Shi *et al. Lipids in Health and Disease* (2025) 24:135
https://doi.org/10.1186/s12944-025-02503-y

Lipids in Health and Disease

RESEARCH Open Access

Effects of remnant cholesterol on adverse renal outcomes in lupus nephritis

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Abstract

Background Remnant cholesterol (RC) causes inflammation and promotes kidney diseases development. However, its role in lupus nephritis (LN) remains unclear. The purpose of this study was to investigate the association between RC and LN.

Methods This observational study was conducted among patients enrolled between 2000 and 2018 in the High Quality Evidence of Guangzhou Lupus Nephritis Cohort. The study outcomes were defined as adverse renal outcomes, including serum creatinine doubled and end-stage renal disease. Patients were stratified into lower and higher RC groups based on the optimal cutoff RC value (86.88 mg/dL) for adverse renal outcomes. To explore the association between renal outcomes and RC, survival analyses, multivariate Cox regression analyses, and subgroup analyses were conducted.

Results Overall, 909 individuals were enrolled. Over a median follow-up of 8.33 (interquartile range, 3.08–12.83) years, 134(14.74%) of them reached renal endpoints. Kaplan-Meier survival analyses indicated that patients with higher RC levels were more susceptible to adverse renal outcomes in LN ($P < 0.001$). After adjusting for confounding factors, higher RC levels exhibited significant correlations with adverse renal outcomes in LN [hazard ratio (HR):1.98, 95% confidence interval (CI):1.16–3.39; $P = 0.012$]. Subgroup analyses revealed a strong relationship between the higher RC and adverse renal outcomes, particularly in patients aged < 40 years, with an estimated glomerular filtration rate < 60 ml/min/1.73m^2 or proliferative pathological changes or nephrotic syndrome ($P < 0.05$).

Conclusions Higher RC levels were significantly associated with poor renal outcomes in LN, indicating that RC may become a non-invasive prognostic tool in clinical assessment of LN.

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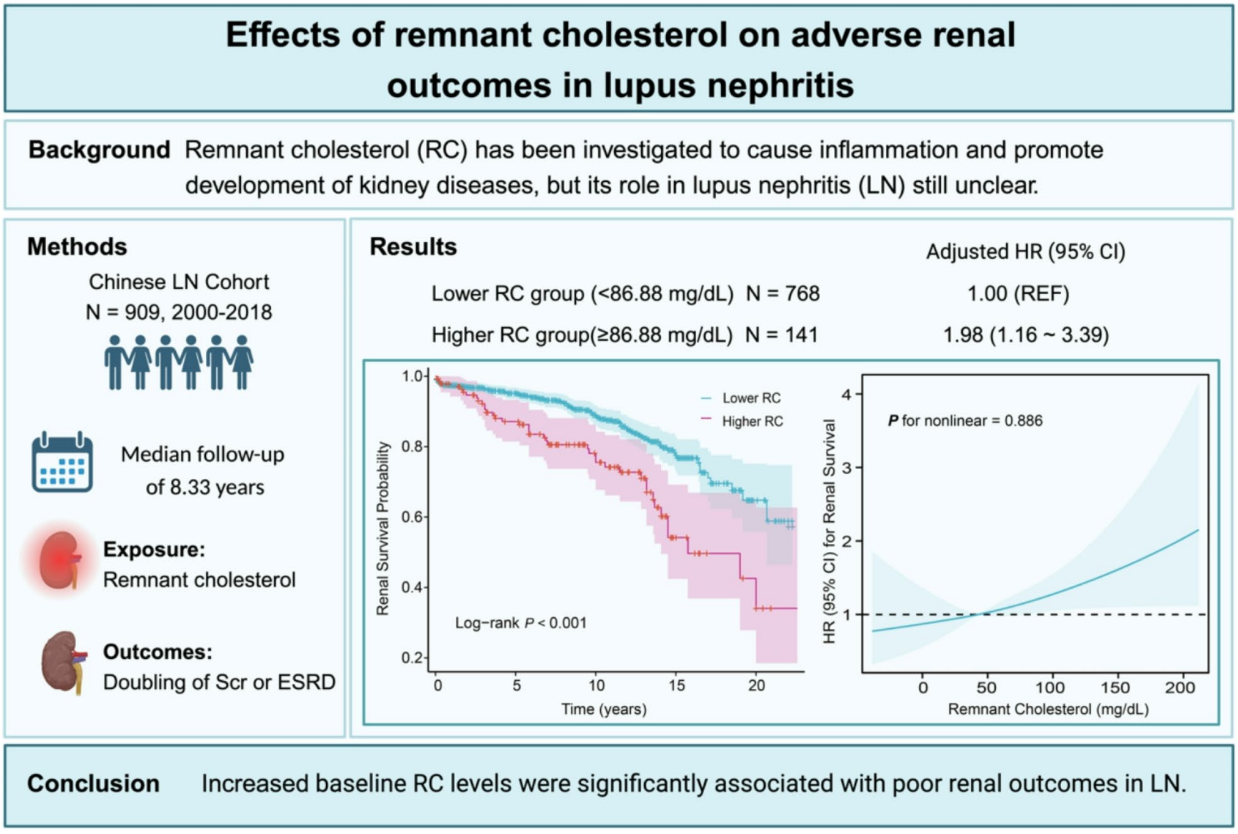
Graphical abstract



Keywords Lupus nephritis, Remnant cholesterol (RC), Lipid profile, Renal outcomes, End-stage renal disease (ESRD)

Introduction

Lupus nephritis (LN) is a type of serious complication of systemic lupus erythematosus (SLE). Research indicates that roughly 50–60% of SLE patients undergo LN, leading to significant distress and considerable socioeconomic burden for patients [1]. Patients with LN face a considerable risk of end-stage renal disease (ESRD) as well as elevated all-cause mortality [2, 3]. However, owing to the heterogeneity of LN, prognostic assessment using noninvasive tools remains challenging.

