Article

Discovery Medicine 2026; 38(214): 3504–3521
https://doi.org/10.24976/Discov.Med.202638214.268

Association of the Triglyceride-Glucose Index With Glomerulosclerosis in Patients With Primary Glomerulonephritis

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Submitted: 18 June 2026 Revised: 27 August 2026 Accepted: 16 September 2026 Published: 25 November 2026

Background: The triglyceride-glucose (TyG) index, a reliable surrogate marker for insulin resistance (IR), has been associated with chronic kidney disease (CKD) progression. The proportion of glomerulosclerosis (GS%) is a key pathological indicator of structural kidney damage and an independent risk factor for CKD progression. However, the associations of the TyG index with glomerulosclerosis and its histological subtypes in primary glomerulonephritis (PGN) remain unclear. This study investigated these associations.

Methods: This cross-sectional study included 377 biopsy-proven PGN patients (CKD stages 1–3). For descriptive comparisons, participants were categorized into low (≤8.49) and high (>8.49) TyG groups according to the median TyG index. Spearman correlation analysis and grouped binomial generalized linear models with a logit link were used to evaluate the associations of the TyG index with total, global, and segmental glomerulosclerosis rates. For each outcome, the corresponding number of sclerotic glomeruli was used as the event count, and the total number of evaluable glomeruli was used as the denominator. The TyG index was modeled as a standardized continuous variable. Odds ratios (ORs) and 95% confidence intervals (CIs) were reported for each 1-standard-deviation increase in the TyG index.

Results: Patients with a high TyG index exhibited more severe metabolic abnormalities, lower estimated glomerular filtration rate (eGFR), higher proteinuria levels, and higher total and global glomerulosclerosis rates. In the overall population, after adjustment, each 1-standard-deviation increase in the TyG index was associated with a higher total glomerulosclerosis rate (adjusted OR = 1.223, 95% CI: 1.073–1.395, $p = 0.003$). Further analysis showed that the TyG index remained associated with global glomerulosclerosis rates after adjustment for measured covariates (adjusted OR = 1.267, 95% CI: 1.109–1.448, $p < 0.001$), but not with segmental glomerulosclerosis rates (adjusted OR = 1.011, 95% CI: 0.841–1.215, $p = 0.906$).

Conclusions: The TyG index was associated with the proportions of total and globally sclerotic glomeruli after adjustment for measured covariates in patients with biopsy-proven PGN. No significant association was observed in the proportion of segmentally sclerotic glomeruli. The TyG index may serve as a candidate marker associated with glomerulosclerotic burden. Further prospective studies are needed to clarify its clinical relevance in relation to glomerulosclerotic burden.

Keywords: triglyceride-glucose index; insulin resistance; glomerulosclerosis; primary glomerulonephritis; chronic kidney disease

Introduction

Primary glomerulonephritis (PGN) is one of the leading causes of chronic kidney disease (CKD) and is an important cause of end-stage renal disease (ESRD) in young adults [1,2]. Global Burden of Disease data indicate a significant upward trend in both the incidence and disease burden of PGN between 1990 and 2019 [3]. As a terminal pathological feature common to various kidney diseases, including PGN, glomerulosclerosis is a crucial indicator for evaluating disease activity, therapeutic response, and prognosis. Notably, glomerulosclerosis reflects structural kidney injury that may develop through maladaptive glomerular hypertension, hyperfiltration, and podocyte stress, thereby providing histological information that complements estimated glomerular filtration rate (eGFR)-based assessment [4]. Multiple studies have demonstrated that the proportion of glomerulosclerosis (GS%) is an independent risk factor for CKD progression [5,6]; specifically, for

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every doubling of GS%, the risk of CKD progression increases by approximately 32% (hazard ratio [HR] = 1.32; 95% confidence interval [CI]: 1.08–1.62; $p < 0.05$) [5]. Therefore, identifying biomarkers associated with GS% severity is critical for the assessment of disease severity.

The triglyceride-glucose (TyG) index is a metabolic index calculated based on fasting triglycerides and fasting blood glucose, commonly using the formula: TyG = Ln [fasting triglycerides (mg/dL) × fasting glucose (mg/dL) / 2] [7]. It is widely regarded as a simple and cost-effective surrogate marker for insulin resistance (IR). Previous evidence shows that a higher TyG index is not only significantly associated with CKD-related outcomes such as proteinuria abnormalities and diabetic nephropathy [8,9] but is also closely related to contrast-associated acute kidney injury [10]. A cohort study further indicated that for every 1-unit increase in TyG, the risk of CKD increases by approximately 59% (HR = 1.59; 95% CI: 1.24–2.05) [11]. Moreover, TyG may mediate approximately half of the association strength between body mass index (BMI) and ESRD in the general population [12]. Although the association between the TyG index and clinical renal function indicators has been extensively studied, the direct relationship between TyG and renal histopathological alterations, specifically glomerulosclerosis, remains unclear.

Epidemiological evidence suggests significant sexual dimorphism in CKD: although the prevalence of CKD stages 3–5 is generally higher in females, males experience a faster rate of renal function decline and are more prone to progressing to ESRD [13]. This sex difference is also reflected in metabolic profiles; females with diabetes typically exhibit higher levels of glycated hemoglobin, total cholesterol, and triglycerides than males. Given that the TyG index reflects lipotoxicity and insulin resistance, it is crucial to investigate whether sex differences exist in its association with glomerulosclerosis.

Therefore, the present study aimed to investigate the association between the TyG index and biopsy-proven glomerulosclerosis in patients with PGN, further exploring its associations with different glomerulosclerosis subtypes and the consistency of these associations across clinical subgroups.

Methods

Study Design and Population

This was a cross-sectional study of 3668 patients who underwent renal biopsy at Xiangya Hospital, Central South University from January 2018 to December 2025. Inclusion criteria were: (1) age 18–65 years; (2) biopsy-confirmed PGN; (3) CKD stage 1–3 (eGFR ≥30 mL/min/1.73 m^2); and (4) complete key biochemical and renal biopsy data. Exclusion criteria included: (1) missing key biochemical or pathological data; (2) age <18 or >65 years; (3) secondary kidney disease, such as lupus nephritis; (4) CKD stage ≥4; (5) fewer than 6 glomeruli in the renal biopsy specimen; (6) co-existing conditions known to substantially affect glucose or lipid metabolism, including diabetes mellitus, thyroid dysfunction, severe liver disease, malignant tumors, autoimmune diseases, or other systemic diseases; and (7) current use of lipid-lowering therapy. After applying the eligibility criteria, 377 individuals met all criteria and constituted the final study cohort.

The patient enrollment process is detailed in Fig. 1. Based on the median TyG index (8.49), eligible participants were divided into two groups: a TyG index ≤8.49 group (n = 191) and a TyG index >8.49 group (n = 186).

This study was approved by the Medical Ethics Committee of Xiangya Hospital, Central South University (ethical approval number: 2026030508). This study was in accordance with the Declaration of Helsinki. The requirement for written informed consent was waived by the institutional review board for this retrospective study.

A total of 3668 patients undergoing renal biopsy at Xiangya Hospital were initially screened. After applying the exclusion criteria, 377 eligible patients with primary glomerulonephritis were enrolled and further classified into two groups based on the median TyG index.

Data Collection

Data regarding participants at the time of renal biopsy were collected by reviewing the electronic medical record system of Xiangya Hospital, Central South University. Collected data included baseline characteristics (age, sex, BMI, history of smoking and alcohol consumption, and comorbidities), laboratory biochemical indicators, renal pathological results, and medication usage. BMI was calculated as weight (kg) divided by the square of height (m). The TyG index was calculated by the following formula: TyG = Ln [fasting triglycerides (mg/dL) × fasting glucose (mg/dL) / 2]. The eGFR was calculated using the CKD-EPI formula [14], expressed in mL/min/1.73 m^2.

Hypertension was defined as a systolic blood pressure ≥140 mmHg or a diastolic blood pressure ≥90 mmHg, according to the 2020 International Society of Hypertension (ISH) guidelines [15]. Chronic kidney disease (CKD) was defined as abnormalities of kidney structure or function, present for a minimum of 3 months, with implications for health [16]. CKD stages were classified as follows: Stage 1: eGFR ≥90 mL/min/1.73 m^2; Stage 2: 60 ≤ eGFR < 90 mL/min/1.73 m^2; Stage 3: 30 ≤ eGFR < 60 mL/min/1.73 m^2; Stage 4: 15 ≤ eGFR < 30 mL/min/1.73 m^2; Stage 5: eGFR <15 mL/min/1.73 m^2 [16]. The pathological subtype classification was based on the final renal biopsy diagnosis recorded in the clinical pathology report, with reference to established principles for the classification, diagnosis, and standardized reporting of glomerulonephritis [17].

