Research Article

Crescents and Global Glomerulosclerosis in Chinese IgA Nephropathy Patients: A Five-Year Follow-Up

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Key Words

IgA nephropathy • Crescent • Global glomerulosclerosis • Renal outcome

Abstract

Background/Aims: This study aims to evaluate the clinical significance of crescent and global glomerulosclerosis formation on renal outcome in patients with IgA nephropathy (IgAN). **Methods:** Biopsy-proven primary IgAN patients from West China Hospital of Sichuan University were studied retrospectively between 2008 and 2015. Clinicopathological features and treatment modalities were recorded. The patients were divided into several groups on the basis of cellular and/or fibrocellular crescents scores and global glomerulosclerosis scores. Crescent (C) was scored according to the updated Oxford classification (C0/C1/C2). Global glomerulosclerosis (G) was scored according to the frequency of global glomerulosclerosis: G0 ($\leq 25\%$ of glomeruli), G1 (26–50% of glomeruli), and G2 ($> 50\%$ of glomeruli). The primary endpoint was defined as a 50% reduction in renal function or end stage renal disease. Patients were followed up for at least 12 months, or shorter if they reached study endpoints. 1328 patients with IgAN were recruited. Mean follow-up time was 46.1 ± 23.6 months. The percentage of patients with C1 and C2 was 19.3% and 5.9% respectively. Higher crescent scores was associated with lower estimated glomerular filtration rates (eGFR), decreased serum albumin levels, increased amounts of urine protein, higher serum creatinine, as well as greater proportions of M1 and E1. The percentage of patients with G0, G1 and G2 was 70.5%, 20.7% and 8.8%, respectively. Elevated glomerulosclerosis scores were associated with lower eGFR levels, increased amounts of urine protein, higher levels of serum creatinine, higher incidences of arterial hypertension, as well as greater proportions of M1. There was a significantly higher proportion of T1/2 in patients with G2. In a multivariate model, crescent and global glomerulosclerosis were identified as independent predictors of decreased renal survival. **Conclusion:** Global glomerulosclerosis and crescents, as detected in renal biopsies, are strong predictors of long-term renal outcome of IgAN.

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Introduction

Immunoglobulin A nephropathy (IgAN), the most common form of glomerulonephritis, is characterized by the accumulation of IgA immune complex deposits in the mesangium of the kidney [1]. The Oxford classification of IgAN has been widely adopted since 2009, which includes several definitive histological features: mesangial hypercellularity (M), endocapillary proliferation (E), segmental sclerosis or adhesion (S) and tubular atrophy/interstitial fibrosis (T) [2]. Validation studies show a correlation between the Oxford classification and renal outcomes [3]. Considering that glomeruli crescents are highly associated with poor renal outcome [4], cellular and/or fibrocellular crescents (C) were included in the updated Oxford classification of IgAN [5]. It is well known that IgAN is a chronic progressive kidney disease that harbors complex clinical manifestations, and 20-40% of patients will develop end-stage renal disease (ESRD) within 10-20 years [6]. It is thought that global glomerulosclerosis, characteristic lesion of chronic pathological changes, may be a prognostic indicator of poor renal outcome of kidney disease. Therefore, this study was performed to clarify the clinical significance of crescents and global glomerulosclerosis formation on the renal outcome in IgAN patients.

Materials and Methods

Patients

Adult IgAN patients (age >14 years), verified via renal biopsy, were retrospectively enrolled in between December 2008 and July 2015 from West China Hospital of Sichuan University. Patients with secondary causes of mesangial IgA deposits (including but not limited to Henoch-Schönlein purpura, rheumatology disease, and liver disease) and those with insufficient clinical and pathologic data (renal biopsies less than 8 glomeruli) were excluded from this study. Patients were followed up for at least 12 months or until study-defined endpoints were reached. This study complies with the principles of the Helsinki Declaration and was approved by The Ethics Committee of West China Hospital of Sichuan University. Written informed consent was collected from all patients prior to treatment.

