk factor for progression to Stage IV periodontitis ($p < 0.001$). Furthermore, RCS analysis demonstrated a significant linear dose-response relationship between SII levels and the risk of Stage IV periodontitis ($p_{overall} = 0.009$), with no evidence of a non-linear threshold effect ($p_{non\text{-}linearity} = 0.069$).

Conclusion: Even after rigorous adjustment for systemic confounders, elevated SII levels are significantly associated with Stage IV periodontitis and exhibit a linear cumulative trend. As a cost-effective and accessible objective indicator, SII not only aids in the precise grading of Stage III and Stage IV periodontitis but also highlights the heightened systemic inflammatory burden in severe cases, thereby supporting the implementation of multidisciplinary management strategies.

Keywords: periodontitis; Systemic Immune-Inflammation Index; grading diagnosis; propensity score matching; systemic inflammation

Introduction

Periodontitis is a chronic multifactorial inflammatory disease initiated by dysbiotic plaque biofilms, characterized by the progressive destruction of periodontal supporting tissues [1,2]. Ranking as the sixth most prevalent condition globally, periodontitis not only causes alveolar bone resorption and tooth loss—compromising masticatory function and aesthetics—but also constitutes a substantial public health burden [3]. To guide clinical decision-making and prognosis more precisely, a novel framework was introduced in the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. This system incorporates "Staging" (Stages I–IV) based on severity and treatment complexity, and "Grading" (Grades A/B/C) based on progression risk and biological characteristics [4]. Specifically, Stages III and IV represent severe and advanced forms of the disease, often complicated by occlusal collapse and extensive tooth loss. Consequently, early identification and precise staging are pivotal for arresting disease progression [5].

However, despite the academic rigor of this new classification, its clinical implementation remains challenging. Currently, diagnosis and staging rely largely on full-mouth probing to assess Probing Depth (PD) and Clinical Attachment Loss (CAL)—the "gold standard" for periodontal assessment [5]. However, this conventional method is labor-intensive and uncomfortable for patients [6]. Furthermore, it is inherently subjective, with measurements susceptible to variations in probing force and angulation [7,8].

Crucially, the relationship between periodontitis and systemic health is well-established. Acting as a reservoir for chronic infection, periodontal pockets allow pathogenic bacteria and their metabolites (e.g., lipopolysaccharide [LPS]) to translocate into the circulation [9]. This translocation triggers a robust host immune response and the release of pro-inflammatory cytokines (e.g., interleukin-1β [IL-1β], interleukin-6 [IL-6], and tumor necrosis factor-α [TNF-α]), thereby inducing a state of low-grade systemic inflammation [10]. Consequently, identifying objective and minimally invasive blood-based biomarkers that reflect this specific inflammatory burden has emerged as a frontier in periodontal research. Although traditional markers, such as white blood cell (WBC) count and C-reactive protein (CRP), have been widely investigated, they are easily influenced by non-specific factors and often lack sufficient sensitivity and specificity for characterizing the specific immune status of periodontitis [11,12].

Against this backdrop, the Systemic Immune-Inflammation Index (SII) has emerged as a promising comprehensive inflammatory marker. Calculated from peripheral blood counts, the SII is defined by the formula: SII = (platelet $\times$ neutrophil) / lymphocyte. Unlike single hematological parameters, SII integrates information from three pivotal pathways: innate immunity (neutrophils), adaptive immunity (lymphocytes), and hemostasis and thrombosis (platelets) [13]. Neutrophils serve as the first line of defense in periodontal tissues and contribute to immunopathological tissue destruction; lymphocytes reflect the host's capacity for immune regulation and surveillance; and platelets play a critical role in inflammatory modulation and soft tissue repair. Consequently, SII provides a more comprehensive and stable reflection of the balance within the host's "inflammation-immunity-thrombosis" network and has demonstrated superior prognostic value in oncology and cardiovascular medicine [14–16].