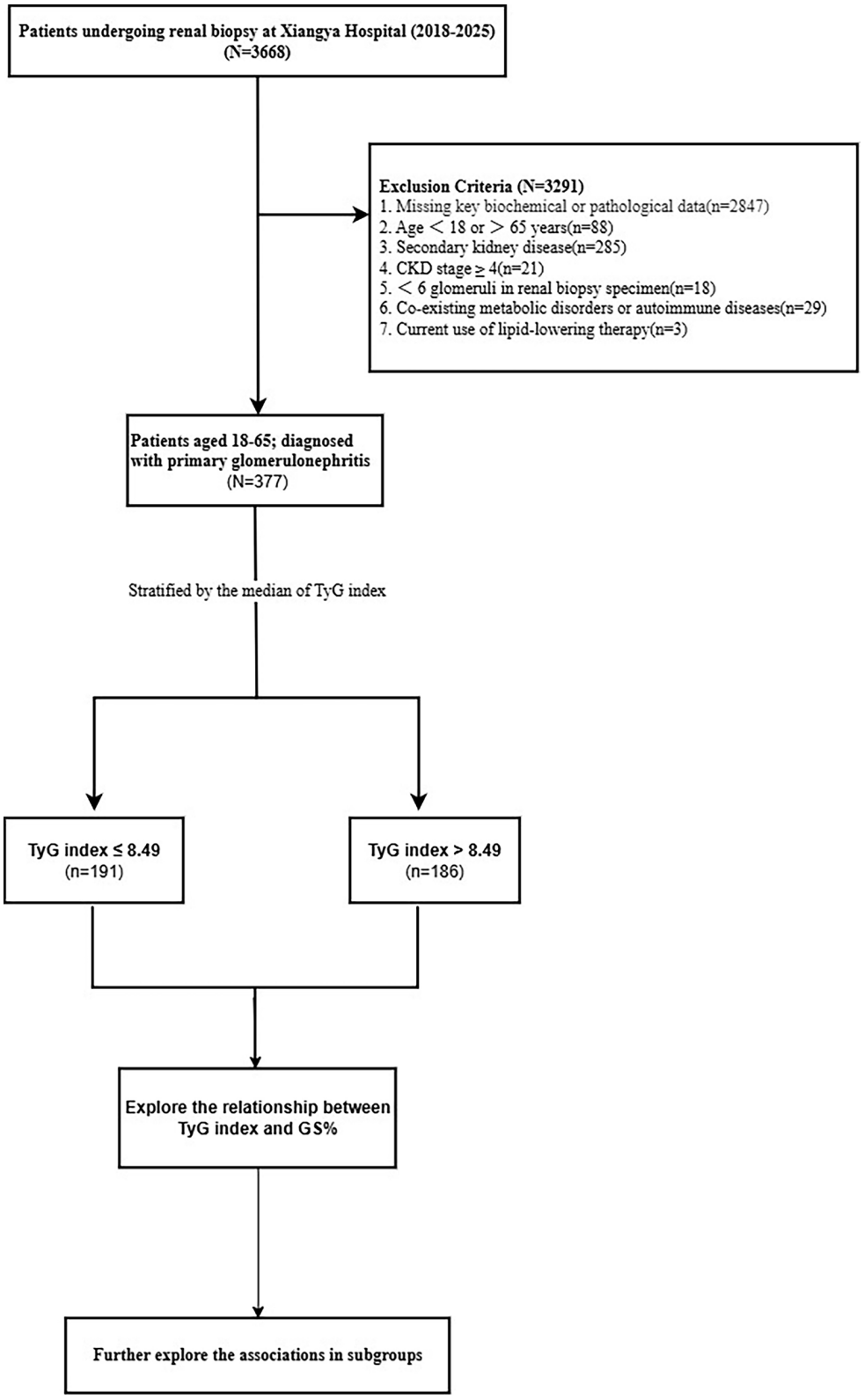

Fig. 1. Flowchart of patient selection and enrollment.

Biochemical Measurements

Blood and urine samples were obtained from all participants. Laboratory examinations were conducted to assess fasting blood glucose (FBG), serum total cholesterol (TC), triglycerides (TG), serum low-density lipoprotein cholesterol (LDL-C), serum high-density lipoprotein cholesterol (HDL-C), total protein, albumin, globulin, direct bilirubin, serum uric acid (SUA), serum creatinine

(SCr), complete blood count, 24-hour urinary microalbumin (24 h mAlb), and 24-hour urinary total protein (24 h U-TP).

TyG Index Calculation

The TyG index was calculated as: TyG = Ln [TG (mg/dL) × FBG (mg/dL) / 2]. FBG levels were measured using the glucose oxidase method, and TG levels using the enzymatic method.

Pathological Assessment

Renal biopsy specimens were processed for light microscopy, immunofluorescence microscopy, and electron microscopy according to routine renal pathology procedures. For light microscopy, renal tissue was fixed in 4% neutral-buffered formalin, routinely processed, embedded in paraffin, and cut into serial 3-μm-thick sections. Tissue for immunofluorescence microscopy was kept fresh in normal saline and processed without fixation. Tissue for electron microscopy was fixed in 2.5% glutaraldehyde. The sections were stained with hematoxylin and eosin, periodic acid–Schiff, periodic acid–methenamine silver, and Masson's trichrome. Glomerulosclerosis, tubular atrophy, interstitial fibrosis, and arteriosclerosis were assessed in all available light-microscopic sections. PAS and silver stains were used to evaluate glomerular extracellular matrix expansion, capillary tuft architecture, and sclerosis, whereas Masson's trichrome staining was used to assess interstitial collagen deposition and fibrosis. Arteriosclerosis was evaluated in routine light-microscopic sections according to the degree of arterial intimal thickening. Immunofluorescence and electron microscopy were used to establish the underlying pathological diagnosis of primary glomerulonephritis rather than to quantify chronic lesions.

Renal histopathological assessment was performed independently by two expert pathologists; in cases of disagreement, a consensus was reached through discussion or by adjudication by a third, more senior pathologist:

Assessment of Glomerulosclerosis

The total number of identifiable glomeruli within the renal cortical region, as well as the count of glomeruli exhibiting sclerosis, was quantified. Glomerulosclerosis was defined by the presence of segmental or global augmentation of the glomerular matrix, segmental or global collapse and obliteration of capillary lumina, hyaline accumulation, and synechial attachments between the glomerular tuft and Bowman's capsule [18,19]. Global glomerulosclerosis was defined as sclerosis involving the entire glomerular tuft, whereas segmental glomerulosclerosis was defined as sclerosis involving only a portion of the tuft, with part of the tuft remaining uninvolved [20]. Subsequently, the percentage of glomerular sclerosis was calculated using the formula:

Glomerulosclerosis rate (total, %) = [(number of globally sclerotic glomeruli + number of segmentally sclerotic glomeruli) / total number of identifiable glomeruli] × 100%.

Global glomerulosclerosis rate (%) = (number of globally sclerotic glomeruli / total number of identifiable glomeruli) × 100%.

Segmental glomerulosclerosis rate (%) = (number of segmentally sclerotic glomeruli / total number of identifiable glomeruli) × 100%.

Evaluation of Renal Tubulointerstitial Lesions

Renal tubular atrophy, interstitial fibrosis, and interstitial inflammatory cell infiltration were assessed. Atrophic tubules were characterized by the presence of thickened basement membranes and/or a reduction in tubule diameter [21]. Renal interstitial fibrosis was characterized by the excessive accumulation of extracellular matrix (ECM) [22].

Assessment of Mesangial Hypercellularity

Mesangial hypercellularity was defined as the presence of more than three mesangial cells per mesangial area in at least one glomerulus [23].

Assessment of Vascular Lesions

Arteriosclerosis was assessed in the arteries present in the biopsy specimen and scored according to the Mayo Clinic/Renal Pathology Society consensus criteria: score 0, intimal thickening less than the thickness of the media; score 1, intimal thickening equal to or exceeding the thickness of the media [19].

Coding of Pathological Variables

The aforementioned pathological manifestations (mesangial hypercellularity, tubular atrophy, interstitial fibrosis, interstitial inflammation and vascular injury) were treated as binary variables (presence/absence) for subsequent statistical analysis.

Sample Size Calculation

Sample size estimation was based on data from a pilot study involving 77 subjects. The pilot results showed that the mean proportions of glomerulosclerosis in the low TyG group and the high TyG group were 13.82% and 20.81%, with standard deviations of 15.77% and 18.64%, respectively. Calculations were performed using PASS 2023 software with $\alpha = 0.05$ and a statistical power of 90%. The results indicated that at least 130 subjects were required per group. Accounting for a potential missing-data or attrition rate of approximately 20%, the study planned to recruit a total of at least 326 subjects (163 per group).

Statistical Analysis

Continuous variables were first assessed for normality using the Kolmogorov–Smirnov test. Normally distributed variables are presented as mean ± standard devi-

ation and were compared using the independent samples *t*-test, whereas non-normally distributed variables are presented as median (Q1, Q3) and were compared using the Mann-Whitney U test. Categorical variables are presented as numbers (%) and were compared using Pearson's chi-square test, continuity-corrected chi-square test, Fisher's exact test, or the Fisher-Freeman-Halton exact test as appropriate.

Spearman's rank correlation analysis was conducted to evaluate the correlations of the TyG index and total glomerulosclerosis proportion with other variables. Glomerulosclerosis outcomes were analyzed as grouped binomial data. Each patient was entered into the model as a single record. The total number of evaluable glomeruli was used as the binomial denominator. For total glomerulosclerosis, the numerator was the sum of globally and segmentally sclerotic glomeruli. For global glomerulosclerosis, the numerator was the number of globally sclerotic glomeruli. For segmental glomerulosclerosis, the numerator was the number of segmentally sclerotic glomeruli. No additional sampling or frequency weights were applied. The binomial denominator allowed biopsies with more evaluable glomeruli to contribute more information to the model. Generalized linear models with a binomial distribution and logit link were used. The scale parameter was estimated using the Pearson chi-square statistic to account for overdispersion. Continuous predictors were standardized, and their ORs were reported per 1-standard deviation (SD) increase. Exploratory stratified analyses were further conducted according to sex, age, CKD stage, and vascular injury status.

All statistical analyses were performed using SPSS Statistics version 27.0 (IBM Corp., Armonk, NY, USA), and a two-sided p-value < 0.05 was considered statistically significant.

Results

Baseline Characteristics

A total of 377 patients with no history of metabolic or autoimmune diseases and not receiving lipid-lowering therapy were ultimately included in this study. The median age of the overall population was 32 years, and 38.5% were male. Patients were categorized into a low TyG group (TyG ≤8.49) and a high TyG group (TyG >8.49) based on the median TyG index of 8.49.

As shown in Table 1, the proportion of male patients was higher in the high TyG group than in the low TyG group (45.7% vs. 31.4%, $\chi^2 = 8.125$, $p = 0.004$). Patients in the high TyG group were also older (median 33 [interquartile range (IQR) 28–41] vs. 30 [24–36] years, $p < 0.001$), had a higher prevalence of hypertension (25.3% vs. 7.3%, $p < 0.001$), and showed a more pronounced metabolic disturbance, including higher BMI, FBG, TC, TG, LDL-C, and TG/HDL-C levels, as well as lower HDL-C levels (all $p < 0.001$). Smoking was also more frequent in the high TyG group (17.2% vs. 9.9%, $p = 0.039$), whereas alcohol consumption did not differ significantly between groups (14.5% vs. 9.4%, $p = 0.127$).

