Am J Transl Res 2026;18(2):1489-1503
www.ajtr.org /ISSN:1943-8141/AJTR0170050

Original Article

Clinical value of combined serum galectin-9 and urine MCP-1 testing for assessment of systemic lupus erythematosus disease activity and early diagnosis of lupus nephritis

Fangwei Ma[1], Yuanhong Ou[2], Yunxiang Liu[1], Shiyan Ge[1]

[1]*Department of Rheumatology and Immunology, Liangshan Hospital of Integrated Traditional and Western Medicine, Liangshan Yi Autonomous Prefecture 615000, Sichuan, China;* [2]*Department of Urology, Liangshan Hospital of Integrated Traditional and Western Medicine, Liangshan Yi Autonomous Prefecture 615000, Sichuan, China*

Received November 17, 2025; Accepted January 30, 2026; Epub February 15, 2026; Published February 28, 2026

Abstract: Objectives: To investigate whether combined measurement of serum galectin-9 and urinary monocyte chemoattractant protein-1 (MCP-1) can serve as non-invasive biomarkers for assessing disease activity in systemic lupus erythematosus (SLE) and for the early identification of lupus nephritis (LN). Methods: This retrospective study included 148 SLE patients hospitalized between June 2022 and May 2025. Patients were divided into three groups: inactive SLE group (n=48), active SLE without LN group (n=40), and active SLE with LN group (n=60). Serum galectin-9, urinary MCP-1, and routine indices (e.g., complement levels, autoantibodies) were measured at admission. Results: Serum markers increased progressively with disease progression: galectin-9 levels (8.59 ± 0.63 vs. 9.68 ± 1.87 vs. 11.72 ± 2.14 ng/mL) and urinary MCP-1 levels (1.58 ± 0.42 vs. 2.85 ± 0.92 vs. 10.45 ± 3.18 pg/mg creatinine, all P<0.05). Correlation analysis showed that both biomarkers were associated with SLE disease activity (both P<0.05). Regarding the diagnosis of LN, the area under the curve (AUC) was 0.782 for galectin-9 and 0.796 for MCP-1. Combined detection further improved diagnostic performance, yielding an AUC of 0.866. Moreover, urinary MCP-1 levels were significantly higher in patients with proliferative LN than in those with non-proliferative LN (12.36 ± 3.28 vs. 8.25 ± 2.84 pg/mg creatinine; P<0.001). Conclusions: Combined assessment of serum galectin-9 and urine MCP-1 provides a non-invasive approach for evaluating overall disease activity in SLE and may facilitate early identification of LN. Compared to traditional indicators, this strategy had superior diagnostic accuracy.

Keywords: Systemic lupus erythematosus, lupus nephritis, galectin-9, monocyte chemoattractant protein-1, autoimmune disease biomarkers, early diagnosis

Introduction

Systemic lupus erythematosus (SLE) is a complex autoimmune disease characterized by abnormal immune system activation and multisystem involvement, with the kidneys being among the most frequently affected organs [1]. Consequently, lupus nephritis (LN) represents one of the most common complications of SLE. The clinical manifestations of SLE are highly heterogeneous. While some patients present with mild symptoms such as rash or joint pain, others may develop severe organ damage [2]. About 60% of SLE patients develop LN, which remains a major cause of morbidity and mortality [3].

In recent years, immunosuppressive agents such as mycophenolate mofetil (MMF) have been increasingly applied in clinical practice. However, the management of SLE remains challenging [4]. Despite advanced understandings of the pathogenic roles of immune complexes, cytokines, and complement activation [5], accurate assessment of disease activity remains difficult. Commonly used scoring tools like SLE disease activity index (SLEDAI) have inherent limitations in subjectivity and specificity. Moreover, early diagnosis of LN still largely relies on renal biopsy, an invasive procedure associated with risks and potential sampling bias, which may limit its ability to detect early kidney inflammation in a timely manner [6]. Therefore,

https://doi.org/10.62347/TGOA6215

there is an urgent need to identify reliable, non-invasive biomarkers for monitoring disease activity and facilitating early detection of renal damage.

Recent studies have increasingly focused on the molecular mechanisms underlying SLE and LN, both of which are closely related to dysregulation of innate and adaptive immune responses [7]. Galactin-9, a β-galactoside-binding lectin, plays an important role in immune regulation by promoting helper T cell apoptosis and inducing regulatory T-cell differentiation, thereby modulating immune homeostasis [8]. Under inflammatory conditions, the expression of galectin-9 is usually upregulated and contributes to the regulation of dendritic cell function [9]. Monocyte chemoattractant protein-1 (MCP-1) is a key chemokine responsible for recruiting monocytes and T lymphocytes to the site of inflammation [10]. In renal injury, MCP-1 levels are significantly elevated in renal tubular epithelial cells and mesangial cells, further promoting inflammatory cell infiltration and contributing to the progression of LN [11]. Evidence suggests that serum galectin-9 level may reflect disease severity, while urinary MCP-1 has been recognized as a sensitive marker of active renal inflammation [12, 13]. However, studies evaluating the combined detection of serum galectin-9 and urinary MCP-1 for assessing overall SLE disease activity and identifying LN remain limited.

To address this gap, this study aimed to evaluate the clinical significance of serum galectin-9 and urinary MCP-1 in assessing SLE disease activity and facilitating the early diagnosis of LN. This study represents a novel attempt to explore whether this novel biomarker combination can serve as a reliable and non-invasive tool for improving disease monitoring and early detection of renal injury, allowing more personalized and effective clinical management for SLE patients.

Materials and methods

Study objects and design

This retrospective study included a total of 148 patients with SLE who were admitted to Liangshan Yi Autonomous Prefecture Hospital of Integrated Traditional Chinese and Western Medicine between June 2022 and May 2025. All patients fulfilled the 2019 European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) classification criteria for SLE [14]. Disease activity was assessed using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) as recommended by the American College of Rheumatology and the Systemic Lupus International Collaborating Clinics (SLICC) [15]. The revised SLEDAI-2000 scoring system was applied in this study [16].

Based on SLEDAI-2000 scores and renal biopsy findings for LN, patients were divided into three groups: an inactive SLE group (n=48), an active SLE without LN group (n=40), and an active SLE with LN group (n=60). Inactive SLE was defined as a SLEDAI score ≤4 with no clinical or serological evidence of disease activity. Active SLE without LN was defined as a SLEDAI score >4 in the absence of renal involvement (24-hour proteinuria <500 mg and negative renal biopsy findings). Active SLE with LN was defined as a SLEDAI score >4 with LN. Renal involvement was classified according to the International Society of Nephrology/Renal Pathology Society (ISN/RPS) criteria [17].

Exclusion criteria: (1) pregnancy or lactation; (2) presence of other autoimmune diseases; (3) end-stage renal disease (estimated glomerular filtration rate [eGFR] <15 mL/min/1.73 m^2), severe hepatic dysfunction (Child-Pugh B/C), or malignancy; (4) active infection; (5) thrombotic events or treatment for antiphospholipid syndrome within the past 3 months; (6) use of corticosteroids (prednisone ≥10 mg/day), immunosuppressants, nonsteroidal anti-inflammatory drugs (NSAIDs), or biologics within the past 3 months; (7) major surgery or trauma within the past 3 months; (8) renal injury unrelated to LN (e.g., diabetic nephropathy, amyloidosis).

The indications for renal biopsy in active SLE patients (SLEDAI >4) included: (1) persistent 24-hour urinary protein excretion ≥0.5 g; (2) acute deterioration of renal function (serum creatinine increase >30% or eGFR decrease >30%); (3) active urinary sediment on urinalysis (including hematuria, leukocyte casts, or granular casts). Renal biopsies were performed within 72 hours of hospital admission. The preliminary diagnosis of all pathology slides was independently completed by a senior renal

pathologist with over 15 years of experience in renal pathology diagnosis at our institution.

Laboratory procedures

All samples were collected within 24 hours of patient admission prior to the initiation of any immunosuppressive treatment. Fasting was not required for sample collection; however, patients were advised to avoid high-protein meals on the day of sample collection to minimize variations in urine protein levels. Venous blood (7 mL) was drawn from the antecubital vein between 7:00 AM and 9:00 AM on the first morning after admission. For 24-hour urine collection, patients were provided with sterile containers and instructed to collect all urine over a complete 24-hour period, starting from the first morning void and ending with the first void the following morning.

(A) Routine blood tests: Complete blood count (CBC) and erythrocyte sedimentation rate (ESR) were measured using an automated hematology analyzer (XT-1800i, Sysmex, Japan) and an ESR analyzer (Monitor-100, Alifax, Italy), respectively. Liver function indices (alanine aminotransferase [ALT], aspartate aminotransferase [AST], total bilirubin, albumin [ALB]), c-reactive protein (CRP), and renal function indicators (serum creatinine and eGFR) were measured using an automated biochemical analyzer (Cobas e601, Roche, France).

(B) Complement and autoantibody testing: Serum complement C3 and C4 levels were determined by nephelometry (BN ProSpec, Siemens, Germany). Antinuclear antibodies (ANA) were detected by indirect immunofluorescence (EUROIMMUN Hep-2 cell slides, Germany), with a positive threshold defined as a titer ≥1:160. Anti-double-stranded DNA (anti-dsDNA) antibodies were measured using an ELISA kit (Quantikine ELISA Kit, Catalog No. MBS269122, MyBioSource, USA; positive threshold ≥30 IU/mL).

(C) Serum galectin-9 measurement: Serum galectin-9 concentrations were quantified utilizing a human galectin-9 ELISA kit (Catalog No. DGAL90, R&D Systems, USA) according to the manufacturer's instructions. Optical density was measured at 450 nm with a reference wavelength of 630 nm using a microplate reader (Infinite M200 Pro, Tecan, Switzerland).