Although a limited number of studies have examined the association between SII and periodontitis [17–19], most have failed to adequately account for confounding factors. Shared risk factors—such as age, smoking status, obesity, and metabolic syndrome—not only predispose individuals to periodontitis but also significantly alter hematological parameters, thereby obscuring the true associations [20,21]. To address these limitations, this retrospective case-control study focuses specifically on patients with severe (Stage III/IV) periodontitis. Propensity Score Matching (PSM) was employed to rigorously mitigate the influence of potent confounders, particularly smoking and diabetes mellitus. We hypothesized that SII levels positively correlate with the severity of periodontal staging and grading. Through rigorous statistical analyses, this study aims to validate the clinical utility of SII as a novel biomarker for the adjunctive diagnosis and precise grading of Stage III and IV periodontitis.

Methods

Study Design and Participants

This retrospective study enrolled patients diagnosed with periodontitis at the Department of Stomatology, Cangnan Hospital of Wenzhou Medical University (The People's Hospital of Cangnan) between February 2022 and January 2025. Diagnosis and staging were strictly based on the consensus report of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions [4]. Based on disease severity and complexity, patients with severe periodontitis were categorized into two groups: the Stage III group (serving as the control) and the Stage IV group (serving as the case). Participants were included based on the following criteria: (1) Age between 18 and 75 years; (2) Availability of comprehensive periodontal charts, including Probing Depth (PD), Clinical Attachment Loss (CAL), and Bleeding on Probing (BOP), along with complete radiographic evaluation (full-mouth periapical radiographs or panoramic X-rays); (3) Availability of routine complete blood count (CBC) results obtained within 24 hours relative to the periodontal examination, specifically including neutrophil, lymphocyte, and platelet counts. In this retrospective cohort, CBC tests were performed either as part of the standard pre-operative assessment for periodontal surgery or as a routine screening protocol for patients with severe periodontal destruction to exclude underlying hematological pathologies. To ensure diagnostic accuracy, all cases were independently reviewed by two experienced periodontists, with any discrepancies resolved through discussion to reach a consensus.

To ensure that SII specifically reflects the periodontal inflammatory burden and to minimize potential confounding variables, strict exclusion criteria were applied. Patients were excluded if they presented with: (1) A history of systemic diseases known to significantly modulate the immune-inflammatory status, including autoimmune disorders (e.g., rheumatoid arthritis), malignancies, hematological disorders, or severe hepatic/renal impairment; (2) A history of acute infection, major surgery, or physical trauma within the preceding three months; (3) Use of antibiotics, non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, or immunosuppressants within three months prior to blood sampling; (4) Receipt of non-surgical or surgical periodontal therapy within the past six months; (5) Pregnancy or lactation; (6) Presence of concomitant oral mu-

Table 1. Baseline characteristics of patients before propensity score matching.

Variables	Total (n = 298)	Stage III (n = 163)	Stage IV (n = 135)	Statistic	*p*	SMD
Age, M (Q_1, Q_3)	51.00 (45.00, 58.00)	49.00 (43.50, 56.00)	53.00 (47.00, 59.00)	Z = –3.29	<0.001	0.407
BMI, M (Q_1, Q_3)	24.65 (22.92, 26.37)	24.70 (23.20, 26.40)	24.60 (22.40, 26.20)	Z = –1.30	0.192	–0.162
SII, M (Q_1, Q_3)	548.38 (490.71, 623.32)	526.63 (485.57, 593.23)	582.41 (514.44, 673.00)	Z = –4.28	<0.001	0.494
Gender, n (%)				χ^2 = 1.07	0.301	
Male	178 (59.73)	93 (57.06)	85 (62.96)			0.122
Female	120 (40.27)	70 (42.94)	50 (37.04)			–0.122
Smoking status, n (%)				χ^2 = 11.81	<0.001	
Non-current smokers	167 (56.04)	106 (65.03)	61 (45.19)			–0.399
Current smokers	131 (43.96)	57 (34.97)	74 (54.81)			0.399
Diabetes mellitus, n (%)				χ^2 = 16.42	<0.001	
NO	227 (76.17)	139 (85.28)	88 (65.19)			–0.422
YES	71 (23.83)	24 (14.72)	47 (34.81)			0.422
Hypertension, n (%)				χ^2 = 3.63	0.057	
NO	181 (60.74)	107 (65.64)	74 (54.81)			–0.218
YES	117 (39.26)	56 (34.36)	61 (45.19)			0.218
Educational level, n (%)				χ^2 = 11.13	<0.001	
Junior high school and above	117 (39.26)	50 (30.67)	67 (49.63)			0.379
Below junior high school	181 (60.74)	113 (69.33)	68 (50.37)			–0.379

Z, Mann-Whitney test; χ^2, Chi-square test.