Regarding renal function, patients in the high TyG group had significantly lower eGFR levels than those in the low TyG group (median 94.67 [IQR 65.87–111.10] vs. 105.05 [85.76–121.39] mL/min/1.73 m^2, $p < 0.001$), while both 24 h mAlb (median 713.32 [359.66–1449.88] vs. 452.25 [201.84–836.50] mg/24 h, $p < 0.001$) and 24 h U-TP (median 1.09 [0.58–2.16] vs. 0.69 [0.33–1.30] g/24 h, $p < 0.001$) were significantly elevated.

Renal pathological analysis revealed that the high TyG group exhibited more severe structural injury. Compared with the low TyG group, patients in the high TyG group had a significantly higher total glomerulosclerosis rate (median 21.24% [IQR 9.52–42.17] vs. 15.38% [5.56–28.57], $p < 0.001$) and global glomerulosclerosis rate (median 16.67% [6.67–35.34] vs. 11.11% [2.86–22.73], $p < 0.001$), whereas the segmental glomerulosclerosis rate did not differ significantly between groups (median 0.00% [0.00–8.33] vs. 0.00% [0.00–7.69], $p = 0.265$). In addition, the high TyG group had higher proportions of tubular atrophy (94.1% vs. 86.4%, $p = 0.012$) and vascular injury (33.3% vs. 18.8%, $p = 0.001$), whereas interstitial fibrosis and interstitial inflammation showed no statistically significant differences. The distribution of pathological subtypes also differed between the two TyG groups (Fisher-Freeman-Halton exact test, $p = 0.033$).

Relationship Between TyG Index, Total Glomerulosclerosis Proportion, and Other Variables

To explore the relationships between the TyG index, total glomerulosclerosis proportion, and clinical indicators, Spearman correlation analysis was performed (Fig. 2).

As shown in Fig. 2, age, BMI, lipid-related parameters (TC, TG, LDL-C, TG/HDL-C), serum uric acid, as well as 24 h mAlb and 24 h U-TP were all positively correlated with both the TyG index and total glomerulosclerosis proportion. Conversely, direct bilirubin and eGFR were negatively correlated with both indices. Serum total protein showed a positive correlation with the TyG index but a negative correlation with GS%. Some indicators exhibited specific correlations: FBG, HDL, globulin, RBC and hemoglobin were correlated only with the TyG index, whereas serum albumin was correlated only with GS%. All correlations described above were statistically significant (all $p < 0.01$).

Based on the correlation analysis and clinical relevance, sex, age, SBP, smoking history, alcohol consumption, BMI, and uric acid were included as covariates in the multivariable regression models.

To examine the association between the TyG index and glomerulosclerosis in patients with PGN, regression analyses were performed. As shown in Table 2, the TyG index was significantly associated with total glomerulosclerosis rate in the overall population in both univariate analysis

Table 1. Baseline characteristics of the study population classified based on TyG index.

	Total cases (n = 377)	TyG index ≤8.49 (n = 191)	TyG index >8.49 (n = 186)	Statistic	*p* value
Male, n (%)	145 (38.5%)	60 (31.4%)	85 (45.7%)	$\chi^2 = 8.125$	0.004
Age (years)	32 (26, 38)	30 (24, 36)	33 (28, 41)	$U = 13671$	<0.001
Hypertension (%)	61 (16.2%)	14 (7.3%)	47 (25.3%)	$\chi^2 = 22.360$	<0.001
Smoking history (%)	51 (13.5%)	19 (9.9%)	32 (17.2%)	$\chi^2 = 4.242$	0.039
Alcohol consumption (%)	45 (11.9%)	18 (9.4%)	27 (14.5%)	$\chi^2 = 2.324$	0.127
BMI (kg/m^2)	23.07 (20.37, 25.30)	21.45 (19.43, 23.88)	24.43 (22.38, 27.06)	$U = 9407$	<0.001
FBG (mmol/L)	4.53 (4.22, 4.90)	4.38 (4.14, 4.69)	4.68 (4.34, 4.99)	$U = 12,163.5$	<0.001
Serum lipids					
TC (mmol/L)	4.64 (4.07, 5.40)	4.49 (3.92, 5.09)	4.92 (4.20, 5.62)	$U = 13,498.5$	<0.001
TG (mmol/L)	1.35 (0.94, 2.11)	0.95 (0.78, 1.17)	2.12 (1.69, 2.76)	$U = 659$	<0.001
LDL (mmol/L)	2.90 (2.47, 3.44)	2.76 (2.29, 3.16)	3.15 (2.59, 3.60)	$U = 12,978$	<0.001
HDL (mmol/L)	1.12 (0.95, 1.32)	1.22 (1.05, 1.48)	1.04 (0.88, 1.18)	$U = 10,068$	<0.001
TG/HDL-C	1.22 (0.76, 2.08)	0.77 (0.57, 1.04)	2.08 (1.54, 2.92)	$U = 1451$	<0.001
Liver function					
Total protein (g/L)	63.42 ± 6.59	62.65 ± 6.57	64.22 ± 6.54	$t = –2.313$	0.021
Alb (g/L)	38.10 (34.90, 40.75)	38.10 (34.80, 40.50)	38.20 (34.98, 41.23)	$U = 16,882.5$	0.405
Globulin (g/L)	25.50 (23.10, 28.15)	25.00 (22.50, 27.90)	26.35 (23.88, 28.63)	$U = 14,627.5$	0.003
DBIL (μmol/L)	3.1 (2.3, 4.1)	3.3 (2.6, 4.5)	3.0 (2.2, 3.8)	$U = 14,468.5$	0.002
Complete blood count					
RBC (10^{12}/L)	4.25 (3.89, 4.63)	4.10 (3.73, 4.49)	4.38 (4.02, 4.69)	$U = 12,709.5$	<0.001
Hemoglobin (g/L)	127 (115, 137)	123 (113, 133)	130 (122, 139)	$U = 13,206.5$	<0.001
PLT (10^9/L)	216 (178, 254)	210 (174, 251)	218 (183, 266)	$U = 15,861$	0.072
Kidney					
UA (μmol/L)	359.60 (296.70, 428.15)	341.10 (284.70, 409.40)	372.35 (322.00, 442.85)	$U = 14,047.5$	<0.001
eGFR (mL/min/1.73 m^2)	101.06 (75.76, 118.07)	105.05 (85.76, 121.39)	94.67 (65.87, 111.10)	$U = 13,042$	<0.001
24 h mAlb (mg/24 h)	612.68 (267.95, 1142.45)	452.25 (201.84, 836.50)	713.32 (359.66, 1449.88)	$U = 13,261.5$	<0.001
24 h U-TP (g/24 h)	0.89 (0.45, 1.74)	0.69 (0.33, 1.30)	1.09 (0.58, 2.16)	$U = 12,835$	<0.001
Renal pathology					
Glomerulosclerosis rate, %	17.65 (8.33, 33.33)	15.38 (5.56, 28.57)	21.24 (9.52, 42.17)	$U = 13,843.5$	<0.001
Global glomerulosclerosis rate, %	13.33 (4.76, 28.57)	11.11 (2.86, 22.73)	16.67 (6.67, 35.34)	$U = 13,930.5$	<0.001
Segmental glomerulosclerosis rate, %	0.00 (0.00, 8.33)	0.00 (0.00, 7.69)	0.00 (0.00, 8.33)	$U = 16,682$	0.265

Table 1. Continued.

	Total cases (n = 377)	TyG index ≤8.49 (n = 191)	TyG index >8.49 (n = 186)	Statistic	*p* value
Mesangial hypercellularity, n (%)	376 (99.7%)	190 (99.5%)	186 (100%)	Fisher	1.000
Tubular atrophy, n (%)	340 (90.2%)	165 (86.4%)	175 (94.1%)	$\chi^2 = 6.310$	0.012
Interstitial fibrosis, n (%)	322 (85.4%)	157 (82.2%)	165 (88.7%)	$\chi^2 = 3.206$	0.073
Interstitial inflammation, n (%)	341 (90.5%)	168 (88.0%)	173 (93.0%)	$\chi^2 = 2.785$	0.095
Vascular injury, n (%)	98 (26.0%)	36 (18.8%)	62 (33.3%)	$\chi^2 = 10.278$	0.001
Medication use					
Antihypertensives	137 (36.3%)	60 (31.4%)	77 (41.4%)	$\chi^2 = 4.061$	0.044
Urate-lowering therapy	8 (2.1%)	1 (0.5%)	7 (3.8%)	$\chi^2 = 3.330$	0.068
Immunosuppressive therapy	64 (17.0%)	33 (17.3%)	31 (16.7%)	$\chi^2 = 0.025$	0.875
Traditional Chinese medicine	140 (37.1%)	70 (36.6%)	70 (37.6%)	$\chi^2 = 0.039$	0.843
Medication unknown	14 (3.7%)	5 (2.6%)	9 (4.8%)	$\chi^2 = 1.300$	0.254
Pathological subtype				Fisher-Freeman-Halton exact test	0.033
IgA nephropathy	326 (86.5%)	170 (89.0%)	156 (83.9%)		
Mesangial proliferative GN	28 (7.4%)	15 (7.9%)	13 (7.0%)		
FSGS	12 (3.2%)	4 (2.1%)	8 (4.3%)		
Sclerosing/proliferative sclerosing GN	10 (2.7%)	1 (0.5%)	9 (4.8%)		
Endocapillary proliferative GN	1 (0.3%)	1 (0.5%)	0 (0.0%)		

Note: Data are presented as mean ± standard deviation (SD), median (Q1, Q3), or number (%). The TyG index was calculated as ln [fasting triglycerides (mg/dL) × fasting glucose (mg/dL) / 2].

Abbreviations: BMI, body mass index; FBG, fasting blood glucose; TC, total cholesterol; TG, triglycerides; LDL, low-density lipoprotein; HDL, high-density lipoprotein; Alb, albumin; DBIL, direct bilirubin; UA, uric acid; eGFR, estimated glomerular filtration rate; 24 h mAlb, 24-hour urinary microalbumin; 24 h U-TP, 24-hour urinary total protein; PLT, platelet count; GN, glomerulonephritis; FSGS, focal segmental glomerulosclerosis.