(D) 24-hour proteinuria: 24-hour urine protein was measured using an automated biochemical analyzer (AU5800, Beckman Coulter, USA) with a urine protein quantification kit (Catalog No. OSR6136, Beckman Coulter, USA).

(E) Urine MCP-1 detection: Urine MCP-1 levels were measured using the Quantikine Human MCP-1 ELISA kit (Catalog No. DCP00, R&D Systems, USA) according to protocols described by the manufacturer. Urinary creatinine concentrations were measured using the Beckman Coulter AU5800 analyzer (USA) and expressed as pg/mg creatinine.

Ethics statement

The study was approved by the Ethics Committee of Liangshan Yi Autonomous Prefecture Hospital of Integrated Traditional Chinese and Western Medicine. All procedures were conducted in accordance with the ethical guidelines detailed in the Declaration of Helsinki. To protect patient privacy, all personally identifiable information was anonymized, and only clinical features and outcome data related to the study were retained for analysis. Given the retrospective nature, the requirement for informed consent was waived by the Ethics Committee.

Statistical methods

Statistical analyses were performed using SPSS software (version 29.0; SPSS Inc., Chicago, IL, USA). Categorical variables were presented as frequencies and percentages [n (%)] and compared between groups using the χ^2 test. Continuous variables were first assessed for normality using the Shapiro-Wilk test. All continuous variables were in a normal distribution and were presented as mean ± standard deviation (SD). Comparisons among multiple groups were conducted using one-way analysis of variance (ANOVA), followed by Tukey's honestly significant difference (HSD) test for post hoc pairwise comparisons. The complete statistical details, including t-values and χ^2 values, are provided in the Tables S1, S2, S3.

Correlation analyses were performed to assess the relationships between variables and SLE disease activity. Pearson correlation analysis was used to evaluate the linear relationship between continuous variables, while Spearman

correlation was used to assess the monotonic relationship between categorical variables.

To identify independent predictors of LN among SLE patients, multivariate logistic regression analysis was performed, considering LN status as the dependent variable. In constructing the multivariate logistic regression model, the selection of independent variables was based on the following steps: First, variables significantly associated (P<0.1) with LN status in the univariate analysis (serum galectin-9 and urinary MCP-1), along with key variables considered potentially relevant to LN based on clinical knowledge (anti-dsDNA positivity and complement C3), were included in the initial candidate variable set. Subsequently, a forward likelihood ratio method was employed for variable selection, with an inclusion criterion of P<0.05 and an exclusion criterion of P>0.1. This automated stepwise regression process aimed to identify the most significant independent predictors while controlling for model complexity and avoiding overfitting. The diagnostic performance of serum galectin-9, urine MCP-1, and their combined use for identifying LN was assessed by constructing receiver operating characteristic (ROC) curves and calculating the area under the curve (AUC).

Due to the retrospective design of the study, the sample size was not calculated a priori but was based on the actual available data collected. However, a post hoc evaluation of sample size adequacy was performed. In the multivariate logistic regression analysis, LN status was defined as the outcome variable, with 60 events observed, and four independent variables included (C3, anti-dsDNA positivity, serum Galectin-9, and urine MCP-1). The events per variable (EPV) ratio was 60/4=15, exceeding the commonly used threshold (EPV≥10), suggesting that the sample size was adequate to avoid overfitting.

Results

Basic characteristics

Baseline demographic and clinical characteristics of the three groups are detailed in **Table 1**. No significant differences were observed in sex or age distribution among groups. Body mass index (BMI) was significantly higher in both active SLE groups than in the inactive group (both P<0.05).

In terms of comorbidities, the prevalence of hypertension was significantly higher in both active groups, especially in the LN group (both P<0.05). However, no significant differences were observed in the prevalence of diabetes mellitus or cardiovascular disease among the three groups.

The proportions of patients receiving corticosteroids, hydroxychloroquine, MMF, and azathioprine (AZA) in the active groups were significantly higher than that in the inactive group (all P<0.05). A similar trend was observed in the cumulative corticosteroid dose and disease duration. The SLEDAI score progressively increased with disease activity (P<0.05).

Notably, the SLICC/ACR Damage Index was significantly higher in the active SLE with LN group compared to the inactive SLE group (P<0.05), while no significant difference was found between the active SLE without LN group and the inactive group. These findings demonstrate that, as SLE progresses from an inactive state to an active state (with or without LN), disease activity, medication requirements, and complications such as hypertension and kidney involvement substantially increase.

Laboratory indicators

Comparison of laboratory indices among the three groups are presented in **Table 2**. There were no significant differences in ALT, AST, total bilirubin, or ALB among the three groups (all P>0.05). In contrast, platelet count, white blood cell count (WBC), hemoglobin levels, ESR, CRP, proteinuria, serum creatinine, eGFR, C3, and C4 levels differed significantly across groups, showing progressive alterations from inactive SLE to active SLE with LN (all P<0.05). Specifically, WBC, hemoglobin, ESR, CRP, proteinuria, serum creatinine, eGFR, C3, and C4 levels were notably altered in both active groups compared to the inactive group. Furthermore, proteinuria, serum creatinine, eGFR, C3, C4, and anti-dsDNA positivity showed significant differences between the active SLE without LN and active SLE with LN groups (all P<0.05).

Table 1. Comparison of baseline characteristics among the three groups

Indicator	Inactive SLE group (n=48)	Active SLE without LN group (n=40)	Active SLE with LN group (n=60)
Female/Male [n (%)]	40 (83.33%)/8 (16.67%)	35 (87.50%)/5 (12.50%)	52 (86.67%)/8 (13.33%)
Age (years)	36.15 ± 6.84	37.48 ± 5.02	38.72 ± 7.21
BMI (kg/m^2)	23.85 ± 3.21	25.67 ± 4.12*	26.13 ± 3.35*
Ethnicity [n (%)]			
Yi	26 (54.16%)	21 (52.50%)	30 (50.00%)
Han	20 (41.67%)	15 (37.50%)	26 (43.33%)
Others	2 (4.17%)	4 (10.00%)	4 (6.67%)
Family history of SLE [n (%)]	5 (10.42%)	3 (7.50%)	9 (15.00%)
Smoking history [n (%)]	8 (16.67%)	7 (17.50%)	11 (18.33%)
Drinking history [n (%)]	5 (10.42%)	6 (15.00%)	8 (13.33%)
Comorbidities [n (%)]			
Hypertension	12 (25.00%)	15 (37.50%)	36 (60.00%)*,#
Diabetes	4 (8.33%)	5 (12.50%)	9 (15.00%)
Cardiovascular disease	3 (6.25%)	1 (2.50%)	7 (11.67%)
Medication history [n (%)]			
Corticosteroids	18 (37.50%)	28 (70.00%)*	45 (75.00%)*
HCQ	28 (58.33%)	30 (75.00%)	48 (80.00%)*
MMF	5 (10.42%)	12 (30.00%)*	28 (46.67%)*
AZA	2 (4.17%)	8 (20.00%)*	15 (25.00%)*
Cumulative corticosteroids dose (mg, prednisone equivalent)	1250.53 ± 320.15	1450.75 ± 350.24*	1820.61 ± 420.18*,#
Disease duration (months)	85.16 ± 20.36	96.24 ± 22.15*	107.37 ± 25.83*,#
SLEDAI (scores)	2.88 ± 0.52	9.19 ± 2.32*	14.75 ± 3.14*,#
SLICC SLE damage index (scores)	4.15 ± 1.03	4.37 ± 0.78	4.62 ± 0.95*
LN pathological grading [n (%)]			
Class I	-	-	7 (11.67%)
Class II	-	-	18 (30.00%)
Class III	-	-	25 (41.67%)
Class IV	-	-	8 (13.33%)
Class V	-	-	2 (3.33%)

SLE, Systemic Lupus Erythematosus; LN, Lupus Nephritis; BMI, Body Mass Index; HCQ, Hydroxychloroquine; MMF, Mycophenolate Mofetil; AZA, Azathioprine; SLEDAI, Systemic Lupus Erythematosus Disease Activity Index; SLICC, Systemic Lupus International Collaborating Clinics; *P<0.05, compared to the inactive SLE group; #P<0.05, compared to the active SLE without LN group.

Table 2. Comparison of laboratory indicators among the three groups

Indicator	Inactive SLE group (n=48)	Active SLE without LN group (n=40)	Active SLE with LN group (n=60)
Platelets (×10^9/L)	245.36 ± 52.14	238.36 ± 47.62	225.24 ± 45.28*
WBC (×10^9/L)	6.52 ± 1.83	5.52 ± 1.67*	5.34 ± 1.53*
Hemoglobin (g/L)	125.36 ± 12.45	112.45 ± 10.36*	110.47 ± 10.82*
ESR (mm/h)	18.45 ± 5.18	24.45 ± 6.21*	26.69 ± 7.53*
CRP (mg/L)	3.52 ± 1.12	4.87 ± 1.53*	5.87 ± 1.55*,#
ALT (U/L)	25.08 ± 5.41	26.54 ± 5.23	27.15 ± 5.51
AST (U/L)	24.56 ± 4.83	25.81 ± 5.05	26.34 ± 5.33
Total bilirubin (mg/dL)	0.85 ± 0.15	0.88 ± 0.16	0.91 ± 0.18
ALB (g/L)	4.27 ± 0.35	4.19 ± 0.32	4.14 ± 0.37
Proteinuria (g/24 h)	0.25 ± 0.08	0.29 ± 0.08*	1.22 ± 0.35*,#
Serum creatinine (mg/dl)	0.72 ± 0.15	0.85 ± 0.18*	1.18 ± 0.24*,#
eGFR (mL/min/1.73 m^2)	117.63 ± 15.45	108.45 ± 12.36*	88.52 ± 20.14*,#
C3 (g/L)	1.05 ± 0.16	0.85 ± 0.14*	0.78 ± 0.12*,#
C4 (g/L)	0.18 ± 0.05	0.14 ± 0.03*	0.12 ± 0.03*,#

SLE, Systemic Lupus Erythematosus; LN, Lupus Nephritis; WBC, White Blood Cell Count; ESR, Erythrocyte Sedimentation Rate; CRP, C-Reaction Protein; ALT, Alanine Aminotransferase; AST, Aspartate Aminotransferase; ALB, Albumin; eGFR, estimated Glomerular Filtration Rate; C3, Complement3; C4, Complement4; *P<0.05, compared to the inactive SLE group; #P<0.05, compared to the active SLE without LN group.