M, Median; Q_1, 1st Quartile; Q_3, 3rd Quartile.

SMD, Standardized Mean Difference; BMI, body mass index; SII, Systemic Immune-Inflammation Index.

cosal pathologies or acute odontogenic infections. Beyond the comorbidities of diabetes mellitus and hypertension, which were adjusted for in the analysis, other concurrent chronic systemic conditions occurred only sporadically and were negligible, ensuring that they did not significantly confound the assessment of systemic inflammatory burden.

The study was conducted in accordance with the Declaration of Helsinki. This study protocol was approved by the Ethics Committee of Cangnan Hospital of Wenzhou Medical University (The People's Hospital of Cangnan) (Approval No.: 2025087). All patient information was anonymized to protect privacy. As a retrospective observational study, the Ethics Committee granted a waiver for the requirement of informed consent.

Propensity Score Matching

To minimize selection bias and ensure comparability between the Stage III and Stage IV cohorts, PSM was performed. The propensity scores were estimated using a multivariable logistic regression model incorporating the following baseline covariates: age, gender, body mass index (BMI), smoking status, diabetes mellitus, hypertension, and educational level. A 1:1 nearest-neighbor matching algorithm was applied to pair patients from the Stage III and Stage IV groups. The balance of covariates between the matched groups was assessed using the Standardized Mean Difference (SMD), with an absolute SMD value of <0.1 considered indicative of adequate balance and negligible between-group differences.

Statistical Analysis

All analyses were performed using R software (Version 4.3.3; R Foundation for Statistical Computing, Vienna, Austria). Continuous variables were first evaluated for normality using the Shapiro-Wilk test. Data following a normal distribution were expressed as mean $\pm$ standard deviation (SD) and compared between groups using the independent Student's *t*-test, whereas non-normally distributed data were presented as median [interquartile range (IQR)] and analyzed via the Mann-Whitney U test. Categorical variables were reported as frequencies and percentages [*n* (%)] and compared using the Chi-square (χ^2) test. To investigate the specific association between SII levels and the risk of Stage IV periodontitis, univariate and multivariate logistic regression analyses were conducted. Given the wide range of SII values, the variable was rescaled by dividing by 100 (per 100-unit increase) to facilitate clinical interpretation of the Odds Ratios (ORs). The results were expressed as ORs and 95% confidence intervals (CIs). The multivariate model was adjusted for potential confounders, including age, gender, smoking status, diabetes mellitus, hypertension, educational level, and BMI. Subsequently, following PSM, a multivariate logistic regression analysis was further performed to adjust for any potential residual confounding and to ensure the robustness of the results (doubly robust estimation). Furthermore, to evaluate potential non-linear dose-response relationships between SII levels and periodontitis severity, a restricted cubic spline (RCS) model with specified knots was constructed, characterizing both overall associations and non-linear trends. All statis-

Table 2. Baseline characteristics of patients after propensity score matching.

Variables	Total (n = 212)	Stage III (n = 106)	Stage IV (n = 106)	Statistic	*p*	SMD
Age, M (Q_1, Q_3)	52.00 (45.00, 58.00)	53.00 (45.00, 58.75)	52.00 (46.00, 58.00)	Z = –0.01	0.994	0.037
BMI, M (Q_1, Q_3)	24.45 (22.90, 26.10)	24.35 (23.20, 25.90)	24.65 (22.50, 26.20)	Z = –0.11	0.913	–0.010
SII, M (Q_1, Q_3)	550.52 (495.23, 620.46)	529.06 (491.34, 593.92)	577.23 (503.59, 658.92)	Z = –2.93	0.003	0.436
Gender, n (%)				χ^2 = 0.00	1.000	
Male	126 (59.43)	63 (59.43)	63 (59.43)			0.000
Female	86 (40.57)	43 (40.57)	43 (40.57)			0.000
Smoking, n (%)				χ^2 = 0.08	0.782	
Non-current smokers	118 (55.66)	60 (56.60)	58 (54.72)			–0.038
Current smokers	94 (44.34)	46 (43.40)	48 (45.28)			0.038
Diabetes mellitus, n (%)				χ^2 = 0.03	0.871	
NO	163 (76.89)	82 (77.36)	81 (76.42)			–0.022
YES	49 (23.11)	24 (22.64)	25 (23.58)			0.022
Hypertension, n (%)				χ^2 = 0.18	0.668	
NO	135 (63.68)	69 (65.09)	66 (62.26)			–0.058
YES	77 (36.32)	37 (34.91)	40 (37.74)			0.058
Educational level, n (%)				χ^2 = 0.00	1.000	
Junior high school and above	92 (43.40)	46 (43.40)	46 (43.40)			0.000
Below junior high school	120 (56.60)	60 (56.60)	60 (56.60)			0.000