Dyslipidemia, often defined as aberrant levels of the fasting total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), or high-density lipoprotein cholesterol (HDL-C), is frequently observed among patients with LN [4, 5]. Previous studies have revealed that dyslipidemia may induce adverse clinical outcomes in kidney diseases by promoting oxidative stress, endoplasmic reticulum stress, and inflammatory stress [6]. SLE patients suffered renal injury have more severe dyslipidemia compared to those without renal involvement [7]. Therefore, dyslipidemia may play a vital role in the prognosis of LN.

Remnant cholesterol (RC), which represents the level of triglycerides and cholesterol transported in triglyceride-rich lipoproteins in circulation, is an emerging composite index derived from TC minus LDL-C and HDL-C [8, 9]. RC and its variability are connected with the occurrence and prognosis of multiple diseases, such as cardiovascular disease, depression, rheumatoid arthritis, kidney stones, breast cancer and type II diabetes mellitus (T2DM) [10–14]. In addition, RC has been proved to have a positive correlation with chronic kidney disease (CKD) practically by mediating proinflammatory state [15]. Although the conventional lipid indices are well-controlled, T2DM patients with increased RC still show a high risk of incident CKD [12]. These results indicate that RC may significantly affect multiple organs, including kidney. Based on the vital role that RC plays in promoting inflammation and the development of kidney diseases, we speculated that RC may be significantly associated with prognosis of LN [16].

To address this knowledge gap, the current study concentrated on the correlation between RC and poor clinical outcomes in patients with LN, potentially offering

valuable insights into therapeutic strategies and prognosis in this distinct cohort.

Methods

Study design and enrolled patients

The current study was carried out using the data from January 1, 2000 to December 31, 2018 from the High Quality Evidence of Guangzhou Lupus Nephritis Cohort (HOPE Cohort, NCT06682507), a single-center, ambispective, observational cohort study at the First Affiliated Hospital of Sun Yat-sen University in China. Individuals who had biopsy proven lupus nephritis were included. Diagnostic criteria followed the American College of Rheumatology 1997 revised criteria [17]. Exclusion criteria were (1) younger than 14 years old, (2) baseline diagnosis of ESRD, (3) diagnosis of a malignant tumor, (4) drug-induced lupus erythematosus, (5) absence of serum fasting lipid data, (6) renal biopsy specimens with fewer than 10 glomeruli, and (7) absence of follow-up data. Patients from 2000 to 2016 were retrospectively enrolled, whereas the patients starting from 2017 were prospectively enrolled. Patients were required to receive medical evaluation in our hospital or telephone interviews by experienced clinicians at least twice a year, which was for clinical purposes not specially for this study. All patients were followed up until they reached the study endpoints or censored on September 30, 2023.

Data collection

Baseline demographic information, clinical data, and biochemical parameters were collected from each patient upon their initial hospital admission for renal biopsy. Renal pathological data were collected from the first renal biopsy performed for the diagnosis of LN. Blood samples for hemoglobin, fasting blood glucose, serum creatinine, uric acid, serum albumin, lipid profiles, antibodies, complement, and erythrocyte sedimentation rate (ESR) were obtained after overnight fasting. Data were extracted from the LN database. RC was calculated according to a previous study [18]. The Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) scores were employed for assessing the activity of LN [17]. The estimated glomerular filtration rate (eGFR) was derived from the CKD-EPI equation formula [19].

Study outcomes and definitions

The study endpoints were defined as adverse renal outcomes, including serum creatinine doubled and ESRD (eGFR under 15 ml/min/1.73m^2 or maintenance dialysis, or kidney transplantation). Hypertension was defined as repeated systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg. Nephrotic syndrome was defined as nephrotic proteinuria (> 3.5 g/24 h) and hypoalbuminemia (serum albumin level < 30 g/L). Pathological classifications were defined as proliferative (including Class III, Class IV, Class III/IV plus V, and Class VI) and non-proliferative LN (Class I, Class II, and purely Class V) according to our previous research [20].

Statistical analysis

The optimal RC value for predicting the study endpoints was 86.88 mg/dL, determined by receiver operating characteristic (ROC) curve analysis (Table S1). Based on this optimal cutoff value, patients were divided into the lower (< 86.88 mg/dL) and higher (≥ 86.88 mg/dL) RC groups, respectively. Missing data (< 10%) were replaced with the mean or median. The Kruskal-Wallis test or the chi-square test was used to compare the differences among the groups. Categorical variables were presented as numbers and percentages. Continuous variables were described as mean ± standard deviation or median with interquartile range. Spearman's rank correlation coefficients were used to estimate the correlation between baseline lipid fractions and disease characteristics of LN.

Adverse renal outcomes were assessed using the Kaplan-Meier (K-M) method. Unadjusted and adjusted multivariate Cox regression models were performed to assess the relationship between poor renal outcomes and RC. Three models were used based on the adjustment of different indicators for each analysis. In the fully adjusted model (Model 3), variables considered to be potential confounders for the adverse prognosis of LN were adjusted for, including gender, age, weight, eGFR, ESR, activity index, chronicity index, disease duration, total cholesterol, triglyceride and high-density lipoprotein cholesterol, immunosuppressants and lipid-lowing treatment. Due to the potential multicollinearity among the cholesterol-related variables, variance inflation factors were calculated to assess the multicollinearity (Table S2). All the variance inflation factors values were well below the threshold of 5. Three-knot restricted cubic spline (RCS) analyses were conducted to assess the nonlinear and exposure-dose relationships between the continuous RC and adverse renal outcomes based on the Model 3. Subgroup analyses stratified by gender, age, nephrotic syndrome, eGFR categories and pathological classification were performed in the Model 3 to confirm the consistent prognostic influence of RC on renal outcomes. Significance was set at $P < 0.05$. Packages from R (4.3.2) were utilized for all statistical analyses in this study.

