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ORIGINAL RESEARCH

Impact of Early Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio Decrease After Continuous Positive Airway Pressure on Glycaemic Control in Type 2 Diabetes with Obstructive Sleep Apnea

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Purpose: The aim of this study is to evaluate the relationship between changes in Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR) within 7 days after Continuous positive airway pressure (CPAP) treatment and long-term glycaemic control.
Methods: This study retrospectively included 650 Type 2 diabetes (T2DM) and Obstructive sleep apnea (OSA) patients treated with CPAP. Patients were divided into two groups based on whether long-term glycaemic control was effective or ineffective, and differences in baseline and disease-related characteristics between the two groups were compared. We constructed a multi factor logistic regression model to analyze the impact of the decrease in NLR and PLR within the first 7 days after treatment on long-term glycaemic control. We used restricted cubic spline analysis and Receiver Operating Characteristic (ROC) curve analysis to evaluate the relationship between the decrease in NLR and PLR and long-term glycaemic control.
Results: In three multiple logistic regression models, it was observed that the decrease in NLR and PLR was an independent factor affecting long-term glycaemic improvement. The limited cubic spline analysis showed that the decrease in NLR and PLR was linearly or approximately linearly positively correlated with long-term glycaemic improvement. The interaction indicates that in patients who use CPAP for a longer period of time every night, the decrease in NLR has a stronger impact on long-term glycaemic improvement. The ROC curve indicates that both NLR and PLR have good and similar predictive abilities in terms of the magnitude of decline.
Conclusion: The decrease in NLR and PLR within 7 days after the start of CPAP treatment is significantly correlated with long-term glycaemic improvement in T2DM patients with OSA, and there is a significant interaction with the duration of CPAP use per night. This study suggests that the decrease in NLR and PLR can serve as potential predictors of CPAP efficacy, providing new ideas for early intervention and optimization of treatment plans.

Keywords: continuous positive airway pressure, CPAP, type 2 diabetes mellitus, T2DM, obstructive sleep apnea, OSA, inflammatory factors, efficacy prediction

Introduction

Type 2 diabetes (T2DM) is a chronic metabolic disorder characterized primarily by insulin resistance and relative insulin deficiency.[1,2] The global prevalence continues to rise, representing a growing public health concern. Populations most commonly affected include individuals with obesity, the elderly, and other high-risk groups. The main symptoms include polyuria, polydipsia, and fatigue.[3,4] Obstructive sleep apnea (OSA) is a common sleep-related breathing disorder characterized by recurrent episodes of partial or complete upper airway obstruction during sleep, leading to intermittent pauses in respiration.[5] The primary symptoms include snoring, sudden awakenings during sleep, daytime sleepiness, and

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difficulty concentrating. OSA is closely linked to T2DM. Studies have shown that diabetes can exacerbate the occurrence of sleep apnea, while sleep apnea further worsens glucose metabolism abnormalities, creating a vicious cycle through various metabolic pathways such as hypoxemia, sympathetic nervous system activation, and elevated inflammatory factors.[6,7]

Continuous Positive Airway Pressure (CPAP) therapy is widely regarded as the standard and most effective treatment for obstructive sleep apnea (OSA).[8] By continuously providing positive pressure airflow to patients, positive pressure ventilation can maintain the opening of the upper airway, prevent respiratory collapse, and significantly improve nighttime breathing disorders.[9] Positive pressure ventilation not only improves sleep quality and alleviates daytime sleepiness but has also been reported to potentially enhance metabolic function in patients with metabolic syndrome or diabetes.[10] Preliminary studies have suggested that positive pressure ventilation therapy may indirectly affect glucose metabolism, improve insulin sensitivity, and help control blood sugar by reducing sympathetic nervous system excitation, improving oxygenation status, and alleviating chronic hypoxemia.[11,12] In addition to improving respiratory function and sleep quality, CPAP treatment has been shown to confer beneficial effects on various metabolic parameters. Studies have indicated that CPAP can reduce systemic inflammation, alleviate oxidative stress, and regulate abnormal lipid metabolism, thereby lowering cardiovascular risk.[13] Furthermore, CPAP improves sleep architecture and supports hormonal regulation, thereby facilitating weight management and enhancing energy metabolism.[14] In patients with diabetes, the metabolic benefits of CPAP include improved insulin resistance and potentially better glycemic control, highlighting its important role in glucose metabolism regulation.[15]

In recent years, many studies have shown that Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR) are associated with the development of T2DM and OSA.[16,17] However, there is still a lack of systematic research on whether NLR and PLR are related to the long-term efficacy of CPAP treatment. Therefore, we hope to predict the long-term glycaemic control effect of CPAP through early changes in NLR and PLR after treatment, in order to identify high-risk patients for early warning and intervention.