Clinical data

Demographics (gender, ethnicity, age) and clinical data (blood pressure (BP), serum creatinine, albumin, estimated glomerular filtration rate (eGFR), 24 h urine protein, and urine red blood cell counts) were collected. Hypertension was defined as BP >140/90 mmHg or requiring the use of antihypertensive agents. eGFR levels were calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation. Treatment modalities were recorded. Patients received optimized supportive care with full dose angiotensin-converting-enzyme inhibitor (ACEi) or angiotensin receptor blockers (ARB) to achieve target blood pressure (BP < 140/90 mmHg). Corticosteroids (0.5 - 1 mg/kg Prednisone daily, tapering down within 6 - 8 months) and immunosuppressant therapy (Cyclophosphamide 2mg/kg daily for 3 months, or Mycophenolate Mofetil 1-2 g daily for 6-8 months) were used based on pathological and clinical severity.

Renal pathology data

Renal biopsy samples from all patients were reviewed by a pathologist and a nephrologist. The updated Oxford Classification (MEST-C) was used in this study (mesangial hypercellularity (M0/M1, <or equal to >50% of glomeruli with >4 mesangial cells/area); endocapillary hypercellularity (E0/E1, present/absent); segmental glomerulosclerosis (S0/S1, present/absent); tubular atrophy/interstitial fibrosis (T0/T1/T2, <25%, 25-50%, >50%) [2], and cellular or fibrocellular crescents (C0/C1/C2, no crescents/crescent in at least 1 glomerulus/crescents in at least 25% of glomeruli) [5]. A crescent was defined as an extracapillary lesion of any size containing more than two cell layers. A cellular crescent was defined by >50% of the lesion occupied by cells, and a fibrocellular crescent was defined by <50% of the lesion occupied by cells

and <90% occupied by matrix. Fibrous crescents (composed of >90% matrix) were not taken into account [7]. Global glomerulosclerosis was defined as hyaline deposition or scarring lesion occurring in more than 50% of any one glomerulus. Global glomerulosclerosis (G) was scored according to the percentage of global glomerulosclerosis: G0 ($\leq 25\%$ of glomeruli), G1 (26–50% of glomeruli), and G2 (>50% of glomeruli).

Outcomes

Responses to therapy included complete remission (CR), partial remission (PR), no response (NR), and ESRD. CR was defined as urinary protein excretion <0.5 g/24 h and eGFR decrease <10% of baseline measurements. PR was defined as a decrease in proteinuria >50% of baseline and eGFR decrease <10% of baseline. NR was defined as a decrease in proteinuria < 50% of baseline, and decrease of eGFR >10% of baseline. Responses to therapy were determined at 6–8 months after the initiation of treatment. ESRD was defined as eGFR <15 mL/min/1.73 m² or need renal replacement treatment. The primary endpoint was a combination of a 50% decline in eGFR and/or ESRD.

Statistical analysis

SPSS 22.0 software (SPSS, Chicago, IL, USA) was used for statistical analysis. Categorical data was described with percentages and analyzed using Chi-square tests. Continuous variables were expressed as mean $\pm$ SD or median (first–third interquartile range), and analyzed with ANOVA, Student's t-test or nonparametric Mann–Whitney U test. Survival analysis was performed using log-rank test and Cox regression model. Results were expressed as hazard ratios (HR) with 95% confidence intervals (CI). Statistical significance was considered if $P < 0.05$. Five year renal survival was predicted using the nearest neighbor estimation method for censored survival data [8]. Prediction accuracy was measured using receiver operating characteristic (ROC) curves and area under ROC curves (AUCs).

Results

Clinicopathological characteristics

1328 IgAN patients (45.6% male and 54.4% female) were recruited. The mean age was 34.2 ± 11.2 years. The mean follow-up time was 46.1 ± 23.6 months. During follow-up, the majority of patients received renin-angiotensin system inhibitors (RASi), and 60.5% received immunosuppressant. 221 (16.6%) patients reached combined primary endpoints during follow-up, and 171 (12.9%) patients reached ESRD. Patients were further divided based on crescent and global glomerulosclerosis. Patients with crescents and global glomerulosclerosis were divided into C0/1/2 and G0/1/2 groups. Patients with higher portion of crescents and global glomerulosclerosis seem to have severer disease with lower eGFR, serum albumin and higher proteinuria, and pathological changes (Table 1 and 2)