Results

Correlation between baseline lipid fractions and disease characteristics of LN

After screening using the inclusion and exclusion criteria, 909 patients diagnosed with LN were enrolled (Fig S1). Table 1 presents the lipid profiles characteristics in LN patients with and without adverse renal outcomes.

Table 1 Baseline lipid profiles of LN patients by adverse renal outcomes

Variables	Total ($n=909$)	Patients without adverse renal outcomes ($n=775$)	Patients with adverse renal outcomes ($n=134$)	*P*
Total cholesterol, md/dL	224.46 (181.89, 282.51)	220.59 (178.02, 278.64)	241.49 (185.76, 324.11)	0.030*
Triglyceride, md/dL	187.83 (132.01, 263.14)	185.17 (132.90, 256.05)	203.78 (130.24, 309.88)	0.043*
HDL-C, md/dL	40.63 (29.80, 54.18)	41.02 (30.19, 54.95)	37.35 (26.80, 51.37)	0.103
LDL-C, md/dL	134.68 (99.85, 174.92)	133.51 (99.85, 172.80)	137.19 (101.39, 182.28)	0.565
RC, mg/dL	42.96 (27.09, 67.34)	42.18 (26.32, 63.27)	50.50 (29.90, 90.85)	0.001*

Abbreviations: HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; RC, remnant cholesterol. * Patients without vs. with adverse renal outcomes: $P<0.05$

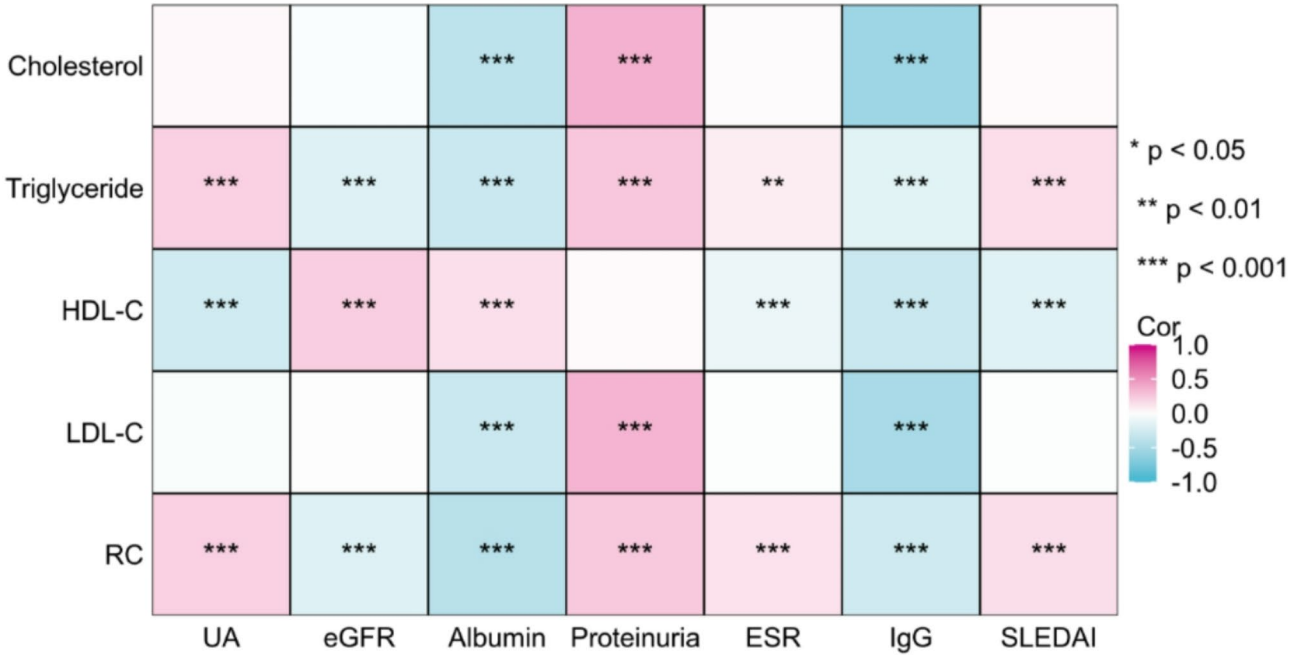


Fig. 1 Correlation between baseline lipid fractions and disease characteristics in LN
Abbreviations: HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; RC, remnant cholesterol; UA, urine acid; eGFR, estimated glomerular filtration rate; ESR, erythrocyte sedimentation rate; IgG, immunoglobulin G; SLEDAI, systemic lupus erythematosus disease activity index

Significant higher levels of total cholesterol, triglyceride, and RC were observed in patients with adverse renal outcomes than those without (all $P<0.05$).

Spearman's rank correlation analyses demonstrated that the levels of RC and TG were significantly related to all the disease characteristics of LN, including urine acid, eGFR, ESR, SELDAI scores, serum albumin, proteinuria and serum immunoglobulin G (all $P<0.05$). However, the TC and LDL-C levels were not statistically correlated with uric acid levels, eGFR, ESR, or SELDAI scores. HDL-C levels did not correlate with proteinuria (Fig. 1). As RC is an emerging comprehensive index and the ROC curve indicated that the area under the curve of RC was higher than that of other lipid indices, we further investigated the relation between RC and adverse renal outcomes in LN (Table S1).

