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ORIGINAL RESEARCH

Clinicopathological Characteristics and Risk Factors for Rapid eGFR Decline in Chinese Patients with Biopsy-Proven Obesity-Related Glomerulopathy

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Aim: To investigate the clinicopathologic features and the related risk factors for rapid estimated glomerular filtration rate (eGFR) decline in Chinese obesity-related glomerulopathy (ORG) patients.

Methods: A total of 63 ORG patients, who underwent a renal biopsy and received follow-up for at least 12 months, were recruited in our study. These patients were classified as rapid decliners and slow decliners based on the eGFR slope value (−5.0 mL/min/1.73 m^2/year). Logistic regression analysis was used to determine the risk factors for rapid eGFR decline.

Results: Of the 63 ORG patients, 48 (76.2%) were male, the mean age was 38.7 ± 9.0 years, the median of urinary protein excretion was 1.62 g/24 h, 27.0% of them had nephrotic-range proteinuria, while hypoalbuminemia was observed in 7.9% of them. The incidence of obvious hypertriglyceridemia, hypertension, glucose dysmetabolism and hyperuricemia were 71.4%, 60.3%, 36.5% and 27.0%, respectively. 13 (20.6%) patients became rapid decliners during the median 45 months of follow-up. Their mean BMI was 31.8 ± 3.6 kg/m^2, the median of baseline eGFR and urinary protein excretion were 71.8 (range of 30.5–118.2) mL/min/1.73 m^2/year and 3.57 g/24 h, respectively. Multivariate logistic regression analysis showed that smoking (OR 9.205, 95% CI 1.704–49.740, P = 0.01), hyperuricemia (OR 5.541, 95% CI 1.079–28.460, P = 0.04) and nephrotic-range proteinuria (OR 6.128, 95% CI 1.311–28.637, P = 0.021) were the independent risk factors for rapid eGFR decline.

Conclusion: Chinese ORG patients were more likely to have clinical characteristics with hypertriglyceridemia, hypertension and hyperuricemia, and mild to severe degrees of urinary protein excretion at diagnosis, while patients with nephrotic-range proteinuria lacked hypoalbuminemia and hypercholesterolemia. Smoking, hyperuricemia and nephrotic-range proteinuria were independent risk factors for rapid eGFR decline in ORG patients.

Keywords: obesity-related glomerulopathy, clinical features, rapid eGFR decline, risk factors

Introduction

Obesity-related glomerulopathy (ORG) is a relatively uncommon kidney disease occurring in association with obesity. Worldwide prevalence of obesity increased at an alarming rate in adult from 3.2% to 10.8% in men and 6.4% to 14.9% in women between 1975 and 2014.[1] According to the latest data from the Chinese Center for Disease Control and Prevention, obesity prevalence among Chinese adults rose from 3.1% in 2004 to 8.1% in 2018.[2] The prevalence of ORG also had increased over the past several decades, owing to the emerging epidemic of obesity. A 10-year retrospective study based on 34,630 renal biopsy cases in Central China reported that the frequency of ORG increased from 0.62% in 2009 to 2.25% in 2018.[3]

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It typically shows an insidious onset and a slow progress with varying degrees of proteinuria.[4] The definite diagnosis of ORG relies on the pathological features of adaptive glomerular hypertrophy with or without focal segmental glomerulosclerosis (FSGS).[5–7] Increased metabolic demand results in glomerular hyperfiltration, renin-angiotensin-aldosterone system (RAAS) activation and abnormal lipid metabolism. Consequent glomerular hypertrophy with low podocyte density leads to proteinuria, increased glomerulosclerosis and chronic renal insufficiency eventually.[8,9]

A handful of studies have addressed kidney biopsy findings and prognosis in patients with ORG, and the follow-up is available on 15 to 50 patients in these studies, which do not involve the Chinese people.[10–12] A study showed the clinical and histopathological characteristics of 90 Chinese subjects with biopsy-proven ORG, while associated long-term outcomes have not been reported.[13] Renal function trajectory is important for managing patients with chronic kidney disease, rapid estimated glomerular filtration rate (eGFR) decline relates to a need for closer renal follow-up and increased risk for end-stage renal disease (ESRD).[14,15] As we know, there is no associated report in patients with ORG. For little data is available, we retrospectively reviewed 63 patients with ORG in a single center of west China to explore the clinicopathological characteristics and risk factors of rapid eGFR decline on patients with ORG.