Materials and Methods

Research Object

This study retrospectively recruited the type 2 diabetes patients with obstructive sleep apnea who received positive pressure ventilation from January 2020 to January 2023. Participants were eligible if they: (1) were ≥ 18 years old; (2) met American Academy of Sleep Medicine (AASM) diagnostic criteria for obstructive sleep apnea (OSA)—either moderate-to-severe disease (apnea–hypopnea index [AHI] ≥ 15 events·h^{-1}) confirmed by polysomnography (PSG) or mild disease ($5 \leq \text{AHI} < 15$ events·h^{-1}) accompanied by clinically significant daytime sleepiness,[18] nocturnal choking, nadir oxygen saturation $< 85\%$, or comorbid hypertension, coronary artery disease, or poorly controlled diabetes warranting CPAP therapy;[19] and (3) possessed complete clinical records. Patients were excluded if they: (1) received concurrent alternative therapeutic interventions; (2) had malignant neoplasms or other severe systemic disorders; (3) exhibited marked hepatic or renal impairment; (4) suffered from major psychiatric illness or demonstrated poor treatment compliance; or (5) had incomplete laboratory data. CPAP adherence was assessed using usage data recorded by the device memory card. CPAP Adherence was quantified via device memory–card downloads. Consistent with established clinical standards, adequate adherence was defined as CPAP use ≥ 4 h·night^{-1} for $\geq 70\%$ of nights per week.[9] Only participants meeting this threshold were retained for analysis. Assuming a medium effect size ($d = 0.5$), 80% statistical power, and $\alpha = 0.05$, power analysis indicated minimum enrolment of 64 participants per group for continuous outcomes, 272 per group for categorical outcomes, and a total of ≥ 118 participants for multivariable logistic-regression modelling.

Treatment Methods

Patients received standardized antihyperglycemic therapy followed by nocturnal CPAP ventilation via nasal mask. During the initial treatment night, optimal positive pressure was titrated with the mask securely fitted. Subsequently, nightly CPAP therapy was administered for 4–8 hours at a pressure range of 4.0–20 cm H_2O (1 cm H_2O = 0.098 kPa), maintained consistently for 6 months.

Data Collection

We collected baseline information and disease-related features of patients, including Age, Gender, Body Mass Index (BMI), Smoking, Drinking, Cardiovascular Disease, Diabetic Complications, Physical Activity, Duration of diabetes, Apnea-Hypopnea Index (AHI), Lowest Peripheral Oxygen Saturation (SpO2), Sleep duration, Percentage of deep sleep. CPAP adherence was assessed using usage data recorded by the device's memory card. The evaluation indicators included Nightly Usage Time and Frequency of Use. Hemoglobin A1c (HbA1c), Fasting Blood Glucose (FBG), Homeostasis Model Assessment of Insulin Resistance (HOMA-IR).

We collected baseline and 7-day post-treatment NLR and PLR values, and calculated the absolute reductions by subtracting post-treatment levels from baseline measurements to quantify the magnitude of NLR and PLR decline. We also collected HbA1c and FBG levels 6 months after treatment. According to established criteria reported in the literature,[20] effective glycemic control was defined as achieving a post-treatment hemoglobin A1c (HbA1c) level of <7% or a reduction of >0.5%, and/or a fasting blood glucose (FBG) level of <7.2 mmol/L or a decrease of >10% from baseline.

Statistical Analysis

All analyses were performed in R (v 4.4.0). Continuous variables are presented as median (minimum–maximum) and compared with either the independent-samples *t*-test or the Mann–Whitney *U*-test, as appropriate. Categorical variables are expressed as frequency (percentage) and analysed with the χ^2-test or Fisher's exact test. Reductions in NLR and PLR were stratified into quartiles (Q1–Q4), glycaemic control status (effective vs ineffective) served as the dependent variable. Three multivariable logistic-regression models were fitted. Model 1 included only the NLR and PLR reductions. Model 2 additionally adjusted for age, sex, and BMI. Model 3 further adjusted for AHI, nadir oxygen saturation, nightly CPAP usage duration, weekly CPAP usage frequency, baseline HbA1c, FBG, and HOMA-IR. Interaction analyses were conducted with Model 3. Restricted cubic-spline functions were employed to explore potential linear or non-linear associations between NLR/PLR reductions and long-term glycaemic control. Predictive performance was evaluated with receiver-operating-characteristic (ROC) analysis; areas under the curve (AUCs) were calculated and compared using DeLong's test to determine whether NLR or PLR offered superior prognostic accuracy.

Results

Differences in Baseline and Disease Characteristics Between Patients with Effective and Ineffective Glycaemic Control

The results showed that the proportion of males in the ineffective group was significantly higher than that in the effective group (71.7% vs 62.94%, P=0.02198). The apnea hypopnea index (AHI) was significantly higher in the ineffective group compared to the effective group (23 vs 20, P=0.00634). The lowest blood oxygen saturation was significantly lower in the ineffective group than in the effective group (87.3% vs 89.5%, P=0.00516).

Additionally, the duration of CPAP device use per night was shorter in the ineffective group (5.1 vs 5.4 hours, P=0.0399). The percentage of patients using the device for ≥ 3 days/week was also lower in the ineffective group compared to the effective group (46.7% vs 58.04%, P=0.01038).

Glycated hemoglobin (HbA1c), fasting blood glucose (FBG), and HOMA-IR were all significantly higher in the ineffective group than in the effective group (FBG: 10.8 vs 10.3, P=0.043; HOMA-IR: 3.0 vs 2.7, P=0.017). Other indicators such as age and BMI showed no significant differences between the two groups (Table 1).