Treatment response

Treatment responses were assessed in relation to pathological lesions (Table 3 and 4). CR rate was significantly lower in patients in C2 group (C0 60.3%, C1 62.6% and C2 42.3%), however ESRD rate was remarkably higher in patients in C2 group (C0 15.4%, C1 13.6%, C2 35.9%). It was found that patients with crescents were more likely to receive immunosuppressive treatment than those without crescents (C0 54.1%, C1 77.0%, C2 88.5%). Moreover, immunosuppressant treatment was apparently associated with, higher CR and PR rate in patients in crescent groups. In our study cohort, higher portion of globe glomerulosclerosis was associated with lower CR and PR rate and higher ESRD (G0 4.3%, G1 32.0%, G2 75.2%) rate. The percentages of patients receiving immunosuppressant were similar in different G groups (G0 59.3%, G1 66.9%, G2 55.6%). Only 1 patient died during follow-up due to severe pulmonary infection.

Table 1. Baseline clinicopathological characteristics of IgAN patients in different crescent scores. Data presented as number (percentage) or mean $\pm$ SD or median (first-third interquartile range) eGFR, estimated glomerular filtration rate; NS, nephrotic syndrome; RBC, red blood cell; Scr, serum creatinine. *P<0.05 compared to C0, **P<0.05 compared to C0 and C1

Variables	All n=1328	0 n=993	Crescent 1 n=257	2 n=78	P
Gender					0.956
Male	605(45.6)	454(45.7)	115(44.7)	36(46.2)	
Female	723(54.4)	559(54.3)	142(55.3)	42(53.8)	
Age, year	34.2 $\pm$ 11.2	34.6 $\pm$ 11.3	33.7 $\pm$ 10.6	31.2 $\pm$ 11.3*	0.025
Disease duration, month	15.0 $\pm$ 24.1	16.0 $\pm$ 25.1	12.7 $\pm$ 22.0	9.5 $\pm$ 15.8*	0.017
eGFR, (ml/min per 1.73 m ²)	84.0 $\pm$ 34.9	86.2 $\pm$ 34.7	78.8 $\pm$ 32.9*	72.7 $\pm$ 40.1*	<0.001
CKD stage					<0.001
1	620 (46.7)	490 (49.3)	107 (41.6)	23 (29.5)	
2	329 (24.8)	242 (24.4)	65 (25.3)	22 (28.2)	
3	287 (21.6)	197 (19.8)	66 (25.7)	24 (30.8)	
4	92 (6.9)	64 (6.4)	19 (7.4)	9 (11.5)	
Hypertension	494 (37.2)	367 (37.0)	96 (37.4)	31 (39.7)	0.886
Oxford classification					
M1	1043(78.5)	747(75.2)	220(85.6)	76 (97.4)	<0.001
E1	64(4.8)	12(1.2)	25(9.7)	27(34.6)	<0.001
S1	675(50.8)	473(47.6)	155(60.3)	47(60.3)	<0.001
T1/2	328(24.7)	234 (23.6)	68 (26.5)	26 (33.3)	0.133
Proteinuria, g/24h	2.8 $\pm$ 3.0	2.6 $\pm$ 3.0	3.1 $\pm$ 3.1*	4.4 $\pm$ 2.9**	<0.001
Albumin, g/L	37.7 $\pm$ 11.8	38.0 $\pm$ 13.0	37.5 $\pm$ 6.5	33.0 $\pm$ 7.3**	0.001
NS	223(16.9)	156 (15.7)	40 (15.6)	27 (34.6)	<0.001
Scr, mg/dL	1.20 $\pm$ 0.64	1.16 $\pm$ 0.62	1.29 $\pm$ 0.65*	1.47 $\pm$ 0.82**	<0.001
Immunosuppression	804(60.5)	537(54.1)	198(77.0)	69(88.5)	<0.001

Table 2. Baseline clinicopathological characteristics of IgAN patients in different glomerulosclerosis scores. Data presented as number (percentage) or mean $\pm$ SD or median (first-third interquartile range)