Methods

Study Sample

We examined 7963 patients who underwent percutaneous renal biopsy in the West China Hospital of Sichuan University from 2010 to 2021 for evidence of ORG. Usual indications for kidney biopsy included renal insufficiency and/or proteinuria and/or hematuria in this institute. The diagnosis of ORG required all of the following: (1) body mass index (BMI) ≥28 kg/m^2, (2) obesity-associated glomerulomegaly with or without FSGS. Patients with one of the following diseases that could cause FSGS or glomerulomegaly were excluded carefully: (1) primary FSGS, (2) other secondary FSGS (such as HIV infection, solitary kidney, congenital heart disease, and sickle cell disease), (3) diabetic nephropathy, (4) hypertensive nephrosclerosis, (5) kidney transplant, (6) superimposed on IgA nephropathy or other renal conditions, (7) follow-up less than 12 months.

Data Collection

The demographic information, clinical and laboratory data at the time of biopsy, renal histology, treatment, and follow-up were obtained from the electronic medical records. The following clinical definitions were used: hypertension, persistent blood pressure ≥140/90 mmHg or ongoing use of antihypertensive medications; glucose dysmetabolism, fasting plasma glucose >6.1 mmol/L or 2-hour plasma glucose >7.8 to 11.1 mmol/L after a standard 75-g glucose load; dyslipidemia involved a combination of total cholesterol >6.2 mmol/L, triglyceride >2.2 mmol/L, low-density lipoprotein cholesterol >3.1 mmol/L and/or high-density lipoprotein cholesterol <1.0 mmol/L; hyperuricemia serum uric acid >380 mmol/L (female) or >490 mmol/L (male); estimated glomerular filtration rate (eGFR) was calculated by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation. The standard processing of kidney biopsy specimens consists of light microscopy, immunofluorescence and electron microscopy. The light microscopy was performed on tissues stained with hematoxylin and eosin, periodic acid–Schiff, Masson trichrome, and Jones methenamine silver. Our observations included global sclerosis, segmental sclerosis, tubular atrophy/interstitial fibrosis (TA/IF) and arteriolosclerosis. The semiquantitative scoring criteria of TA/IF focused on the percentage of cortical area affected: 0, absent; 1+, 1–25%; 2+, 26–50% and 3+, >50%. The arteriolosclerosis was graded as follows: 0, absent; 1+, mild; 2+, moderate; 3+, severe.[10] The foot process fusion, mesangial lesions, glomerular basement membrane (GBM) lesions and capillary lumen lesions were observed by electron microscopy. The rapid eGFR decline (rapid decliners) was defined as a sustainable ≥5 mL/min/1.73 m^2/year decline of the eGFR value according to the Kidney Disease: Improving Global Outcomes guidelines.[16]

Statistical Analysis

The statistical analysis was conducted using SPSS version 26.0 (IBM, USA). The quantitative data were expressed as mean ± standard deviation (SD) or median with range, and compared by using one-way analysis of variance or Mann–

Whitney *U*-test. The categorical data were described as sample sizes (number of cases) and percentages, analyzed by using χ^2 test or Fisher exact test. The risk factors for rapid decline in eGFR were performed by univariable and multivariable logistic regression analyses. The statistical significance was assumed at $p < 0.05$.

Results

Clinical and Histopathological Characteristics of the Patients with ORG

7963 patients were reviewed. A total of 63 cases diagnosed with biopsy-proven ORG and with more than 12 months of follow-up were analyzed (Figure 1). Clinical and histopathological baseline characteristics of the study were summarized in Table 1. For the overall patients, the mean age was 38.7 ± 9.0 years, 76.2% were men, and the mean BMI value was 32.4 ± 3.6 kg/m^2. The clinical manifestations included hypercholesterolemia (22.2%), obvious hypertriglyceridemia (71.4%), low HDL cholesterol (36.5%), high LDL cholesterol (11.1%), glucose dysmetabolism (36.5%), hypertension (60.3%), hyperuricemia (27.0%), fatty liver (34.9%) and obstructive sleep apnea (7.9%). The median of proteinuria was 1.62 g/24 h (range of 0.04–16.64 g/24 h), 17 (27.0%) patients had nephrotic-range proteinuria at the time of their kidney biopsy, while hypoalbuminemia was only present in 5 patients (7.9%). All cases were characterized by pathological changes of glomerulomegaly, the pathological change of FSGS was found in 46 (73.0%) cases, with a mean 11.4 ± 9.3% of global sclerosis and a mean 11.6 ± 10.0% of segmental sclerosis. The incidence rate of foot process fusion was 68.3%.

