BMC Nephrology

RESEARCH

Open Access

Clinicopathological characteristics and predictors of renal outcomes in diffuse crescentic glomerulonephritis : a retrospective single-center study from Western China

Shan Wen[1†], Shasha Chen[1†], Yingying Lin[1], Guisen Li[1], Ping Zhang[1*] and Wei Wang[1*]

Abstract

Background The factors influencing diffuse crescentic glomerulonephritis renal survival and prognosis remain uncertain. Additionally, there's no literature on the clinical outcomes of IgA nephropathy, lupus nephritis, and IgA vasculitis nephritis in type II patients.

Methods This study retrospectively examined 107 patients diagnosed with diffuse crescentic glomerulonephritis through biopsy. Analytical methods included Cox regression models and Kaplan-Meier survival analysis to assess the data.

Results Among the 107 enrolled patients, 12 patients had Type I diffuse crescentic glomerulonephritis, 70 patients had Type II, and 25 patients had Type III. The respective 5-year kidney survival rates were 0%, 57.5%, and 18.6% for type I, type II, and type III. Furthermore, among Type II patients, IgA nephropathy emerged as the most prevalent condition. The cumulative 5-year kidney survival rates were 50% for patients with IgA nephropathy, 64% for lupus nephritis, and 70% for Henoch-Schönlein purpura nephritis. A significant association between the risk of ESKD development and several factors was revealed by a multivariate Cox regression analysis: estimated glomerular filtration rate ($P=0.004$), initial kidney replacement therapy (KRT) at presentation ($P=0.002$), global glomerulosclerosis ($P<0.001$).

Conclusions Type II diffuse crescentic glomerulonephritis was the most prevalent type in DCGN, and favors better renal prognosis than type I and III DCGN, in which IgA nephropathy was the most common entity of Type II DCGN. Additionally, estimated glomerular filtration rate, initial KRT at presentation and global glomerulosclerosis were identified as predictors of renal outcomes in diffuse crescentic glomerulonephritis.

Keywords Crescentic glomerulonephritis, End stage kidney disease, Prognosis, Risk factors

†Shan Wen and Shasha Chen are co-first authors who contributed equally to the study.

*Correspondence:
Ping Zhang
zhangping415@126.com

Wei Wang
wangweisz@med.uestc.edu.cn
[1]Renal Department and Nephrology Institute, Sichuan Provincial People's Hospital, School of Medicine, University of Electronic Science and Technology of China, Chengdu 610072, China

Background

Characterized by a swift and progressive decline in kidney function, diffuse crescentic glomerulonephritis (DCGN) is recognized as a severe renal disease. The hallmark pathological feature of DCGN is the formation of crescents in over 50% of the glomeruli [1]. The primary immunopathological classifications of DCGN encompass anti-glomerular basement membrane antibody-mediated glomerulonephritis, immune complex-mediated glomerulonephritis, and pauci-immune glomerulonephritis [2]. These three types have different clinical and pathological features as well as outcomes [1–5]. The etiology of DCGN patients varies in different geographical regions worldwide. In regions such as North China [6], East China [3], the United States [7], and Spain [8], pauci-immune glomerulonephritis was predominant. Conversely, in Southern China [2], India [4, 9], South Asia [10], Turkey [11], Germany [12], Saudi Arabia [13], and Egypt [14], there was a relatively higher incidence of glomerulonephritis mediated by immune complexes, with lupus nephritis being the most common type within immune complex-mediated glomerulonephritis [1, 2, 10, 13, 14]. A study from Hunan, China reported an equal occurrence rate of type II (39%) and type III (39%) DCGN [5]. Furthermore, while the majority of past studies indicated that type I patients had the poorest renal prognosis [2–4, 6, 10, 15], a few studies suggested that type II [16] or III patients [11]. may have had the worst prognosis. The prognosis of different types of DCGN still remains controversial. Some research indicated that elevated serum creatinine levels, Severe-to-extreme interstitial fibrosis and tubular atrophy, and oliguria/anuria could predict adverse kidney outcomes [4]. Other studies reported that the severity of clinical conditions reflected by the need for dialysis during initial hospitalization was more associated with lower short-term kidney survival rates [3]. However, the risk factors and long-term prognosis that affect the renal survival rate of DCGN are still unclear. In addition, there is no literature reporting the clinical manifestations and prognosis of the three most common diseases among type II patients: IgA nephropathy, lupus nephritis, and IgA vasculitis nephritis. Therefore, this retrospective study aims to evaluate the clinical and pathological features of patients with diffuse crescentic glomerulonephritis (DCGN), with a particular emphasis on Type II DCGN. Additionally, the study endeavors to identify risk factors that may have an impact on the overall prognosis of these patients.