Conversion factors for units: FBG in mg/dL to mmol/L, ×0.05551; TC, LDL, and HDL in mg/dL to mmol/L, ×0.02586; TG in mg/dL to mmol/L, ×0.01129; total protein, Alb and globulin in g/dL to g/L, ×10; DBIL in mg/dL to μmol/L, ×17.1; UA in mg/dL to μmol/L, ×59.48.

(OR = 1.364, 95% CI: 1.216–1.530, $p < 0.001$) and multivariate analysis adjusted for sex, age, SBP, smoking history, alcohol consumption, BMI, and uric acid (OR = 1.223, 95% CI: 1.073–1.395, $p = 0.003$). Further analysis showed that TyG remained associated with global glomerulosclerosis rates after adjustment for measured covariates (adjusted OR = 1.267, 95% CI: 1.109–1.448, $p < 0.001$), but not with segmental glomerulosclerosis rates (adjusted OR = 1.011, 95% CI: 0.841–1.215, $p = 0.906$).

The TyG index was associated with the total glomerulosclerosis proportion after adjustment for measured covariates in the overall analysis. Exploratory stratified analyses were subsequently performed according to sex, age, CKD stage, and vascular injury status to assess the consistency of this association.

Baseline Characteristics Stratified by Sex

As shown in Table 3, a higher TyG index was associated with older age, higher BMI, a higher prevalence of hypertension, less favorable lipid profiles, lower eGFR, and a higher proportion of vascular injury in both sexes. Among males, patients in the high TyG group were older than those in the low TyG group (median 33 [IQR 25–41] vs. 28 [22–32] years, $p = 0.003$), had a higher prevalence of hypertension (28.2% vs. 8.3%, $p = 0.003$), higher BMI (25.18 ± 3.81 vs. 22.68 ± 2.95 kg/m^2, $p < 0.001$), and a higher proportion of vascular injury (32.9% vs. 15.0%, $p = 0.015$). Similarly, among females, the patients in the high TyG group were older (34 [29–41] vs. 31 [25–37] years, $p = 0.002$), had a higher prevalence of hypertension (22.8% vs. 6.9%, $p < 0.001$), higher BMI (24.17 [22.00–26.21] vs. 20.70 [19.20–23.12] kg/m^2, $p < 0.001$), and a higher proportion of vascular injury (33.7% vs. 20.6%, $p = 0.025$). In both sexes, the high TyG group also showed higher fasting blood glucose, triglycerides, LDL-C, and lower HDL-C and eGFR levels. Total cholesterol was significantly higher in the high TyG group in males ($p < 0.001$) and females ($p = 0.008$).

However, differences between male and female subgroups were observed in the distribution of renal injury-related indicators. In females, the high TyG group showed a significantly greater proteinuria burden, with higher 24 h mAlb levels (672.00 [352.28–1236.63] vs. 431.90 [168.95–806.40] mg/24 h, $p < 0.001$) and 24 h U-TP levels (1.07 [0.59–1.98] vs. 0.68 [0.28–1.24] g/24 h, $p < 0.001$), as well as higher uric acid levels (351.60 [273.10–401.45] vs.

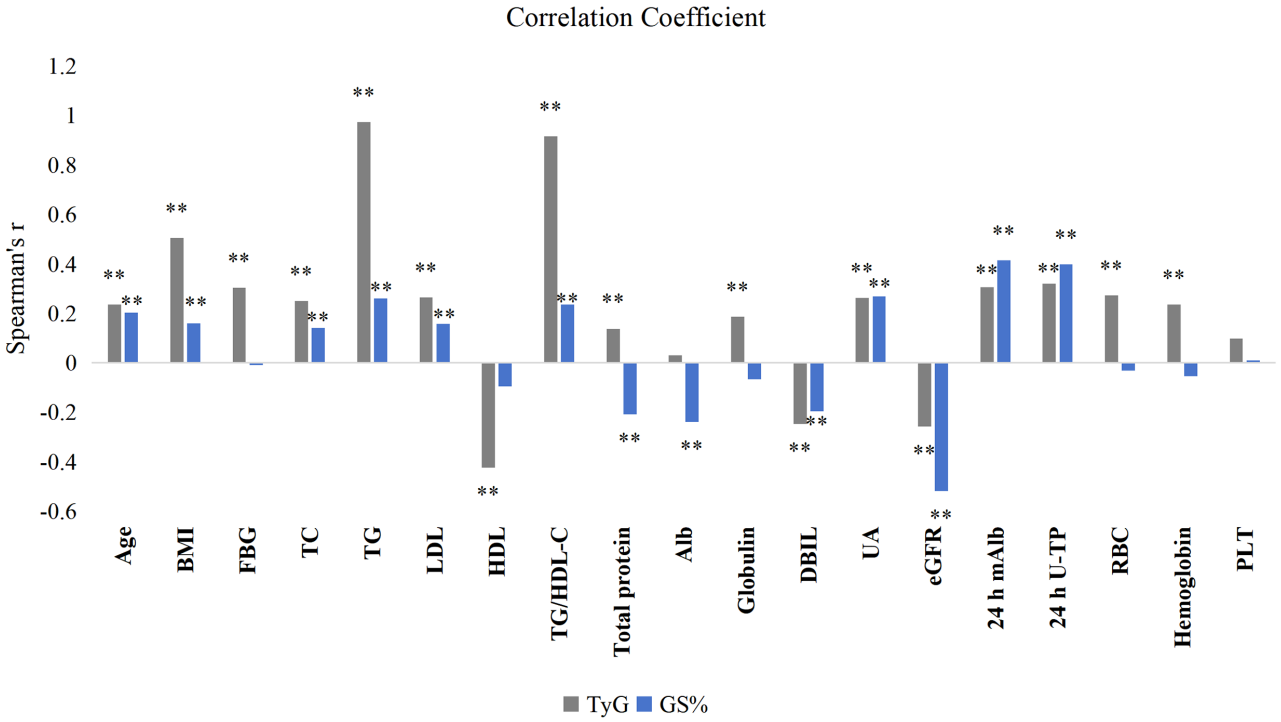

Fig. 2. Correlation analysis of the TyG index and total glomerulosclerosis proportion with clinical and laboratory variables. Note: The bar chart displays the correlation coefficients (r) between the TyG index (gray bars), total glomerulosclerosis proportion (blue bars), and various clinical parameters. $^{**}p < 0.01$. Abbreviations: TyG, triglyceride-glucose; GS%, glomerulosclerosis rate; BMI, body mass index; FBG, fasting blood glucose; TC, total cholesterol; TG, triglycerides; LDL, low-density lipoprotein; HDL, high-density lipoprotein; TG/HDL-C, triglyceride to high-density lipoprotein cholesterol ratio; Alb, albumin; DBIL, direct bilirubin; UA, uric acid; eGFR, estimated glomerular filtration rate; 24 h mAlb, 24-hour urinary microalbumin; 24 h U-TP, 24-hour urinary total protein; RBC, red blood cell count; PLT, platelet count.

Table 2. Generalized linear regression analyses of factors associated with glomerulosclerosis and its histological subtypes.

Outcome	Variable	Univariate analysis			Multivariate analysis		
Total glomerulosclerosis rate		OR	95% CI	*p* value	OR	95% CI	*p* value
	Male	1.224	0.963–1.556	0.098	0.710	0.524–0.961	0.026
	Age	1.195	1.062–1.345	0.003	1.099	0.980–1.233	0.106
	SBP	1.233	1.096–1.387	<0.001	1.151	1.022–1.298	0.020
	Smoking history	1.873	1.381–2.542	<0.001	1.701	1.170–2.472	0.005
	Alcohol consumption	1.572	1.116–2.214	0.010	1.147	0.783–1.681	0.481
	BMI	1.206	1.074–1.353	0.002	0.984	0.860–1.125	0.812
	UA	1.326	1.186–1.481	<0.001	1.239	1.092–1.407	<0.001
	TyG	1.364	1.216–1.530	<0.001	1.223	1.073–1.395	0.003
Global glomerulosclerosis rate	TyG	1.402	1.248–1.576	<0.001	1.267	1.109–1.448	<0.001
Segmental glomerulosclerosis rate	TyG	1.106	0.941–1.300	0.220	1.011	0.841–1.215	0.906

Note: Generalized linear models with a binomial distribution and logit link were used. Outcomes included total, global, and segmental glomerulosclerosis rates. Multivariable models were adjusted for sex, age, SBP, smoking history, alcohol consumption, BMI, and uric acid. For global and segmental glomerulosclerosis rates, only the results for the TyG index are shown. ORs for continuous variables are presented per 1-SD increase; binary variables are presented as category comparisons.

Abbreviations: BMI, body mass index; SBP, systolic blood pressure; UA, uric acid; TyG, triglyceride-glucose index; OR, odds ratio; CI, confidence interval.

Multicollinearity among covariates was assessed using variance inflation factors (VIFs), and all VIF values ranged from 1.095 to 1.604, indicating no obvious multicollinearity.

Table 3. Baseline characteristics of the study population stratified by sex and TyG index.