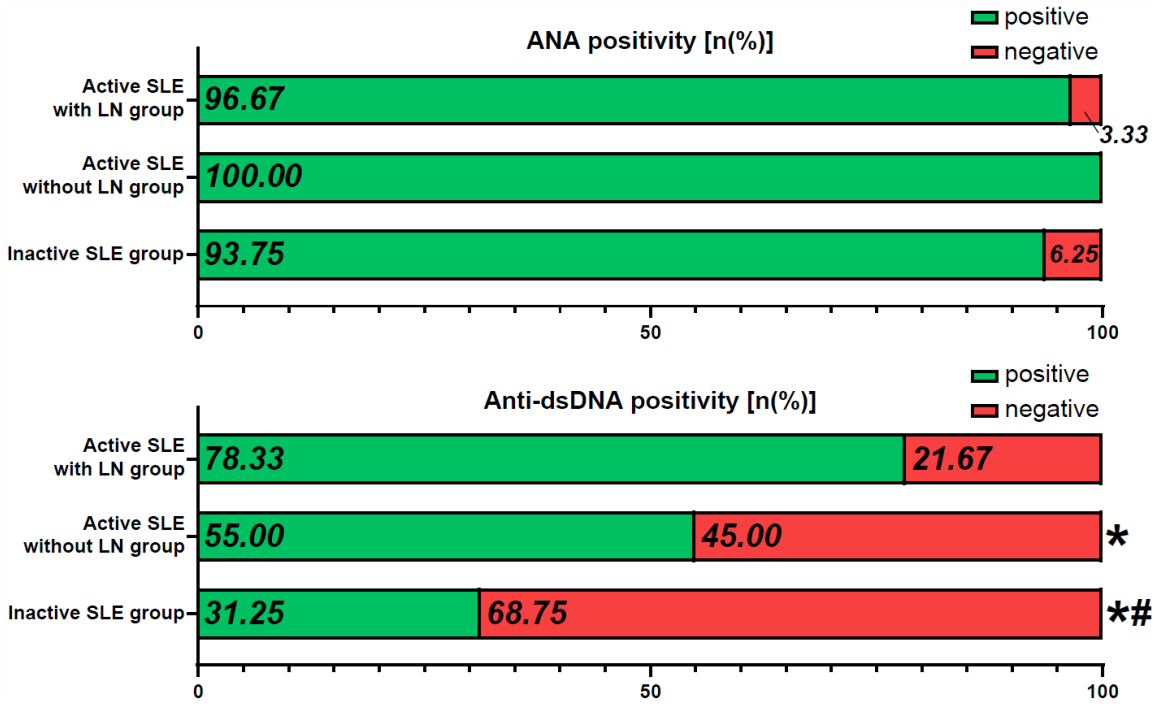

Figure 1. Autoantibody positivity in study cohort. SLE, Systemic Lupus Erythematosus; LN, Lupus Nephritis; ANA, Antinuclear Antibodies; dsDNA, double-stranded Deoxyribonucleic Acid. Data are presented as the number (n) of positive cases and their percentage within the group. Inactive SLE group, n=48; Active SLE without LN group, n=40; Active SLE with LN group, n=60. Comparisons between groups were performed using the Chi-square test. *, P<0.05 compared to the inactive SLE group; #, P<0.05 compared to the active SLE without LN group.

ANA positivity was consistently high across all groups. In contrast, anti-dsDNA positivity increased significantly from the inactive SLE to the active SLE with LN group, indicating a higher level of disease activity and severity (**Figure 1**). Overall, these findings suggest a clear trend of

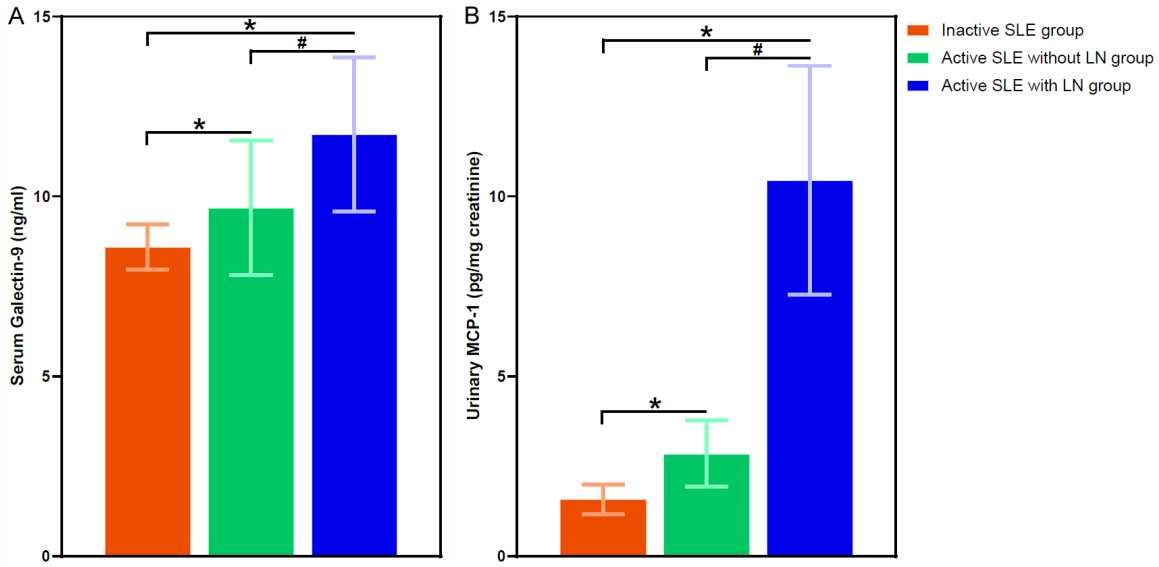

Figure 2. Comparison of serum galectin-9 and urinary MCP-1 level among the three groups. A: Serum Galectin-9 (ng/ml); B: Urinary MCP-1 (pg/mg creatinine). SLE, Systemic Lupus Erythematosus; LN, Lupus Nephritis; MCP-1, Monocyte Chemoattractant Protein-1. *P<0.05 compared to the inactive SLE group; #P<0.05 compared to the active SLE without LN group.

worsening hematologic and immunological indices as SLE progresses from an inactive state to active disease with renal involvement.

Serum galectin-9 and urinary MCP-1

Comparisons of serum galectin-9 and urinary MCP-1 levels among the three groups are shown in **Figure 2**. Serum galectin-9 levels progressively increased as disease activity of SLE increased, showing significant inter-group differences (8.59 ± 0.63 ng/mL in the inactive group, 9.68 ± 1.87 ng/mL in the active but without LN group, and 11.72 ± 2.14 ng/mL in the active with LN group; all P<0.001). Similar trend was observed in urinary MCP-1 levels, with significant inter-group differences (1.58 ± 0.42 pg/mg creatinine in the inactive group, 2.85 ± 0.92 pg/mg creatinine in the active but without LN group, and 10.45 ± 3.18 pg/mg creatinine in the active with LN group; all P<0.001). These results suggest that both serum Galectin-9 and urinary MCP-1 increase in parallel with SLE disease activity and are markedly elevated in patients with LN.

Correlation analysis

In the inactive SLE and active SLE without LN groups (**Figure 3**), BMI, corticosteroid use, MMF use, AZA use, cumulative corticosteroid dose and disease duration were positively correlated with disease activity (all P<0.05). The SLEDAI scores were strongly positively correlated with serum galectin-9 and urine MCP-1 levels (all P<0.001), suggesting close associations with disease activity. In contrast, WBC, and complement C3 and C4 were negatively correlated with disease activity. ESR, CRP, proteinuria and serum creatinine were positively associated with disease activity. Anti-dsDNA antibody positivity was also positively correlated with disease activity. These results indicate that serum galectin-9 and urine MCP-1 may serve as valuable biomarkers for assessing SLE disease activity. Similar to established markers such as SLEDAI scores, complement levels, and inflammatory markers, these biomarkers may be involved in the pathophysiology of SLE and may provide utility in monitoring disease progression and treatment response.