Relationship Between the Decrease in NLR and PLR and Improvement in Blood Glucose Levels

In Model 1, a significant positive correlation was observed between the decrease in NLR and improvement in blood glucose levels (Q3 vs Q1, OR=1.085, P=0.001) (Q4 vs Q1, OR=1.560, P<0.0001). In Model 2, it was also found that there was a significant positive correlation between the decrease in NLR and the improvement in blood glucose (Q4 vs

Table 1 The Baseline Information and Disease Characteristics Differences Between Effective and Ineffective Blood Sugar Control

	All Patients (n=650)	**Effective (n=286)**	**Ineffective (n=364)**	**P-value**
Age	52 (34–69)	51 (34–69)	52 (34–69)	0.67
Gender*				0.021983
Male	441 (67.85%)	180 (62.94%)	261 (71.7%)	
Female	209 (32.15%)	106 (37.06%)	103 (28.3%)	
BMI	28.3 (23.4–33.2)	28.1 (23.4–33.2)	28.4 (23.4–33.2)	0.419
Smoking				0.723406
Yes	144 (22.15%)	61 (21.33%)	83 (22.8%)	
No	506 (77.85%)	225 (78.67%)	281 (77.2%)	
Drinking				0.069728
Yes	141 (21.69%)	72 (25.17%)	69 (18.96%)	
No	509 (78.31%)	214 (74.83%)	295 (81.04%)	
Cardiovascular Disease				0.128501
Yes	228 (35.08%)	110 (38.46%)	118 (32.42%)	
No	422 (64.92%)	176 (61.54%)	246 (67.58%)	
Diabetic Complications				0.627576
Yes	351 (54%)	158 (55.24%)	193 (53.02%)	
No	299 (46%)	128 (44.76%)	171 (46.98%)	
Physical Activity				0.849615
Low	385 (59.23%)	169 (59.09%)	216 (59.34%)	
Moderate	218 (33.54%)	98 (34.27%)	120 (32.97%)	
High	47 (7.23%)	19 (6.64%)	28 (7.69%)	
Duration of diabetes				0.129392
< 5 years	229 (35.23%)	95 (33.22%)	134 (36.81%)	
5–10 years	265 (40.77%)	129 (45.1%)	136 (37.36%)	
> 10 years	156 (24%)	62 (21.68%)	94 (25.82%)	
Apnea-Hypopnea Index, AHI*	21 (9–32)	20 (9–32)	23 (9–32)	0.00634
Lowest SpO2*	88.2 (82.0–95.0)	89.5 (82.1–95.0)	87.3 (82.0–95.0)	0.00516
Sleep duration	6.0 (4.5–7.8)	6.2 (4.5–7.8)	6.0 (4.5–7.8)	0.225
Percentage of deep sleep				0.09894
< 20%	244 (37.54%)	120 (41.96%)	124 (34.07%)	
20–40%	350 (53.85%)	141 (49.3%)	209 (57.42%)	
> 40%	56 (8.62%)	25 (8.74%)	31 (8.52%)	
Nightly Usage Time*	5.3 (3.2–7.1)	5.4 (3.2–7.1)	5.1 (3.2–7.1)	0.0399
Frequency of Use*				0.010384
< 3 days	160 (24.62%)	57 (19.93%)	103 (28.3%)	
3–5 days	336 (51.69%)	166 (58.04%)	170 (46.7%)	
> 5 days	154 (23.69%)	63 (22.03%)	91 (25%)	
Hemoglobin A1c, HbA1c (%)*	7.2 (6.5–7.9)	7.1 (6.5–7.9)	7.2 (6.5–7.9)	0.00548
Fasting Blood Glucose, FBG (mmol/L)*	10.5 (7.2–13.9)	10.3 (7.2–13.9)	10.8 (7.2–13.9)	0.043
Homeostasis Model Assessment of Insulin Resistance, HOMA-IR*	2.9 (1.8–4.0)	2.7 (1.8–4.0)	3.0 (1.8–4.0)	0.017

Note: *Indicates statistical significance.

Q1, OR=1.555, P<0.0001). After adjusting multiple confounding factors in model 3, the decline of NLR was still positively correlated with the improvement of blood glucose (Q4 vs Q1, OR=1.530, P<0.0001) (Table 2).

In Model 1, Q2, Q3, and Q4 showed a significant positive correlation with glycaemic improvement compared to Q1 (Q2 vs Q1, OR=1.166, P=0.004) (Q3 vs Q1, OR=1.209, P<0.0001) (Q4 vs Q1, OR=1.438, P<0.0001). In Model 2, there was a significant positive correlation between Q2, Q3, and Q4 and glycaemic improvement (Q2 vs Q1, OR=1.165, P=0.004) (Q3 vs Q1, OR=1.206, P<0.0001) (Q4 vs Q1, OR=1.442, P<0.0001). In Model 3, the effects of Q2, Q3, and Q4 on glycaemic improvement were still significant compared to the reference group (Q2 vs Q1, OR=1.143, P=0.010) (Q3 vs Q1, OR=1.200, P<0.0001) (Q4 vs Q1, OR=1.449, P<0.0001), but the OR values were lower than those of Model 1 and Model 2, indicating a weaker effect (Table 3).