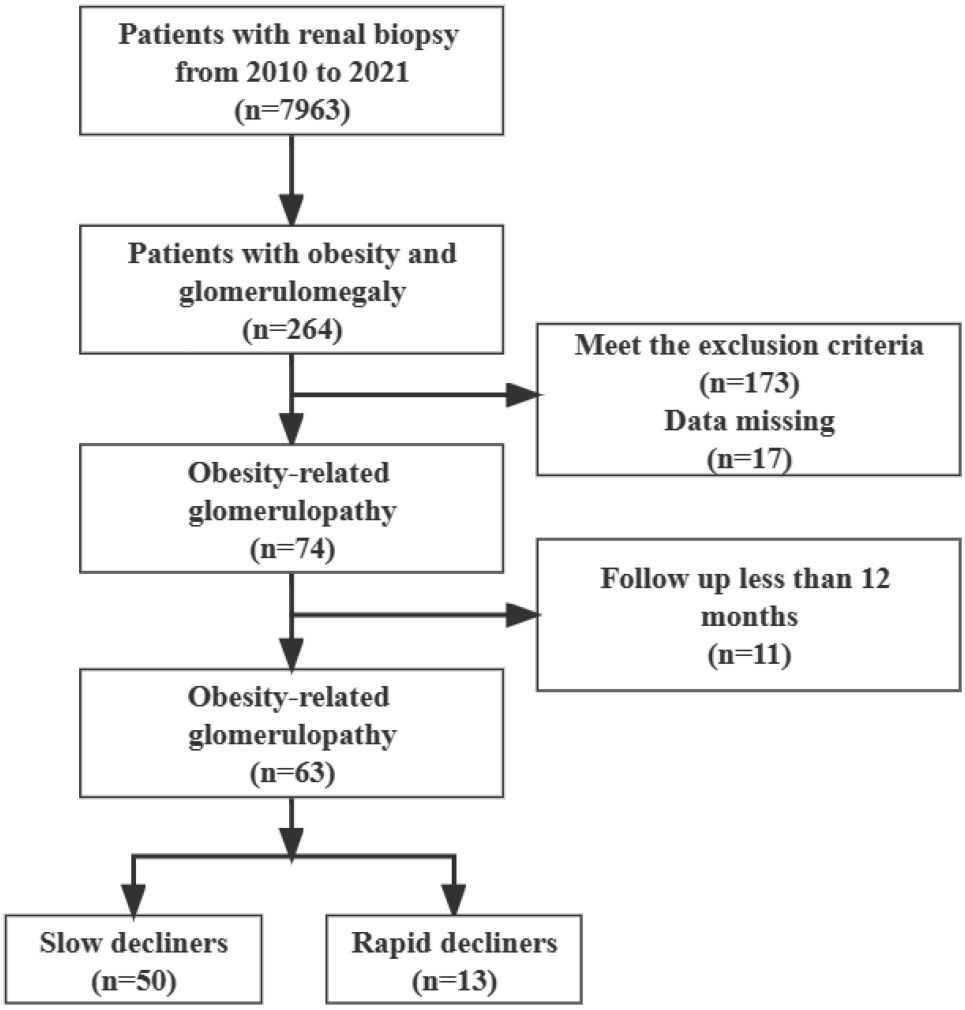

Figure 1 Flowchart of study participants.

Table 1 Comparison of the Clinical Findings at Biopsy Between Rapid Decliners and Slow Decliners

