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RESEARCH ARTICLE

Liang et al: CRP–TyG index and lupus nephritis risk

Association between the CRP–TyG index and lupus nephritis risk

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ABSTRACT

Assessment of insulin resistance is increasingly emphasized in patients with systemic lupus erythematosus (SLE) due to its significant role in predicting kidney injury and cardiovascular risk. Given that sustained inflammation is a hallmark of SLE, the novel C-reactive protein (CRP)-triglyceride-glucose (TyG) index (CTI), which comprehensively reflects insulin resistance and inflammation, has emerged as a valuable biomarker. This study aimed to investigate the association between the CTI and the risk of lupus nephritis (LN) risk and further explore its predictive potential in SLE patients. A cohort of 195 SLE patients stratified by renal involvement or CTI tertiles were included. Spearman's correlation analysis was performed to assess the relationship between the CTI and clinical parameters of lupus activity. Logistic regression analysis was utilized to identify the association between the CTI and risk of LN. The receiver operating characteristic (ROC) curve was employed to evaluate the CTI and the TyG index in predicting LN. The results demonstrated significantly elevated CTI levels in the LN group compared to the non-LN group. Multivariate-adjusted regression analysis indicated that a unit increase in CTI corresponded to enhanced risk of LN (adjusted OR =2.062; 95% CI: 1.208 – 3.522), particularly among patients in the third tertile compared to those in the first tertile (adjusted OR = 4.368; 95% CI: 1.411 – 13.520). Subgroup analysis revealed that SLE patients with a SLEDAI-2K score greater than 6 exhibited an increased LN risk associated with higher CTI levels. ROC analysis illustrated the higher sensitivity of CTI (AUC = 0.6592; 95%CI, 0.576 – 0.742) compared to the TyG index (AUC = 0.6327; 95%CI, 0.546 – 0.719) in predicting LN risk. These findings indicate that elevated CTI is strongly associated with an increased risk of LN, suggesting its potential as a valuable predictor of LN risk in SLE patients.

Keywords: C-reactive protein-triglyceride-glucose index, systemic lupus erythematosus, lupus nephritis, proteinuria.

INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by the production of multiple autoantibodies, severe organ damage, frequent disease flares and sustained inflammation [1,2]. Lupus nephritis (LN) is one of the most common and serious manifestations in SLE patients, which can progress to end-stage renal disease and significantly increase mortality risk [3,4]. The early diagnosis and effective treatment strategies of kidney involvement are therefore of utmost importance for improving the prognosis of these patients.

Metabolic disturbance, including insulin resistance or dyslipidemia, has drawn more attention in SLE patients due to its positive correlation with disease progression. Insulin resistance contributes to complement activation, immune dysregulation and enhanced secretion of inflammatory cytokines, potentially exacerbating systemic inflammation and nephritis activity [5–9].

The triglyceride-glucose (TyG) index serves as a clinically valuable marker for insulin resistance assessment. Increasing evidence demonstrates that elevated TyG index is associated with renal impairment, including higher proteinuria levels and accelerated chronic kidney disease (CKD) progression in diabetes populations [10–12]. In particular, the TyG index is linked to increased risk of carotid atherosclerosis, retinal microvascular damage and hypertension in patients with autoimmune diseases [13–15]. Recently, C-reactive protein-triglyceride-glucose index (CTI), which serves as a biomarker integrating insulin resistance and systemic inflammation, has been demonstrated as a valuable predictor of cardiovascular disease, stroke risk and liver fibrosis progression [16–18]. CTI reflects systemic inflammation and metabolic dysfunction by incorporating CRP and TyG index parameters. However, evidence regarding the association between the CTI and LN risk in SLE patients remains rare. In this study, we focus on investigating the association and further exploring the predictive efficacy between the CTI and LN risk in SLE patients.

MATERIALS AND METHODS

Study population

A total of 195 patients with SLE were enrolled from the Third Affiliated Hospital of Southern Medical University from January 2018 to December 2022 in this

retrospective study. The inclusion criteria included (1) satisfying the European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) classification criteria (2019) for systemic lupus erythematosus; (2) available data of fasting triglycerides, glucose concentrations and C-reactive protein (CRP) level; and (3) over 18 years old. SLE patients in the LN group should also meet the following conditions: (1) persistent proteinuria over 0.5g/day or urine protein >3+ in routine urinalysis; and/or persistent cellular casts; or active urinary sediment (>5 red blood cells/high-power field, >5 white blood cells/high-power field and infection excluded; (2) and/or renal biopsy pathology confirming LN. Also, patients meeting any of the following criteria were excluded: (1) pregnant women; (2) aged under 18 years old; (3) history of gastrointestinal surgery; (4) severe liver dysfunction; (5) history of malignant tumors; (6) history of diabetes; (7) history of hypertension; (8) with infections. The systemic lupus erythematosus disease activity index-2000 (SLEDAI-2K) score was used to evaluate the disease activity for SLE patients.

Data collection

Demographic, laboratory data and clinical characteristics of SLE patients were collected from medical records. The data included age, sex, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), anti-dsDNA antibody, anti-Sm antibody, 24-hour proteinuria, blood creatinine, blood urea nitrogen, blood uric acid, estimated glomerular filtration rate (eGFR), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), fasting triglyceride (TG), total cholesterol (TC), fasting glucose, complements (C3, C4 and C1q) and 25-hydroxyvitaminD (25(OH)D).

The TyG index and CTI assessment

The TyG index was assessed using the following formula: Ln [Blood triglyceride concentration (mg/dL) × Blood glucose concentration (mg/dL) /2]. The value of the CTI was calculated according to the following formula: TyG index+0.412×Ln [CRP (mg/L)] [17].