Methods

Study design and patients

This retrospective study included a total of 107 patients with biopsy-proven diffuse crescentic glomerulonephritis (DCGN) from January 2012 to July 2022. These patients were admitted to the Sichuan Provincial People's Hospital. Inclusion criteria for the study encompassed the following: (1) age ≥ 14 years; (2) more than 50% of the analyzed glomeruli have crescents [1]; (3) at least eight glomeruli per biopsy section. The following criteria were used for exclusion: (1) insufficient medical records; (2) patients who had less than 6 months of follow-up in the follow-up cohort. The follow-up cutoff date was February 15, 2023.

Clinical and laboratory variables

Laboratory variables included sex, age, blood pressure, serum creatinine levels (normal range: 67–107 μmol/L), albumin levels (normal range: 40–55 g/L), estimated glomerular filtration rate (eGFR), 24-hour urine protein quantification (normal range: 0.028–0.270 g/24 h), urine red blood cell count, uric acid (normal range: 202–417 μmol/L), urea (normal range: 3.1-8 mmol/L), hemoglobin (normal range: 130–175 g/L), total cholesterol (TC; normal range: 3.9–5.2 mmol/L), triglycerides (TG; normal range: 0.6–1.7 mmol/L), low-density lipoprotein (LDL; normal range: 1-3.34 mmol/L), plasma immunoglobulin levels (IgG: normal range 7–16 g/L; IgA: normal range 0.7–4 g/L; IgM: normal range 0.4–2.8 g/L), plasma complement levels (C3: normal range 0.9–1.8 g/L; C4: normal range 0.1–0.4 g/L), C-reactive protein (CRP), initial symptoms, extrarenal manifestations, and whether dialysis was administered during hospitalization. Pathological data included levels of glomerular immunoglobulin deposits (IgG, IgA, IgM, C3, C1q) and the percentages of glomerulosclerosis, interstitial fibrosis, crescent formation. Interstitial inflammation was defined as the extent of inflammatory cell infiltration in the renal interstitium, encompassing lymphocytes, monocytes, and plasma cells.

Renal histopathology and outcomes

Based on immunofluorescence staining, the patients were categorized into three types: Type I was characterized by the linear deposition of immunoglobulin along the glomerular basement membrane; Type II showed significant accumulation of immune complexes in the glomeruli; Type III exhibited minimal presence of immune complexes in the glomeruli. Renal biopsy samples were fixed in 10% formalin and embedded in paraffin. Multiple continuous sections, each 4 μm thick, were prepared from the paraffin-embedded tissue. All biopsy samples were stained with hematoxylin-eosin (H&E), periodic acid-Schiff (PAS), periodic acid-methenamine silver (PASM), and Masson's trichrome (MT) stain. Staining for immunoglobulins (IgG, IgM, IgA) and complement components (C3, C1q) was conducted using fluorochrome-conjugated antibodies. For electron microscopy examination, specimens were contrasted with potassium

dichromate. Crescents identified in the glomeruli were included in the crescent count, without differentiation between large and small crescents. Two experienced nephropathologists independently evaluated all pathological sections, ensuring their blindness to the clinical data.

The primary endpoint was defined as end-stage kidney disease (ESKD), indicated by the initiation of dialysis therapy for a duration of 3 months or kidney transplantation.

Statistical analysis

We utilized SPSS 27.0 software for data analysis. Normally distributed variables were expressed as mean ± standard deviation, and comparisons were appropriately conducted using t-tests, analysis of variance (ANOVA), or Kruskal-Wallis tests as appropriate. The non-parametric variables were presented as median (interquartile range) and compared using the Mann-Whitney U test. Categorical variables were presented as frequencies (percentages) and compared using the chi-square test. Kaplan-Meier survival analysis was used to evaluate renal survival rate. To assess the independent risk factors associated with renal survival, both univariate and multivariate Cox regression analyses were conducted. The results were presented as hazard ratios (HR) along with their corresponding 95% confidence intervals (95% CI). A p-value < 0.05 was considered statistically significant.