Baseline characteristics of enrolled participants

Table 2 presents the clinical and pathological characteristics at baseline in the lower ($n=768$) and higher ($n=141$) RC groups. The median patient age was 27 years. Among these patients, 82.84% were female, 33.44% had hypertension, and 27.50% manifested as nephrotic syndrome. Compared to the lower RC group, the percentages of patients with musculoskeletal involvement, hypertension, nephrotic syndrome, immunosuppressants treatment, and lipid-lowering therapy were significantly higher in the higher RC group (all $P<0.05$). Additionally, proteinuria, serum creatinine, SLEDAI scores, complement C4 levels, and ESR significantly increased in LN patients with higher RC (all $P<0.05$). However, in this group, the levels of eGFR, serum albumin, and serum immunoglobulin G were significantly lower than LN patients with lower RC (all $P<0.001$). Regarding pathological characteristics, the group with higher RC exhibited more severe

Table 2 Baseline characteristics between remnant cholesterol (RC) groups

Variables	Total ($n=909$)	Lower RC ($n=768$)	Higher RC ($n=141$)	*P*
Female, %	753 (82.84)	630 (82.03)	123 (87.23)	0.132
Age, years	27 (21, 36)	28 (21, 36)	26 (20, 37)	0.214
LN duration, months	3 (1, 13)	3 (1, 13)	4 (2, 24)	< 0.001*
Fever, %	255 (28.05)	221 (28.78)	34 (24.11)	0.257
Rash, %	282 (31.02)	229 (29.82)	53 (37.59)	0.067
Mucous ulcer, %	46 (5.06)	37 (4.82)	9 (6.38)	0.436
Alopecia, %	139 (15.29)	112 (14.58)	27 (19.15)	0.166
Musculoskeletal, %	558 (61.39)	460 (59.90)	98 (69.50)	0.031*
Smoking, %	26 (2.86)	24 (3.12)	2 (1.42)	0.399
Drinking, %	10 (1.10)	9 (1.17)	1 (0.71)	0.964
Hypertension, %	304 (33.44)	240 (31.25)	64 (45.39)	0.001*
Nephrotic syndrome, %	250 (27.50)	200 (26.04)	50 (35.46)	0.021*
Weight, kg	53 (49, 58)	53 (49, 58)	53 (49, 58)	0.749
Hemoglobin, g/L	100.60 ± 22.73	100.78 ± 22.54	99.64 ± 23.80	0.584
Serum creatinine, μmol/L	80 (58, 128)	77 (56, 117)	102 (67, 171)	< 0.001*
eGFR, ml/min/1.73 m^2	89.73 (51.44, 121.02)	94.81 (56.91, 121.80)	66.60 (34.38, 109.69)	< 0.001*
Serum albumin, g/L	26.0 (21.0, 31.3)	27.0 (22.0, 32.3)	21.0 (18.0, 25.0)	< 0.001*
Proteinuria, g/24 h	2.05 (0.89, 4.09)	1.93 (0.81, 3.92)	2.90 (1.65, 5.19)	< 0.001*
SLEDAI scores	16 (12, 19)	16 (12, 19)	16 (12, 20)	0.030*
Positive ANA, %	889 (97.80)	749 (97.53)	140 (99.29)	0.317
Positive anti-dsDNA, %	759 (83.50)	651 (84.77)	108 (76.60)	0.016*
Complement C3, g/L	0.45 (0.30, 0.63)	0.44 (0.29, 0.63)	0.47 (0.32, 0.62)	0.244
Complement C4, g/L	0.10 (0.06, 0.18)	0.10 (0.06, 0.17)	0.11 (0.07, 0.21)	0.006*
Serum immunoglobulin G, g/L	10.90 (7.13, 15.60)	11.55 (7.66, 16.40)	8.32 (4.77, 11.60)	< 0.001*
ESR, mm/h	41 (24, 45)	41 (22, 43)	41 (34, 57)	< 0.001*
Lipid-lowing treatment, %	293 (32.23)	224 (29.17)	69 (48.94)	< 0.001*
Glucocorticoids, %	895 (98.46)	754 (98.18)	141 (100)	0.214
Immunosuppressants, %	559 (61.50)	461 (60.03)	98 (69.50)	0.034*
Pathological classification				0.783
proliferative LN	647 (71.18)	548 (71.35)	99 (70.21)	
non-proliferative LN	262 (28.82)	220 (28.65)	42 (29.79)	
Activity index	7 (5, 9)	7 (5, 9)	7 (5, 9)	0.412
Chronicity index	3 (2, 4)	3 (2, 4)	4 (2, 4)	0.006*
Crescents, %	468 (51.49)	388 (50.52)	80 (56.74)	0.175
Glomerular sclerosis, %	376 (41.36)	303 (39.45)	73 (51.77)	0.007*
Wire-loop lesions, %	238 (26.18)	192 (25.00)	46 (32.62)	0.058
Renal tubular necrosis	29 (3.19)	23 (2.99)	6 (4.26)	0.602
Nuclear fragmentation(n,%)				0.116
0%	647 (71.18)	536 (69.79)	111 (78.72)	
<25%	211 (23.21)	185 (24.09)	26 (18.44)	
25-50%	40 (4.40)	36 (4.69)	4 (2.84)	
>50%	11 (1.21)	11 (1.43)	0 (0.00)	
Mesangial cell and matrix hyperplasia(n, %)				0.082
0%	42 (4.62)	33 (4.30)	9 (6.38)	
<25%	269 (29.59)	233 (30.34)	36 (25.53)	
25-50%	314 (34.54)	273 (35.55)	41 (29.08)	
>50%	284 (31.24)	229 (29.82)	55 (39.01)	
Interstitial inflammation (n, %)				< 0.001*
0%	270 (29.70)	244 (31.77)	26 (18.44)	
<25%	462 (50.83)	392 (51.04)	70 (49.65)	
25%~50%	120 (13.20)	88 (11.46)	32 (22.70)	
50%~75%	24 (2.64)	18 (2.34)	6 (4.26)	

Table 2 (continued)