Variables	All	Rapid Decliners (n = 50)	Slow Decliners (n = 13)	p value
Age (years)	38.7±9.0	38.9±9.3	37.9±8.0	0.732
Male (n/%)	48 (76.2%)	36 (72.0%)	12 (92.3%)	0.162
Body mass index (kg/m^2)	32.4±3.6	32.6±3.6	31.8±3.6	0.458
Smoking (n/%)	26 (41.3%)	16 (32.0%)	10 (76.9%)	0.005
Drink (n/%)	23 (36.5%)	15 (30.0%)	8(61.5%)	0.053
High cholesterol (n/%)	14 (22.2%)	11 (22.0%)	3 (23.1%)	1.000
High triglycerides (n/%)	45 (71.4%)	36 (72.0%)	9 (69.2%)	1.000
Low HDL cholesterol (n/%)	23 (36.5%)	17 (34.0%)	6 (23.0%)	0.522
High LDL cholesterol (n/%)	7 (11.1%)	7(14.0%)	0 (0.0%)	0.328
Glucose dysmetabolism (n/%)	23 (36.5%)	16 (32.0%)	7 (53.8%)	0.198
Hypertension (n/%)	38 (60.3%)	32 (64.0%)	6 (46.2%)	0.341
Hyperuricemia (n/%)	17 (27.0%)	10 (20.0%)	7 (53.8%)	0.031
Fatty liver (n/%)	22 (34.9%)	19 (38.0%)	3 (23.1%)	0.515
Obstructive sleep apnea (n/%)	5 (7.9%)	4 (8.0%)	1 (7.7%)	1.000
Proteinuria (g/24 h)	1.62 (0.04–16.64)	1.36 (0.04–16.64)	3.57 (0.7–14.2)	0.051
<1.0 (n/%)	20 (31.7%)	18 (36.0%)	2 (15.4%)	
1.0–3.5 (n/%)	26 (41.3%)	22 (44.0%)	4 (30.8%)	
≥3.5 (n/%)	17 (27.0%)	9 (18.0%)	8 (61.5%)	
Serum albumin (g/dl)	41.0±6.9	41.4±7.5	39.5±3.3	0.389
<3.5 (n/%)	5 (7.9%)	4 (8.0%)	1 (7.7%)	1.000
eGFR (mL/min/1.73 m^2)	89.5 (30.5–137.9)	99.7 (37.1–137.9)	71.8 (30.5–118.2)	0.138
>90	30 (47.6%)	27 (54.0%)	3 (6.2%)	
60–90	19(30.2%)	13(26.0%)	6 (46.2%)	
30–60	14 (22.2%)	10 (20.0%)	4 (30.8%)	
Global sclerosis (%)	11.4±9.3	11.3±9.0	12.1±10.0	0.788
Segmental sclerosis (%)	11.6±10.0	12.6±9.9	7.8±5.7	0.125
TA/IF (n/%)				0.172
0	12 (19.0%)	11 (22.0%)	1(2.5%)	
1	47 (74.6%)	37 (74.0%)	10 (76.9%)	
2	3 (4.8%)	2 (4.0%)	1 (7.7%)	
3	1 (1.6%)	0 (0.0%)	1 (7.7%)	
Arteriolosclerosis (n/%)				0.256
0	36 (57.1%)	30 (60.0%)	6 (46.2%)	
1	15 (23.8%)	12 (24.0%)	3 (23.1%)	
2	9 (14.3%)	7 (14.0%)	2 (15.4%)	
3	3 (4.8%)	1 (2.0%)	2 (15.4%)	
Foot process fusion (n/%)	43 (68.3%)	35 (70.0%)	8 (61.5%)	1.000

Notes: Data are presented as a mean ± SD, or median [IQR], or count (percentage). A two-tailed p< 0.05 was considered statistically significant.
Abbreviations: HDL, high-density lipoprotein; LDL, low-density lipoprotein; eGFR, estimated glomerular filtration rate; TA/IF, tubular atrophy and interstitial fibrosis.

The grading of tubular atrophy and interstitial fibrosis was typically mild (median 1), as was arteriolosclerosis (median 1).

Treatment and Renal Outcomes

Median follow-up time was 45 (range of 12–116) months after biopsy. 53 patients (84.1%) were treated with either angiotensin converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB), of whom 15 received steroids or cytotoxic agents before admission to our hospital because of unexplained proteinuria. 11 (17.5%) patients received fenofibrate treatment and 19 (30.2%) patients received atorvastatin treatment. The number of these patients who underwent sodium-glucose cotransporter 2 (SGLT-2) inhibitors and glucagon-like peptide 1 (GLP-1) receptor agonists

treatment were 6 (9.5%) and 4 (6.35%), respectively. At the last follow-up, 3 (4.8%) patients progressed to ESRD requiring renal replacement therapy.