The eGFR assessment

The estimated glomerular filtration rate (eGFR) was assessed using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation (2021) [19].

Ethical statement

This study was conducted in accordance with the ethical principles outlined in the *Declaration of Helsinki* and relevant national clinical research regulations. Ethical approval was granted by the Ethics Committee of the Third Affiliated Hospital of Southern Medical University.

Statistical analysis

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) software version 23.0. GraphPad Prism software version 8 and RStudio were used to produce the graphs. The extent of missing data in this study is shown in Table S1, and we utilized complete cases to address the issue of missing values. Continuous variables were expressed as the mean ± standard deviation (SD) or median (interquartile range, IQR), and categorical variables were presented as numbers or percentages. Data normality was assessed using the Shapiro-Wilk test. Comparisons between the LN and non-LN groups were performed using Student's t-test for symmetrically distributed data and the Mann-Whitney *U* test for skewed distribution data. For comparisons across CTI tertiles, ANOVA was used for continuous parametric variables and the Kruskal-Wallis test for nonparametric data. Comparisons between categorical variables were performed using the chi-square test. Correlations between CTI and clinical parameters were evaluated using Spearman's correlation coefficient. To identify the risk factors associated with LN, we conducted logistic regression models and the results were expressed as odds ratios (ORs) and 95% confidence intervals (CIs). Based on the logistic model with continuous CTI values and 65 observed LN events, we conducted power calculations assuming a two-tailed α of 0.05, and the post-hoc power showed as 91.5%, confirming sufficient coefficient stability for analysis. Three logistic models were employed to investigate the association between the CTI and LN. Model 1 remained unadjusted. Model 2 adjusted for age and sex. Model 3 adjusted for age, erythrocyte sedimentation rate, anti-dsDNA antibody, use of glucocorticoid and use of lipid-lowering agents. The variance inflation factors (VIFs) were used to measure potential collinearity between the CTI and other covariates. All covariates demonstrated VIFs less than 5 (shown in Table S2), indicating the absence of significant multicollinearity in regression models. All corresponding ORs and 95%CIs are presented in Table S3. The Hosmer-Lemeshow test was employed to assess the calibration of logistic regression models incorporating

CTI for discriminative performance in identifying LN, and the results showed adequate calibration of the prediction models incorporating CTI for LN (all $P > 0.05$, as shown in Table S4). To evaluate the potential effect of modification, stratified analyses were performed for potential covariables (age, eGFR, SLEDAI-2K scores, and glucocorticoid use) on the relationship between CTI and LN risk. The distributions of LN and non-LN events in each subgroup are summarized in Table S5. The Benjamini–Hochberg false-discovery rate was applied to control multiplicity, including CTI tertiles comparisons, correlation analysis and subgroup interaction tests. Additionally, we performed operating characteristic curve (ROC) analysis to assess the predictive capacity for LN risk, with the area under the ROC curve (AUC) assessing the incremental effect of CTI. The restricted cubic spline (RCS) with four knots (placed at the 5th, 35th, 65th, and 95th percentiles) to explore the dose-response relationship between CTI and the LN risk. The RCS plot was conducted in RStudio software using the rms R package. A P value < 0.05 was considered statistically significant.

RESULTS

Demographic and clinical characteristics of the SLE patients according to LN status and CTI tertiles

We analyzed 195 SLE patients with available CTI in this study. As shown in Table 1, significantly higher levels of SLEDAI-2K score, 24-hour proteinuria, BUN, Cr, UA, ESR, CRP, anti-dsDNA antibody, D-dimer, TG, TC and LDL-C were observed in the LN group compared to the non-LN group (all $P < 0.01$). Additionally, LN patients performed significantly lower levels of eGFR, C3, C4, C1q and 25(OH)D (all $P < 0.05$). Overall, SLE patients with LN had significantly higher CTI compared with those without (8.78±0.97 vs 8.25±0.88, $P < 0.001$). Furthermore, we divided the patients into three groups according to CTI tertiles, and the average values of the CTI were 6.31 – 7.88 in tertile 1, 7.88 – 8.93 in tertile 2 and 8.93 – 10.98 in tertile 3, respectively. Table 2 lists the comparisons of demographic, laboratory and clinical characteristics among the CTI tertiles. We found significantly enhanced levels of SLEDAI-2K score, UA, ESR, CRP, anti-dsDNA antibody, GLU, TG and TC while decreasing levels of eGFR and HDL-C with elevation in the tertiles of the CTI (all $P < 0.05$).

Correlations of CTI with clinical parameters in SLE patients

Figure 1 shows the Spearman's correlations of the CTI with clinical parameters in SLE patients. CTI was positively correlated with SLEDAI-2K score, 24-hour proteinuria, Cr, BUN, UA, ESR, D-Dimer, TC and anti-dsDNA antibody levels, while negatively correlated with eGFR, HDL-C and C4 levels in SLE patients (all $P <$ 0.05).

Relationship between CTI and LN risk in SLE patients

Table 3 presents the multivariate regression analysis for the relationship between CTI and LN risk. The results showed that following all covariates adjusted in Model 3, every unit increase in CTI was associated with a 106.2% higher LN risk (OR = 2.062, 95%CI: 1.208 – 3.522), and each SD increase in CTI (SD = 0.94) predicted a 97.5% higher LN risk (OR = 1.975, 95%CI: 1.194 – 3.266). Next, we stratified CTI into tertiles for sensitivity analysis. In comparison to the tertile 1 of the CTI group, tertile 3 was significantly associated with higher LN risk (OR = 3.879; 95%CI: 1.781 – 8.447, *P* for trend 0.002) in Model 1 and age and sex-adjusted in Model 2 (OR = 4.497; 95%CI: 2.016 – 10.03, *P* for trend 0.001). Furthermore, after adjusting for all covariates in Model 3, the positive link remained significantly consistent (OR = 4.368; 95%CI: 1.411 – 13.520, *P* for trend 0.031). Additionally, we used the restricted cubic splines (RCS) regression model to evaluate the association between CTI and LN risk, as shown in Figure 2. The CTI displayed a dose-response relationship with LN risk in the full-adjusted model 3 (*P* for total = 0.010, *P* for nonlinearity = 0.068).