Variables	Total (*n* = 909)	Lower RC (*n* = 768)	Higher RC (*n* = 141)	*P*
>75%	33 (3.63)	26 (3.39)	7 (4.96)	
Interstitial fibrosis (n, %)				0.045*
0%	518 (56.99)	447 (58.20)	71 (50.35)	
<25%	297 (32.67)	247 (32.16)	50 (35.46)	
25%~50%	79 (8.69)	63 (8.20)	16 (11.35)	
50%~75%	10 (1.10)	9 (1.17)	1 (0.71)	
>75%	5 (0.55)	2 (0.26)	3 (2.13)	
Tubular atrophy(n,%)				0.157
0%	390 (42.90)	341 (44.40)	49 (34.75)	
<25%	359 (39.49)	299 (38.93)	60 (42.55)	
25%~50%	111 (12.21)	91 (11.85)	20 (14.18)	
50%~75%	27 (2.97)	20 (2.60)	7 (4.96)	
>75%	22 (2.42)	17 (2.21)	5 (3.55)	

Abbreviations: eGFR, estimated glomerular filtration rate; SLEDAI, systemic lupus erythematosus disease activity index; ESR, erythrocyte sedimentation rate. * Lower RC vs. Higher RC: $P < 0.05$

degree of renal damage. Interstitial inflammation and interstitial fibrosis were more severe in this group, and the chronicity index was much higher than that in the lower RC group (all $P < 0.05$).

RC and renal outcomes of LN

Over a median follow-up of 8.33 (interquartile range, 3.08–12.83) years, the loss to follow-up rate was 7.24% and the rates between the lower ($n = 61$, 7.36%) and higher ($n = 10$, 6.62%) RC groups showed no statistical difference ($P = 0.748$). The adverse renal events occurred in 134 (14.74%) patients. The rates of adverse renal outcomes in lower and higher RC groups were 12.24% and 28.37%, respectively. Of all the 909 patients enrolled, 620 had available data for flare assessment. The rate of flare was significantly higher in the higher RC group (31/92, 33.70%) than in the lower RC group (111/528, 21.02%) ($P = 0.008$). The K-M analysis showed statistical significance between the lower and higher RC groups, revealing significantly worse renal survival in the higher RC group ($P < 0.001$) (Fig. 2).

Further multivariate Cox regression models were performed to assess the adverse renal outcomes by the continuous RC and RC categories (Table 3). The reference group was defined as the lower RC group. After adjusting for gender, age, weight, eGFR, ESR, activity index, chronicity index, disease duration, total cholesterol, triglyceride and high-density lipoprotein cholesterol, immunosuppressants and lipid-lowing treatment in Model 3, in comparison to the reference group, the hazard ratios (HRs) for adverse renal outcomes in the higher RC group were 1.98 (95% confidence interval [CI]: 1.16–3.39; $P = 0.012$). The prognostic value of continuous RC for adverse renal outcomes (HR: 1.01, 95%CI: 1.01–1.01; $P = 0.030$) in LN was also detected in Model 3.

According to the results of the three-knot RCS models, linear correlations were observed between adverse renal outcomes and the continuous RC in LN (*P* for nonlinear = 0.886) (Fig. 3). Furthermore, the linear connections were also observed in subgroups according to age, gender and eGFR.

Subgroup analyses

Subgroup analyses were performed based on gender, age, nephrotic syndrome, eGFR categories and pathological classification to examine the impact of population stratification on the relationships between RC and renal outcomes in LN (Fig. 4). The results showed that LN patients who were aged < 40 years of age, manifested as nephrotic syndrome, with eGFR under 60 mL/min/1.73m^2 or proliferative pathological changes showed a statistically increased likelihood of adverse renal outcomes (all $P < 0.05$).

Discussion

Based on an extensive literature review, this study, conducted in Southeast China, is the most comprehensive investigation to date on exploring the association between the baseline RC levels and adverse renal outcomes in LN. For the first time, we identified that RC levels are statistically correlated with indicators of disease activity and prognosis of LN. Moreover, our results provide compelling evidence linking an elevated RC levels to poor renal outcomes in LN patients, underscoring the potential prognostic value of RC.

LN is characterized by immune complex-mediated glomerulonephritis, with a complex but unclear pathogenesis. All LN patients have CKD, and they are more likely to progress to ESRD [21, 22]. Dyslipidemia has been identified to occur in roughly 50–70% LN patients and is known to impact the long-term prognosis of LN [4, 5].