Comparison of the Clinical Findings at Biopsy and During the Follow-Up Between Rapid Decliners and Slow Decliners

Then we compared the differences of the clinical findings at biopsy and treatment between rapid decliners and slow decliners. As shown in Table 1, compared with the slow decliners group, the rapid decliners group had a higher proportion of smoking (76.9% vs 32.0%) and drinking (61.5% vs 30.0%). Patients with ORG and rapid eGFR decline had a significantly higher incidence of hyperuricemia than those with slow eGFR decline (53.8% vs 20.0%). They also had more overt proteinuria, with a greater prevalence of nephrotic-range proteinuria (61.5% vs 18.0%). Other clinical findings including age, BMI, the incidence of dyslipidemia, glucose dysmetabolism and hypertension, baseline eGFR and the degrees of pathological lesion (FSGS, arteriolosclerosis and foot process fusion) were not significantly different between the two groups. In Table 2, there was no statistical difference in the use of ACEI/ARB, glucocorticoids/immunosuppressors, fenofibrate/atorvastatin, SGLT-2 inhibitors and GLP-1 receptor agonists between the two groups.

Multivariate Logistic Regression Analysis for the Factors That Influence the Slope of the eGFR

Based on the results of the comparison between rapid decliners and slow decliners, the predictors of rapid eGFR decline by univariate logistic regression analysis are shown in Table 3. Smoking, drinking, hyperuricemia, nephrotic-range proteinuria and TA/IF > 25% were significantly associated with the rapid eGFR decline. The multivariate logistic regression analysis showed that smoking (OR 9.205, 95% CI 1.704–49.740, P = 0.01), hyperuricemia (OR 5.541, 95% CI 1.079–28.460, P = 0.04) and nephrotic-range proteinuria (OR 6.128, 95% CI 1.311–28.637, P = 0.021) were independent risk factors for rapid eGFR decline, while drinking and TA/IF > 25% were not independent risk factors for rapid eGFR decline.

Table 2 Treatment and Renal Outcomes During Follow-Up

Variables	All	Rapid Decliners (n = 50)	Slow Decliners (n = 13)	p value
ACEI/ARB (n/%)	53 (84.1%)	44 (88.0%)	9 (69.2%)	0.194
Glucocorticoids/immunosuppressors (n/%)	15 (23.8%)	11 (22.0%)	4 (30.8%)	0.489
Fenofibrate (n/%)	11 (17.5%)	8 (16.0%)	3 (23.1%)	0.683
Atorvastatin (n/%)	19 (30.2%)	14 (28.0%)	5 (38.5%)	0.508
SGLT-2 inhibitors (n/%)	6 (9.5%)	5 (10.0%)	1 (7.7%)	1.000
GLP-1 receptor agonists (n/%)	4 (6.3%)	3 (6.0%)	1 (7.7%)	1.000
ESRD (n/%)	3 (6.0%)	3 (6.0%)	0 (0.0%)	0.007
Length of follow-up (months)	45 (12–116)	46 (12–116)	37 (12–111)	0.747

Notes: Data are presented as a median [IQR], or count (percentage). A two-tailed p< 0.05 was considered statistically significant.
Abbreviations: ACEI, angiotensin converting enzyme inhibitors; ARB, angiotensin receptor blocker; SGLT-2, sodium-glucose cotransporter 2; GLP-1, glucagon-like peptide 1; ESRD, end-stage renal disease.

Table 3 Risk Factors for Rapid eGFR Decline Using Univariate/Multivariate Logistic Regression Analysis

	Univariate Analysis OR (95% CI)	*P* value	Multivariate Analysis OR (95% CI)	*P* value
Smoking	7.083 (1.711–29.318)	0.007	9.205 (1.704–49.740)	0.010
Drinking	3.733 (1.048–13.301)	0.042	3.460 (0.511–14.618)	0.624
Hyperuricemia	4.667 (1.282–16.987)	0.019	5.541 (1.079–28.460)	0.040
Nephrotic-range proteinuria	4.667 (1.282–16.987)	0.019	6.128 (1.311–28.637)	0.021
TA/IF>25%	7.125 (1.857–27.341)	0.004	5.115 (0.958–22.726)	0.061

Note: A two-tailed p< 0.05 was considered statistically significant.
Abbreviations: OR, odds ratio; CI, confidence interval; TA/IF, tubular atrophy and interstitial fibrosis.