Z, Mann-Whitney test; χ^2, Chi-square test.

M, Median; Q_1, 1st Quartile; Q_3, 3rd Quartile.

tical tests were two-sided, and a $p < 0.05$ was considered statistically significant.

Results

Baseline Characteristics Before PSM

A total of 298 participants were initially included in the study, comprising 163 patients with Stage III periodontitis and 135 with Stage IV periodontitis. Prior to PSM, significant differences in baseline characteristics were observed between the two cohorts. Specifically, patients in the Stage IV group were significantly older ($p < 0.05$) and exhibited significantly higher prevalences of smoking and diabetes mellitus compared to those in the Stage III group ($p < 0.05$). Notably, baseline SII levels were also significantly elevated in the Stage IV cohort ($p < 0.05$). These observed imbalances underscored the presence of potential confounding factors, necessitating statistical adjustment to ensure comparability. Detailed baseline characteristics of the unmatched population are summarized in Table 1.

Baseline Characteristics After PSM

Following the application of PSM, a total of 212 patients were successfully matched, yielding 106 matched pairs. Post-matching analysis revealed no statistically significant differences in any baseline covariates—including age, gender, BMI, smoking status, diabetes mellitus, hypertension, and educational level—between the two groups ($p > 0.05$). Furthermore, analysis of Standardized Mean Differences (SMDs) confirmed that covariate imbalances were substantially mitigated, with all absolute SMD values below the threshold of 0.1. Consistently, the histograms of propensity scores exhibited a high degree of overlap, indicating that adequate baseline balance and comparability were achieved between the cohorts. The characteristics of the matched population are detailed in Table 2, and the covariate balance plot is illustrated in Figs 1,2.

Association Between SII and Periodontal Staging

Within the matched cohort, comparative analysis demonstrated that SII levels were significantly elevated in the Stage IV group compared to the Stage III group [Median (IQR): 577.23 (503.59, 658.92) vs. 529.06 (491.34, 593.92), $p = 0.003$]. Logistic regression analysis (Table 3) further elucidated this association. In univariate analysis, elevated SII levels were significantly associated with an increased risk of progression to Stage IV periodontitis ($p < 0.001$). Crucially, after adjusting for potential confounders, multivariate analysis confirmed that elevated SII remained an independent risk factor for Stage IV periodontitis ($p < 0.001$).

To characterize the dose-response relationship, Restricted Cubic Spline (RCS) analysis was performed (Fig. 3). Univariate RCS analysis revealed a significant overall association ($p_{overall} = 0.009$) with no evidence of non-linearity ($p_{non\text{-}linearity} = 0.073$). Similar results were observed in the multivariate RCS model adjusted for covariates with the positive association remaining significant ($p_{overall} = 0.009$) and the test for non-linearity remaining non-significant ($p_{non\text{-}linearity} = 0.069$), suggesting a linear dose-response relationship between systemic inflammatory burden and periodontal disease severity.