Results

Etiology

This retrospective study recorded a total of 107 eligible patients with biopsy-proven diffuse crescentic glomerulonephritis (DCGN) from January 2012 to July 2022 at the Sichuan Provincial People's Hospita. The flow chart of this retrospective study was displayed in Fig. 1. The number of newly diagnosed diseases by DCGN during the study period is shown in Supplementary Fig. 1a.

Baseline demographic data and kidney manifestation

Among the 107 patients diagnosed with DCGN, 46 (43%) were male and 61 (57%) were female, and the average age at biopsy was 41.2 ± 17.9 years (Table 1). The disease course was relatively shorter for type I patients. There was a large difference between time of first clinical symptoms and kidney biopsy for type II and III patients (range 6-1200 days) (Supplementary Fig. 1b).

Laboratory and serologic data

All the patients with DCGN had hematuria. Patients with type I had a higher prevalence of anemia and elevated serum creatinine levels. Type II patients had higher prevalence of females, higher proteinuria and more severe hypoproteinemia. Type III patients were mostly seen in middle aged and elderly people(Table 1).The eGFR in each disease group was shown in Supplementary Fig. 1c. Type II patients exhibited lower serum complement levels compared to both type I and type III patients.

Among the three most common diseases in type II patients, IgA nephropathy (IgAN) showed more severe hematuria. Lupus nephritis (LN) had a higher prevalence in females, with higher rates of hypertension and anemia(Table 1). IgA vasculitis nephritis (IgAVN) patients exhibited higher levels of proteinuria.

Pathological features

Table 2 showed the pathologic features of diffuse crescentic glomerulonephritis. A higher percentage of type I patients had ruptured Bowman's capsule and severe interstitial inflammation compared to other groups. In type II patients, there was a lower incidence of balloon sclerosis and milder interstitial inflammation. In type III patients, there was a higher occurrence of glomerular fibrinoid necrosis.

IgAN had a higher proportion of chronic glomerular lesions compared to LN and HSPN, including the percentage of fibrocellular crescents and mesangial sclerosis.

Supplementary Fig. 2 showed the fluorescence, light microscopy, and electron microscopy findings of different types of crescentic glomerulonephritis. Type II Diffuse Crescentic Glomerulonephritis commonly exhibited mesangial or intracapillary proliferation, with more orderly arrangement of crescent cells and deposition of immune complexes in the mesangial area, often accompanied by significant infiltration of inflammatory cells.

Extrarenal manifestations

Patients with different types of DCGN exhibited distinct extrarenal manifestations. Type I patients had a higher frequency of pulmonary involvement (66.7%) and gastrointestinal symptoms (33.3%). Patients with type II had a greater prevalence of skin rash (24.3%) and arthritis (17.1%). Type III patients had a higher frequency of pulmonary infections (72%) and cardiovascular diseases (20%).

IgAN was dominated by upper respiratory (42.9%) and gastrointestinal (39.3%) symptoms. Arthritis (33.3%) was more frequent in LN. Rash (100%) predominated in IgAVN.

Treatment and outcomes of follow-up queue patients

Treatment and follow-up data were presented in Table 3. Among the 37 cases (34.6%) of patients, initial kidney replacement therapy (KRT) was required. Over the follow-up period, Among the patients requiring KRT, six individuals regained kidney function and no longer needed dialysis, including one type I patient, four type