Subgroup analysis

Table 4 presents the subgroup analyses assessing the stability of the association between CTI and LN risk in SLE patients. SLE patients were categorized into subgroups according to age, eGFR, disease activity (SLEDAI-2K score) and use of glucocorticoid. When stratified by age or use of glucocorticoid, their interaction *P* values were non-significant (both $P > 0.05$), indicating no age-related or glucocorticoid usage modification. In eGFR subgroups, patients with preserved renal function (eGFR $\geq$ 90 mL/min/1.73m^2) demonstrated a significantly higher LN risk associated with the elevated CTI (OR = 1.901, 95%CI: 1.213 – 2.978, $P = 0.005$). Importantly, disease activity interacted this association (*P* for interaction < 0.001), and patients with high disease activity (SLEDAI-2K score > 6) exhibited significantly

higher LN risk (OR = 1.535, 95%CI: 1.017 – 2.315, $P = 0.041$) compared to those with low disease activity (SLEDAI-2K score ≤ 6). These results indicated that patients with active SLE exhibited a high-risk subgroup for CTI-associated LN development.

Potential predictive value of the CTI for LN risk

The receiver operating characteristic (ROC) curves were generated to directly compare the predictive capability of CTI and TyG index for LN risk. As shown in Figure 3, the CTI presented an AUC of 0.6592 (95%CI: 0.576 – 0.742), and the TyG index performed an AUC of 0.6327 (95%CI: 0.546 – 0.719). The CTI cut-off value of 8.46 with 66.2% sensitivity and 63.1% specificity, which outperforms the TyG index cut-off of 8.50 (sensitivity = 52.3%, specificity = 73.1%). CTI demonstrated higher sensitivity for detecting LN risk compared to the TyG index, which may significantly improve the early identification of high-risk patients.

DISCUSSION

Kidney involvement is one of the most common and severe clinical manifestations of SLE, presenting significant challenges to achieving disease remission. End-stage renal disease remains a leading cause of mortality in this population [20,21]. Although invasive renal biopsy serves as the diagnostic gold standard for LN, the risk of procedure-related complications requires careful consideration. These limitations highlight the critical need for non-invasive and accurate predictive markers to enable earlier diagnosis of LN.

Previous studies have indicated the TyG index as an important metabolic marker in predicting renal damage in diabetes and cardiovascular disease populations [10,22–24]. Recently, the TyG index has been confirmed as a reliable screening indicator for insulin resistance in the SLE population [25], which also demonstrated the predictor for SLE comorbidities, including cardiovascular risk, myosteatosis, hypertension incidence and LN risk [9,14,15]. Specifically, CTI synergistically integrates CRP and the TyG index parameters, thus comprehensively reflecting systemic inflammation and metabolic dysfunction. Chronic inflammation constitutes a hallmark of SLE pathogenesis, especially in LN progression, but the association between CTI and LN risk remains unknown.

In our study, we observed significantly elevated CTI in LN patients compared to non-LN patients. Also, CTI demonstrated strong positive correlations with LDL-C, TC, ESR and anti-dsDNA antibody, alongside a negative correlation with C3 and HDL-C levels in SLE patients. These results were consistent with the former studies that insulin resistance and activated inflammation play crucial roles in the pathogenesis of LN [26–28]. Similarly, elevated TyG index is linked to LN risk, and our data also found that CTI potentially serves as a predictive indicator for identifying LN and showed higher sensitivity compared to the TyG index. Moreover, subgroup analysis revealed a robust association between the CTI and LN specifically in patients with high disease activity (SLEDAI-2K score＞6) or with preserved renal function (eGFR ≥90 mL/min/1.73m^2), indicating the relevance of CTI to autoimmune-driven renal injury, especially in active SLE patients.

Growing evidence indicates that insulin resistance exacerbates renal injury through non-immunological and immunodulatory pathways. First, insulin resistance drives non-immune renal damage through adipocytokine-driven fibrotic remodeling, mitochondrial dysfunction-induced oxidative stress, accumulation of advanced glycation end-products and vitamin D deficiency [8,26,28–31]. Our research revealed that LN patients exhibited metabolic dysregulation, including elevated TC, TG and LDL-C as well as decreased 25(OH)D levels compared to non-LN patients, which may mechanistically contribute to renal injury independent of autoimmunity. Second, insulin resistance may disrupt immune homeostasis through enhanced immune-complex deposition, complement activation and inflammation amplification [32,33]. Specifically, inflammation and insulin resistance can form a self-perpetuating cycle, in which sustained inflammatory cytokines worsen insulin resistance, while hyperglycemia and hyperinsulinism amplify inflammation responses. Together, these pathways synergistically cause renal hemodynamics dysregulation, glomerular endothelial damage and podocyte foot process fusion, collectively driving LN progression.

While insulin resistance is implicated in LN, therapeutic strategies directly targeting insulin resistance for LN management remain limited. Among conventional immunomodulators commonly used in LN treatment, hydroxychloroquine (HCQ) ameliorates insulin resistance whereas glucocorticoids application exerts an opposing effect [34,35]. It emphasizes the attention on glucocorticoids-induced metabolic

complications and the clinical significance of exploring novel insulin resistance-specific therapies in SLE patients.