Discussion

In this study, we analyzed the clinicopathological features and renal outcomes of 63 patients with ORG in a single center from west China. To our knowledge, this is the largest experience of ORG with prognosis and the first report in China. The main findings of the current study were as follows. Young and middle-aged male were susceptible. Chinese ORG patients were more likely to have clinical characteristics with hypertriglyceridemia, hypertension and hyperuricemia, mild to severe degrees of urinary protein excretion at diagnosis, while patients with nephrotic-range proteinuria lacked hypoalbuminemia and hypercholesterolemia. During the median 45 months of follow-up, 20.6% of these patients developed more than a 5 mL/min/1.73 m^2/year reduction of eGFR by the last observation. The smoking, drinking, hyperuricemia, nephrotic-range proteinuria, and TA/IF > 25% were found to be predictive of rapid eGFR decline by the univariate logistic regression analysis. However, the multivariate logistic regression analysis only supported smoking, hyperuricemia and nephrotic-range proteinuria as independent risk factors.

The presentation of ORG is typically by varying degrees of proteinuria with or without renal impairment. The nephrotic-range proteinuria occurs in 10–48% patients, but the incidence of nephrotic syndrome is relatively low (0–6%).[10–13] The nephrotic-range proteinuria, but without hypoalbuminemia and hypercholesterolemia, might be a clinical clue to differentiate ORG from other primary nephrotic syndromes. More than half of the patients had accompanying dyslipidaemia and hypertension.[10–13] Consistent with previous studies,[10,12] our present study suggested that proteinuria at diagnosis was one of the independent predictors of the renal outcome. A study on 20 Japanese ORG patients identified that the time-averaged proteinuria during mean 6.2 years follow-up is better to predict the renal outcome compared to the urinary protein excretion at diagnosis.[12] Proteinuria level is related directly with BMI, waist circumference, visceral obesity and levels of total cholesterol, fasting glucose, insulin resistance in ORG patients.[13,17] Consistent with the reported study, baseline lower eGFR was not an independent risk factor for renal outcome in our and the Japanese ORG cohort,[12] but more large clinical studies are needed to support that.

The pathological lesions of ORG are characterized by glomerular hypertrophy with or without FSGS. A previous study showed that the glomerular diameter of patients with ORG (mean 226 μm ± 24.6 μm; range 172 to 300 μm) is significantly greater than that of normal controls (mean 168 ± 12 μm; range 138 to 186 μm).[10] The reported percentage of ORG patients with FSGS ranges from 70.0% to 80.3%. Foot-process fusion has been seen in 36–40% of patients, mean foot-process width is 534 nm.[12,13] Our study had observed higher degrees of TA/IF in ORG patients with a progressive decline of eGFR, but not as an independent risk factor, which was consistent with the previous study.[11,12] The abnormal triglyceride accumulation located in proximal tubule cells predominantly has been reported as being associated with renal tubule lesions via steatosis and lipotoxicity in the human kidney.[18] Like other chronic renal diseases,[19,20] tubulointerstitial injuries caused by protein overload may play a part in the progression of renal impairment in ORG patients.

Although all the pathogenesis of ORG are not fully clarified, it is acknowledged that the glomerular hyperfiltration caused by failure of glomerulotubular and tubuloglomerular interactions play a central part in the pathogenesis of renal injury.[21,22] Overactivation of the renin-angiotensin-aldosterone system (RAAS), which is closely related to altered renal haemodynamics, may lead to obesity-induced hypertension and hyperfiltration.[23,24] The chronic inflammation induced by obesity is well accepted to participate in the pathogenesis of ORG, and several flammatory agents including TNF-α, NF-κB, MAPK and NLRP3 may exert a relevant role.[25,26] Hyperlipidemia is highly prevalent in ORG patients, abnormal accumulation of triglyceride and cholesterol result in kidney injury by lipotoxicity immediately and abnormal hemodynamic immediately.[27] Other factors including insulin resistance, oxidative stress and genetics may also affect to different degrees.[28]

Consistent with previous studies,[10–12] our data showed that the use of ACEI/ARB was not independently correlated with renal outcome in ORG patients. Except for the influence of possible body weight gain in the follow-up time, the occurrence of aldosterone escape may explain the result. A study has demonstrated that under stable treatment with ACEI/ARB, the concentration of plasma aldosterone concentration in patients with BMI ≥35 kg/m^2 is higher than that in patients with BMI <35 kg/m^2.[29] Adipocyte-derived factors stimulating aldosterone secretion directly and reduced natriuretic peptide activity mitigating the inhibition of aldosterone secretion in obesity have been observed.[30,31] Adding aldosterone receptor antagonist to a traditional blockade of the RAAS is beneficial for long-term renal function of patients with obesity and proteinuria,[32] which implies a mineralocorticoid receptor antagonist may be a promising drug for obesity with kidney damage. Meanwhile,

elevated levels of circulating angiotensinogen derived from adipose tissue in obese humans suggests that a sufficient dose of ACEI/ARB may be important for the inhibition of RAAS in ORG patients.[33]