Table 2 Multivariate Logistic Regression Analysis of the Association Between the Reduction in NLR and Improvement in Blood Glucose Control

	NLR Decrease	Estimate	std.error	Statistic	p.value	OR	CI_lower	CI_upper
Model 1	Q1 (Reference)	Ref	Ref	Ref	Ref	Ref	Ref	Ref
	Q2	0.061	0.051	1.194	0.233	1.063	0.961	1.176
	Q3*	0.081	0.025	3.201	0.001	1.085	1.032	1.140
	Q4*	0.445	0.052	8.628	0.000	1.560	1.410	1.726
Model 2	Q1 (Reference)	Ref	Ref	Ref	Ref	Ref	Ref	Ref
	Q2	0.060	0.051	1.161	0.246	1.062	0.960	1.174
	Q3	0.030	0.051	0.591	0.555	1.031	0.932	1.140
	Q4*	0.442	0.052	8.554	0.000	1.555	1.406	1.721
Model 3	Q1 (Reference)	Ref	Ref	Ref	Ref	Ref	Ref	Ref
	Q2	0.055	0.050	1.081	0.280	1.056	0.957	1.166
	Q3	0.042	0.050	0.831	0.406	1.043	0.945	1.151
	Q4*	0.425	0.051	8.388	0.000	1.530	1.385	1.690

Notes: Model 1: Unadjusted. Model 2: Adjusted for age, gender, and BMI. Model 3: Adjusted for age, gender, BMI, AHI, lowest blood oxygen, nightly CPAP usage duration, weekly CPAP usage frequency, HbA1c, FBG, and HOMA-IR. "Reference" or "ref" in the table indicates the reference group used for comparison of relative risks among other groups, and does not refer to a bibliographic citation. *Indicates statistical significance.

Table 3 Multivariate Logistic Regression Analysis of the Association Between the Reduction in PLR and Improvement in Blood Glucose Control

	PLR Decrease	Estimate	std.error	Statistic	p.value	OR	CI_lower	CI_upper
Model 1	Q1 (Reference)	Ref	Ref	Ref	Ref	Ref	Ref	Ref
	Q2*	0.153	0.053	2.880	0.004	1.166	1.050	1.294
	Q3*	0.190	0.053	3.571	0.000	1.209	1.090	1.343
	Q4*	0.364	0.053	6.805	0.000	1.438	1.295	1.597
Model 2	Q1 (Reference)	Ref	Ref	Ref	Ref	Ref	Ref	Ref
	Q2*	0.153	0.053	2.875	0.004	1.165	1.050	1.293
	Q3*	0.188	0.053	3.533	0.000	1.206	1.087	1.339
	Q4*	0.366	0.053	6.861	0.000	1.442	1.299	1.601
Model 3	Q1 (Reference)	Ref	Ref	Ref	Ref	Ref	Ref	Ref
	Q2*	0.134	0.052	2.581	0.010	1.143	1.033	1.266
	Q3*	0.182	0.052	3.509	0.000	1.200	1.084	1.329
	Q4*	0.371	0.052	7.137	0.000	1.449	1.309	1.605

Notes: Model 1: Unadjusted. Model 2: Adjusted for age, gender, and BMI. Model 3: Adjusted for age, gender, BMI, AHI, lowest blood oxygen, nightly CPAP usage duration, weekly CPAP usage frequency, HbA1c, FBG, and HOMA-IR. "Reference" or "ref" in the table indicates the reference group used for comparison of relative risks among other groups, and does not refer to a bibliographic citation. *Indicates statistical significance.

Restricted cubic spline analysis showed that there was a significant correlation between the decrease in NLR and PLR and glycaemic improvement (P for TOTAL was less than 0.05). Nonlinear analysis shows that there is no significant nonlinear relationship between the decrease in NLR and PLR and glycaemic improvement (P for Nonlinear is greater than 0.05), indicating that there may be a linear or near linear relationship between them, and the greater the decrease in NLR and PLR, the higher the possibility of glycaemic improvement (Figure 1A and B).

Interaction Analysis Between NLR and PLR Decrease and Other Covariates

The interaction analysis demonstrated that the reduction in NLR and the duration of CPAP use per night were significantly positively correlated with glycaemic improvement (interaction term β=0.057, p=0.032, OR=1.059, 95% CI: 1.005–1.115). This finding suggested that the beneficial effect of NLR reduction on glycaemic control was progressively enhanced with longer nightly CPAP usage. No significant interactions were found between the decrease