Despite having comprehensively analyzed the association between the CTI and LN risk in this study, several limitations still need to be pointed out. First, as a constituent of CTI, CRP reflects SLE disease activity and nonspecific inflammation [36]. CRP is mainly driven by interleukin-6 (IL-6) in active SLE, and a significantly higher CRP level is associated with renal damage in SLE [37]. However, the production of CRP involves various regulatory factors, including interferon-dependent suppression of hepatic CRP production and concurrent infections [36,38], which may limit the significance of CRP as an important inflammation marker in SLE patients. Second, the limited availability of renal biopsy classifications among biopsied patients in this study prevented examination of correlations between CTI and renal histopathological outcomes. Additionally, this retrospective cross-sectional study only contains Chinese individuals and was conducted in a single research center. Also, the limited sample size restricted the statistical power, particularly for subgroup analysis. Further multicenter studies with larger and ethnically diverse cohorts are required to validate these findings. In addition, our study primarily focused on the relationship between the CTI and LN risk while lacking longitudinal data to further prove their causation.

CONCLUSION

In conclusion, this study identified CTI as an inflammation and metabolic integration biomarker to independently predict lupus nephritis risk. Our data demonstrate a significant association between elevated CTI and increased LN risk. CTI may provide a valuable implication for identifying SLE patients at heightened risk of renal involvement, and serve as an effective and simple indicator for LN risk assessment in clinical practice. Future research is needed to explore the causality and mechanistic links between CTI and renal immune disorder.

Conflicts of interest: Authors declare no conflicts of interest.

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Data availability: The data sets supporting the conclusions of this article and its supporting information are available from the corresponding author upon reasonable request.

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TABLES AND FIGURES WITH LEGENDS

Table 1. Baseline characteristics of the SLE patients with or without LN

Parameter	LN (n = 65)	Non-LN (n = 130)	p value
Demographic characteristics			
Age (years)	31.60±9.33	34.26±10.59	0.087
Sex			0.504
Male, *n* (%)	8 (12.3)	12 (9.2)	
Female, *n* (%)	57 (87.7)	118 (90.8)	
Clinical features			
SLEDAI-2K score	18 (8.5-22)	6.5 (3.25-10)	**<0.001**
Glucocorticoid treatment, *n* (%)	52 (80.0)	86 (66.2)	**0.045**
Renal function			
eGFR (mL/min/1.73m^2)	96.4 (68.78-120.08)	117.15 (96.95-125.5)	**<0.001**
24-hour proteinuria (mg/d)	736.81 (201.18-1840.31)	109.64 (78.90-155.12)	**<0.001**
BUN (mmol/L)	6.02 (4.46-9.62)	4.14 (3.51-5.25)	**<0.001**
Cr (μmol/L)	75 (63.5-88.5)	58.5 (51-73)	**<0.001**
UA (μmol/L)	406.5 (315.75-478.75)	340.5 (276-386.25)	**<0.001**
Hematuria, *n* (%)	48 (73.8)	40 (30.8)	**<0.001**
Inflammation and immunity			
ESR (mm/h)	39 (18.25-71.5)	21 (12.25-29.75)	**0.001**
CRP (mg/L)	2.05 (0.54-7.91)	0.99 (0.39-3.00)	**0.009**
C3 (g/L)	0.53 (0.37-0.97)	0.86 (0.64-0.97)	**<0.001**
C4 (g/L)	0.09 (0.04-0.21)	0.14 (0.1-0.24)	**0.003**
C1q (mg/L)	145.54±33.85	158.67±36.44	**0.016**
Anti-dsDNA antibody (IU/ml)	36.86 (1.82-283.21)	9.46 (2.08-41.56)	**0.001**
Anti-Sm antibody (RU/ml)	2.64 (2-23.47)	3.49 (2-51.80)	0.568

D-dimer (μg/L)	329.5 (135-764.5)	168 (112-348.5)	**<0.001**
Metabolic profile			
GLU (mg/dL)	78.56 (72.07-89.01)	81.98 (74.41-87.21)	0.542
TG (mg/dL)	123.11 (80.60-178.91)	90.34 (64.66-124.00)	**0.001**
TyG index	8.51±0.61	8.22±0.49	**0.002**
CTI	8.78±0.97	8.25±0.88	**<0.001**
TC (mmol/L)	4.38 (3.83-5.08)	3.82 (3.18-4.46)	**<0.001**
LDL-C (mmol/L)	2.46 (2.02-3.16)	2.2 (1.47-2.87)	**0.001**
HDL-C (mmol/L)	1.1 (0.87-1.49)	1.09 (0.91-1.30)	0.539
25(OH)D (nmol/L)	48.05±20.01	55.72±17.69	**0.007**

Data were presented as n, median (interquartile range, IQR) or mean ± standard deviation. Abbreviations: LN: Lupus nephritis; SLEDAI-2K: Systemic lupus erythematosus disease activity index-2000; eGFR: Estimated glomerular filtration rate; BUN: Blood urea nitrogen; Cr: Creatinine; UA: Uric acid; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; C3: Complement 3; C4: Complement 4; GLU: Glucose; TG: Triglyceride; TyG index: Triglyceride-glucose index; CTI: C-reactive protein (CRP)-triglyceride glucose index; TC: Total cholesterol; LDL-C: Low-density lipoprotein cholesterol; HDL-C: High-density lipoprotein cholesterol; 25(OH)D: 25-HydroxyvitaminD.