In the inactive SLE and active SLE with LN groups (**Figure 4**), BMI, hypertension, corticosteroid use, MMF use, AZA use, HCQ use, cumulative corticosteroid dose, and disease duration were positively correlated with disease activity (all *P*<0.05). Notably, SLEDAI scores, serum galectin-9, and urinary MCP-1 were strongly correlated with disease activity (all *P*<0.001). Conversely, WBC count, hemoglobin, eGFR, C3, and C4 (all P<0.001) were

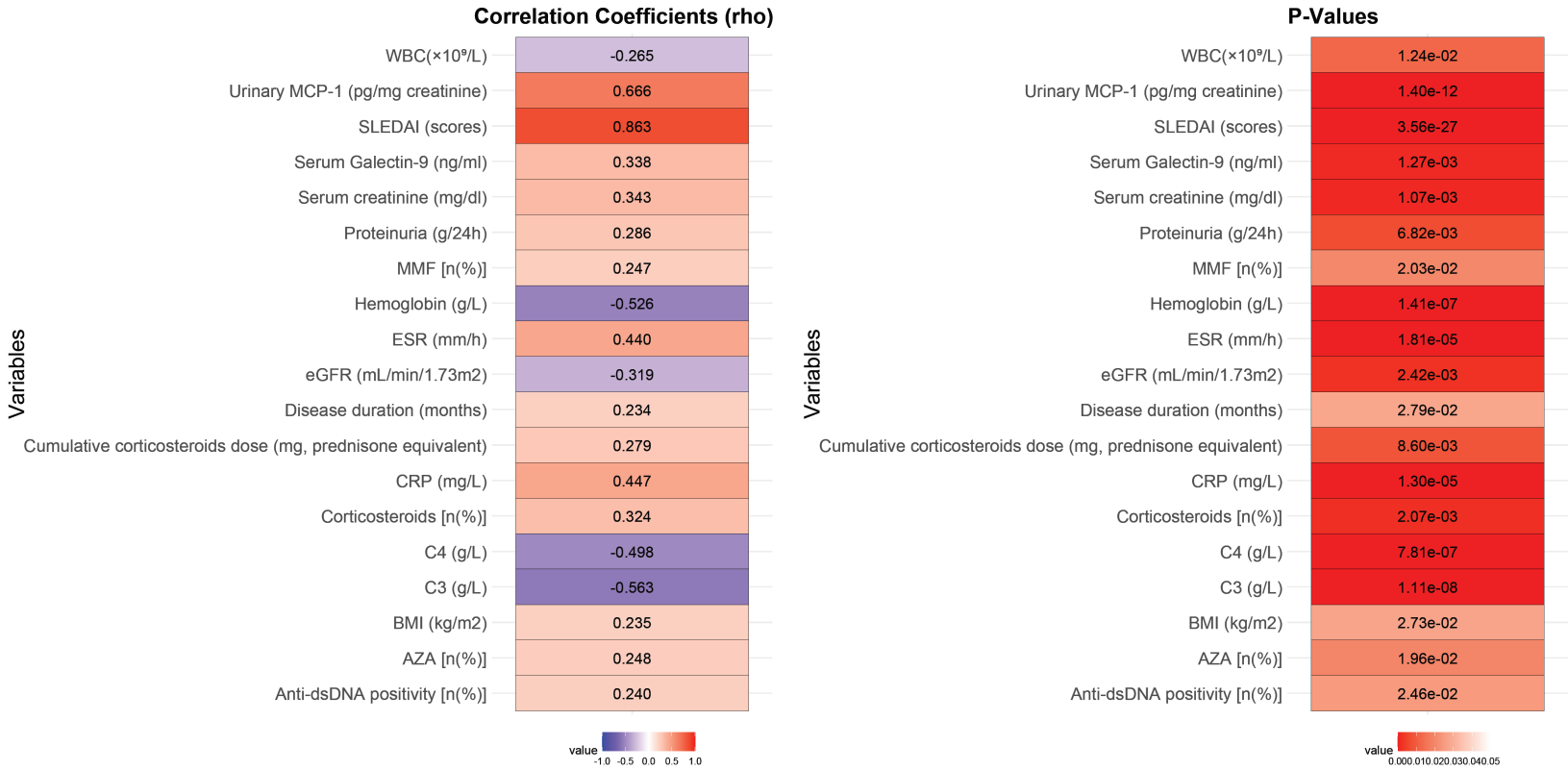

Figure 3. Correlation analysis of serum galectin-9, urinary MCP-1, and SLE disease activity between inactive SLE group and active SLE without LN group. BMI, Body Mass Index; HMMF, Mycophenolate Mofetil; AZA, Azathioprine; SLEDAI, Systemic Lupus Erythematosus Disease Activity Index; WBC, White Blood Cell Count; ESR, Erythrocyte Sedimentation Rate; CRP, C-Reaction Protein; eGFR, estimated Glomerular Filtration Rate; C3, Complement3; C4, Complement4; dsDNA: double-stranded Deoxyribonucleic Acid; MCP-1, Monocyte Chemoattractant Protein-1.

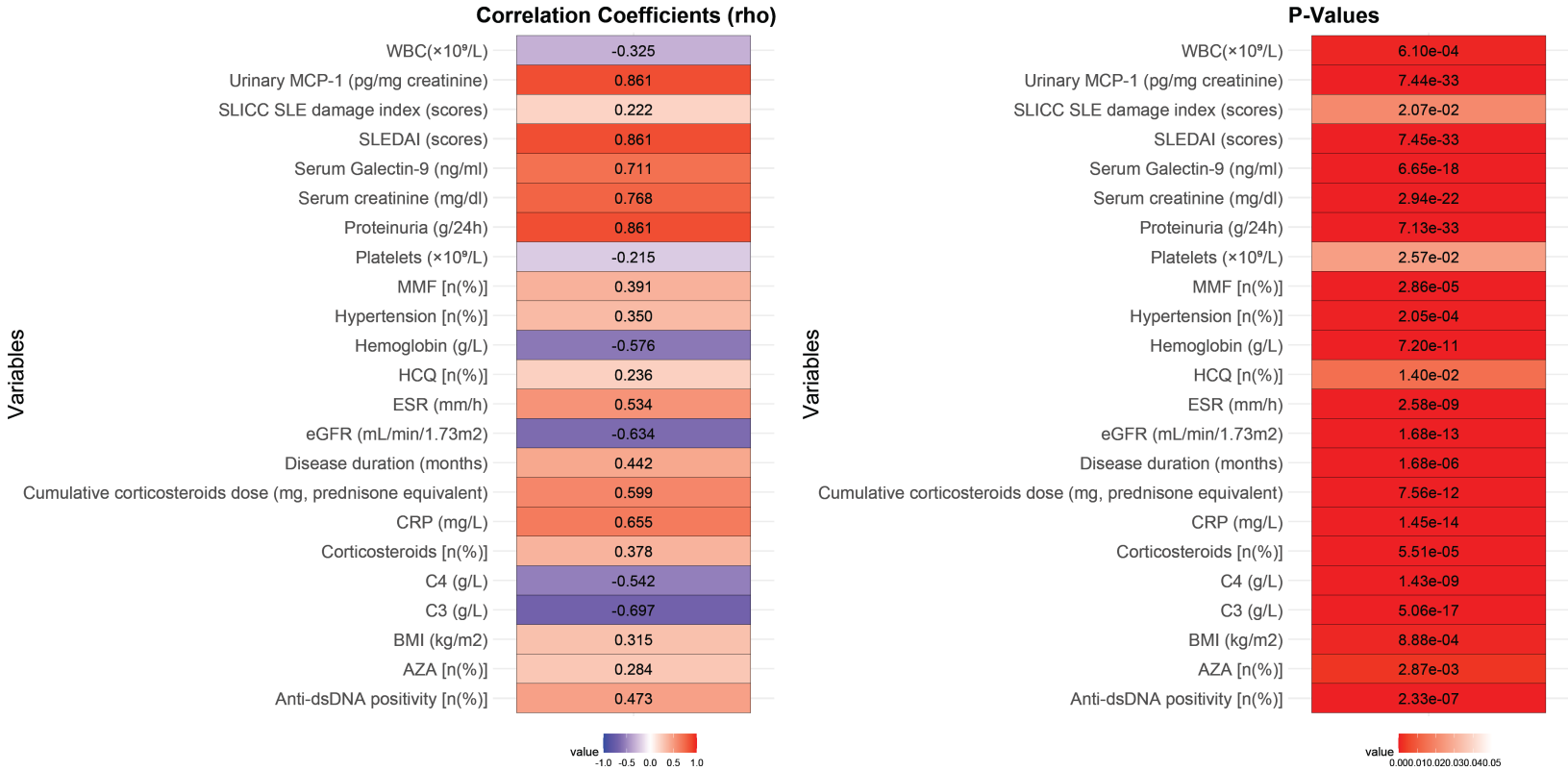

Figure 4. Correlation analysis between serum galectin-9, urinary MCP-1, and SLE disease activity between inactive SLE group and active SLE with LN group. BMI, Body Mass Index; HMMF, Mycophenolate Mofetil; AZA, Azathioprine; SLEDAI, Systemic Lupus Erythematosus Disease Activity Index; WBC, White Blood Cell Count; ESR, Erythrocyte Sedimentation Rate; CRP, C-Reaction Protein; eGFR, estimated Glomerular Filtration Rate; C3, Complement3; C4, Complement4; dsDNA, double-stranded Deoxyribonucleic Acid; MCP-1, Monocyte Chemoattractant Protein-1.

Table 3. Multivariate logistic regression analysis of the risk factors for SLE combined with LN

Indicator	Coefficient	Std. Error	Wald Stat	P	OR	95% CI Lower	95% CI Upper
C3 (g/L)	-3.215	1.024	9.857	0.002	0.040	0.005	0.304
Anti-dsDNA positivity [n (%)]	1.576	0.642	6.025	0.014	4.835	1.374	17.016
Serum Galectin-9 (ng/ml)	0.284	0.098	8.392	0.004	1.328	1.096	1.610
Urinary MCP-1 (pg/mg creatinine)	0.042	0.011	14.562	<0.001	1.043	1.021	1.065

C3, Complement3; dsDNA, double-stranded Deoxyribonucleic Acid; MCP-1, Monocyte Chemoattractant Protein-1.