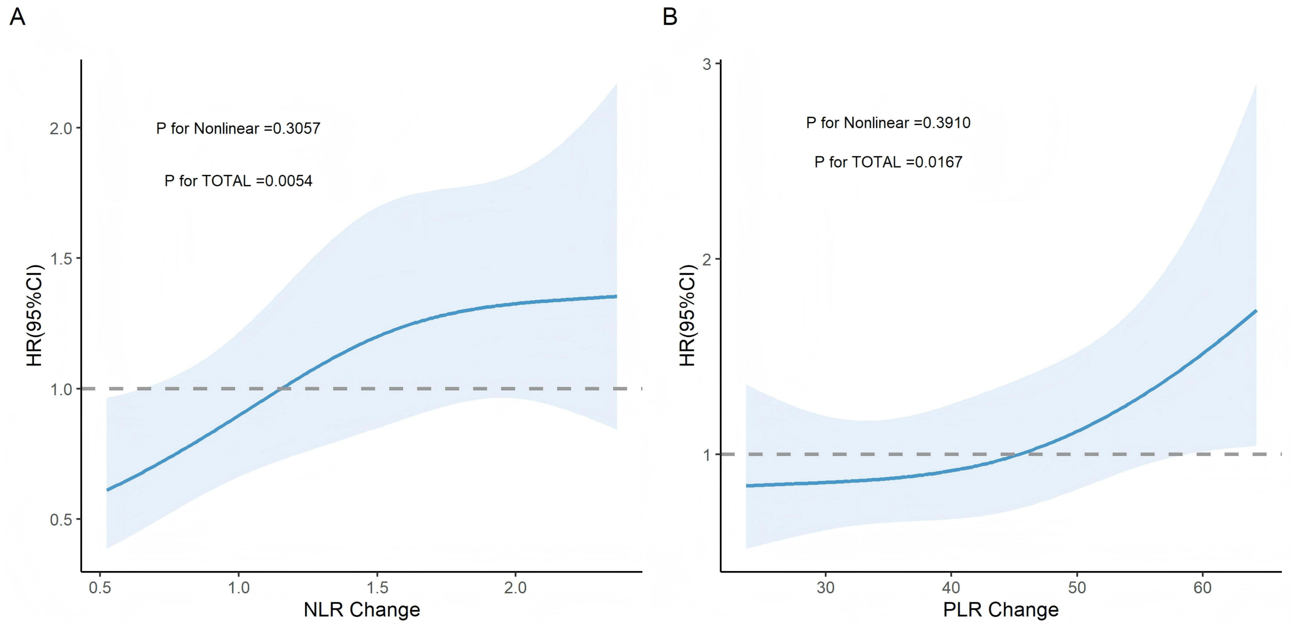

Figure 1 RCS Analysis (**A**) The association between the decrease in Neutrophil-to-Lymphocyte Ratio (NLR) and glycaemic improvement (P for Nonlinear = 0.3057, P for TOTAL = 0.0054) (**B**) The association between the decrease in Platelet-to-Lymphocyte Ratio (PLR) and glycaemic improvement (P for Nonlinear = 0.3910, P for TOTAL = 0.0167).

in NLR and other factors such as gender (p=0.833), AHI (p=0.819), or minimum blood oxygen saturation (p=0.742). Similarly, there were no significant interactions between the decline in PLR and gender, AHI, or the lowest blood oxygen levels (Table 4).

ROC Curve Evaluation of the Predictive Effect of the Decrease in NLR and PLR on Glycaemic Improvement

The results demonstrated that the AUCs values for NLR and PLR were 0.602 and 0.601, respectively, indicating comparable predictive performance. Glycaemic improvement was observed when reductions in NLR and PLR surpassed thresholds of 1.538 and 38.232, respectively. Further analysis using DeLong's test yielded a P-value of 0.7023, confirming that both the decrease in NLR and PLR effectively predict glycaemic improvement, with no significant difference in their predictive abilities (Figure 2A and B).

Table 4 Interaction Analysis Between the Reductions in NLR and PLR and Other Covariates

	Estimate	Std error	Statistic	P value	OR	CI-lower	CI-upper
NLR×Gender	0.015	0.071	0.211	0.833	1.015	0.883	1.167
NLR×AHI	0.001	0.005	0.229	0.819	1.001	0.992	1.011
NLR×Lowest.SpO2	0.003	0.009	0.329	0.742	1.003	0.986	1.020
NLR×Usage Time*	0.057	0.026	2.148	0.032	1.059	1.005	1.115
NLR×HbA1c	−0.020	0.082	−0.239	0.811	0.981	0.835	1.151
NLR×HOMA.IR	−0.084	0.051	−1.652	0.099	0.920	0.832	1.016
PLR×Gender	−0.001	0.004	−0.424	0.672	0.999	0.992	1.005
PLR×AHI	0.000	0.000	−0.427	0.670	1.000	0.999	1.000
PLR×Lowest.SpO2	0.000	0.000	−0.743	0.458	1.000	0.999	1.001
PLR×Usage Time	−0.001	0.001	−0.724	0.469	0.999	0.996	1.002
PLR×HbA1c	−0.005	0.004	−1.216	0.224	0.995	0.988	1.003
PLR×FBG	0.001	0.001	0.749	0.454	1.001	0.999	1.002
PLR×HOMA.IR	−0.001	0.002	−0.361	0.718	0.999	0.994	1.004

Notes: ×Indicates interaction. *Indicates statistical significance.