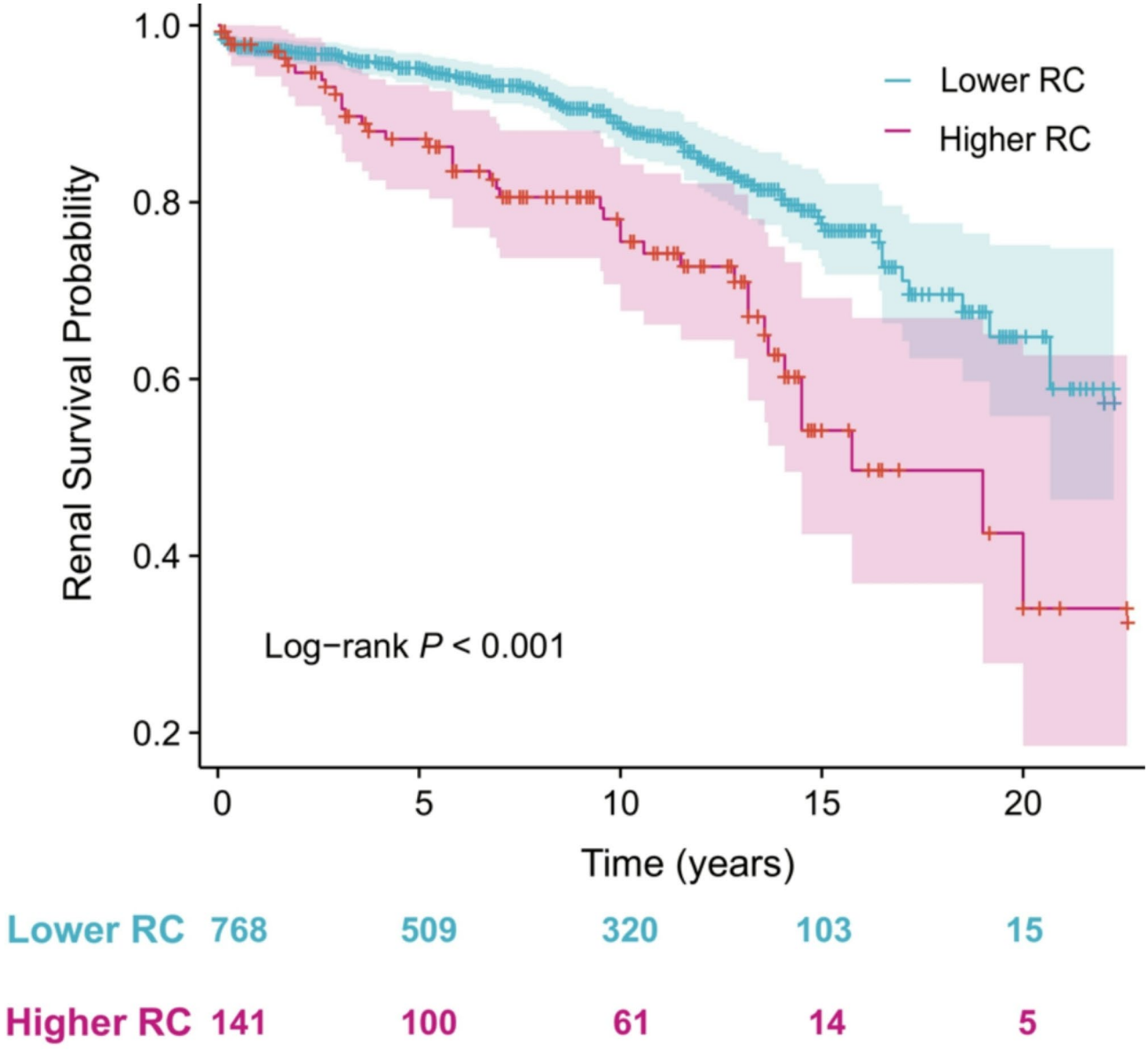


Fig. 2 Kaplan-Meier survival curves for adverse renal outcomes in the RC groups of LN patients

Table 3 The relationship between RC and the renal endpoint events

	Model1		Model2		Model3	
	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
RC (continuous)	1.01 (1.01 ~ 1.01)	< 0.001	1.01 (1.01 ~ 1.01)	0.008	1.01 (1.01 ~ 1.01)	0.030
RC Categories						
Lower RC	Ref		Ref		Ref	
Higher RC	2.22 (1.53 ~ 3.21)	< 0.001	1.84 (1.23 ~ 2.75)	0.003	1.98 (1.16 ~ 3.39)	0.012

HR: Hazard Ratio, CI: Confidence Interval

Model 1: Crude

Model 2: Adjusted for gender, age, weight, eGFR, ESR, activity index, chronicity index, disease duration, immunosuppressants and lipid-lowing treatment

Model 3: Adjusted for Model 2 plus total cholesterol, triglyceride and high-density lipoprotein cholesterol