Table 4. ROC analysis of risk factors for early diagnosis of LN

Indicator	Best threshold	Sensitivities	Specificities	AUC	Youden index	F1 score
C3 (g/L)	0.850	0.675	0.725	0.685	0.400	0.648
Anti-dsDNA positivity [n (%)]	0.500	0.725	0.775	0.742	0.500	0.725
Serum Galectin-9 (ng/ml)	9.850	0.783	0.833	0.782	0.500	0.742
Urinary MCP-1 (pg/mg creatinine)	6.150	0.823	0.875	0.796	0.658	0.824

AUC, Area Under the Curve; C3, Complement3; dsDNA, double-stranded Deoxyribonucleic Acid; MCP-1, Monocyte Chemoattractant Protein-1.

negatively correlated with disease activity. ESR, CRP, proteinuria, serum creatinine, and anti-dsDNA positivity (all P<0.001) were all positively correlated. These results demonstrate that serum galectin-9 and urinary MCP-1 are strongly associated with disease activity and severity in SLE patients, particularly those with LN.

Multivariate logistic regression analysis

Multivariate logistic regression analysis was performed to identify independent risk factors for LN among patients with SLE (**Table 3**). Lower C3 (P=0.002) and anti-dsDNA positivity (P=0.014) were independently associated with increased LN risk. Furthermore, elevated serum galectin-9 (P=0.004) and urinary MCP-1 levels (P<0.001) were also identified as independent risk factors. The Hosmer-Lemeshow goodness-of-fit test yielded a *P* value of 0.78, indicating adequate model calibration.

ROC analysis

ROC analysis was conducted to evaluate the diagnostic performance of each risk factor for early detection of LN (**Table 4**). C3 demonstrated an AUC of 0.685, with an optimal cutoff of 0.850 g/L, yielding a sensitivity of 0.675 and specificity of 0.725. Anti-dsDNA positivity had an AUC of 0.742, with a cutoff of 0.500, sensitivity of 0.725 and specificity of 0.775. Serum galectin-9 achieved an AUC of 0.782, with an optimal cutoff of 9.850 ng/ml, sensitivity of 0.783, and specificity of 0.833. Urinary MCP-1 showed a slightly higher AUC of 0.796, with a cutoff of 6.150 pg/mg creatinine, sensitivity of 0.823, and specificity of 0.875. These results indicate that both serum galectin-9 and urinary MCP-1 are effective biomarkers for the early detection of LN, with urinary MCP-1 demonstrating marginally better performance in terms of sensitivity, specificity, and overall discriminatory power.

Joint testing model

The combined diagnostic model incorporating serum galectin-9 and urinary MCP-1 demonstrated improved diagnostic performance, with an AUC of 0.866 (**Figure 5**). The ROC curve approached the upper left corner, reflecting a favorable balance between sensitivity and specificity.

Subgroup analysis

In the group of the active SLE with LN (n=60), patients were further divided into a non-proliferative LN group (Class I/II/V, n=27) and a proliferative LN group (Class III/IV, n=33), based on the ISN/RPS pathologic grading criteria (**Table 5**). Hypertension did not show a notable difference between groups (P=0.244). However, significant differences were observed in

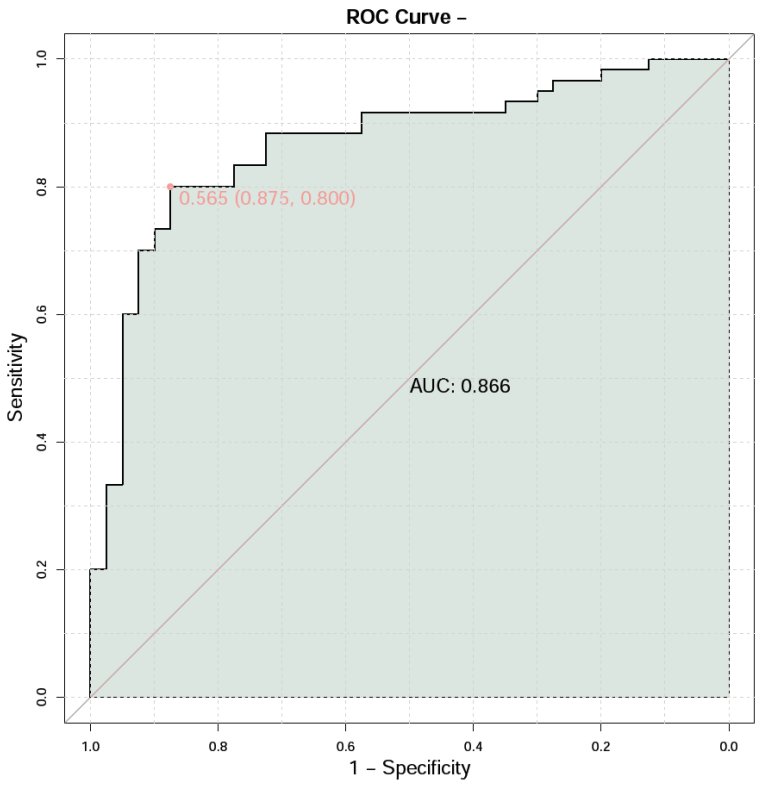

Figure 5. ROC curve of joint testing. ROC, Receiver Operating Characteristic; AUC, Area Under the Curve.

SLEDAI score (P=0.002), proteinuria (P<0.001), serum creatinine (P<0.001), eGFR (P=0.01), C3 (P=0.007), anti-dsDNA positivity (P=0.047), serum galectin-9 (P=0.006), and urinary MCP-1 (P<0.001). These findings underscore the distinctions in disease severity and renal involvement between non-proliferative and proliferative LN types, emphasizing the importance of these markers for differentiating LN classes.

Discussion

The results of this study support that the combined detection of serum galectin-9 and urinary MCP-1 can significantly improve the non-invasive assessment of SLE. These two biomarkers not only reflect overall disease activity, but also demonstrate unique value in the early identification of LN, a critical determinant of patient prognosis. Galactin-9 mainly reflects systemic immune disorders, while urinary MCP-1 more directly reflects local renal inflammation. Combining these two provides a more comprehensive view of the pathologic processes underlying disease progression and kidney injury from different perspectives. Compared to traditional indicators, this combination improves diagnostic efficiency and provides a more comprehensive basis for clinical decision-making, potentially facilitating earlier and more precise interventions.

In patients with active SLE, we observed significantly elevated serum galectin-9 levels, particularly in patients with biopsy-confirmed LN. Galactin-9 is involved in various immune regulatory processes, including induction of pro-inflammatory Th1 cell apoptosis, enhancement of Treg cell function, and modulation of dendritic cell activity [18]. Its upregulation may therefore represent a complex regulatory response to systemic inflammation [19]. Increasing evidence has linked elevated galectin-9 level to SLE disease activity. For example, reports have shown that its elevation is associated with disease recurrence and the presence of anti dsDNA antibodies [20]. Our research further extends these observations by demonstrating that galectin-9 is not only associated with overall SLE disease activity but also closely related to the presence and histologic severity of LN. These findings suggest that galectin-9 is not merely a bystander in the disease process. Instead, it may actively participate in the immune dysregulation leading to target organ damage, especially renal involvement. Correlation between galectin-9 and complement depletion (C3, C4) and anti-dsDNA positivity further support its involvement in the core immunopathogenic cascade in SLE [21]. Galectin-9 may serve as a key molecular link between innate immune activation (such as complement system and IFN signature) and adaptive immune dysregulation [22].

Notably, in the analyses of **Table 3** (comparison between inactive group and active SLE without LN group) and **Table 4** (comparison between inactive group and active SLE with LN group), the correlation coefficients between serum galectin-9 and SLEDAI scores differ. This differ-

Table 5. Comparison of clinical and laboratory characteristics between active SLE patients with non-proliferative and proliferative LN (n=60)

Indicator	Non-Proliferative LN group (class I/II/V, n=27)	Proliferative LN group (class III/IV, n=33)	t/χ^2	P
Age (years)	37.85 ± 6.92	38.72 ± 7.15	0.479	0.634
Female/Male [n (%)]	22 (81.48%)/5 (18.52%)	30 (90.91%)/3 (9.09%)	0.472	0.492
Hypertension [n (%)]	14 (51.85%)	22 (66.67%)	1.358	0.244
SLEDAI score	13.25 ± 2.84	15.87 ± 3.26	3.287	0.002
Proteinuria (g/24h)	0.98 ± 0.22	1.42 ± 0.45	4.883	<0.001
Serum creatinine (mg/dL)	1.05 ± 0.21	1.28 ± 0.26	3.664	<0.001
eGFR (mL/min/1.73 m^2)	95.36 ± 18.25	82.15 ± 19.63	2.677	0.010
C3 (g/L)	0.82 ± 0.11	0.73 ± 0.13	2.800	0.007
Anti-dsDNA positivity [n (%)]	18 (66.67%)	29 (87.88%)	3.937	0.047
Serum Galectin-9 (ng/mL)	10.85 ± 1.92	12.42 ± 2.25	2.880	0.006
Urinary MCP-1 (pg/mg creatinine)	8.25 ± 2.84	12.36 ± 3.28	5.123	<0.001

LN, Lupus Nephritis; SLE, Systemic Lupus Erythematosus; SLEDAI, Systemic Lupus Erythematosus Disease Activity Index; eGFR, estimated Glomerular Filtration Rate; C3, Complement3; dsDNA, double-stranded Deoxyribonucleic Acid; MCP-1, Monocyte Chemoattractant Protein-1.

ence is primarily due to the varying spectrum of disease activity in the analyzed populations. The SLEDAI score range in the population of **Table 3** is relatively limited, whereas **Table 4**, which includes patients with more active LN, exhibits a broader range and greater variability in SLEDAI scores. This wider range of disease activity results in a stronger positive correlation between galectin-9 and SLEDAI. These findings underscore that serum galectin-9 is closely associated with SLE disease activity, particularly in patients with higher disease activity and major organ involvement such as the kidneys, where this association becomes more pronounced.