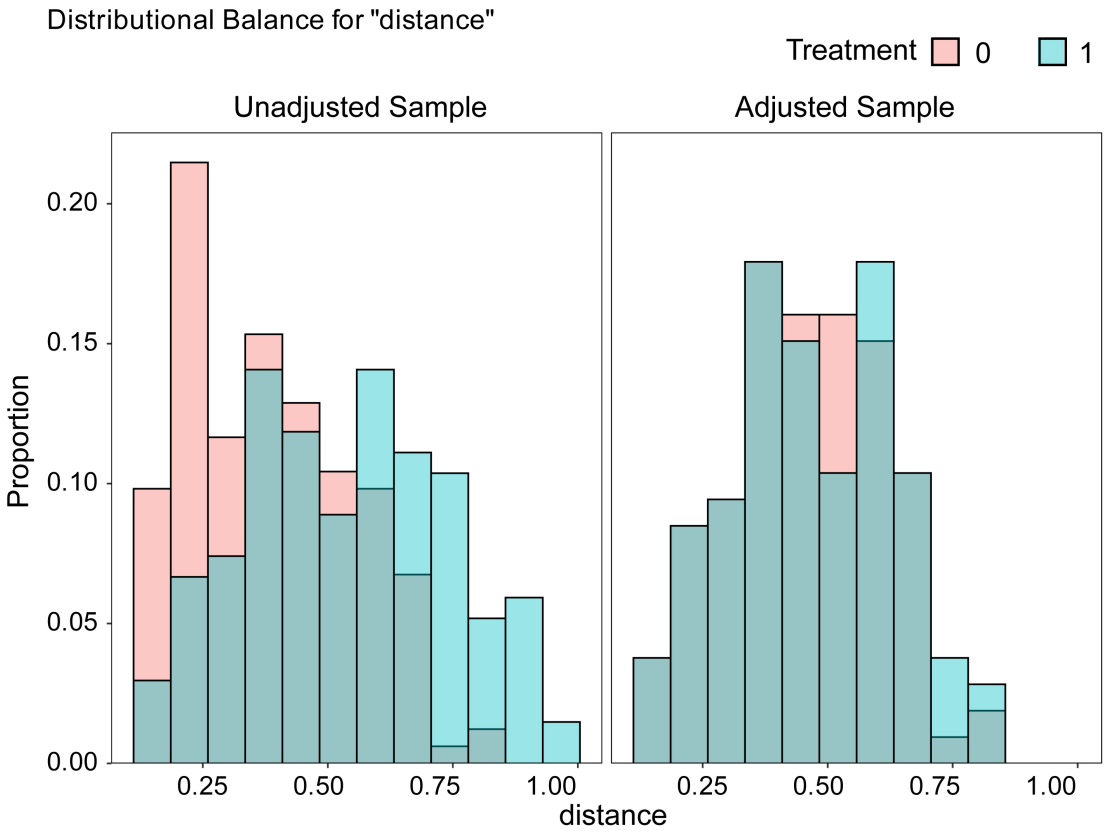

Fig. 1. Probability density analysis plot.