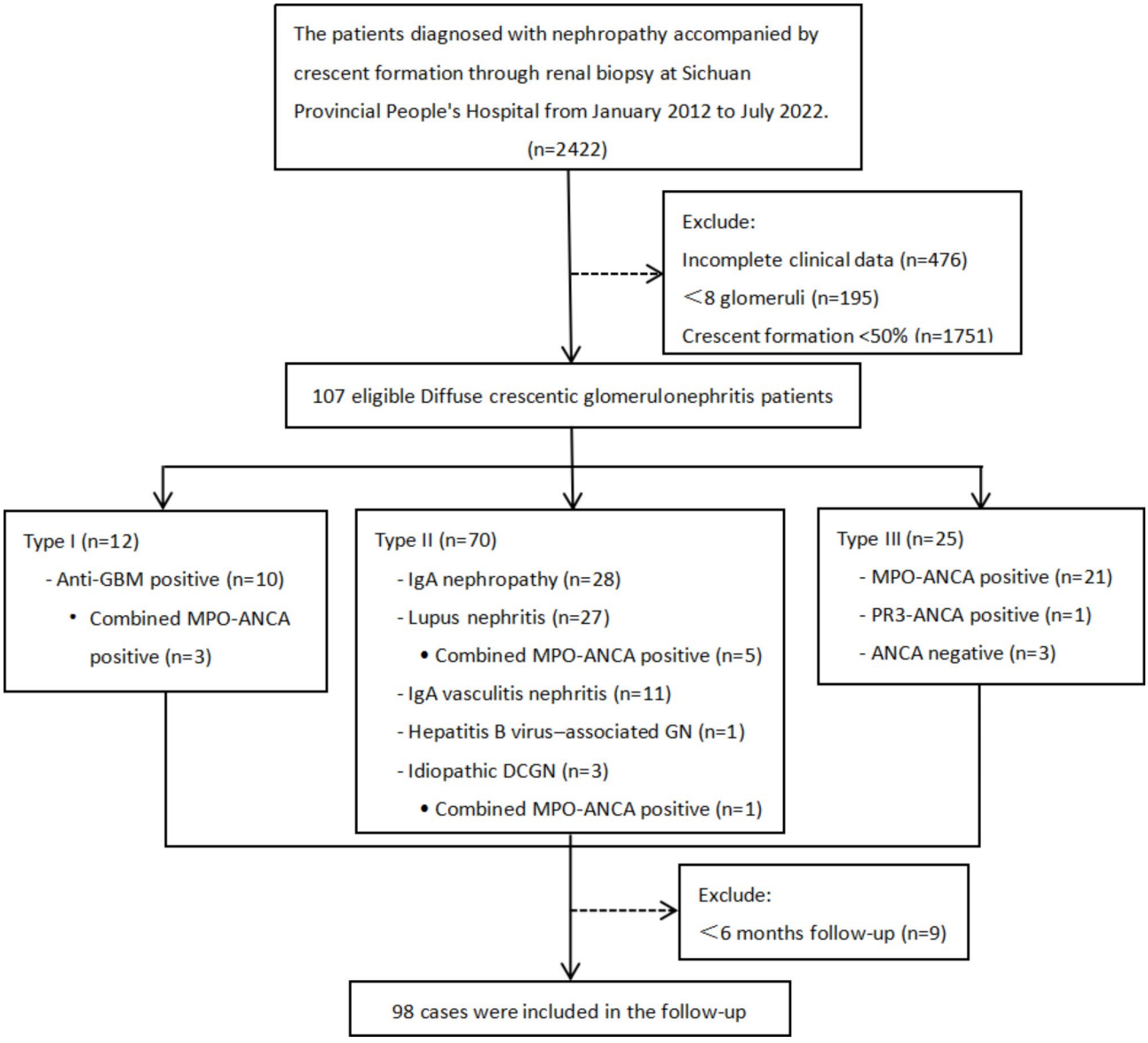

Fig. 1 The flow chart of the enrolment of Diffuse crescentic glomerulonephritis patients
ANCA: antineutrophil cytoplasmic antibody, GBM: glomerular basement membrane, GN: glomerulonephritis, MPO: myeloperoxidase, PR3:proteinase 3, DCGN: diffuse crescentic glomerulonephritis

II patients, and one type III patient. 46 DCGN patients (46.9%) progressed to ESKD. According to Fig. 2, the kidney survival rate in type II patients was significantly greater than that of the other two groups ($P < 0.001$).

At the end of follow-up, ESKD was achieved in 10 (38.5%), 7 (28%), and 2 (25%) patients with IgAN, LN, and IgAVN, respectively (Table 3). 5-year cumulative renal survival was 52%, 64%, and 70%, respectively (Supplementary Fig. 3).

Predictors of renal survival in DCGN

Kaplan-Meier survival analysis (Supplementary Fig. 3) showed that global glomerulosclerosis ($P = 0.008$), Initial KRT ($P < 0.001$), fibrous crescents > 50% ($P = 0.004$), and serum creatinine ≥ 290 μmol/L ($P < 0.001$) were linked to the advancement to ESKD.