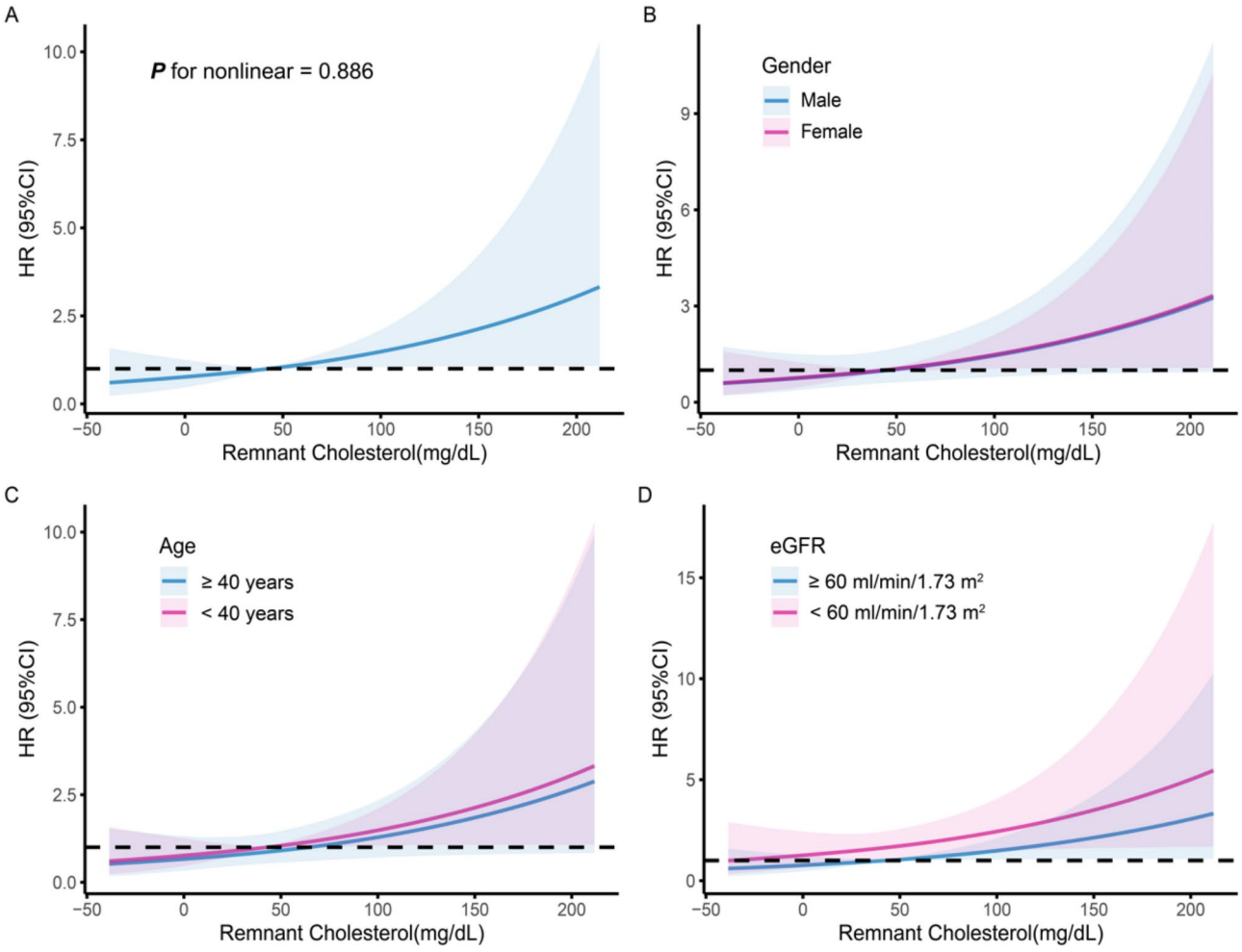


Fig. 3 Results of adjusted three-knot RCS models. Adjusted three-knot RCS models for the association between RC and adverse renal outcomes (**A**) in subgroups of gender (**B**), age (**C**), and eGFR (**D**)

Several studies have examined the relationship between the lipid profiles and LN. Liu et al. demonstrated that the increase of TC, TG and LDL-C levels were related to the development of pediatric LN [23]. Huang et al. revealed that the circulating TC and LDL-C concentrations were positively correlated to proteinuria and serum creatinine levels [7]. Furthermore, Feng et al. investigated the role of TC as an independent risk indicator of kidney involvement in patients with SLE [24]. We previously demonstrated the connection between adverse renal outcomes and decreased circulating HDL-C levels in LN [25]. These results highlight the close relationship between dyslipidemia and LN. RC, a new type of lipid metabolism index, has received increasing attention in recent years due to its significant influence on multiple diseases independent of traditional lipid profiles. Previous studies have confirmed that increased RC can cause low-grade inflammation, and some scholars have suggested that RC could be a target for lipid reduction management; however, further research is needed to confirm this [16, 26, 27].

Strong correlations have been consistently observed across diverse populations, linking RC to poor renal outcomes. RC has already been demonstrated to be an independent risk factor for developing renal dysfunction among patients with T2DM in the United States, Korea and China, even when conventional lipid parameters are well controlled [12, 28, 29]. In addition, a longitudinal study conducted using a Chinese cohort consisting of T2DM patients with diabetic nephropathy (DN) confirmed by renal biopsy revealed that DN patients with higher RC were more likely to progress to ESRD [30]. Among patients with hypertension in China, circulating RC levels exhibited a positive linear relationship with the danger of developing into CKD [31]. Yan et al. also proved that RC was significantly related to incident CKD among general middle-aged and elderly Chinese populations [32]. A number of studies have proved that increased serum RC concentrations are positively correlated with renal dysfunction even in the general population [33–35]. In line with previous research, this study