Table 2. Clinical and laboratory characteristics based on CTI tertiles

Parameter	Overall (*n* = 195) (6.31 – 10.98)	CTI			*p* value
		Tertile 1 (*n* = 65) (6.31 – 7.88)	Tertile 2 (*n* = 65) (7.88 – 8.93)	Tertile 3 (*n* = 65) (8.93 – 10.98)	
Demographic characteristics					
Age (years)	33.37±10.24	31.6±9.31	34.14±12.09	34.38±8.97	0.085
Sex					0.946
Male, *n* (%)	20 (10.3)	7 (10.8)	7 (10.8)	6 (9.2)	
Female, *n* (%)	175 (89.7)	58 (89.2)	58 (89.2)	59 (90.8)	
Clinical features					
SLEDAI-2K score	9 (4-16)	5 (2-10)	8 (4-14.5) †	14 (7.25-20) ††, #	**<0.001**
Renal function					
BUN (mmol/L)	4.76 (3.72 - 6.49)	4.61 (3.38-6.04)	4.38 (3.73-5.37)	5.63 (4.13-7.28) †	**0.021**
Cr (μmol/L)	65 (52.02-79.75)	59 (51-68)	60.5 (50.5-78.25)	75 (60.75-100.25)	0.081
UA (μmol/L)	345.5 (296.25-439.75)	308 (269-416)	344 (315-439.25)	367 (311.5-474.75) †	**0.025**
eGFR (mL/min/1.73m^2)	111.95 (84.18-123.25)	117.3 (100.7-125.5)	117.55 (89.5-123.25)	87.05 (62.85-116.1) †	**0.025**
24-hour proteinuria (mg/d)	152.65 (88.36-495.53)	122.15 (69.12-176.39)	116.105 (82.92-427.52)	284.305 (154.30-1062.78) ††, ##	**<0.001**
Inflammation and immunity					
ESR (mm/h)	25 (14-42.75)	18 (12-25)	20.5 (10-27.25)	45.5 (29.25-71.5) †, #	**<0.001**

CRP (mg/L)	1.25 (0.43-4.00)	0.28 (0.19-0.53)	1.36 (0.58-2.19) †††	7 (3.23-12.19) †††, ###	**<0.001**
C3 (g/L)	0.81 (0.51-0.97)	0.78 (0.57-0.97)	0.9 (0.50-1.08)	0.74 (0.47-0.93)	0.256
C4 (g/L)	0.13 (0.07-0.23)	0.15 (0.1-0.24)	0.12 (0.07-0.21)	0.12 (0.06-0.20)	0.085
C1q (mg/L)	142 (124.25-164.5)	145 (128-166)	139 (115.75-164.5)	141.5 (126.5-163.75)	0.797
Anti-dsDNA antibody (IU/ml)	13.95 (2.01-93.81)	4.17 (1-47.67)	15.5 (1.75-84.65)	28.01 (2.59-264.78) †	**0.002**
Anti-Sm antibody (RU/ml)	3.18 (2-28.51)	5.62 (2-59.35)	2 (2-10.36)	3.35 (2-35.94)	0.435
D-dimer (μg/L)	182 (124-477.75)	159 (106-329.5)	147 (100-335)	429.5 (156-1213.5) ††, ##	**<0.001**
Metabolic profile					
GLU (mg/dL)	80.90 (72.97-87.39)	77.66 (71.17-84.50)	80.36 (71.89-86.58)	85.23 (79.01-95.14) ††, ##	**<0.001**
TG (mg/dL)	95.66 (70.86-142.60)	65.54 (55.36-85.47)	103.63 (76.17-124.00) ††	148.80 (112.04-211.24) ††, ##	**<0.001**
TC (mmol/L)	4.03 (3.41-4.78)	3.91 (3.32-4.59)	4.15 (3.54-4.62)	4.34 (3.47-5.20) †	**0.032**
LDL-C (mmol/L)	2.35 (1.78-3.01)	2.15 (1.63-2.75)	2.20 (1.99-2.92)	2.41 (1.64-3.12)	0.736
HDL-C (mmol/L)	1.09 (0.91-1.32)	1.28 (0.97-1.46)	1.11 (0.93-1.33)	1.02 (0.83-1.31)	**0.032**
25(OH)D (nmol/L)	53.16±18.80	55.58±18.61	49.85±19.65	54.05±17.91	0.632
TyG index	8.32±0.55	7.88±0.30	8.29±0.45 ††	8.79±0.45 †††, ###	**<0.001**

CTI	8.43±0.94	7.40±0.40	8.38±0.29 ††	9.51±0.42 †††, ###	**<0.001**

Data were presented as n, median (interquartile range, IQR) or mean ± standard deviation. †, compared with tertile 1, $p < 0.05$; ††, $p < 0.01$; †††, $p < 0.001$. #, compared with tertile 2, ##, $p < 0.01$; ###, $p < 0.001$. Abbreviations: SLEDAI-2K: Systemic lupus erythematosus disease activity index-2000; eGFR: Estimated glomerular filtration rate; BUN: Blood urea nitrogen; Cr: Creatinine; UA: Uric acid; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; C3: Complement 3; C4: Complement 4; GLU: Glucose; TG: Triglyceride; CTI: C-reactive protein (CRP)-triglyceride glucose index; TyG index: Triglyceride-glucose index; TC: Total cholesterol; LDL-C: Low-density lipoprotein cholesterol; HDL-C: High-density lipoprotein cholesterol; 25(OH)D: 25-HydroxyvitaminD.