After correcting for baseline clinicopathologic parameters, multifactorial Cox regression analyses indicated that estimated glomerular filtration rate(0.004), initial KRT at presentation ($P = 0.002$) and global glomerulosclerosis ($P<0.001$) were significantly linked to the risk of patients progressing to ESKD (Table 4).

Table 1 The baseline demographic characteristics and renal/extra-renal manifestations of the study population

Characteristic	Type I(*n* = 12)	Type II(*n* = 70)				Type III(*n* = 25)	*P* value
		Total(*n* = 70)	IgAN(*n* = 28)	LN(*n* = 27)	*P* value		
Age(years, mean ± SD)	38.1 ± 17.5	37.3 ± 17.1	38.3 ± 18.4	34.8 ± 14.1	0.756	53.7 ± 15.0	<0.001[b, c]
Gender(male: female (ratio))	6:6(1.00)	31:39(0.79)	18: 10(1.8)	5: 22(0.23)	<0.001[d]	9:16(0.56)	0.675
Duration of disease, mo	0.9(0.4,1)	1.4(0.7,3.2)	2.1(1.0,3.4)	1.0(0.7,5.0)	0.234	2.0(1.0,3.0)	0.060
MAP, mmHg	108.1 ± 17.7	105.2 ± 18.7	104.5 ± 19.7	111.9 ± 18.4	0.016	109.9 ± 16.1	0.514
Hb, g/L	83.9 ± 18.4	101.1 ± 24.6	114.8 ± 22.7	84.6 ± 16.6	<0.001[d]	85.0 ± 19.1	0.003[c]
Albumin, g/L	32.4 ± 2.9	26.0 ± 5.7	28.0 ± 5.7	24.6 ± 4.4	0.018[d]	30.2 ± 4.9	<0.001[a, c]
Globulin, g/L	26.4 ± 6.7	25.1 ± 6.5	24.6 ± 5.8	26.0 ± 6.7	0.185	30.4 ± 5.6	0.002[c]
Neutrophil,10^9/L	5.9(4.6,9.9)	5.6(4.1,8.2)	5.8(4.1,7.3)	4.4(3.4,7.7)	0.004	7.4(4.6,11.6)	0.540
Lymphocyte,10^9/L	1.0(0.9,1.2)	1.3(0.9,1.9)	1.9(1.0,2.4)	1.0(0.5,1.3)	<0.001[d]	1.1(0.8,1.5)	0.243
BUN, mmol/L	21.0 ± 6.4	13.8 ± 8.9	11.4 ± 6.4	16.8 ± 11.3	<0.001[d]	19.3 ± 9.9	0.004[a, c]
Scr,μmol/L	789.6 ± 440.5	253.2 ± 227.4	252.2 ± 246.6	239.7 ± 211	0.632	420.5 ± 249.8	<0.001[a, c]
Proteinuria, g/d	2.0(0.7,2.9)	5.2(3.2,8.1)	4.2(2.8,8.2)	5.3(3.8,6.7)	0.617	2.5(1.0,3.5)	<0.001[a, c]
Urine RBC count,×10^4/mL	1315(85,2000)	363(181,1884)	671(304,3267)	268(73,501)	0.009[d]	993(253,2501)	0.516
eGFR, mL/min/1.73m^2	6.7(5.2,9.2)	34(18,75)	43(16,94)	34.4(21.9,47.3)	0.413	13.8(8.1,20.0)	<0.001[a, c]
Low C3,n/N(%)	5/11(45.5)	36/68(52.9)	5/28(17.9)	27/27(100)	<0.001[d]	12/23(52.2)	0.953
Low C4,n/N(%)	0	16/68(23.5)	0	16/27(59.3)	<0.001[d]	1/23(4.3)	0.031[c]
IgA, g/L	2.0(1.4,3.1)	2.3(1.8,3.3)	2.2(1.8,3.1)	2.3(1.7,3.2)	0.523	2.8(2.1,3.7)	0.259
IgG, g/L	12.7 ± 5.9	9.6 ± 5.6	6.9 ± 3.3	12.9 ± 6.0	<0.001[d]	15.0 ± 4.3	0.001[c]
IgM, g/L	1.1(0.7,1.5)	0.9(0.7,1.4)	1.0(0.8,1.6)	0.9(0.7,1.0)	0.310	1.1(0.8,1.6)	0.324
ANA positive	3(25)	25(35.7)	0	25/27(92.6)	<0.001[d]	11(44)	0.519
Anti-dsDNA positive	0	20(28.6)	0	20/27(74.1)	<0.001[d]	1(4)	0.005[c]
ANCA positive	3(25)	6(8.6)	0	5/27(18.5)		22(88)	<0.001[b, c]
MPO-ANCA positive	3(25)	6(8.6)	0	5/27(18.5)		21(84)	<0.001[b, c]
PR3-ANCA positive	0	0	0	0		1(4)	0.346
Anti-GBM positive	10(83.3)	0	0	0		0	<0.001[a, b]