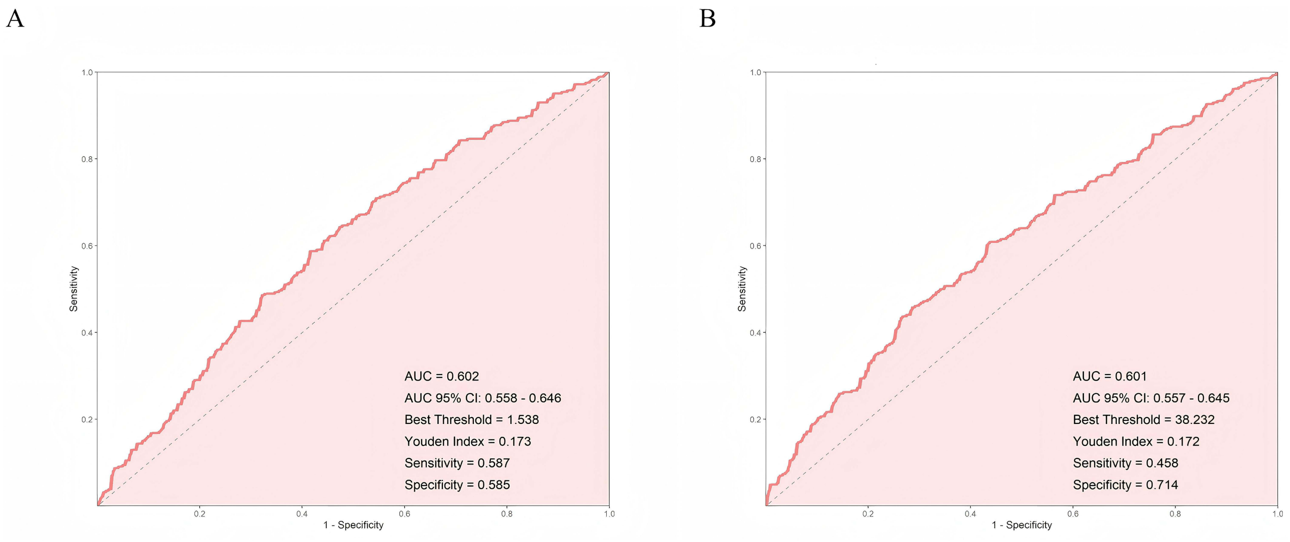

Figure 2 (**A**) ROC curve of the decrease in NLR (AUC= 0.602, AUC 95% CI: 0.558–0.646, Threshold = 1.538, Youden index = 0.173, Sensitivity= 0.587, Specificity = 0.585) (**B**) ROC curve of the decrease in PLR (AUC= 0.601, AUC 95% CI: 0.557–0.645, Threshold = 38.232, Youden index = 0.172, Sensitivity= 0.458, Specificity = 0.714).

Discussion

Glycaemic control is essential for patients with type 2 diabetes complicated by obstructive sleep apnea. Evidence suggests that intermittent hypoxia characteristic of OSA induces oxidative stress and elevates systemic inflammation, thereby exacerbating insulin resistance. Consequently, blood glucose levels rise, and chronic hyperglycemia can impair autonomic nervous system function, further exacerbating obstructive sleep apnea. Moreover, sustained poor glycaemic control contributes to endothelial dysfunction and increases the risk of atherosclerosis, hypertension, and other cardiovascular diseases.

This study demonstrated that the reductions in NLR and PLR within seven days after CPAP treatment are closely associated with long-term glycaemic control outcomes. NLR, as a common inflammatory marker, is usually associated with the systemic inflammatory state and immune balance of the body.[21] Patients with T2DM and OSA typically exhibit elevated NLR levels, potentially due to hyperglycemia–induced upregulation of pro-inflammatory cytokines.[22,23] The intermittent hypoxia (IH) symptoms observed by patients at night can increase the activity of the NF-κB pathway, further elevating the levels of inflammatory factors.[24] CPAP treatment addresses the fundamental pathological issue of OSA—intermittent hypoxia and reoxygenation caused by repeated nighttime breathing pauses—by maintaining the openness of the upper airway. This, in turn, reduces the levels of oxidative stress markers.[25,26] As a result, the patient's sleep architecture was significantly improved, accompanied by reduced sympathetic nervous system activity, lowered cortisol levels, and decreased neutrophil release, leading to a reduction in NLR levels. Additionally, PLR serves as a biomarker for inflammation and thrombosis. In T2DM, elevated blood glucose levels promote platelet activation and worsen endothelial damage.[27,28] Long term chronic low-grade inflammation can lead to a decrease in lymphocytes, resulting in further elevation of PLR.[29] Intermittent hypoxia and sleep fragmentation in OSA contribute to platelet activation and heightened inflammatory responses, resulting in increased PLR levels.[30] CPAP treatment reduces HIF-1 α levels by improving intermittent hypoxia, thereby lowering platelet levels.[31] Optimizing the patient's sleep structure also reduces cortisol levels, inhibits lymphocyte apoptosis, and increases lymphocyte counts, resulting in a decrease in PLR levels. Patients who show a significant reduction in NLR and PLR levels early in treatment demonstrate marked improvement in inflammatory status and exhibit greater sensitivity to therapy. Consequently, these patients are more likely to benefit from long-term treatment.

Interaction analysis indicates that among patients with longer nightly CPAP usage, reductions in NLR exert a more pronounced effect on long-term treatment outcomes, underscoring the critical role of adherence. This also suggests that clinicians should emphasize consistent CPAP use when advising patients to achieve better glycaemic control.

Our ROC analysis indicates comparable predictive performance between reductions in NLR and PLR. Although both NLR and PLR are inflammatory indicators, they have different mechanisms. NLR is often associated with acute inflammation and activation of immune responses, while PLR is often associated with chronic inflammation or blood coagulation. These two factors predict the long-term efficacy of CPAP from different perspectives and can both serve as potential predictors of glycaemic improvement, providing more choices for clinical doctors' judgment. The development of these biomarkers also provides a new method for predicting the long-term efficacy of CPAP treatment in T2DM patients with OSA, which helps to develop personalized treatment plans.