Table 3. Odds ratios for the association of the CTI with LN in patients with SLE

	Per 1 unit CTI increase	Per 1 SD CTI increase	CTI			*p* for trend
			Tertile 1 (*n* = 65) (6.31 – 7.88)	Tertile 2 (*n* = 65) (7.88 – 8.93)	Tertile 3 (*n* = 65) (8.93 – 10.98)	
			OR (95%CI), *p* value			
Model 1	1.879 (1.331-2.653) *p* < 0.001	1.810 (1.309-2.502) *p* < 0.001	Ref.	1.778 (0.795-3.973) *p* = 0.161	3.879 (1.781-8.447) *p* = 0.001	0.002
Model 2	2.004 (1.407-2.853) *p* < 0.001	1.922 (1.379-2.680) *p* < 0.001	Ref.	1.938 (0.856-4.388) *p* = 0.113	4.497 (2.016-10.03) *p* = 0.001	0.001
Model 3	2.062 (1.208-3.522) *p* = 0.008	1.975 (1.194-3.266) *p* = 0.008	Ref.	2.857 (1.034-7.893) *p* = 0.043	4.368 (1.411-13.520) *p* = 0.011	0.031

Model 1: No covariates were adjusted; Model 2: Adjusted for age and sex; Model 3: Adjusted for age, erythrocyte sedimentation rate (ESR), anti-dsDNA antibody, use of glucocorticoid and use of lipid-lowering agents. Abbreviations: LN: Lupus nephritis; SLE: Systemic lupus erythematosus.

Table 4. Associations between the CTI and LN in subgroup analysis

Variables	N	OR (95%CI)	*p* value	*p* for interaction
Age (years)				0.813
> 35	70	4.357 (1.906-9.958)	0.001	
≤ 35	125	1.608 (1.054-2.453)	0.028	
eGFR (mL/min/1.73m^2)				0.005
eGFR <60	21	1.351 (0.545-3.348)	0.516	
60≤ eGFR <90	30	1.340 (0.593-3.028)	0.482	
eGFR ≥ 90	144	1.901 (1.213-2.978)	0.005	
SLEDAI-2K score				<0.001
> 6	102	1.535 (1.017-2.315)	0.041	
≤ 6	93	1.827 (0.906-3.686)	0.092	
Use of glucocorticoid				0.089
Yes	138	2.480 (1.146-5.369)	0.021	
No	57	1.672 (1.135-2.464)	0.009	

Abbreviations: eGFR: Estimated glomerular filtration rate; SLEDAI-2K: Systemic lupus erythematosus disease activity index-2000.