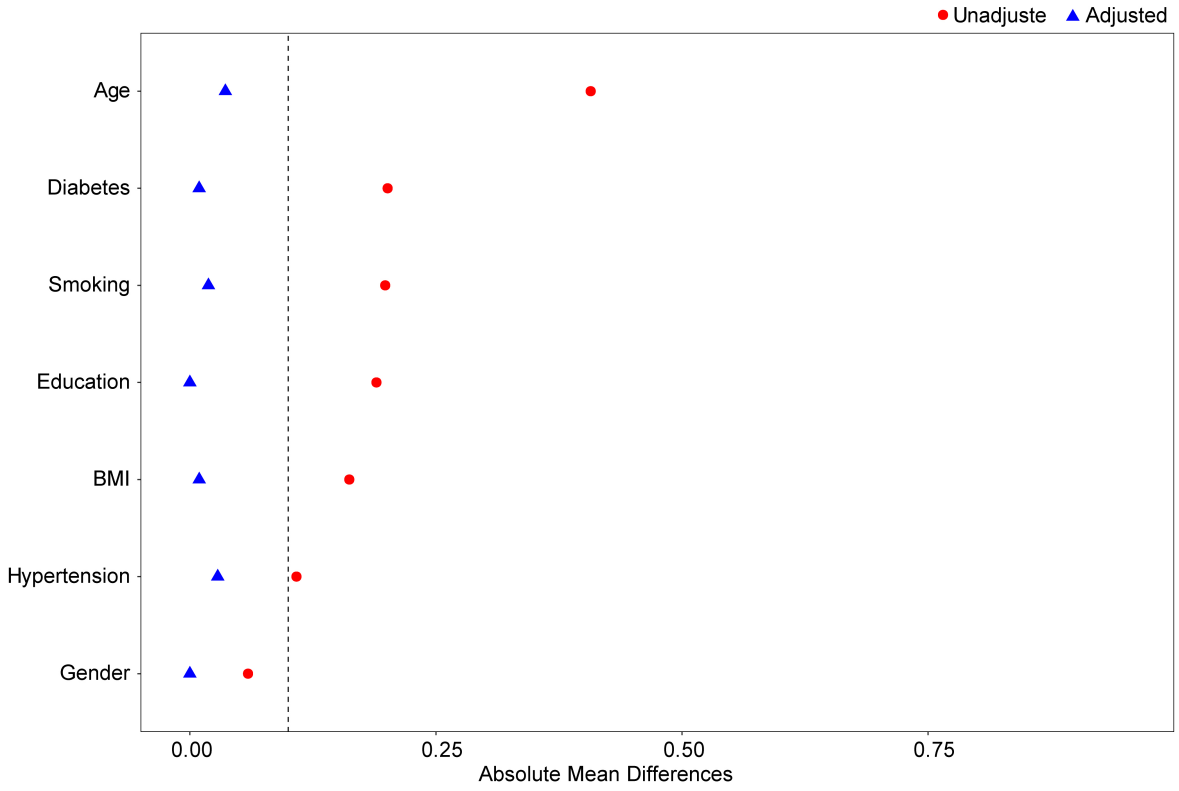

Fig. 2. Standardized Mean Difference (SMD) analysis plot.

Table 3. Single and multiple factor logistic regression results.

Variables	Univariate analysis					Multivariable analysis				
	β	SE	Z	*p*	OR (95% CI)	*β*	SE	Z	*p*	OR (95% CI)
SII (per 100 units)	0.48	0.14	3.46	<0.001	1.62 (1.23~2.13)	0.49	0.14	3.43	<0.001	1.63 (1.23~2.16)
Gender										
Male					1.00 (Reference)					1.00 (Reference)
Female	0.00	0.28	0.00	1.000	1.00 (0.58~1.73)	0.05	0.30	0.17	0.867	1.05 (0.58~1.89)
Smoking status										
Non-current smokers					1.00 (Reference)					1.00 (Reference)
Current smokers	0.08	0.28	0.28	0.782	1.08 (0.63~1.86)	–0.03	0.30	–0.09	0.930	0.97 (0.54~1.74)
Diabetes mellitus										
NO					1.00 (Reference)					1.00 (Reference)
YES	0.05	0.33	0.16	0.871	1.05 (0.56~2.00)	0.08	0.36	0.23	0.818	1.09 (0.53~2.21)
Hypertension										
NO					1.00 (Reference)					1.00 (Reference)
YES	0.12	0.29	0.43	0.668	1.13 (0.65~1.98)	–0.02	0.30	–0.07	0.947	0.98 (0.54~1.78)
Educational level										
Junior high school and above					1.00 (Reference)					1.00 (Reference)
Below junior high school	0.00	0.28	0.00	1.000	1.00 (0.58~1.72)	–0.05	0.38	–0.13	0.896	0.95 (0.45~2.00)
Age	0.00	0.02	0.26	0.793	1.00 (0.97~1.04)	0.00	0.02	0.03	0.979	1.00 (0.96~1.05)
BMI	–0.01	0.07	–0.08	0.939	0.99 (0.87~1.13)	–0.02	0.07	–0.35	0.726	0.98 (0.85~1.12)

OR, Odds Ratio; CI, Confidence Interval.