NLR and PLR, as simple, economical, and easily obtainable blood inflammatory markers, have certain clinical monitoring value. In patients with T2DM combined with OSA, evaluating changes in NLR and PLR within 7 days after CPAP treatment not only helps assess the trend of inflammatory responses but may also provide information for predicting glycaemic control after CPAP therapy.

This study has several limitations. First, its retrospective design introduces potential selection bias. Second, the relatively small sample size limits the ability to fully exclude the influence of other factors on long-term glycaemic control. Therefore, in the future, more comprehensive influencing factors can be included, and dynamic analysis of factor changes can be incorporated to conduct prospective, larger scale randomized controlled trials. The AUC values for the reductions in NLR and PLR were 0.602 and 0.601, respectively, demonstrating a moderate predictive capability. However, the relatively low AUC values suggest that these markers alone may have limited effectiveness in predicting glycaemic control following CPAP treatment. Future studies should consider integrating NLR and PLR with additional metabolic and inflammatory markers to develop a multifactorial prediction models, thereby improving overall predictive accuracy.

Conclusion

This study indicates that reductions in NLR and PLR within seven days following CPAP treatment independently predict long-term glycaemic control, with comparable predictive efficacy. The reduction in NLR exhibits a stronger association with glycaemic control among patients who maintain longer nightly CPAP usage. This study provides a reference for predicting CPAP efficacy in patients with T2DM and OSA.

Data Sharing Statement

Due to the nature of this research, participants of this study did not agree for their data to be shared publicly, so supporting data is not available. Mengmeng Zhang is the lead author; Fuzai Yin is the correspondence author.

Ethics Clearance

This paper has been reviewed by relevant departments of our hospital, such as the Science and Education Department, Medical Department and Ethics Committee of Qinhuangdao First Hospital. The research content involved in this research meets the requirements of medical ethics and academic morality of our hospital, and the research content is reasonable, the risks are controllable, and there are no violations. The relevant research carried out is in line with the safe, standardized and true scientific research guiding principles, and in line with the requirements of the clinical research ethics code.

Informed Consent

All the selected patients were informed and agreed to the study and provided an informed consent to participate.

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Disclosure

The authors declare that there is no competing interest associated with the manuscript.

References

1. Javeed N, Matveyenko AV. Circadian etiology of type 2 diabetes mellitus. *Physiology*. 2018;33(2):138–150. doi:10.1152/physiol.00003.2018