In patients with active LN, urinary MCP-1 levels were markedly elevated, further supporting the role of MCP-1 as a major regulator of renal inflammation. MCP-1 primarily functions by recruiting monocytes/macrophages and T cells, which are critical effector cells in the pathogenesis of LN [23]. Previous studies had shown that urine MCP-1 is a sensitive marker of acute renal attack in LN [24]. Consistent with these reports, in this study, urinary MCP-1 was significantly elevated in LN patients compared to inactive and active SLE patients without LN, indicating its high specificity for kidney injury. Our findings not only confirm but also extend existing evidence by demonstrating a positive correlation between urinary MCP-1 and SLE disease activity. This relationship suggests that urinary MCP-1 directly reflects the severity of inflammatory reaction in the kidney and the degree of renal function damage [25]. Elevated urinary MCP-1 levels often precede definitive histologic damage on biopsy and is therefore an important biomarker for early diagnosis of LN [26]. In patients with proliferative LN, urinary MCP-1 levels were significantly higher than those of non-proliferative LN, providing strong evidence that this chemokine is associated with the most aggressive and destructive forms of kidney inflammation, which are typically characterized by capillary necrosis and endocapillary proliferation [27].

The innovation of this study lies in the combined application of galectin-9 and MCP-1 for disease evaluation. Although each biomarker has demonstrated diagnostic value for LN, their combined assessment achieved significantly improved diagnostic performance. This improvement may stem from the fact that they each reflect different but interrelated pathologic processes. Serum galectin-9 reflects systemic immune dysregulation and overall disease burden, whereas urinary MCP-1 more directly reflects local inflammatory response in the kidneys [28]. The combined detection model effectively compensates for the limitations of commonly used biomarkers, which are often insensitive to early subclinical renal involvement and have difficulties in distinguishing renal-specific activity from systemic disease

activity [29]. The joint model achieved higher AUC values than those of individual markers, indicating that, compared to traditional serologica indicators, such as single markers, anti-dsDNA antibodies, or complement levels, simultaneous detection of these two can provide more comprehensive and accurate disease information. This discovery is also in line with the consensus that SLE and LN are driven by multiple overlapping pathogenic mechanisms. Therefore, a multiindices biomarker strategy is essential for comprehensive evaluation [30]. In multiple logistic regression analysis, even after adjusting for known predictive factors such as proteinuria, serum creatinine, eGFR, and complement levels, serum galectin-9 and urinary MCP-1 remained independently associated with LN, further highlighting their unique and cumulative clinical value.

In addition to their diagnostic value, our correlation analysis also found a close relationship between these two biomarkers and the degree of SLE disease activity. In both groups of active SLE, galectin-9 and MCP-1 levels were positively correlated with disease activity, further supporting their use as reliable indicators for assessing overall SLE activity [31]. Notably, these biomarkers, especially urinary MCP-1, also demonstrated value for distinguishing between proliferative and non-proliferative LN. This has significant clinical implications, as proliferative LN is generally associated with a poor prognosis and often requires more aggressive immunosuppressive therapy. A non-invasive approach to obtain information related to renal pathologic subtypes is expected to reduce the need for repeated renal biopsies. This non-invasive tool is particularly suitable for long-term treatment response monitoring or disease classification evaluation, providing a more convenient basis for clinical management.

Although the results of this study are encouraging, some limitations should be acknowledged. First, this is a retrospective, single-center study, which may have limited the generalizability of the findings and introduced selection bias. Although strict exclusion criteria facilitated a more focused analysis of biomarker signals associated with SLE/LN activity, it also resulted in a relatively homogeneous study population. Consequently, this study may not fully represent the heterogeneity of SLE patients in real clinical settings, particularly those with severe comorbidities or recent use of immunosuppressants. Second, this study adopted a cross-sectional design with assessment of biomarker levels at a single time point only. To monitor disease progression, predict recurrence, or evaluate treatment response, longitudinal studies with repeated measurements before, during, and after disease recurrence are required to track their dynamic changes and prognostic value. Third, although SLEDAI-2000 is a widely used evaluation tool, it has certain limitations. Future studies may use novel indices, such as SELENA-SLEDAI or BILAG-2004, to further validate the results of this study. Additionally, in the subgroup analysis of LN, patients were classified only into proliferative and non-proliferative subgroups. Although this classification has significant clinical guidance value, the limited sample size in each specific pathological stage (Classes I-V) precluded a more detailed analysis of the gradient relationship between serum galectin-9, urinary MCP-1, and the severity of pathologic damage. Future studies with larger sample size, particularly including a broader distribution of pathological classes, are warranted to verify the potential of these two biomarkers in distinguishing fine pathologic types of LN and predicting disease progression.

Conclusion

Combined measurement of serum galectin-9 and urinary MCP-1 represents a promising non-invasive tool for assessing SLE disease activity and aiding the early diagnosis of LN. By simultaneously reflecting both systemic and renal-specific inflammatory signals, this dual-biomarker approach demonstrated superior diagnostic performance than individual markers or conventional indicators. While these preliminary findings are encouraging, they require validation in larger, prospective, and multi-center studies. Future research should focus on longitudinal evaluation, mechanistic exploration of the precise roles of these molecules in LN pathogenesis, and rigorous assessment of their clinical utility in improving patient management and outcome.

Disclosure of conflict of interest

None.

Address correspondence to: Fangwei Ma, Department of Rheumatology and Immunology, Liangshan Hospital of Integrated Traditional and Western Medicine, No. 60, Section 2, Hedong Avenue, Xichang City, Liangshan Yi Autonomous Prefecture 615000, Sichuan, China. E-mail: mfw1981m@163.com

References

[1] Halfon M, Tankeu AT and Ribi C. Mitochondrial dysfunction in systemic lupus erythematosus with a focus on lupus nephritis. Int J Mol Sci 2024; 25: 6162.

[2] Xiao B, Wu S, Tian Y, Huang W, Chen G, Luo D, Cai Y, Chen M, Zhang Y, Liu C, Zhao J and Li L. Advances of NAT10 in diseases: insights from dual properties as protein and RNA acetyltransferase. Cell Biol Toxicol 2024; 41: 17.

[3] Luo W, Farinha F, Isenberg DA and Rahman A. Survival analysis of mortality and development of lupus nephritis in patients with systemic lupus erythematosus up to 40 years of follow-up. Rheumatology (Oxford) 2022; 62: 200-208.

[4] Tsoi A, Nikolopoulos D and Parodis I. Advances in the pharmacological management of systemic lupus erythematosus. Expert Opin Pharmacother 2024; 25: 705-716.

[5] Naithani U, Jain P, Sachan A, Khare P and Gabrani R. MicroRNA as a potential biomarker for systemic lupus erythematosus: pathogenesis and targeted therapy. Clin Exp Med 2023; 23: 4065-4077.

[6] Yang Y, Huang D, Liu C, Zhong N, Peng Y, Wang L, Xiao L and Zhao W. Early diagnosis and clinical application of systemic lupus erythematosus based on a nomogram model. Heliyon 2024; 10: e24523.

[7] Infante B, Mercuri S, Dello Strologo A, Franzin R, Catalano V, Troise D, Cataldo E, Pontrelli P, Alfieri C, Binda V, Frontini G, Netti GS, Ranieri E, Gesualdo L, Castellano G and Stallone G. Unraveling the link between interferon-α and systemic lupus erythematosus: from the molecular mechanisms to target therapies. Int J Mol Sci 2022; 23: 15998.

[8] Schlichtner S, Meyer NH, Yasinska IM, Aliu N, Berger SM, Gibbs BF, Fasler-Kan E and Sumbayev VV. Functional role of galectin-9 in directing human innate immune reactions to Gram-negative bacteria and T cell apoptosis. Int Immunopharmacol 2021; 100: 108155.

[9] Cao Z, Leng P, Xu H and Li X. The regulating role of galectin-9 in immune cell populations. Front Pharmacol 2024; 15: 1462061.

[10] Zhu S, Liu M, Bennett S, Wang Z, Pfleger KDG and Xu J. The molecular structure and role of CCL2 (MCP-1) and C-C chemokine receptor CCR2 in skeletal biology and diseases. J Cell Physiol 2021; 236: 7211-7222.

[11] Fang Y, Wang B, Pang B, Zhou Z, Xing Y, Pang P, Zheng D, Zhang G and Yang B. Exploring the relations of NLR, hsCRP and MCP-1 with type 2 diabetic kidney disease: a cross-sectional study. Sci Rep 2024; 14: 3211.

[12] Hiramoto K, Saito S, Hanaoka H, Kikuchi J, Fukui H, Hashiguchi A, Suzuki K, Takeuchi T and Kaneko Y. Urinary biomarkers associated with pathogenic pathways reflecting histologic findings in lupus nephritis. Arthritis Rheumatol 2025; 77: 298-310.

[13] Iwasaki-Hozumi H, Chagan-Yasutan H, Ashino Y and Hattori T. Blood levels of galectin-9, an immuno-regulating molecule, reflect the severity for the acute and chronic infectious diseases. Biomolecules 2021; 11: 430.