	Male					Female				
	Total cases (n = 145)	TyG index ≤8.49 (n = 60)	TyG index >8.49 (n = 85)	Statistic	*p* value	Total cases (n = 232)	TyG index ≤8.49 (n = 131)	TyG index >8.49 (n = 101)	Statistic	*p* value
Age (years)	31 (24, 38)	28 (22, 32)	33 (25, 41)	U = 1805.5	0.003	33 (27, 39)	31 (25, 37)	34 (29, 41)	U = 5070.5	0.002
Hypertension (%)	29 (20%)	5 (8.3%)	24 (28.2%)	χ^2 = 8.707	0.003	32 (13.8%)	9 (6.9%)	23 (22.8%)	χ^2 = 12.128	<0.001
Smoking history (%)	49 (33.8%)	18 (30.0%)	31 (36.5%)	χ^2 = 0.658	0.417	2 (0.9%)	1 (0.8%)	1 (1.0%)	Fisher	1.000
Alcohol consumption (%)	41 (28.3%)	15 (25.0%)	26 (30.6%)	χ^2 = 0.542	0.462	4 (1.7%)	3 (2.3%)	1 (1.0%)	χ^2 = 0.06	0.806
BMI (kg/m^2)	24.14 ± 3.68	22.68 ± 2.95	25.18 ± 3.81	t = –4.257	<0.001	22.36 (19.93, 24.64)	20.70 (19.20, 23.12)	24.17 (22.00, 26.21)	U = 3303.5	<0.001
FBG (mmol/L)	4.53 (4.19, 4.88)	4.33 (3.99, 4.67)	4.70 (4.34, 4.94)	U = 1628.5	0.001	4.50 (4.23, 4.91)	4.39 (4.18, 4.70)	4.67 (4.36, 5.09)	U = 4547.5	<0.001
Serum lipids										
TC (mmol/L)	4.68 ± 1.06	4.31 ± 0.87	4.95 ± 1.11	t = –3.901	<0.001	4.69 (4.13, 5.42)	4.55 (4.05, 5.25)	4.91 (4.32, 5.57)	U = 5272	0.008
TG (mmol/L)	1.58 (1.09, 2.21)	1.03 (0.89, 1.19)	2.06 (1.66, 3.18)	U = 144	<0.001	1.24 (0.86, 2.04)	0.90 (0.75, 1.17)	2.13 (1.71, 2.58)	U = 190	<0.001
LDL (mmol/L)	2.99 ± 0.73	2.75 ± 0.65	3.15 ± 0.75	t = –3.35	0.001	2.90 (2.47, 3.43)	2.77 (2.40, 3.23)	3.08 (2.64, 3.51)	U = 4997.5	0.001
HDL (mmol/L)	1.01 (0.87, 1.15)	1.07 (0.93, 1.21)	0.95 (0.82, 1.13)	U = 1831.5	0.004	1.19 (1.04, 1.44)	1.30 (1.14, 1.55)	1.10 (0.93, 1.24)	U = 3362.5	<0.001
TG/HDL–C	1.52 (1.04, 2.38)	1.01 (0.77, 1.15)	2.19 (1.71, 3.73)	U = 290	<0.001	1.01 (0.66, 1.81)	0.70 (0.53, 0.89)	2.03 (1.47, 2.53)	U = 415	<0.001
Liver function										
Total protein (g/L)	63.67 ± 6.66	63.24 ± 6.33	63.98 ± 6.91	t = –0.658	0.512	63.27 ± 6.56	62.39 ± 6.68	64.42 ± 6.25	t = –2.359	0.019
Alb (g/L)	38.58 ± 4.60	38.45 ± 4.45	38.67 ± 4.73	t = –0.274	0.784	37.02 ± 4.18	37.01 ± 4.32	37.04 ± 4.01	t = –0.064	0.949
Globulin (g/L)	24.90 (22.35, 27.10)	24.90 (21.80, 27.33)	24.90 (22.55, 27.10)	U = 2323	0.362	26.25 ± 3.83	25.38 ± 3.65	27.37 ± 3.79	t = –4.059	<0.001
DBIL (μmol/L)	3.2 (2.5, 4.8)	3.7 (2.7, 5.3)	3.1 (2.3, 4.5)	U = 2055	0.047	3.0 (2.2, 3.8)	3.2 (2.5, 4.2)	2.7 (2.1, 3.4)	U = 5072.5	0.002
Complete blood count										
RBC (10^{12}/L)	4.64 ± 0.57	4.63 ± 0.63	4.65 ± 0.53	t = –0.189	0.850	4.01 (3.73, 4.32)	3.91 (3.66, 4.18)	4.20 (3.93, 4.49)	U = 4273.5	<0.001
Hemoglobin (g/L)	138 (131, 147)	136 (129, 146)	141 (132, 148)	U = 2199.5	0.159	120 (112, 128)	116 (110, 126)	124 (114, 131)	U = 4913.5	0.001
PLT (10^9/L)	212.61 ± 54.67	211.72 ± 51.68	213.25 ± 56.98	t = –0.165	0.869	219 (181, 260)	209 (174, 252)	224 (197, 274)	U = 5321	0.011
Kidney										
UA (μmol/L)	410.9 (354.3, 462.1)	411.2 (347.0, 461.4)	410.9 (354.3, 463.7)	U = 2424	0.613	329.10 (270.23, 384.45)	310.90 (269.80, 368.60)	351.60 (273.10, 401.45)	U = 5382.5	0.015
eGFR (mL/min/1.73 m^2)	94.68 (66.30, 112.84)	102.90 (72.01, 121.58)	86.28 (65.62, 105.51)	U = 1807	0.003	103.42 (83.08, 119.65)	107.92 (88.11, 121.39)	99.24 (69.05, 116.78)	U = 5308	0.010
24 h mAlb (mg/24 h)	682.00 (327.75, 1502.35)	595.55 (309.53, 1058.10)	827.20 (359.64, 1706.55)	U = 2092	0.066	581.90 (215.06, 948.38)	431.90 (168.95, 806.40)	672.00 (352.28, 1236.63)	U = 4756.5	<0.001
24 h U–TP (g/24 h)	0.99 (0.52, 2.16)	0.82 (0.45, 1.61)	1.21 (0.54, 2.43)	U = 2085	0.062	0.82 (0.37, 1.53)	0.68 (0.28, 1.24)	1.07 (0.59, 1.98)	U = 4504.5	<0.001

Table 3. Continued.

	Male					Female				
	Total cases (n = 145)	TyG index ≤8.49 (n = 60)	TyG index >8.49 (n = 85)	Statistic	*p* value	Total cases (n = 232)	TyG index ≤8.49 (n = 131)	TyG index >8.49 (n = 101)	Statistic	*p* value
Renal pathology										
Glomerulosclerosis rate, %	19.44 (7.69, 40.59)	15.59 (0.37, 28.57)	21.95 (9.76, 51.19)	U = 1726.5	0.001	16.33 (9.09, 33.33)	15.38 (5.88, 28.57)	20.00 (9.52, 40.00)	U = 5624.5	0.050
Global glomerulosclerosis rate, %	13.33 (4.55, 32.05)	6.90 (0.00, 22.82)	18.52 (8.17, 43.65)	U = 1665.5	<0.001	13.19 (4.76, 25.00)	11.76 (5.00, 21.88)	14.29 (4.76, 32.05)	U = 5777	0.097
Segmental glomerulosclerosis rate, %	0 (0, 8.33)	0.00 (0.00, 7.62)	0.00 (0.00, 9.09)	U = 2479	0.759	0 (0, 7.92)	0 (0, 8.00)	0 (0, 8.01)	U = 6083	0.248
Mesangial hypercellularity, n (%)	145 (100%)	60 (100%)	85 (100%)			231 (99.6%)	130 (99.2%)	101 (100%)	Fisher	1.000
Tubular atrophy, n (%)	130 (89.7%)	48 (80.0%)	82 (96.5%)	χ^2 = 10.288	0.001	210 (90.5%)	117 (89.3%)	93 (92.1%)	χ^2 = 0.508	0.476
Interstitial fibrosis, n (%)	128 (88.3%)	49 (81.7%)	79 (92.9%)	χ^2 = 4.320	0.038	194 (83.6%)	108 (82.4%)	86 (85.1%)	χ^2 = 0.305	0.581
Interstitial inflammation, n (%)	132 (91%)	51 (85.0%)	81 (95.3%)	χ^2 = 4.567	0.033	209 (90.1%)	117 (89.3%)	92 (91.1%)	χ^2 = 0.201	0.654
Vascular injury, n (%)	37 (25.5%)	9 (15.0%)	28 (32.9%)	χ^2 = 5.957	0.015	61 (26.3%)	27 (20.6%)	34 (33.7%)	χ^2 = 5.014	0.025
Medication use										
Antihypertensives	61 (42.1%)	20 (33.3%)	41 (48.2%)	χ^2 = 3.205	0.073	76 (32.8%)	40 (30.5%)	36 (35.6%)	χ^2 = 0.676	0.411
Urate–lowering therapy	6 (4.1%)	1 (1.7%)	5 (5.9%)	χ^2 = 0.692	0.405	2 (0.9%)	0 (0.0%)	2 (2.0%)	Fisher	0.188
Immunosuppressive therapy	25 (17.2%)	10 (16.7%)	15 (17.6%)	χ^2 = 0.024	0.878	39 (16.8%)	23 (17.6%)	16 (15.8%)	χ^2 = 0.120	0.729
Traditional Chinese medicine	52 (35.9%)	23 (38.3%)	29 (34.1%)	χ^2 = 0.272	0.602	88 (37.9%)	47 (35.9%)	41 (40.6%)	χ^2 = 0.539	0.463
Medication unknown	3 (2.1%)	2 (3.3%)	1 (1.2%)	χ^2 = 0.094	0.759	11 (4.7%)	3 (2.3%)	8 (7.9%)	χ^2 = 2.854	0.091

Note: Data are presented as mean ± SD, median (Q1, Q3), or number (%). TyG index was calculated as Ln [fasting triglycerides (mg/dL) × fasting glucose (mg/dL) / 2].

Abbreviations: BMI, body mass index; FBG, fasting blood glucose; TC, total cholesterol; TG, triglycerides; LDL, low-density lipoprotein; HDL, high-density lipoprotein; TG/HDL-C, triglyceride to high-density lipoprotein cholesterol ratio; Alb, albumin; DBIL, direct bilirubin; RBC, red blood cell count; PLT, platelet count; UA, uric acid; eGFR, estimated glomerular filtration rate; 24 h mAlb, 24-hour urinary microalbumin; 24 h U-TP, 24-hour urinary total protein.

310.90 [269.80–368.60] μmol/L, $p = 0.015$). In contrast, among males, the differences in 24 h mAlb, 24 h U-TP, and uric acid between TyG groups were not statistically significant. Nevertheless, males in the high TyG group exhibited more severe pathological injury, including higher glomerulosclerosis rates, global glomerulosclerosis rates, tubular atrophy, interstitial fibrosis, interstitial inflammation, and vascular injury.