Variables	All n=1328	0 n=936	Glomerulosclerosis 1 n=275	2 n=117	P
Gender					0.136
Male	605(45.6)	414(44.2)	128(46.5)	63(54.3)	
Female	723(54.4)	522(55.8)	147(53.5)	54(46.2)	
Age, year	34.2 $\pm$ 11.2	33.6 $\pm$ 11.6	36.1 $\pm$ 9.5*	34.7 $\pm$ 11.2	0.005
Disease duration, month	15.0 $\pm$ 24.1	13.6 $\pm$ 22.6	19.1 $\pm$ 27.9*	16.4 $\pm$ 25.3	0.003
eGFR, (ml/min per 1.73 m ²)	84.0 $\pm$ 34.9	96.0 $\pm$ 30.2	62.0 $\pm$ 28.3*	39.8 $\pm$ 20.4**	<0.001
CKD stage					<0.001
1	620(46.7)	567 (60.6)	49 (17.8)	4 (3.4)	
2	329(24.8)	239 (25.5)	76 (27.6)	14 (12.0)	
3	287(21.6)	112 (12.0)	118 (42.9)	57 (48.7)	
4	92(6.9)	18 (1.9)	32 (11.6)	42 (35.9)	
Hypertension	494(37.2)	258(27.6)	149(54.2)	96(75.6)	<0.001
Oxford classification					
M1	1043(78.5)	688(73.5)	244(88.7)	111(94.9)	<0.001
E1	64(4.8)	52(5.6)	10(3.6)	2(1.7)	0.074
S1	675(50.8)	401(42.8)	197(71.6)	77(65.8)	<0.001
T1/2	328(24.7)	76 (8.1)	145 (52.7)	107 (91.5)	<0.001
Proteinuria, g/24h	2.8 $\pm$ 3.0	2.7 $\pm$ 3.3	2.8 $\pm$ 2.2	3.6 $\pm$ 2.4**	0.009
Albumin, g/L	37.7 $\pm$ 11.8	37.8 $\pm$ 13.5	37.8 $\pm$ 5.9	35.6 $\pm$ 6.2	0.149
NS	223(16.9)	164 (17.5)	40 (14.7)	19 (16.5)	0.540
Scr, mg/dL	1.20 $\pm$ 0.64	0.98 $\pm$ 0.43	1.51 $\pm$ 0.68*	2.19 $\pm$ 0.76**	<0.001
Immunosuppression	804(60.5)	555(59.3)	184(66.9)	65(55.6)	0.037

Table 3. Treatment responses in IgAN patients with different crescent scores. IT, immunosuppressive therapy; SC, supportive care; CR, complete remission; PR, partial remission; NR, no response; ESRD, end stage renal disease

Response	C0			C1			C2		
	All n=993	IT n=537(54.1%)	SC n=456(45.9%)	All n=257	IT n=198(77.0%)	SC n=59(23.0%)	All n=78	IT n=69(88.5%)	SC n=9(11.5%)
CR	599 (60.3%)	347(64.6%)	252(55.3%)	161(62.6%)	133(67.2%)	28(47.5%)	33(42.3%)	33(47.8%)	0(0.0%)
PR	105 (10.6%)	71(13.2%)	34(7.4%)	27(10.5%)	24(12.1%)	3(5.1%)	10(12.8%)	9(13.0%)	1(11.1%)
NR	135 (13.6%)	47(8.8%)	88(19.3%)	34(13.2%)	16(8.1%)	18(30.5%)	7(9.0%)	4(5.8%)	3(33.3%)
ESRD	153 (15.4%)	71(13.2%)	82(18.0%)	35(13.6%)	25(12.6%)	10(16.9%)	28(35.9%)	23(33.3%)	5(55.6%)

Table 4. Treatment responses in IgAN patients with different glomerulosclerosis scores. IT, immunosuppressive therapy; SC, supportive care; CR, complete remission; PR, partial remission; NR, no response; ESRD, end stage renal disease

Response	G0			G1			G2		
	All n=936	IT n=555(59.3%)	SC n=381(40.7%)	All n=275	IT n=184(66.9%)	SC n=91(33.1%)	All n=117	IT n=65(55.6%)	SC n=52(44.4%)
CR	675(72.1%)	419(75.5%)	256(67.2%)	107(38.9%)	84(45.6%)	23(25.3%)	11(9.4%)	10(15.4%)	1(1.9%)
PR	99(10.6%)	66(11.9%)	33(8.7%)	37(13.5%)	32(17.4%)	5(5.5%)	6(5.1%)	6(9.2%)	0(0.0%)
NR	121(12.9%)	39(7.0%)	82(21.5%)	43(15.6%)	20(10.9%)	23(25.3%)	12(10.3%)	8(12.3%)	4(7.7%)
ESRD	40(4.3%)	30(5.4%)	10(2.6%)	88(32.0%)	48(26.1%)	40(43.9%)	88(75.2%)	41(63.1%)	47(90.4%)