[14] Aringer M, Costenbader K, Daikh D, Brinks R, Mosca M, Ramsey-Goldman R, Smolen JS, Wofsy D, Boumpas DT, Kamen DL, Jayne D, Cervera R, Costedoat-Chalumeau N, Diamond B, Gladman DD, Hahn B, Hiepe F, Jacobsen S, Khanna D, Lerstrøm K, Massarotti E, McCune J, Ruiz-Irastorza G, Sanchez-Guerrero J, Schneider M, Urowitz M, Bertsias G, Hoyer BF, Leuchten N, Tani C, Tedeschi SK, Touma Z, Schmajuk G, Anic B, Assan F, Chan TM, Clarke AE, Crow MK, Czirják L, Doria A, Graninger W, Halda-Kiss B, Hasni S, Izmirly PM, Jung M, Kumánovics G, Mariette X, Padjen I, Pego-Reigosa JM, Romero-Diaz J, Rúa-Figueroa Fernández Í, Seror R, Stummvoll GH, Tanaka Y, Tektonidou MG, Vasconcelos C, Vital EM, Wallace DJ, Yavuz S, Meroni PL, Fritzler MJ, Naden R, Dörner T and Johnson SR. 2019 European League Against Rheumatism/American College of Rheumatology classification criteria for systemic lupus erythematosus. Ann Rheum Dis 2019; 78: 1151-1159.

[15] Gladman D, Ginzler E, Goldsmith C, Fortin P, Liang M, Urowitz M, Bacon P, Bombardieri S, Hanly J, Hay E, Isenberg D, Jones J, Kalunian K, Maddison P, Nived O, Petri M, Richter M, Sanchez-Guerrero J, Snaith M, Sturfelt G, Symmons D and Zoma A. The development and initial validation of the Systemic Lupus International Collaborating Clinics/American College of Rheumatology damage index for systemic lupus erythematosus. Arthritis Rheum 1996; 39: 363-369.

[16] Gladman DD, Ibañez D and Urowitz MB. Systemic lupus erythematosus disease activity index 2000. J Rheumatol 2002; 29: 288-291.

[17] Weening JJ, D'Agati VD, Schwartz MM, Seshan SV, Alpers CE, Appel GB, Balow JE, Bruijn JA, Cook T, Ferrario F, Fogo AB, Ginzler EM, Hebert L, Hill G, Hill P, Jennette JC, Kong NC, Lesavre P, Lockshin M, Looi LM, Makino H, Moura LA

and Nagata M. The classification of glomerulonephritis in systemic lupus erythematosus revisited. J Am Soc Nephrol 2004; 15: 241-250.
[18] Suszczyk D, Skiba W, Pawłowska A, Polak G, Tarkowski R and Wertel I. Expression of Gal-9 on dendritic cells and soluble forms of TIM-3/Gal-9 in patients suffering from endometriosis. Int J Mol Sci 2023; 24: 5948.
[19] Vázquez-Galán YI, Guzmán-Silahua S, Trujillo-Rangel WA and Rodríguez-Lara SQ. Role of ischemia/reperfusion and oxidative stress in shock state. Cells 2025; 14: 808.
[20] Matsuoka N, Fujita Y, Temmoku J, Furuya MY, Asano T, Sato S, Matsumoto H, Kobayashi H, Watanabe H, Suzuki E, Kozuru H, Yastuhashi H and Migita K. Galectin-9 as a biomarker for disease activity in systemic lupus erythematosus. PLoS One 2020; 15: e0227069.
[21] Cai YH, Deng J, Chen ZL, Mei H, Tang L, Luo SS and Hu Y. Brief report on the relation between complement C3a and anti dsDNA antibody in systemic lupus erythematosus. Sci Rep 2022; 12: 7098.
[22] Shil RK, Mohammed NBB and Dimitroff CJ. Galectin-9 - ligand axis: an emerging therapeutic target for multiple myeloma. Front Immunol 2024; 15: 1469794.
[23] Roveta A, Parodi EL, Brezzi B, Tunesi F, Zanetti V, Merlotti G, Francese A, Maconi AG and Quaglia M. Lupus nephritis from pathogenesis to new therapies: an update. Int J Mol Sci 2024; 25: 8981.
[24] Liu Y, Xu K, Xiang Y, Ma B, Li H, Li Y, Shi Y, Li S and Bai Y. Role of MCP-1 as an inflammatory biomarker in nephropathy. Front Immunol 2023; 14: 1303076.
[25] Klocke J, Kim SJ, Skopnik CM, Hinze C, Boltengagen A, Metzke D, Grothgar E, Prskalo L, Wagner L, Freund P, Görlich N, Muench F, Schmidt-Ott KM, Mashreghi MF, Kocks C, Eckardt KU, Rajewsky N and Enghard P. Urinary single-cell sequencing captures kidney injury and repair processes in human acute kidney injury. Kidney Int 2022; 102: 1359-1370.
[26] Lu Z, Ni W, Wu Y, Zhai B, Zhao Q, Zheng T, Liu Q and Ding D. Application of biomarkers in the diagnosis of kidney disease. Front Med (Lausanne) 2025; 12: 1560222.
[27] Guo Q, Qiao P, Wang J, Zhao L, Guo Z, Li X, Fan X, Yu C and Zhang L. Investigating the value of urinary biomarkers in relation to lupus nephritis histopathology: present insights and future prospects. Front Pharmacol 2024; 15: 1421657.
[28] Wang Y, Zhang Y, Ma M, Zhuang X, Lu Y, Miao L, Lu X, Cui Y and Cui W. Mechanisms underlying the involvement of peritoneal macrophages in the pathogenesis and novel therapeutic strategies for dialysis-induced peritoneal fibrosis. Front Immunol 2024; 15: 1507265.
[29] Safdar OY, Baghdadi RM, Alahmadi SA, Fakieh BE and Algaydi AM. Sickle cell nephropathy: a review of novel biomarkers and their potential roles in early detection of renal involvement. World J Clin Pediatr 2022; 11: 14-26.
[30] Ameer MA, Chaudhry H, Mushtaq J, Khan OS, Babar M, Hashim T, Zeb S, Tariq MA, Patlolla SR, Ali J, Hashim SN and Hashim S. An overview of systemic lupus erythematosus (SLE) pathogenesis, classification, and management. Cureus 2022; 14: e30330.
[31] Haynes WA, Haddon DJ, Diep VK, Khatri A, Bongen E, Yiu G, Balboni I, Bolen CR, Mao R, Utz PJ and Khatri P. Integrated, multicohort analysis reveals unified signature of systemic lupus erythematosus. JCI Insight 2020; 5: e122312.

Table S1. Comparison of all data between the inactive SLE and active SLE without LN groups

Indicator	Inactive SLE group (n=48)	Active SLE without LN group (n=40)	t/χ^2	P
Female/Male [n (%)]	40 (83.33%)/8 (16.67%)	35 (87.50%)/5 (12.50%)	0.301	0.583
Age (years)	36.15 ± 6.84	37.48 ± 5.02	1.048	0.298
BMI (kg/m^2)	23.85 ± 3.21	25.67 ± 4.12	2.326	0.022
Ethnicity [n (%)]			0.431	0.512
Han	46 (95.83%)	36 (90.00%)		
Others	2 (4.17%)	4 (10.00%)		
Family history of SLE [n (%)]	5 (10.42%)	3 (7.50%)	0.010	0.919
Smoking history [n (%)]	8 (16.67%)	7 (17.50%)	0.011	0.918
Drinking history [n (%)]	5 (10.42%)	6 (15.00%)	0.419	0.517
Comorbidities [n (%)]				
Hypertension	12 (25.00%)	15 (37.50%)	1.603	0.205
Diabetes	4 (8.33%)	5 (12.50%)	0.084	0.773
Cardiovascular disease	3 (6.25%)	1 (2.50%)	0.107	0.744
Medication history [n (%)]				
Corticosteroids	18 (37.50%)	28 (70.00%)	9.237	0.002
HCQ	28 (58.33%)	30 (75.00%)	2.697	0.101
MMF	5 (10.42%)	12 (30.00%)	5.368	0.021
AZA	2 (4.17%)	8 (20.00%)	3.972	0.046
Cumulative corticosteroids dose (mg, prednisone equivalent)	1250.53 ± 320.15	1450.75 ± 350.24	2.799	0.006
Disease duration (months)	85.16 ± 20.36	96.24 ± 22.15	2.442	0.017
SLEDAI (scores)	2.88 ± 0.52	9.19 ± 2.32	16.887	<0.001
SLICC SLE damage index (scores)	4.15 ± 1.03	4.37 ± 0.78	1.104	0.273
Platelets ($\times 10^9/L$)	245.36 ± 52.14	238.36 ± 47.62	0.653	0.516
WBC ($\times 10^9/L$)	6.52 ± 1.83	5.52 ± 1.67	2.642	0.010
Hemoglobin (g/L)	125.36 ± 12.45	112.45 ± 10.36	5.223	<0.001
ESR (mm/h)	18.45 ± 5.18	24.45 ± 6.21	4.947	<0.001
CRP (mg/L)	3.52 ± 1.12	4.87 ± 1.53	4.651	<0.001
Proteinuria (g/24 h)	0.25 ± 0.08	0.29 ± 0.08	2.488	0.015
Serum creatinine (mg/dl)	0.72 ± 0.15	0.85 ± 0.18	3.537	<0.001
eGFR ($mL/min/1.73\ m^2$)	117.63 ± 15.45	108.45 ± 12.36	3.035	0.003
C3 (g/L)	1.05 ± 0.16	0.85 ± 0.14	6.082	<0.001
C4 (g/L)	0.18 ± 0.05	0.14 ± 0.03	5.520	<0.001
ANA positivity [n (%)]	45 (93.75%)	40 (100%)	1.038	0.308
Anti-dsDNA positivity [n (%)]	15 (31.25%)	22 (55.00%)	5.051	0.025
Serum Galectin-9 (ng/ml)	8.59 ± 0.63	9.68 ± 1.87	3.545	<0.001
Urinary MCP-1 (pg/mg creatinine)	1.58 ± 0.42	2.85 ± 0.92	8.093	<0.001

SLE, Systemic Lupus Erythematosus; LN, Lupus Nephritis; BMI, Body Mass Index; HCQ, Hydroxychloroquine; MMF, Mycophenolate Mofetil; AZA, Azathioprine; SLEDAI, Systemic Lupus Erythematosus Activity Index; SLICC, The Systemic Lupus International Collaborating Clinics Damage Index; WBC, White Blood Cells; ESR, Erythrocyte Sedimentation Rate; CRP, C-Reaction Protein; eGFR, estimated Glomerular Filtration Rate; C3, Complement 3; C4, Complement 4; ANA, Antinuclear Antibodies; dsDNA, double-stranded Deoxyribonucleic Acid; MCP-1, Monocyte Chemoattractant Protein-1.