Besides this, our data showed that there was no statistical difference in the treatment of fenofibrate and atorvastatin between progressors and non-progressors. As far as we know, no clinical trial has previously tested the long-term renal effect of atorvastatin and fenofibrate in ORG patients. The Action to Control Cardiovascular Risk in Diabetes Follow-On (ACCORDION) Study documents that fenofibrate use is associated with the lower rate of eGFR decline, but not the incidence of CKD and/or kidney failure during 6.5 years follow-up time.[34,35] A double-blind, randomized, placebo-controlled study on patients with hypertriglyceridemia and non-alcoholic fatty liver disease has showed that fenofibrate could alleviate hyperlipidemia, but fail to reduce lipid accumulation in the liver and weight gain.[36] ORG patients are more likely to be accompanied with abnormal metabolic state, such as hypertension, hyperlipidemia and glucose dysmetabolism which are well-established risk factors for renal outcomes.[37,38] ORG was associated with a high frequency of hyperuricemia, and similarly, hyperuricemia was an independent risk factor for renal function in our study. Furthermore, an elevated uric acid independently predicts the development of obesity, hypertension, diabetes and fatty liver.[39] Hence, alleviating any part of the changes caused by obesity could not delay or reverse it, and the effective treatment might be integrated management of the risk factors and pathological obesity, which lead to these target's organ damage.[4,40] Our study did not support the renoprotective effect of glucocorticoids or immunosuppressors in ORG patients. Meanwhile, glucocorticoids and immunosuppressors have a high risk of side effects. Hence, for obesity patients with hypertriglyceridemia, hypertension and hyperuricemia, especially those companied with nephrotic-range proteinuria and lack of hypoalbuminemia and hypercholesterolemia at the same time, the use of glucocorticoids or immunosuppressors should be alert before definitely diagnosed by kidney biopsy.

Bariatric surgery has positive effects on renal outcomes in severe obesity patients with or without chronic kidney disease.[40] The main contributor to the improvement of eGFR and alleviation of proteinuria is the integrated improvement of comorbidities as a result of weight loss.[41–43] Previous studies demonstrate that the change in BMI is an important predictor of proteinuria, which is associated with decreased podocyte density and number and mesangial cell proliferation.[4,44,45] SGLT-2 inhibitors, GLP-1 receptor agonist and dual glucose-dependent insulinotropic polypeptide–GLP-1 receptor agonist are new antidiabetic drugs that have been associated with a reduction in weight, proteinuria and/or progression of renal disease.[46–49] The kidney protection of these new antidiabetic drugs has been considered to be a consequence of inhibition of inflammation, restored insulin sensitivity and decreasing the level of autophagy in ORG model mice.[25,50] While our data showed that there were no significant differences of the eGFR trajectory between the two groups after the treatment of SGLT-2 inhibitors or GLP-1 receptor agonists. Considering that the utilization rate of these drugs and sample size are low, devoted clinical trials are needed to verify both of these interventions as effective therapeutic options for patients with ORG.

Some limitations of our study should be recognized. First, the data were collected retrospectively, so some risk variables including the duration of obesity were missed. Second, owing to the variation data of BMI and proteinuria in the follow-up time not being involved in the study, it was difficult to interpret their effects on renal outcome. Third, we only had 10 of 63 (15.9%) patients with at least 50% reduction of eGFR. Moreover, a further validation in cohorts with more patients is warranted before the conclusions may be generalized.

Conclusion

In Chinese ORG patients, hypertriglyceridemia, hypertension and hyperuricemia, and mild to severe degrees of proteinuria were prevalent, while nephrotic-range proteinuria with hypoalbuminemia and hypercholesterolemia was relatively rare. Smoking, hyperuricemia and nephrotic-range proteinuria were associated with the rapid eGFR decline of these patients independently.

Data Sharing Statement

Datasets are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committees of the West China Hospital of Sichuan University. Our retrospective research was in compliance with ethical standards. Informed consent for patients in this study was waived due to the retrospective nature of the review, but we confirmed that the data was maintained with confidentiality and complied with the Declaration of Helsinki.

Consent to Publication

All participants have consented to the submission of the data to the journal.

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Disclosure

The authors report no conflicts of interest in this work.

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