Sex-Stratified Analyses of TyG and Glomerulosclerosis

As shown in Table 4, sex-stratified analyses showed that the association between the TyG index and total glomerulosclerosis proportion reached statistical significance in females after adjustment. In females, TyG was significantly associated with total glomerulosclerosis rate in both univariate analysis (OR = 1.390, 95% CI: 1.199–1.611, $p < 0.001$) and multivariate analysis (adjusted OR = 1.235, 95% CI: 1.048–1.454, $p = 0.012$). In males, TyG was significant in the univariate analysis (OR = 1.309, 95% CI: 1.082–1.583, $p = 0.006$), but the association was attenuated after adjustment (adjusted OR = 1.197, 95% CI: 0.957–1.497, $p = 0.115$). For global glomerulosclerosis rates, TyG remained significant after adjustment in both males (adjusted OR = 1.273, 95% CI: 1.017–1.593, $p = 0.035$) and females (adjusted OR = 1.251, 95% CI: 1.058–1.479, $p = 0.009$). However, no significant association was observed between TyG and segmental glomerulosclerosis rate in either males (adjusted OR = 0.899, 95% CI: 0.662–1.222, $p = 0.498$) or females (adjusted OR = 1.109, 95% CI: 0.876–1.404, $p = 0.390$).

Baseline Characteristics Stratified by CKD Stage

As shown in Table 5, a higher TyG index was associated with adverse metabolic profiles across different CKD stages. In CKD stage 1, patients in the high TyG group were older than those in the low TyG group (median 32 [IQR 26–38] vs. 30 [22–34] years, $p = 0.008$), had a higher prevalence of hypertension (18.6% vs. 4.5%, $p < 0.001$), and had higher BMI levels (24.44 [22.75–27.86] vs. 21.23 [19.42–23.89] kg/m^2, $p < 0.001$). In CKD stages 2–3, the high TyG group had a higher prevalence of hypertension (33.3% vs. 14.0%, $p = 0.010$) and higher BMI levels (24.12 [21.83–26.02] vs. 21.99 [19.35–23.77] kg/m^2, $p < 0.001$). In both CKD strata, the high TyG group showed significantly higher fasting blood glucose, triglycerides, TG/HDL-C, and lower HDL-C levels. Elevated total cholesterol and LDL-C levels were observed only in CKD stage 1, whereas higher serum uric acid levels were significant only in CKD stages 2–3.

Regarding renal-related indicators, the high TyG group showed lower eGFR levels in both CKD strata. However, the pattern of renal injury differed between CKD stages. In CKD stage 1, the high TyG group was characterized by greater proteinuria burden, with higher 24 h mAlb levels (667.50 [323.85–1249.44] vs. 421.80 [188.89–770.40] mg/24 h, $p < 0.001$) and higher 24 h U-TP levels (0.96 [0.53–2.00] vs. 0.62 [0.30–1.13] g/24 h, $p < 0.001$), as well as a higher proportion of tubular atrophy (93.1% vs. 82.8%, $p = 0.019$). In contrast, in CKD stages 2–3, the high TyG group showed more prominent chronic pathological injury, including a higher glomerulosclerosis rate (38.57% [17.13–61.71] vs. 27.27% [15.38–45.56], $p = 0.010$), a higher global glomerulosclerosis rate (31.67% [12.71–51.50] vs. 20.69% [10.56–33.33], $p = 0.008$), and a higher proportion of vascular injury (45.2% vs. 26.3%, $p = 0.023$).

CKD Stage–Stratified Analyses of TyG and Glomerulosclerosis

As shown in Table 6, CKD-stratified analyses showed that the association between the TyG index and total glomerulosclerosis rate reached statistical significance in CKD stages 2–3 after adjustment. In CKD stage 1, TyG was significantly associated with the outcomes in the univariate analysis (OR = 1.231, 95% CI: 1.076–1.408, $p = 0.002$), but not after adjustment (adjusted OR = 1.121, 95% CI: 0.959–1.309, $p = 0.151$). In contrast, in CKD stages 2–3, TyG remained significantly associated with total glomerulosclerosis rate after adjustment (adjusted OR = 1.248, 95% CI: 1.013–1.537, $p = 0.037$). A similar pattern was observed for global glomerulosclerosis rates, with a significant adjusted association in CKD stages 2–3 (adjusted OR = 1.365, 95% CI: 1.110–1.679, $p = 0.003$), but not in CKD stage 1. No significant association was observed between TyG and segmental glomerulosclerosis rate in either CKD stage.

Discussion

This study investigated the association between the TyG index and biopsy-proven glomerulosclerosis in patients with PGN. The results showed that an elevated TyG index was associated with a higher total glomerulosclerosis rate after adjustment for measured covariates. Further analyses suggested that this association was more evident for global glomerulosclerosis, whereas no significant association was observed in segmental glomerulosclerosis.

A substantial body of previous epidemiological research has shown that the TyG index, as a reliable surrogate marker for IR, is closely related to albuminuria, the risk of CKD onset, and the progression to ESRD. A prospective cohort study based on the Austrian Vorarlberg Health Monitoring and Promotion Program (VHM&PP) showed that for every 1-standard-deviation increase in the TyG index, the risk of ESRD increased by approximately 68%; furthermore, mediation analysis suggested that the TyG index mediated approximately 41.7% of the association between BMI and ESRD. Similarly, Xu et al. [24] found in a Chinese cohort that a high TyG index is an independent risk factor for the occurrence of CKD. This is consistent with

Table 4. Generalized linear regression analyses of factors associated with glomerulosclerosis and its histological subtypes stratified by sex.

Outcome	Variable	Univariate analysis			Multivariate analysis		
		OR	95% CI	*p* value	OR	95% CI	*p* value
Total glomerulosclerosis rate	Male						
	Age	1.163	0.963–1.405	0.116	1.057	0.876–1.277	0.562
	SBP	1.153	0.929–1.432	0.195	1.132	0.910–1.410	0.266
	Smoking history	2.056	1.389–3.043	<0.001	1.870	1.208–2.893	0.005
	Alcohol consumption	1.571	1.025–2.410	0.038	1.131	0.709–1.804	0.605
	BMI	1.242	0.993–1.554	0.058	1.008	0.775–1.312	0.952
	UA	1.210	0.979–1.496	0.077	1.126	0.904–1.404	0.289
	TyG	1.309	1.082–1.583	0.006	1.197	0.957–1.497	0.115
Global glomerulosclerosis rate	TyG	1.378	1.141–1.665	<0.001	1.273	1.017–1.593	0.035
Segmental glomerulosclerosis rate	TyG	0.978	0.748–1.279	0.868	0.899	0.662–1.222	0.498
Total glomerulosclerosis rate	Female						
	Age	1.246	1.072–1.447	0.004	1.158	0.999–1.342	0.051
	SBP	1.256	1.090–1.448	0.002	1.131	0.979–1.307	0.094
	Smoking history	0.663	0.114–3.851	0.647	0.312	0.057–1.719	0.181
	Alcohol consumption	1.072	0.407–2.820	0.888	0.856	0.342–2.141	0.739
	BMI	1.171	1.022–1.340	0.023	0.961	0.824–1.121	0.615
	UA	1.450	1.248–1.684	<0.001	1.391	1.185–1.634	<0.001
	TyG	1.390	1.199–1.611	<0.001	1.235	1.048–1.454	0.012
Global glomerulosclerosis rate	TyG	1.403	1.205–1.634	<0.001	1.251	1.058–1.479	0.009
Segmental glomerulosclerosis rate	TyG	1.200	0.974–1.477	0.087	1.109	0.876–1.404	0.390

Note: Generalized linear models with a binomial distribution and logit link were used. Outcomes included total, global, and segmental glomerulosclerosis rates. Multivariable models were adjusted for age, SBP, smoking history, alcohol consumption, BMI, and uric acid within each sex subgroup. For global and segmental glomerulosclerosis rates, only the results for the TyG index are shown. ORs for continuous variables are presented per 1-SD increase; binary variables are presented as category comparisons.

Abbreviations: BMI, body mass index; SBP, systolic blood pressure; UA, uric acid; TyG, triglyceride-glucose index; OR, odds ratio; CI, confidence interval.

the lower eGFR and higher proteinuria levels observed in the high TyG group in our study. However, the aforementioned studies primarily relied on functional indicators such as eGFR or proteinuria to define renal outcomes. Although functional indicators have clinical value, they may not fully capture underlying histological injury, particularly when renal function is relatively preserved. This study addresses the limitations of previous studies that focused solely on biochemical markers. By incorporating renal biopsy findings, our study demonstrated that a higher TyG index was significantly associated with a greater proportion of biopsy-proven glomerulosclerosis, extending previous epidemiological findings with histopathological evidence.

Currently, evidence regarding the association between the TyG index and renal histopathology remains relatively scarce. Choi et al. [25] previously found in patients with immunoglobulin A (IgA) nephropathy that hypertriglyceridemia was associated with more severe glomerulosclerosis, and that the TyG index was significantly positively correlated with proteinuria. Our study not only is consistent with this finding but also extends it to an IgA nephropathy–predominant PGN cohort and further quantifies the association between the TyG index and GS%. Consistent with the findings of Zhao et al. [26], who found that the TyG index was associated with early renal injury markers (microalbuminuria), our study found that TyG was associated with total and global glomerulosclerosis rates after adjustment for measured covariates in biopsy-proven PGN. These findings extend previous evidence based on clinical markers of renal injury to an association with biopsy-defined glomerulosclerotic burden. However, causality cannot be inferred because of the cross-sectional design.

Several possible biological explanations may underlie the observed association. Previous research indicates that adipokines and ectopic lipid accumulation may be related to insulin resistance in podocytes, with possible involvement of impairing the protective phosphoinositide 3-kinase/protein kinase B (PI3K/Akt) signaling pathway and disrupting the cytoskeletal adaptation required to maintain glomerular structure [27]. These maladaptive podocyte responses have been discussed as potential biological processes related to focal segmental glomerulosclerosis (FSGS). Concurrently, compensatory hyperinsulinemia has been hypothesized to be associated with insulin re-

Table 5. Baseline characteristics of the study population stratified by CKD stage and TyG index.