Table S2. Comparison of all data between the inactive SLE and active SLE with LN groups

Indicator	Inactive SLE group (n=48)	Active SLE with LN group (n=60)	t/χ^2	P
Female/Male [n (%)]	40 (83.33%)/8 (16.67%)	52 (86.67%)/8 (13.33%)	0.235	0.628
Age (years)	36.15 ± 6.84	38.72 ± 7.21	1.879	0.063
BMI (kg/m^2)	23.85 ± 3.21	26.13 ± 3.35	3.580	<0.001
Ethnicity [n (%)]			0.020	0.888
Han	46 (95.83%)	56 (93.33%)		
Others	2 (4.17%)	4 (6.67%)		
Family history of SLE [n (%)]	5 (10.42%)	9 (15.00%)	0.497	0.481
Smoking history [n (%)]	8 (16.67%)	11 (18.33%)	0.051	0.821
Drinking history [n (%)]	5 (10.42%)	8 (13.33%)	0.214	0.643
Comorbidities [n (%)]				
Hypertension	12 (25.00%)	36 (60.00%)	13.23	<0.001
Diabetes	4 (8.33%)	9 (15.00%)	1.119	0.29
Cardiovascular disease	3 (6.25%)	7 (11.67%)	0.398	0.528
Medication history [n (%)]				
Corticosteroids	18 (37.50%)	45 (75.00%)	15.429	<0.001
HCQ	28 (58.33%)	48 (80.00%)	6.004	0.014
MMF	5 (10.42%)	28 (46.67%)	16.514	<0.001
AZA	2 (4.17%)	15 (25.00%)	8.727	0.003
Cumulative corticosteroids dose (mg, prednisone equivalent)	1250.53 ± 320.15	1820.61 ± 420.18	7.766	<0.001
Disease duration (months)	85.16 ± 20.36	107.37 ± 25.83	4.867	<0.001
SLEDAI (scores)	2.88 ± 0.52	14.75 ± 3.14	28.810	<0.001
SLICC SLE damage index (scores)	4.15 ± 1.03	4.62 ± 0.95	2.493	0.014
Platelets ($\times 10^9/L$)	245.36 ± 52.14	225.24 ± 45.28	2.145	0.034
WBC ($\times 10^9/L$)	6.52 ± 1.83	5.34 ± 1.53	3.662	<0.001
Hemoglobin (g/L)	125.36 ± 12.45	110.47 ± 10.82	6.645	<0.001
ESR (mm/h)	18.45 ± 5.18	26.69 ± 7.53	6.720	<0.001
CRP (mg/L)	3.52 ± 1.12	5.87 ± 1.55	9.112	<0.001
Proteinuria (g/24 h)	0.25 ± 0.08	1.22 ± 0.35	20.705	<0.001
Serum creatinine (mg/dl)	0.72 ± 0.15	1.18 ± 0.24	12.186	<0.001
eGFR ($mL/min/1.73\ m^2$)	117.63 ± 15.45	88.52 ± 20.14	8.255	<0.001
C3 (g/L)	1.05 ± 0.16	0.78 ± 0.12	9.439	<0.001
C4 (g/L)	0.18 ± 0.05	0.12 ± 0.03	6.466	<0.001
ANA positivity [n (%)]	45 (93.75%)	58 (96.67%)	0.066	0.798
Anti-dsDNA positivity [n (%)]	15 (31.25%)	47 (78.33%)	24.177	<0.001
Serum Galectin-9 (ng/ml)	8.59 ± 0.63	11.72 ± 2.14	10.769	<0.001
Urinary MCP-1 (pg/mg creatinine)	1.58 ± 0.42	10.45 ± 3.18	21.367	<0.001

SLE, Systemic Lupus Erythematosus; LN, Lupus Nephritis; BMI, Body Mass Index; HCQ, Hydroxychloroquine; MMF, Mycophenolate Mofetil; AZA, Azathioprine; SLEDAI, Systemic Lupus Erythematosus Activity Index; SLICC, The Systemic Lupus International Collaborating Clinics Damage Index; WBC, White Blood Cells; ESR, Erythrocyte Sedimentation Rate; CRP, C-Reaction Protein; eGFR, estimated Glomerular Filtration Rate; C3, Complement 3; C4, Complement 4; ANA, Antinuclear Antibodies; dsDNA, double-stranded Deoxyribonucleic Acid; MCP-1, Monocyte Chemoattractant Protein-1.

Table S3. Comparison of all data between the active SLE without LN and active SLE with LN groups

Indicator	Active SLE without LN group (n=40)	Active SLE with LN group (n=60)	t/χ^2	P
Female/Male [n (%)]	35 (87.50%)/5 (12.50%)	52 (86.67%)/8 (13.33%)	0.015	0.903
Age (years)	37.48 ± 5.02	38.72 ± 7.21	1.012	0.314
BMI (kg/m^2)	25.67 ± 4.12	26.13 ± 3.35	0.613	0.541
Ethnicity [n (%)]			0.051	0.821
Han	36 (90.00%)	56 (93.33%)		
Others	4 (10.00%)	4 (6.67%)		
Family history of SLE [n (%)]	3 (7.50%)	9 (15.00%)	0.667	0.414
Smoking history [n (%)]	7 (17.50%)	11 (18.33%)	0.011	0.915
Drinking history [n (%)]	6 (15.00%)	8 (13.33%)	0.055	0.814
Comorbidities [n (%)]				
Hypertension	15 (37.50%)	36 (60.00%)	4.862	0.027
Diabetes	5 (12.50%)	9 (15.00%)	0.125	0.724
Cardiovascular disease	1 (2.50%)	7 (11.67%)	1.636	0.201
Medication history [n (%)]				
Corticosteroids	28 (70.00%)	45 (75.00%)	0.304	0.581
HCQ	30 (75.00%)	48 (80.00%)	0.35	0.554
MMF	12 (30.00%)	28 (46.67%)	2.778	0.096
AZA	8 (20.00%)	15 (25.00%)	0.339	0.561
Cumulative corticosteroids dose (mg, prednisone equivalent)	1450.75 ± 350.24	1820.61 ± 420.18	4.601	<0.001
Disease duration (months)	96.24 ± 22.15	107.37 ± 25.83	2.231	0.028
SLEDAI (scores)	9.19 ± 2.32	14.75 ± 3.14	10.171	<0.001
SLICC SLE damage index (scores)	4.37 ± 0.78	4.62 ± 0.95	1.395	0.166
Platelets (×10^9/L)	238.36 ± 47.62	225.24 ± 45.28	1.391	0.167
WBC (×10^9/L)	5.52 ± 1.67	5.34 ± 1.53	0.547	0.585
Hemoglobin (g/L)	112.45 ± 10.36	110.47 ± 10.82	0.915	0.363
ESR (mm/h)	24.45 ± 6.21	26.69 ± 7.53	1.561	0.122
CRP (mg/L)	4.87 ± 1.53	5.87 ± 1.55	3.178	0.002
Proteinuria (g/24 h)	0.29 ± 0.08	1.22 ± 0.35	19.687	<0.001
Serum creatinine (mg/dl)	0.85 ± 0.18	1.18 ± 0.24	7.826	<0.001
eGFR (mL/min/1.73 m^2)	108.45 ± 12.36	88.52 ± 20.14	6.128	<0.001
C3 (g/L)	0.85 ± 0.14	0.78 ± 0.12	2.601	0.011
C4 (g/L)	0.14 ± 0.03	0.12 ± 0.03	2.787	0.006
ANA positivity [n (%)]	40 (100.00%)	58 (96.67%)	0.191	0.662
Anti-dsDNA positivity [n (%)]	22 (55.00%)	47 (78.33%)	6.109	0.013
Serum Galectin-9 (ng/ml)	9.68 ± 1.87	11.72 ± 2.14	4.911	<0.001
Urinary MCP-1 (pg/mg creatinine)	2.85 ± 0.92	10.45 ± 3.18	17.466	<0.001

SLE, Systemic Lupus Erythematosus; LN, Lupus Nephritis; BMI, Body Mass Index; HCQ, Hydroxychloroquine; MMF, Mycophenolate Mofetil; AZA, Azathioprine; SLEDAI, Systemic Lupus Erythematosus Activity Index; SLICC, The Systemic Lupus International Collaborating Clinics Damage Index; WBC, White Blood Cells; ESR, Erythrocyte Sedimentation Rate; CRP, C-Reaction Protein; eGFR, estimated Glomerular Filtration Rate; C3, Complement 3; C4, Complement 4; ANA, Antinuclear Antibodies; dsDNA, double-stranded Deoxyribonucleic Acid; MCP-1, Monocyte Chemoattractant Protein-1.