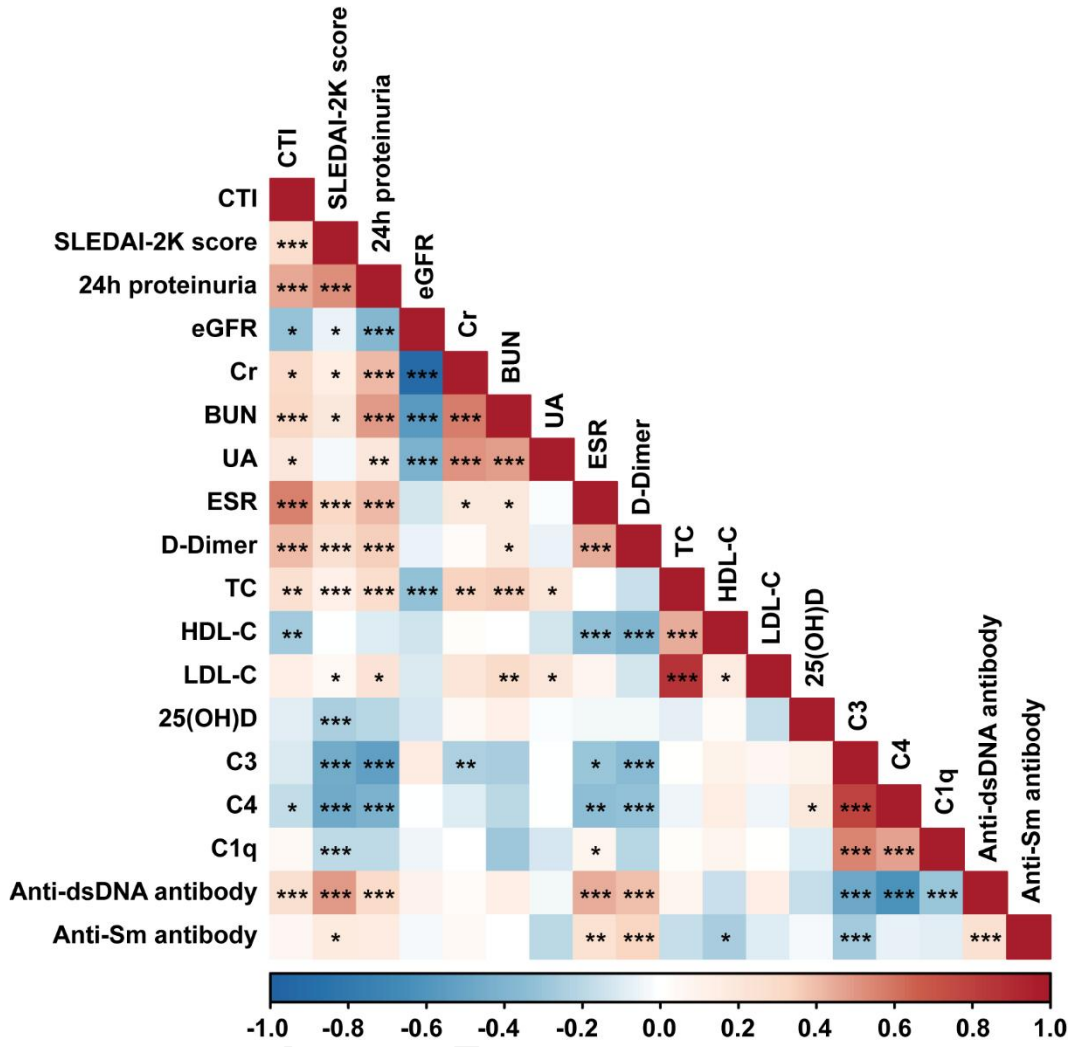

Figure 1. Correlations between the CTI and clinical parameters in SLE patients. *p* values were adjusted for the Benjamini-Hochberg false discovery rate (FDR) method. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. Abbreviations: CTI: C-reactive protein (CRP)-triglyceride glucose index; CTI: C-reactive protein (CRP)-triglyceride glucose index; SLEDAI-2K: Systemic lupus erythematosus disease activity index-2000; eGFR: Estimated glomerular filtration rate; BUN: Blood urea nitrogen; Cr: Creatinine; UA: Uric acid; ESR: Erythrocyte sedimentation rate; C3: Complement 3; C4: Complement 4; TC: Total cholesterol; LDL-C: Low-density lipoprotein cholesterol; HDL-C: High-density lipoprotein cholesterol; 25(OH)D: 25-HydroxyvitaminD.

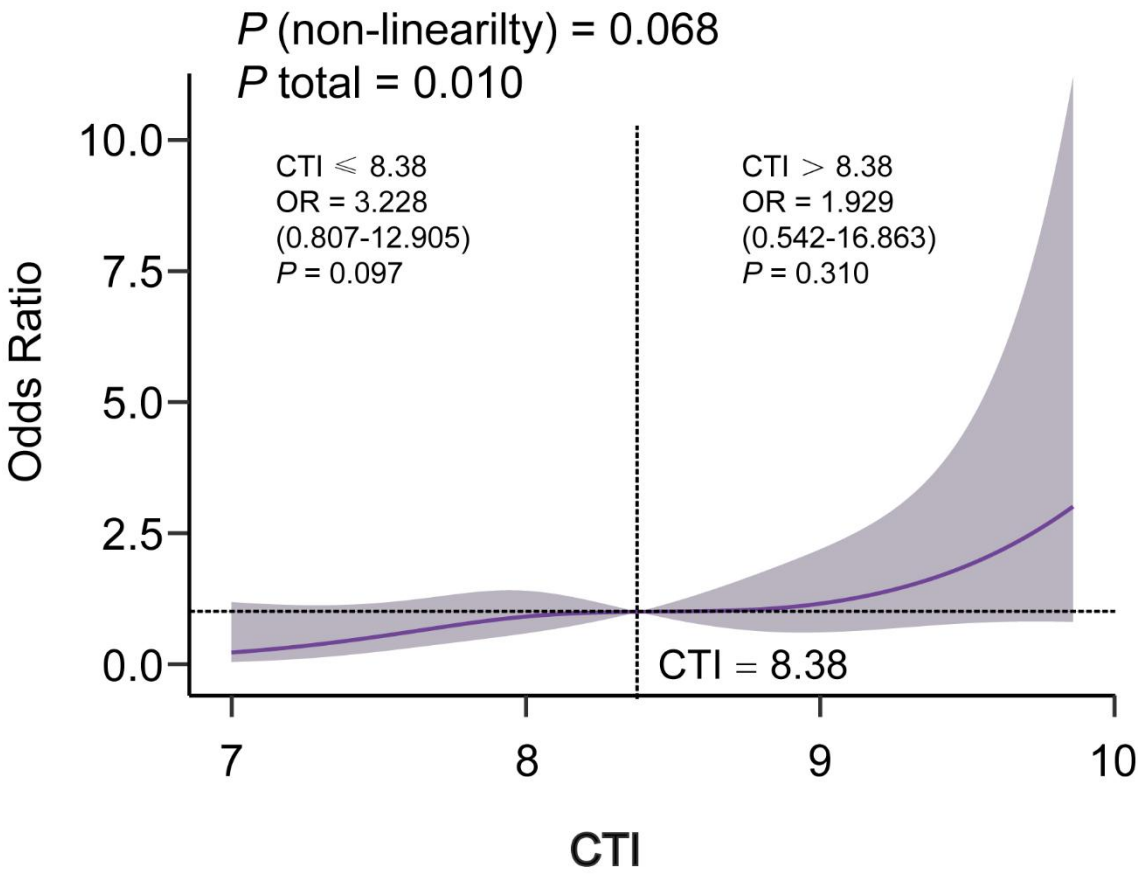

Figure 2. Restricted cubic spline curves for the CTI and LN. Adjusted for age, erythrocyte sedimentation rate, anti-dsDNA antibody, use of glucocorticoid and use of lipid-lowering agents. Abbreviations: CTI: C-reactive protein-triglyceride glucose index; OR: Odds ratio.