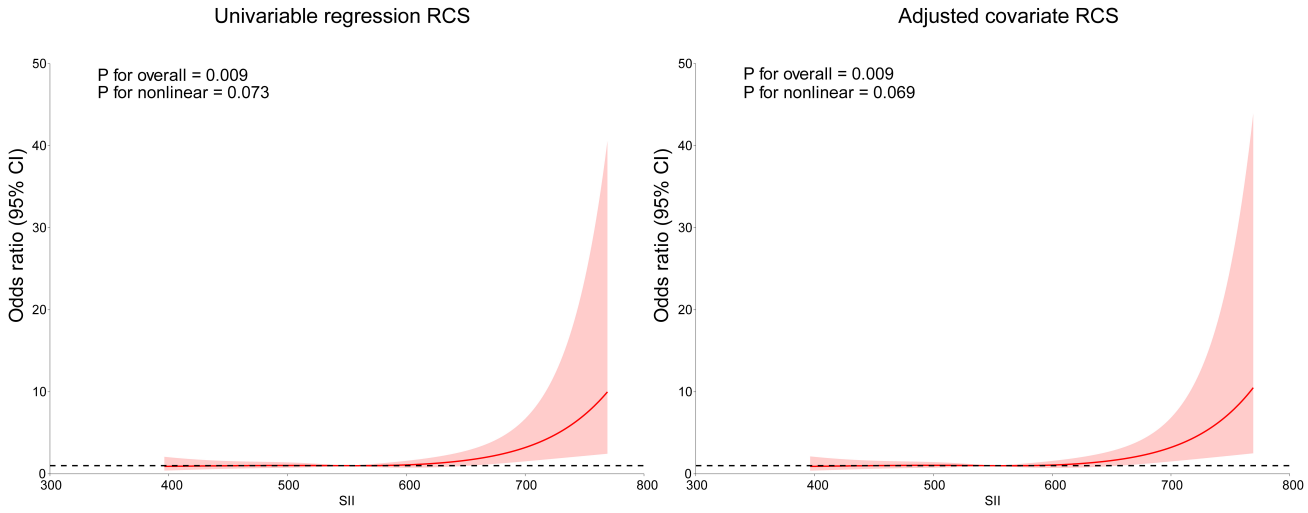

Fig. 3. Restricted Cubic Spline (RCS) plot.

Discussion

To the best of our knowledge, this is the first retrospective study to employ PSM to rigorously evaluate the utility of SII in differentiating between generalized Stage III and Stage IV periodontitis. The principal finding of this study is that, even after rigorous adjustment for systemic confounders—including age, gender, smoking status, diabetes mellitus, and hypertension—SII levels remained significantly elevated in patients with Stage IV periodontitis compared to those with Stage III. Multivariate logistic regression analysis corroborated that elevated SII constitutes an independent risk factor for Stage IV periodontitis. Of particular significance, Restricted Cubic Spline (RCS) analysis unveiled a distinct linear dose-response relationship between SII levels and the risk of Stage IV periodontitis. This implies that the severity of periodontal destruction increases in parallel with the systemic inflammatory burden, without evidence of a non-linear threshold effect. Collectively, these findings support the role of SII as a highly sensitive biomarker capable of precisely capturing the nuanced differences in systemic inflammation across the severity spectrum from Stage III to Stage IV periodontitis.

Mechanistically, SII integrates neutrophil, platelet, and lymphocyte counts, thereby offering a comprehensive reflection of the equilibrium between innate immunity,

thrombotic potential, and adaptive immunity [13]. Relative to Stage III, Stage IV periodontitis is characterized not only by more severe attachment loss but also by extensive tooth loss and complex occlusal collapse [22]. These clinical manifestations result in a larger Periodontal Inflamed Surface Area (PISA) and more frequent masticatory trauma, significantly exacerbating the systemic inflammatory burden [23–25]. As the host's first line of defense against periodontal pathogens, neutrophils are extensively recruited in severe periodontitis. Their activation triggers the release of reactive oxygen species (ROS) and proteases, which contribute to local tissue destruction and may also enter the peripheral circulation [26]. Concurrently, patients with Stage IV disease may experience more frequent episodes of transient bacteremia; the translocation of periodontal pathogens into the bloodstream can activate platelets and induce the release of pro-inflammatory cytokines such as IL-1 and IL-6 [20]. In our study, the observed elevation of SII parallels disease severity. The relative reduction in lymphocytes—the denominator of the index—may reflect immune suppression or lymphocyte exhaustion resulting from chronic inflammatory stress. This lymphopenia synergizes with the upregulation of innate immunity and thrombotic activity, further amplifying and perpetuating the hyper-inflammatory state characteristic of Stage IV patients [27].