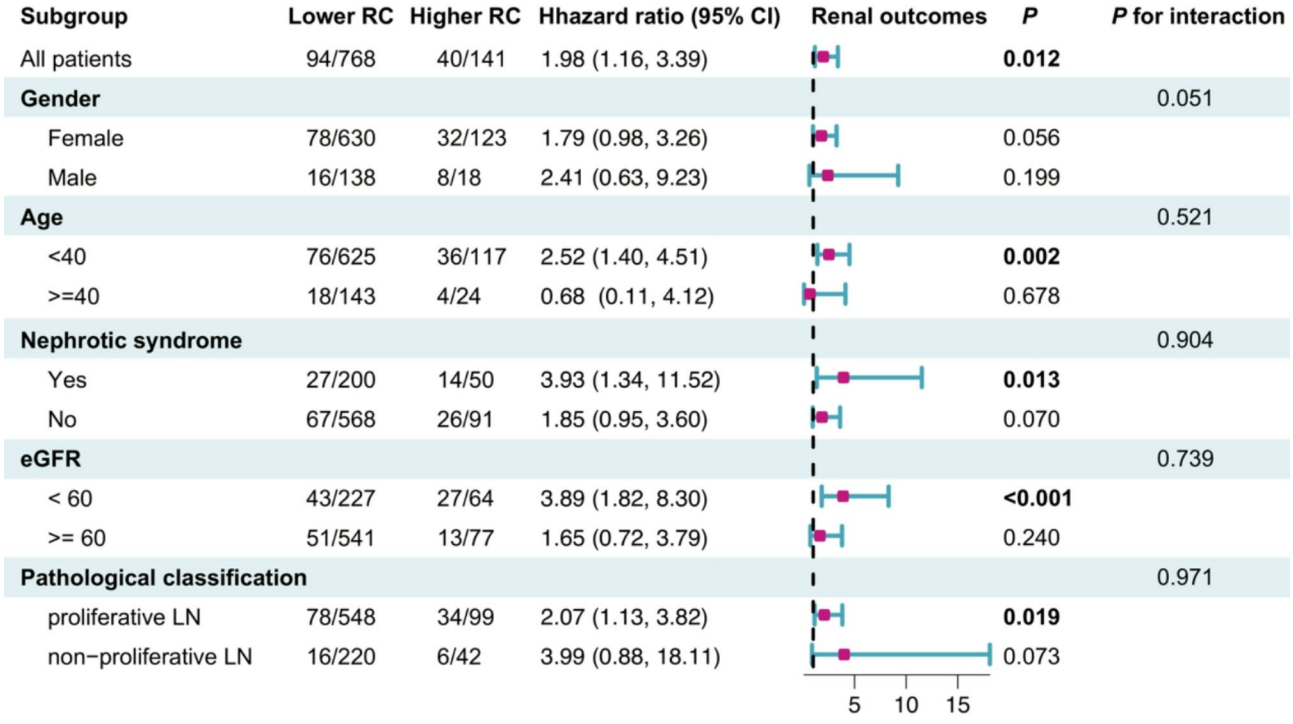


Fig. 4 Subgroup analyses for the association between RC and renal outcomes of LN

established a strong link between poor renal outcomes and elevated baseline RC levels in LN. By adjusting other cholesterol indexes, TC, TG and HDL-C, the independent association of RC with adverse outcomes in LN was further identified.

Subgroup analysis revealed a particularly pronounced impact of increased RC on adverse renal outcomes in patients aged < 40 years, manifested as nephrotic syndrome, with eGFR under 60 mL/min/1.73m^2 or proliferative pathological changes in LN. Studies have elucidated that eGFR at flare and the manifestation of nephrotic syndrome are independent factors for adverse clinical outcomes in LN [36, 37]. Moreover, younger age has also been confirmed to have an association with renal dysfunction in LN [38, 39]. Notably, proliferative pathological injury is associated with poor LN prognosis [40, 41]. These results enhance the significance of this study by demonstrating that RC has substantial predictive potential for those predisposed to poor renal outcomes in LN and underline the importance of considering these variables when utilizing RC to assess the prognosis of LN.

The correlation between dyslipidemia and inflammation has been previously proven, and Yuan et al. found that the connection between RC and CKD is mediated in part by the preinflammatory state [15, 42]. In line with these findings, LN patients with a higher RC exhibited more severe interstitial inflammation in this study. Interstitial fibrosis is a central factor in the prognosis of LN. A recent study found that interstitial fibrosis was an independent risk of ESRD in LN [43]. Our results also indicated that LN patients in the higher RC group showed more serious interstitial fibrosis. However, the mechanism by which the RC is the main culprit or a spectator of the renal dysfunction in LN remains unclear.

To our knowledge, it is the first study to explore the relationship between RC and adverse renal outcomes in patients with LN, suggesting that RC could serve as a noninvasive indicator to assess the prognosis of LN. These findings provide new perspectives on clinical lipid management in patients with LN. Those with RC levels exceeding 86.88 mg/dL should be closely monitored and provided with intensive lipid-lowering therapy to mitigate the risk of progressing to ESRD. Further prospective studies are warranted to confirm whether reducing circulating RC levels can decelerate the progression of LN and to support the formulation of clinical guidelines. Nevertheless, limitations must be acknowledged. Firstly, given the retrospective and nature of the study for patients enrolled between 2000 and 2016, selection and recall biases were unavoidable. And its observational nature precludes establishing causality. Secondly, the dynamic changes in maintenance therapy options may influence the prognosis of LN; however, a limitation of this study is the unavailability of data on treatment changes over time. Thirdly, this single-center cohort study was confined to Chinese patients.

Conclusion

In conclusion, higher baseline RC levels were significantly associated with poor renal outcomes in LN. These results support RC concentration as a non-invasive approach to identify specific LN patient subsets who are more vulnerable to suffer adverse renal outcomes.

Abbreviations

CI	Confidence interval
CKD	Chronic kidney disease
DN	Diabetic nephropathy
eGFR	Estimated glomerular filtration rate
ESR	Erythrocyte sedimentation rate
ESRD	End-stage renal disease
HDL-C	High-density lipoprotein cholesterol
HR	Hazard ratio
Ig	Immunoglobulin
K-M	Kaplan-Meier
LDL-C	Low-density lipoprotein cholesterol
LN	Lupus nephritis
RC	Remnant cholesterol
RCS	Restricted cubic splines
ROC	Receiver operating characteristic
SLE	Systemic lupus erythematosus
SLEDAI	Systemic Lupus Erythematosus Disease Activity Index
T2DM	Type II diabetes mellitus
TC	Total cholesterol
TG	Triglycerides

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12944-025-02503-y.

Supplementary Material 1

Acknowledgements

We thank all the patients for their significant contributions. The graphical abstract was created with biorender.com.

Author contributions

Xiaolei Shi: Writing - original draft, Formal analysis, Investigation, Visualization. Xinxin Zhang: Data curation; Formal analysis. Yuewen Lu: Data curation; Software. Wang Xiang: Data curation; Formal analysis. Xin Wang: Data curation. Jianwen Yu: Data curation. Hongjian Ye: Data curation. Haishan Wu: Data curation. Ruihan Tang: Supervision, Funding acquisition. Xi Xia: Writing - review & editing, Supervision. Wei Chen: Writing - review & editing, Supervision, Project administration, Funding acquisition.

Funding

This study was supported by the National Natural Science Foundation of China (No. 82170737, 82370707, and 82400832), the Guangdong Province High-Level Hospital Construction Project (No. DFJHBF202101), and the National Key Research and Development Project of China (2021YFC2501302) —— Strategy study on lupus nephritis diagnosis and treatment.

Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

This study was performed in line with the principles of the Declaration of Helsinki and approved by the Human Ethics Committee of Sun Yat-sen University (No. 2016 – 215). Informed consent waivers from 2000 to 2016 were approved due to the retrospective nature of the study. Patients enrolled between 2017 and 2020 all signed written informed consent.

Competing interests

The authors declare no competing interests.

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Received: 12 December 2024 / Accepted: 23 February 2025
Published online: 10 April 2025

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