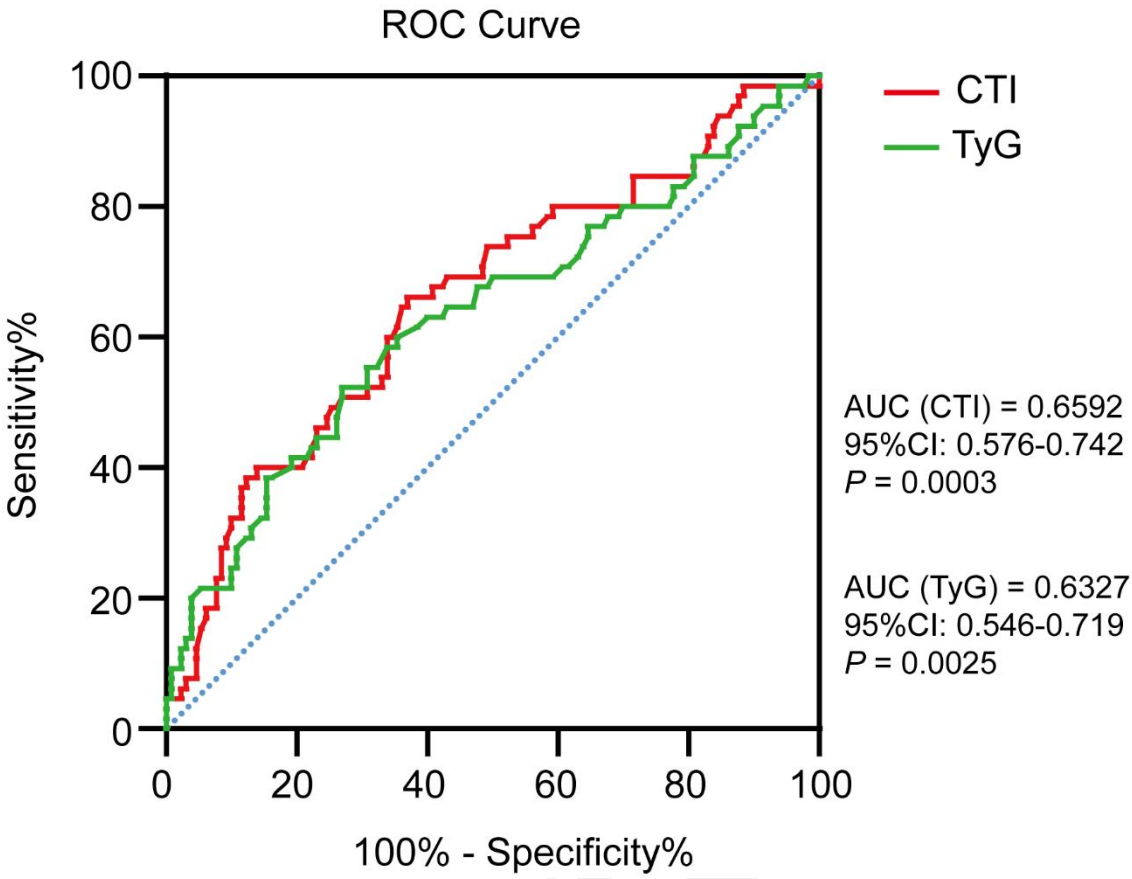

Figure 3. The ROC curves of the CTI and TyG index for predicting LN in patients with SLE. ROC analysis comparing CTI (red) and TyG (green). CTI showed an AUC of 0.6592 (95% CI 0.576–0.742), while TyG had an AUC of 0.6327 (95% CI 0.546–0.719). Optimal cut-offs: CTI 8.46 (sensitivity 66.2%, specificity 63.1%) vs. TyG 8.50 (sensitivity 52.3%, specificity 73.1%). Abbreviations: TyG: Triglyceride–glucose; AUC: Area under the curve; CI: Confidence interval; LN: Lupus nephritis; SLE: Systemic lupus erythematosus.

SUPPLEMENTAL DATA

Table S1. Distribution of variables with missing data

Variables	Number of missing	Missing proportion
24-hour proteinuria	33	16.9%
BUN	28	14.4%
UA	1	0.5%
ESR	3	1.5%
C3	1	0.5%
C4	1	0.5%
C1q	2	1.0%
D-dimer	15	7.7%
Anti-Sm antibody	43	22.1%

Abbreviations: BUN: Blood urea nitrogen; Cr: Creatinine; UA: Uric acid; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; C3: Complement 3; C4: Complement 4.

Table S2. The VIF values for all variables

Covariates	β	*p* value	VIF
Sex	-0.107	0.171	1.035
Age	-0.020	0.795	1.049
ESR	0.316	＜0.001	1.112
Anti-dsDNA antibody	0.092	0.247	1.071
Use of glucocorticoid	0.056	0.469	1.016
Use of lipid-lowering agents	-0.097	0.210	1.028

Abbreviations: VIF: Variance inflation factor; ESR: Erythrocyte sedimentation rate.

Table S3. The ORs and 95%CIs for all variables in Model 3

Variables	OR (95%CI)	*p* value
Age	0.975 (0.933 - 1.018)	0.251
ESR	1.010 (0.992 - 1.029)	0.286
Anti-dsDNA antibody	1.000 (1.000 - 1.001)	0.359
Use of glucocorticoid	1.244 (0.516 - 2.999)	0.627
Use of lipid-lowering agents	0.000	0.999

Abbreviations: ORs: Odds ratios; CIs: Confidence intervals; ESR: Erythrocyte sedimentation rate.

Table S4. Hosmer-Lemeshow test of the Models

Models	χ^2	*p* value
Model 1	9.196	0.326
Model 2	7.778	0.353
Model 2 + CTI	4.430	0.816
Model 3	14.691	0.065
Model 3 + CTI	10.215	0.250

Model 1: No covariates were adjusted; Model 2: Adjusted for age and sex; Model 3: Adjusted for age, erythrocyte sedimentation rate, anti-dsDNA antibody, use of glucocorticoid, use of lipid-lowering agents. Abbreviation: CTI: C-reactive protein-triglyceride glucose index.

Table S5. The distributions of LN and non-LN events in each subgroup

Variables	LN events	Non-LN events
Age (years)		
>35	16	54
≤35	49	76
eGFR (mL/min/1.73m^2)		
eGFR<60	14	7
60≤eGFR<90	15	15
eGFR<60	36	108
SLEDAI-2K score		
>6	50	52
≤6	15	78
Use of glucocorticoid		
Yes	52	86
No	13	44

Abbreviations: LN: Lupus nephritis; eGFR: Estimated glomerular filtration rate; SLEDAI-2K: Systemic lupus erythematosus disease activity index-2000.