	CKD stage 1					CKD stage 2–3				
	Total cases (n = 236)	TyG index ≤8.49 (n = 134)	TyG index >8.49 (n = 102)	Statistic	*p* value	Total cases (n = 141)	TyG index ≤8.49 (n = 57)	TyG index >8.49 (n = 84)	Statistic	*p* value
Male, n (%)	79 (33.5%)	39 (29.1%)	40 (39.2%)	$\chi^2 = 2.659$	0.103	66 (46.8%)	21 (36.8%)	45 (53.6%)	$\chi^2 = 3.817$	0.051
Age (years)	31 (24, 35)	30 (22, 34)	32 (26, 38)	$U = 5456$	0.008	36 (29, 43)	34 (26, 41)	37 (30, 47)	$U =$ 1969.5	0.074
Hypertension (%)	25 (10.6%)	6 (4.5%)	19 (18.6%)	$\chi^2 =$ 12.243	<0.001	36 (25.5%)	8 (14.0%)	28 (33.3%)	$\chi^2 = 6.651$	0.010
Smoking history (%)	22 (9.3%)	9 (6.7%)	13 (12.7%)	$\chi^2 = 2.490$	0.115	29 (20.6%)	10 (17.5%)	19 (22.6%)	$\chi^2 = 0.535$	0.464
Alcohol consumption (%)	19 (8.1%)	11 (8.2%)	8 (7.8%)	$\chi^2 = 0.010$	0.919	26 (18.4%)	7 (12.3%)	19 (22.6%)	$\chi^2 = 2.413$	0.120
BMI (kg/m^2)	23.02 (20.04, 25.30)	21.23 (19.42, 23.89)	24.44 (22.75, 27.86)	$U =$ 3521.5	<0.001	23.36 (20.93, 25.35)	21.99 (19.35, 23.77)	24.12 (21.83, 26.02)	$U =$ 1327.5	<0.001
FBG (mmol/L)	4.53 (4.23, 4.90)	4.41 (4.17, 4.69)	4.72 (4.42, 5.03)	$U = 4698$	<0.001	4.51 (4.20, 4.89)	4.33 (4.10, 4.68)	4.67 (4.31, 4.97)	$U =$ 1515.5	<0.001
Serum lipids										
TC (mmol/L)	4.61 (4.07, 5.27)	4.49 (3.79, 5.00)	4.92 (4.37, 5.55)	$U = 4634$	<0.001	4.75 (4.07, 5.60)	4.52 (4.08, 5.54)	4.91 (4.03, 5.71)	$U =$ 2176.5	0.361
TG (mmol/L)	1.20 (0.88, 1.93)	0.92 (0.77, 1.10)	2.13 (1.64, 3.01)	$U = 153$	<0.001	1.60 (1.19, 2.16)	1.15 (0.84, 1.29)	2.12 (1.73, 2.58)	$U = 163.5$	<0.001
LDL (mmol/L)	2.92 ± 0.69	2.75 ± 0.69	3.15 ± 0.63	$t = –4.579$	<0.001	2.93 (2.48, 3.58)	2.84 (2.50, 3.35)	3.08 (2.48, 3.62)	$U = 2091$	0.203
HDL (mmol/L)	1.13 (0.96, 1.34)	1.19 (1.05, 1.50)	1.07 (0.92, 1.18)	$U =$ 4078.5	<0.001	1.11 (0.90, 1.31)	1.23 (1.05, 1.45)	1.01 (0.84, 1.19)	$U =$ 1244.5	<0.001
TG/HDL-C	1.10 (0.70, 1.82)	0.73 (0.55, 0.95)	2.03 (1.50, 2.92)	$U = 445$	<0.001	1.49 (0.95, 2.23)	0.86 (0.66, 1.13)	2.16 (1.58, 2.94)	$U = 281$	<0.001
Liver function										
Total protein (g/L)	63.93 ± 6.42	63.25 ± 6.33	64.83 ± 6.46	$t = –1.880$	0.061	62.58 ± 6.81	61.26 ± 6.95	63.48 ± 6.61	$t = –1.915$	0.058
Alb (g/L)	38.18 ± 4.23	38.08 ± 4.02	38.32 ± 4.52	$t = –0.425$	0.671	36.69 ± 4.55	36.01 ± 4.94	37.14 ± 4.23	$t = –1.453$	0.148
Globulin (g/L)	25.75 ± 3.92	25.17 ± 3.99	26.51 ± 3.69	$t = –2.640$	0.009	25.89 ± 3.93	25.25 ± 3.43	26.34 ± 4.20	$t = –1.624$	0.107
DBIL (μmol/L)	3.2 (2.4, 4.2)	3.4 (2.5, 4.4)	3.1 (2.2, 4.0)	$U =$ 6028.5	0.121	3.0 (2.2, 4.0)	3.2 (2.7, 4.6)	2.8 (1.9, 3.6)	$U = 1760$	0.008
Complete blood count										
RBC (10^{12}/L)	4.28 (3.94, 4.65)	4.13 (3.82, 4.51)	4.50 (4.08, 4.71)	$U =$ 4493.5	<0.001	4.19 (3.72, 4.54)	3.89 (3.54, 4.47)	4.28 (3.98, 4.62)	$U =$ 1735.5	0.006
Hemoglobin (g/L)	128 (117, 137)	124 (114, 134)	132 (123, 140)	$U =$ 5105.5	0.001	124.11 ± 16.89	118.42 ± 18.21	127.96 ± 14.84	$t = –3.415$	0.001
PLT (10^9/L)	215 (179, 254)	209 (174, 248)	218 (191, 272)	$U =$ 5842.5	0.056	217.49 ± 57.65	213.19 ± 53.17	220.4 ± 60.64	$t = –0.728$	0.468
Kidney										
UA (μmol/L)	336.55 (277.33, 396.18)	326.8 (275.0, 391.1)	350.0 (283.7, 407.1)	$U =$ 5973.5	0.098	406.02 ± 95.53	383.61 ± 93.56	421.23 ± 94.39	$t = –2.331$	0.021
eGFR (mL/min/1.73 m^2)	113.21 (102.17, 123.26)	116.74 (103.31, 124.74)	109.82 (100.09, 120.00)	$U = 5441$	0.007	66.42 (53.36, 80.50)	72.98 (58.86, 82.75)	64.62 (49.80, 77.07)	$U = 1787$	0.011
24 h mAlb (mg/24 h)	533.04 (229.50, 936.53)	421.80 (188.89, 770.40)	667.50 (323.85, 1249.44)	$U = 4903$	<0.001	727.60 (376.93, 1493.35)	628.60 (334.65, 1135.35)	762.90 (412.25, 1568.33)	$U = 2049$	0.147
24 h U-TP (g/24 h)	0.80 (0.37, 1.51)	0.62 (0.30, 1.13)	0.96 (0.53, 2.00)	$U = 4893$	<0.001	1.18 (0.58, 2.23)	0.99 (0.48, 1.73)	1.24 (0.69, 2.37)	$U =$ 1937.5	0.055

Table 5. Continued.

	CKD stage 1					CKD stage 2-3				
	Total cases (n = 236)	TyG index ≤8.49 (n = 134)	TyG index >8.49 (n = 102)	Statistic	*p* value	Total cases (n = 141)	TyG index ≤8.49 (n = 57)	TyG index >8.49 (n = 84)	Statistic	*p* value
Renal pathology										
Glomerulosclerosis rate, %	12.00 (4.40, 23.08)	11.53 (2.78, 21.96)	13.33 (6.67, 27.60)	U = 5926	0.080	33.33 (16.33, 54.86)	27.27 (15.38, 45.56)	38.57 (17.13, 61.71)	U = 1784.5	0.010
Global glomerulosclerosis rate, %	9.09 (2.60, 18.18)	7.95 (0, 16.91)	9.52 (4.13, 20.00)	U = 5959	0.090	25.00 (11.88, 44.44)	20.69 (10.56, 33.33)	31.67 (12.71, 51.50)	U = 1761.5	0.008
Segmental glomerulosclerosis rate, %	0 (0, 6.25)	0 (0, 6.25)	0 (0, 6.51)	U = 6488.5	0.452	4.35 (0.00, 11.11)	4.35 (0.00, 11.56)	4.38 (0.00, 11.11)	U = 2379	0.947
Mesangial hypercellularity, n (%)	235 (99.6%)	133 (99.3%)	102 (100%)	Fisher	1.000	141 (100%)	57 (100%)	84 (100%)		
Tubular atrophy, n (%)	206 (87.3%)	111 (82.8%)	95 (93.1%)	χ^2 = 5.539	0.019	134 (95.0%)	54 (94.7%)	80 (95.2%)	χ^2 = 0	1.000
Interstitial fibrosis, n (%)	194 (82.2%)	105 (78.4%)	89 (87.3%)	χ^2 = 3.133	0.077	128 (90.8%)	52 (91.2%)	76 (90.5%)	χ^2 = 0.023	0.880
Interstitial inflammation, n (%)	206 (87.3%)	114 (85.1%)	92 (90.2%)	χ^2 = 1.369	0.242	135 (95.7%)	54 (94.7%)	81 (96.4%)	χ^2 = 0.004	0.950
Vascular injury, n (%)	45 (19.1%)	21 (15.7%)	24 (23.5%)	χ^2 = 2.317	0.128	53 (37.6%)	15 (26.3%)	38 (45.2%)	χ^2 = 5.183	0.023
Medication use										
Antihypertensives	80 (33.9%)	45 (33.6%)	35 (34.3%)	χ^2 = 0.014	0.906	57 (40.4%)	15 (26.3%)	42 (50.0%)	χ^2 = 7.909	0.005
Urate-lowering therapy	0 (0%)	0 (0%)	0 (0%)			8 (5.7%)	1 (1.8%)	7 (8.3%)	χ^2 = 1.655	0.198
Immunosuppressive therapy	45 (19.1%)	26 (19.4%)	19 (18.6%)	χ^2 = 0.023	0.881	19 (13.5%)	7 (12.3%)	12 (14.3%)	χ^2 = 0.117	0.732
Traditional Chinese medicine	88 (37.3%)	48 (35.8%)	40 (39.2%)	χ^2 = 0.285	0.593	52 (36.9%)	22 (38.6%)	30 (35.7%)	χ^2 = 0.121	0.728
Medication unknown	6 (2.5%)	3 (2.2%)	3 (2.9%)	χ^2 = 0	1.000	8 (5.7%)	2 (3.5%)	6 (7.1%)	χ^2 = 0.296	0.586

Note: Data are presented as mean ± SD, median (Q1, Q3), or number (%). *p*-values were calculated using the Student's *t*-test, Mann-Whitney U test, Chi-square test, or Fisher's exact test, as appropriate.