Predictive assessment of clinical outcomes

In the present study, 221 patients (16.6 %) reached combined primary end point (C0: 164 cases, C1: 31 cases, C2: 26 cases, and G0: 44 cases, G1: 87 cases, G2: 90 cases). Kaplan-Meier analysis showed that C and G were significantly associated with renal outcome (log rank: C1 vs C0, $P=0.200$, C2 vs C0, $P<0.001$, C2 vs C1, $P<0.001$; G1 vs G0, $P<0.001$, G2 vs G0, $P<0.001$, G2 vs G1, $P<0.001$) (Fig. 1 and 2). The correlation between clinicopathological parameters and renal outcome were also analyzed in COX regression model (Table 5). In univariate analysis, all variables except age and disease duration prior to renal biopsy were associated with an increased risk for the combined endpoint. In multivariate analysis, independent predictors of poor renal survival included T1/2, C2, G1, G2, serum creatinine levels, arterial hypertension, and nephrotic syndrome at the time of biopsy.

Effects of C and G on discrimination of survival models

ROC curves were used to further investigate the predictive power of crescents and global glomerulosclerosis in evaluating 5-year renal survival. Model 1 in Fig. 3 comprised the statistically significant variables in univariate analysis in Table 5. The AUC value of model 1 was 0.9234. When G was removed from the model, the AUC value was 0.9020. And when C and G were both removed, the AUC value was 0.9001. These results indicate that C and G scores contribute to improved discrimination of the survival model.

Discussion

In this study, we found that global glomerulosclerosis (>25% of glomeruli) and crescents (>25% of glomeruli) were independently associated with renal survival of IgAN patients. We observed a more than two-fold increased risk (C2 vs C0 2.366, G1 vs G0 2.552, G2 vs G0 4.678) of poor renal outcome (50% reduction of eGFR and ESRD), suggesting high prognostic significance of crescent and glomerulosclerosis in renal biopsy.

Although the predictive value of crescents was not confirmed in the original Oxford study (excluding individuals with severe renal insufficiency) [9], new studies found that crescents was strong predictors of unfavorable prognosis of IgAN [10]. Therefore, the Oxford classification was revised to add the crescent score [5]. It is important to note that this only applies to well defined cellular or fibrocellular crescents and not to fibrous crescents. In the

Fig. 1. Kaplan-Meier analysis for the probability of primary endpoint in patients with different C scores.

Fig. 2. Kaplan-Meier analysis for the probability of primary endpoint in patients with different G scores.

current study, we found that C2 (HR 2.366; 95% CI 1.434 to 3.904) was a predictor of poor renal survival. Patients in C2 group experienced a lower CR rate and higher ESRD rate. These results suggested that presence of crescents in more than 25% of glomeruli indicated aggressive disease progression and required early initiation of steroids and immunosuppressant. Nevertheless, the 2012 KDIGO Guidelines recommended immunosuppressive therapy only for crescentic IgAN, which defined as IgAN with crescents in more than 50% of glomeruli in the renal biopsy [11]. This may compromise the application of adequate treatment and lead to poor renal survival in IgAN patients with crescents. In the current cohort, we found that more patients in C2 group received immunosuppressant than patients in C1 and C0 groups. Moreover, aggressive treatment contain immunosuppressant could effectively improve the renal outcome of IgAN patients (especially patients with crescents), which is similar to several other studies [12] [13]. Inconsistent with previous reports [10], C1 did not independently predict renal outcome in our cohort, and treatment responses were similar in patients in C1 and C0 groups. Because patients with crescent in a least 1 glomerulus was included in C1 group, the exact number and portion of glomeruli with crescents were relatively low in our cohort. Moreover, patients in C1 group received considerably aggressive treatment (contained corticosteroid and immunosuppressant) than patients in C0 group. These may be the reason why no significant difference was observed in renal prognosis between C1 and C0 groups in the current cohort. However, these findings need to be validated in further study.