2. Fletcher B, Gulanick M, Lamendola C. Risk factors for type 2 diabetes mellitus. *J Cardiovasc Nurs*. 2002;16(2):17–23. doi:10.1097/00005082-200201000-00003
3. Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. *Nat Rev Endocrinol*. 2018;14(2):88–98. doi:10.1038/nrendo.2017.151
4. Ali MK, Pearson-Stuttard J, Selvin E, et al. Interpreting global trends in type 2 diabetes complications and mortality. *Diabetologia*. 2022;65(1):3–13. doi:10.1007/s00125-021-05585-2
5. Muraki I, Wada H, Tanigawa T. Sleep apnea and type 2 diabetes. *J Diabetes Investig*. 2018;9(5):991–997. doi:10.1111/jdi.12823
6. Paschou SA, Bletsa E, Saltiki K, et al. Sleep apnea and cardiovascular risk in patients with prediabetes and type 2 diabetes. *Nutrients*. 2022;14:23. doi:10.3390/nu14234989
7. Ota H, Fujita Y, Yamauchi M, et al. Relationship between intermittent hypoxia and type 2 diabetes in sleep apnea syndrome. *Int J Mol Sci*. 2019;20:19. doi:10.3390/ijms20194756
8. Jordan AS, McSharry DG, Malhotra A. Adult obstructive sleep apnoea. *Lancet*. 2014;383(9918):736–747. doi:10.1016/s0140-6736(13)60734-5
9. Mehrtash M, Bakker JP, Ayas N. Predictors of continuous positive airway pressure adherence in patients with obstructive sleep apnea. *Lung*. 2019;197(2):115–121. doi:10.1007/s00408-018-00193-1
10. Pengo MF, Bonafini S, Fava C, et al. Cardiorespiratory interaction with continuous positive airway pressure. *J Thorac Dis*. 2018;10(Suppl 1):S57–s70. doi:10.21037/jtd.2018.01.39
11. Zhao X, Zhang W, Xin S, et al. Effect of CPAP on blood glucose fluctuation in patients with type 2 diabetes mellitus and obstructive sleep apnea. *Sleep Breath*. 2022;26(4):1875–1883. doi:10.1007/s11325-021-02556-0
12. Wei CY, Wang HL, Li J, et al. [Effect of continuous positive airway pressure upon 24 h changes of blood glucose level in patients with obstructive sleep apnea hypopnea syndrome and type 2 diabetes]. *Zhonghua Yi Xue Za Zhi*. 2009;89(38):2686–2689. Danish
13. Mahboub B, Kharaba Z, Ramakrishnan RK, et al. Continuous positive airway pressure therapy suppresses inflammatory cytokines and improves glucocorticoid responsiveness in patients with obstructive sleep apnea and asthma: a case-control study. *Ann Thorac Med*. 2022;17(3):166–172. doi:10.4103/atm.atm_37_22
14. O'Donnell C, Crilly S, O'Mahony A, et al. Continuous positive airway pressure but not GLP1-mediated weight loss improves early cardiovascular disease in obstructive sleep apnea: a randomized proof-of-concept study. *Ann Am Thorac Soc*. 2024;21(3):464–473. doi:10.1513/AnnalsATS.202309-821OC
15. Shang W, Zhang Y, Wang G, et al. Benefits of continuous positive airway pressure on glycaemic control and insulin resistance in patients with type 2 diabetes and obstructive sleep apnoea: a meta-analysis. *Diabetes Obes Metab*. 2021;23(2):540–548. doi:10.1111/dom.14247
16. Chen HL, Wu C, Cao L, et al. The association between the neutrophil-to-lymphocyte ratio and type 2 diabetes mellitus: a cross-sectional study. *BMC Endocr Disord*. 2024;24(1):107. doi:10.1186/s12902-024-01637-x
17. Adane T, Melku M, Worku YB, et al. The association between neutrophil-to-lymphocyte ratio and glycemic control in type 2 diabetes mellitus: a systematic review and meta-analysis. *J Diabetes Res*. 2023;2023:3117396. doi:10.1155/2023/3117396
18. Kapur VK, Auckley DH, Chowdhuri S, et al. Clinical practice guideline for diagnostic testing for adult obstructive sleep apnea: an American Academy of Sleep Medicine clinical practice guideline. *J Clin Sleep Med*. 2017;13(3):479–504. doi:10.5664/jcsm.6506
19. Patil SP, Ayappa IA, Caples SM, et al. Treatment of adult obstructive sleep apnea with positive airway pressure: an American Academy of Sleep Medicine clinical practice guideline. *J Clin Sleep Med*. 2019;15(2):335–343. doi:10.5664/jcsm.7640
20. Serdar MA, Serteser M, Ucal Y, et al. An assessment of HbA1c in diabetes mellitus and pre-diabetes diagnosis: a multi-centered data mining study. *Appl Biochem Biotechnol*. 2020;190(1):44–56. doi:10.1007/s12010-019-03080-4
21. Islam MM, Satici MO, Eroglu SE. Unraveling the clinical significance and prognostic value of the neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, systemic immune-inflammation index, systemic inflammation response index, and delta neutrophil index: an extensive literature review. *Turk J Emerg Med*. 2024;24(1):8–19. doi:10.4103/tjem.tjem_198_23
22. Shetty S, Chandrashekhar S, Chaya SK, et al. Role of neutrophil to lymphocyte ratio in predicting severity of obstructive sleep apnea. *Indian J Otolaryngol Head Neck Surg*. 2022;74(Suppl 3):5003–5007. doi:10.1007/s12070-021-02613-w
23. Altintas N, Çetinoğlu E, Yuceege M, et al. Neutrophil-to-lymphocyte ratio in obstructive sleep apnea; a multi center, retrospective study. *Eur Rev Med Pharmacol Sci*. 2015;19(17):3234–3240.
24. Lee MY, Wang Y, Mak JC, et al. Intermittent hypoxia induces NF-κB-dependent endothelial activation via adipocyte-derived mediators. *Am J Physiol Cell Physiol*. 2016;310(6):C446–55. doi:10.1152/ajpcell.00240.2015
25. Floras JS. Obstructive sleep apnea syndrome, continuous positive airway pressure and treatment of hypertension. *Eur J Pharmacol*. 2015;763(Pt A):28–37. doi:10.1016/j.ejphar.2015.06.024
26. Feinsilver SH. Obstructive sleep apnea: treatment with positive airway pressure. *Clin Geriatr Med*. 2021;37(3):417–427. doi:10.1016/j.cger.2021.04.004
27. Zaccardi F, Rocca B, Rizzi A, et al. Platelet indices and glucose control in type 1 and type 2 diabetes mellitus: a case-control study. *Nutr Metab Cardiovasc Dis*. 2017;27(10):902–909. doi:10.1016/j.numecd.2017.06.016
28. Kaur R, Kaur M, Singh J. Endothelial dysfunction and platelet hyperactivity in type 2 diabetes mellitus: molecular insights and therapeutic strategies. *Cardiovasc Diabetol*. 2018;17(1):121. doi:10.1186/s12933-018-0763-3
29. Atak B, Aktas G, Duman TT, et al. Diabetes control could through platelet-to-lymphocyte ratio in hemograms. *Rev Assoc Med Bras*. 2019;65(1):38–42. doi:10.1590/1806-9282.65.1.38
30. Attia MM, Qasim MA, Alhamwi HS, et al. Using the neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio as prognostic markers for obstructive sleep apnea: a systematic review and meta-analysis of observational studies. *Cureus*. 2024;16(10):e72539. doi:10.7759/cureus.72539
31. Yang C, Zhou Y, Liu H, et al. The role of inflammation in cognitive impairment of obstructive sleep apnea syndrome. *Brain Sci*. 2022;12:10. doi:10.3390/brainsci12101303