Abbreviations: CKD, chronic kidney disease; TyG, triglyceride-glucose; BMI, body mass index; FBG, fasting blood glucose; TC, total cholesterol; TG, triglycerides; LDL, low-density lipoprotein; HDL, high-density lipoprotein; DBIL, direct bilirubin; RBC, red blood cell; PLT, platelet; UA, uric acid; eGFR, estimated glomerular filtration rate; 24 h mAlb, 24-hour urinary microalbumin; 24 h U-TP, 24-hour urinary total protein.

Table 6. Generalized linear regression analyses of factors associated with glomerulosclerosis and its histological subtypes stratified by CKD stage.

Outcome	Variable	Univariate analysis			Multivariate analysis		
		OR	95% CI	*p* value	OR	95% CI	*p* value
Total glomerulosclerosis rate	CKD stage 1						
	Male	1.041	0.777–1.395	0.787	0.675	0.458–0.995	0.047
	Age	1.086	0.928–1.270	0.304	1.081	0.923–1.265	0.333
	SBP	1.132	0.985–1.301	0.079	1.076	0.928–1.247	0.332
	Smoking history	1.548	1.022–2.343	0.039	1.831	1.055–3.176	0.032
	Alcohol consumption	1.035	0.622–1.721	0.896	0.738	0.395–1.381	0.342
	BMI	1.158	1.019–1.316	0.024	1.009	0.863–1.179	0.914
	UA	1.252	1.081–1.450	0.003	1.263	1.047–1.524	0.015
	TyG	1.231	1.076–1.408	0.002	1.121	0.959–1.309	0.151
Global glomerulosclerosis rate	TyG	1.238	1.075–1.426	0.003	1.118	0.950–1.315	0.179
Segmental glomerulosclerosis rate	TyG	1.149	0.941–1.402	0.173	1.101	0.872–1.391	0.419
Total glomerulosclerosis rate	CKD stage 2–3						
	Male	1.164	0.835–1.622	0.372	0.758	0.490–1.172	0.213
	Age	0.968	0.824–1.138	0.694	0.896	0.755–1.064	0.212
	SBP	1.148	0.963–1.369	0.124	1.119	0.932–1.343	0.228
	Smoking history	1.519	1.025–2.251	0.037	1.570	0.973–2.534	0.065
	Alcohol consumption	1.431	0.934–2.193	0.100	1.150	0.715–1.848	0.565
	BMI	1.349	1.114–1.633	0.002	1.235	0.979–1.558	0.075
	UA	1.038	0.890–1.211	0.634	0.956	0.808–1.130	0.595
	TyG	1.370	1.148–1.636	<0.001	1.248	1.013–1.537	0.037
Global glomerulosclerosis rate	TyG	1.449	1.218–1.724	<0.001	1.365	1.110–1.679	0.003
Segmental glomerulosclerosis rate	TyG	0.943	0.732–1.216	0.653	0.820	0.610–1.104	0.192

Note: Generalized linear models with a binomial distribution and logit link were used. Outcomes included total, global, and segmental glomerulosclerosis rates. Multivariable models were adjusted for sex, age, SBP, smoking history, alcohol consumption, BMI, and uric acid within each CKD stage subgroup. For global and segmental glomerulosclerosis rates, only the results for the TyG index are shown. ORs for continuous variables are presented per 1-SD increase; binary variables are presented as category comparisons.

Abbreviations: CKD, chronic kidney disease; BMI, body mass index; SBP, systolic blood pressure; UA, uric acid; TyG, triglyceride-glucose index; OR, odds ratio; CI, confidence interval.

Additional exploratory analyses were performed according to age and vascular injury status (**Supplementary Tables 1–4**). In patients aged <45 years, the TyG index was associated with total glomerulosclerosis after adjustment (adjusted OR = 1.188, 95% CI: 1.032–1.368, $p = 0.016$). The association was not statistically significant in patients aged ≥45 years (adjusted OR = 1.361, 95% CI: 0.980–1.890, $p = 0.065$). The TyG index was also associated with total glomerulosclerosis in patients without vascular injury (adjusted OR = 1.223, 95% CI: 1.053–1.421, $p = 0.008$). No significant association was observed in patients with vascular injury (adjusted OR = 1.092, 95% CI: 0.847–1.409, $p = 0.497$). Similar results were observed for global glomerulosclerosis. No significant association with segmental glomerulosclerosis was observed in these subgroups.

sponsiveness and sodium reabsorption in renal tubular epithelial cells, as well as with altered tubuloglomerular feedback, afferent arteriolar tone, glomerular hyperfiltration, elevated filtration pressure, and glomerular hemodynamic stress [28]. These metabolic and hemodynamic abnormalities may provide possible biological explanations for the observed association with glomerulosclerosis. In our data, the association with TyG index was more consistently observed for total and global glomerulosclerosis than for segmental glomerulosclerosis.

In the exploratory sex-stratified analysis, the association between the TyG index and total glomerulosclerosis was significant in females but was attenuated after adjustment in males. This result is consistent with the large-scale longitudinal study by Wang et al. [29], which found that a high TyG index was associated with increased CKD risk and eGFR decline only in females. A previous study also reported that a similar hypertriglyceridemic waist phenotype is associated with CKD in women [30]. This may stem from multiple mechanisms: First, lipid handling and glucose homeostasis differ between females and males [31]. Second, sex hormone-related pathways, including estrogen receptor signaling, may be involved in metabolic regulation and susceptibility to metabolic abnormalities [31]. Furthermore, females may face a greater burden of insulin resistance during the stage of impaired glucose tolerance, and

specific genetic backgrounds may increase their susceptibility to metabolic renal injury [32]. These mechanisms may contribute to the statistically significant association observed in the female subgroup in this exploratory analysis. The non-significant adjusted association in males should not be interpreted as evidence of absence of effect and may reflect limited statistical precision.

In addition, CKD-stratified analysis showed that the TyG index remained associated with total and global glomerulosclerosis rates after adjustment for measured covariates in patients with CKD stages 2–3, whereas these associations did not reach statistical significance in CKD stage 1. One possible explanation for this discrepancy may be that, although insulin resistance appears early in CKD [33], during early disease, podocyte loss may not have reached the critical threshold (approximately 20%–40%) required to trigger significant sclerosis [34], and the kidney still possesses strong compensatory capacity. As kidney function declines, lower eGFR is associated with reduced peripheral insulin sensitivity [35]. At this point, podocyte injury or loss may become more apparent; further metabolic injury may compromise the function and survival of the remaining podocytes, thereby establishing a potential pathway through which a high TyG index may contribute to irreversible glomerulosclerosis.

These findings suggest that the TyG index may serve as a candidate marker associated with glomerulosclerotic burden in patients with PGN. However, given the cross-sectional nature of this study, prospective cohorts and interventional trials are warranted to validate the potential role of the TyG index as a candidate marker associated with glomerulosclerotic burden.

This study has several limitations. First, the cross-sectional design prevents the establishment of a causal relationship between elevated TyG index and glomerulosclerosis; it can only suggest an association between metabolic abnormalities and histological damage. Second, selection bias cannot be completely excluded. Since the study population consisted of PGN patients who underwent renal biopsy, the included participants may not fully represent the broader PGN population, potentially limiting the external generalizability of our findings. In addition, a considerable proportion of patients lacked height and/or weight measurements and were therefore excluded from the analysis. Although this approach ensured the accuracy of BMI classification, the exclusion of these patients may have introduced additional selection bias. Third, the relatively limited sample size of renal biopsy-confirmed PGN patients may have reduced statistical power, particularly in subgroup analyses and in analyses of segmental glomerulosclerosis, which was infrequent in this cohort. Fourth, as a surrogate marker for IR, the TyG index is susceptible to interference from factors such as fasting state, acute stress, and hepatic steatosis, and the optimal cutoff value for defining IR using the TyG index has not yet been standardized. Fifth, as a surrogate marker for insulin resistance, the TyG index cannot fully replace direct measures of insulin resistance. In addition, residual confounding cannot be excluded. In particular, the distribution of pathological subtypes differed between the high- and low-TyG groups, and different PGN subtypes may be associated with different degrees of chronic glomerular injury. Because pathological subtype was not additionally included in the multivariable models, its potential contribution to the observed association between the TyG index and glomerulosclerosis could not be fully accounted for. Residual confounding related to disease duration and detailed treatment exposure also cannot be excluded. Therefore, prospective multicenter studies are needed to validate these findings.

Conclusions

In conclusion, the TyG index was associated with the proportions of total and globally sclerotic glomeruli after adjustment for measured covariates in patients with biopsy-proven PGN. No significant association was observed in the proportion of segmentally sclerotic glomeruli. The TyG index may serve as a candidate marker associated with glomerulosclerotic burden. Further prospective studies are needed to validate its potential role as a candidate marker associated with glomerulosclerotic burden.

Availability of Data and Materials

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

Author Contributions

CC and JW designed the research study. HLC performed the research. YKW, PC, JJL and YWZ contributed to data collection. HLC, QPL and LHZ analyzed the data. CC and HLC have been involved in drafting the manuscript and all authors contributed to important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was approved by the Medical Ethics Committee of Xiangya Hospital, Central South University (ethical approval number: 2026030508). This study was in accordance with the Declaration of Helsinki. The requirement for written informed consent was waived by the institutional review board for this retrospective study.

Acknowledgment

Not applicable.

Funding

This work was funded by The 2023 Hunan Provincial Health High-Level Talents Major Scientific Research Project (Grant No. R2023052) and the Fund of Xiangya Hospital Partnership Support with Hunan University of Medicine General Hospital for Clinical Research and Cohort Development (Grant No. XYDL-ZB02).

Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.24976/Discov.Med.202638214.268.

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