Table 5. Variable associated with renal survival in the cox analysis. HTN, hypertension; NS, nephrotic syndrome; Scr, serum creatinine

Variable	Renal survival		
	Univariate analysis P-value	Multivariate analysis HR(95% CI)	P-value
Gender	0.006		
Male		1 (Referent)	
Female		1.216(0.910-1.624)	0.186
Age (per year)	0.154		
Duration (per month)	0.054		
Oxford classification			
M1 vs M0	<0.001	2.131(0.929-4.891)	0.074
E1 vs E0	0.006	1.886(1.013-3.513)	0.045
S1 vs S0	<0.001	1.193(0.874-1.628)	0.267
T1/2 vs T0	<0.001	2.582(1.650-4.010)	<0.001
C1 vs C0	0.231	0.764(0.508-1.148)	0.196
C2 vs C0	<0.001	2.366(1.434-3.904)	0.001
G1 vs G0	<0.001	2.552(1.630-3.996)	<0.001
G2 vs G0	<0.001	4.678(2.758-7.936)	<0.001
HTN	<0.001	2.210(1.577-3.097)	<0.001
NS	<0.001	2.178(1.548-3.065)	0.002
Scr (per mg/dL)	<0.001	2.184(1.772-2.691)	<0.001
Immunosuppression	<0.001	0.577(0.426-0.780)	<0.001

Fig. 3. ROC curves for each model

It is well accepted that chronic pathological changes such as glomerular sclerosis, tubular atrophy and interstitial fibrosis are strongly associated with poor long term renal survival of kidney disease. However, previous studies only emphasized the association between tubular atrophy and interstitial fibrosis (T) and renal survival [14]. Several investigators found that global glomerulosclerosis was an independent risk factor for ESRD of IgAN [15], but no further study was performed. Although a correlation between global glomerulosclerosis and tubulointerstitial atrophy and fibrosis has been reported previously [16], in certain conditions tubulointerstitial changes may not be consistent with glomerulosclerosis. This is especially true in patients with a history of hypertension, analgesic use, or traditional Chinese medicine exposure. Considering that global glomerulosclerosis is an indicator of advanced irreversible lesion and it also suggests poor response to treatment, we thought that global glomerulosclerosis may also be a predictor of poor renal outcome of IgAN. In this study we found that higher proportion of glomeruli with global sclerosis were significantly associated with poor renal outcome (G1: HR 2.552; 95% CI 1.630 to 3.996 and G2: HR 4.678; 95% CI 2.758 to 7.936). It should further be noted that combination of G and C score could improve discrimination for the prediction of renal survival (Fig. 3). Therefore, it is reasonable to add global glomerulosclerosis (G) in the pathology score system of IgAN patients.

In this study we found that treatment responses in patients of G2 group were poor, and 90% patients reached primary endpoint during follow up in spite of the treatment. Previously, it was reported that glomerular sclerosis (>40%) was a predictor of poor renal outcome [17], while our study identified that >25% glomerulosclerosis was strongly correlated with renal survival. These results suggested that aggressive treatment (corticosteroids and immunosuppressant) may not be appropriate in patients with high portion of global glomerulosclerosis (>25%). However, additional studies are required to confirm our findings.

Results of our study suggested that both pathological change and clinical character are closely related to the disease prognosis. Patients with active proliferative lesions (cellular or fibrocellular crescents), should receive more aggressive treatment such as steroids and/or immunosuppressant as these changes are potentially reversible. Although STOP Trial showed no significant effect of adding immunosuppression to supportive care, pathological changes were not considered [18]. It was reported that mycophenolate mofetil and prednisone or prednisone alone could achieve good treatment response in IgAN patients with active proliferative lesions [19]. However, in patients with apparent chronic pathological changes (G2), corticosteroids and immunosuppressant may not be beneficial.

Our novel findings should be interpreted within the context of the study's limitations. First, this is a retrospective study in a single center in China. It is not verified whether our participants have distinctive demographic or ethnic backgrounds. Second, the therapeutic interventions were varied as were specific immunosuppressive regimens, which may impair data interpretation. Besides, the immunosuppression related complications were not elucidated in this study. Third, 5-year follow-up was relatively short, and IgAN is known to progress slowly. Patient follow-ups should be continuous and extended.

Conclusion

Cellular and fibrocellular crescents and global glomerulosclerosis were independently associated with unfavorable prognosis of IgA nephropathy at 5 years, even after adjusting for clinical factors and MEST pathological parameters. Results of the current study strongly suggest that pathological activity should be included when determining treatment strategy for IgAN patients.

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Disclosure Statement

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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