A principal methodological strength of this study lies in the application of PSM to maximally mitigate the selection bias inherent in observational research [28]. As evidenced by our pre-matching baseline data, patients with Stage IV periodontitis were significantly older and exhibited a higher prevalence of smoking, diabetes mellitus, and hypertension compared to those with Stage III disease. Given that these factors are intrinsically associated with elevated systemic inflammatory markers, without rigorous control, it would be challenging to disentangle whether the observed elevation in SII stems from the aggravation of periodontal pathology or merely from advanced age and comorbid burdens [29]. By creating a cohort balanced across all covariates using PSM, we effectively isolated the independent impact of periodontal staging on SII. The persistence of significant differences in SII levels post-matching further corroborates that periodontal disease severity per se is a pivotal driver of systemic immune-inflammatory dysregulation, providing greater robustness compared to conventional multivariate regression models alone.

The findings of this study exhibit substantial clinical and translational value. Although the distinction between Stage III and Stage IV periodontitis in the 2017 classification is primarily predicated on tooth loss and the complexity of occlusal rehabilitation [5], our RCS analysis suggested a positive linear correlation, indicating that patients with Stage IV periodontitis endure not only greater challenges in oral rehabilitation but also a significantly heightened systemic inflammatory burden. Unlike sophisticated molecular biomarkers (e.g., cytokine assays) that necessitate specific testing, SII can be derived from routine blood counts without additional expenditure, thereby positioning it as a highly cost-effective and accessible adjunctive tool for stratifying systemic health risks. Specifically, in Stage IV patients with aberrantly elevated SII levels, clinicians should remain alert to potential underlying cardiovascular or metabolic risks [30]. Consequently, our findings strongly advocate for a paradigm shift from a strictly periodontal-focused treatment approach toward a multidisciplinary management model, thereby facilitating the early identification and intervention for systemic risk factors [20].

Despite the rigorous design, this study has several limitations. First, as a retrospective study, we could only establish a strong association between SII and periodontal staging rather than a causal relationship; whether elevated inflammatory levels drive progression to Stage IV, or Stage IV pathology leads to elevated SII, still requires verification in prospective cohort studies. Second, although PSM effectively controlled for major confounding factors, the retrospective nature of the data precluded adjustment for potential variables such as oral hygiene habits and genetic background. Third, given that SII is a non-specific inflammatory marker, its diagnostic specificity for periodontal staging may be compromised in patients with concurrent autoimmune or hematologic disorders, which can obscure the periodontal inflammatory signal; thus, our findings are primarily applicable to patients without severe active systemic comorbidities. Finally, this single-center design and predominance of patients from a tertiary hospital may limit the generalizability of the conclusions. Therefore, further validation in more diverse populations is warranted.

Conclusion

In conclusion, utilizing propensity score matching analysis, this study provides robust evidence that, even after rigorous adjustment for systemic confounders, elevated SII is independently associated with the diagnosis of Stage IV periodontitis. Furthermore, restricted cubic spline analysis elucidated a significant linear dose-response relationship between SII levels and the risk of Stage IV periodontitis, indicating that the systemic inflammatory burden increases progressively with the severity of periodontal destruction. As a cost-effective and readily accessible hematological parameter, SII shows promise not only as an objective biomarker for the adjunctive differentiation between Stage III and Stage IV periodontitis but also provides novel insights for assessing the systemic inflammatory status in patients with severe periodontitis. These findings highlight critical clinical implications: in patients with Stage IV periodontitis, clinicians should address both oral functional rehabilitation and potential systemic health risks, adopting a multidisciplinary management strategy.

Availability of Data and Materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions

YW and DDZ designed the research study. DDZ performed the research. YW and DDZ analyzed the data. YW drafted the article. Both authors contributed to important editorial changes in the manuscript. Both authors read and approved the final manuscript. Both authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The study was conducted in accordance with the Declaration of Helsinki. This study protocol was approved by the Ethics Committee of Cangnan Hospital of Wenzhou Medical University (The People's Hospital of Cangnan) (Approval No.: 2025087). All patient information was anonymized to protect privacy. As a retrospective observational study, the Ethics Committee granted a waiver for the requirement of informed consent.

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Conflict of Interest

The authors declare no conflict of interest.

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