Note: Values for categorical variables are given as number(percentage); values for continuous variables, as mean ± standard deviation or median [interquartile range].

Abbreviations: MAP, mean arterial pressure; IgAN, IgA nephropathy; LN, lupus nephritis; eGFR, estimated glomerular filtration rate; RBC, red blood cell; Scr, serum creatinine; BMI, Body Mass Index; MAP, mean arterial pressure; CRP, C-reactive protein; UA, uric acid; BUN, blood urea nitrogen; ANCA, antineutrophil cytoplasmic antibody; C3, complement 3;C4, complement 4;GBM, glomerular basement membrane; MPO, myeloperoxidase; PR3,proteinase3;ANCA: antineutrophil cytoplasmic antibody.[a]P <0.05 between typesland II; [b]P <0.05 between typesland III; [c]P <0.05 between types II and III.[d]P <0.05 between IgAN and LN.

Discussion

The incidence of patients with diffuse crescentic glomerulonephritis(DCGN) is increasing year by year [2], and defining its clinicopathologic features and prognosis is important for treatment decisions. This study provided detailed data on a single-center study of DCGN in Western China, specifically focusing on type II DCGN. This study found that type II DCGN was the most common and had the best prognosis among DCGN types. Among them, the most common condition observed was IgA nephropathy, with lupus nephritis following closely behind. Among the three most common diseases in type II patients, IgA nephropathy had the lowest five-year kidney survival rate, followed by lupus nephritis and IgA vasculitis nephritis.

The epidemiological characteristics of DCGN vary significantly in different regions. It has been found that lupus nephritis is the main type in southern China [2], Saudi Arabia [13], and Egypt [14], while type III DCGN is the main pathological type in India [4], northern China [6], the United States [7], Spain [8], and Shanxi province in China [5]. However, in our cohort, IgA nephropathy was the most common, which had been rarely mentioned in previous studies. In this retrospective study, the patients' age was lower compared to Shanxi province in China [5] and the United States [7], but similar to southern China [2] and India [4]. In our cohort (Supplementary Table 1), the average serum creatinine concentration was lower compared to studies conducted in southern China [2], India [4], and Shanxi province in China [5], while the average urine protein level was higher than in previous research [2, 4, 5]. Our crescent proportion was similar to that of India [4] but lower than that of Shanxi province in China [2].

In our cohort, we observed that 52% of patients with type III disease exhibited low serum complement C3 levels. This finding may be attributed to the activation of the complement system in diffuse crescentic glomerulonephritis, which plays a significant role in the immune response and becomes extensively consumed, resulting

Table 2 Pathological features

Characteristic	Type I($n=12$)	Type II($n=70$)				Type III($n=25$)	*P* value
		Total($n=70$)	IgAN($n=28$)	LN($n=27$)	*P* value		
Histological characteristics							
Number of glomeruli	11(9,14)	13(11,16)	12(10,14)	13(12,17)	0.131	12(9,15)	0.183
Crescents(%)	71(57,83)	62.5(54.5,72.9)	63(55,69)	66.7(54.5,75.0)	0.523	66.7(51.7,75.0)	0.153
Cellular crescents(%)	17(10,49)	26.1(11.6,50.0)	22(13,36)	37.5(7.7,52.4)	0.340	15.8(0.0,29.7)	0.028[c]
Fibrocellular crescent(%)	28.15 ± 15.09	25.07 ± 15.51	25.5 ± 16.1	25.8 ± 15.7	0.792	29.61 ± 10.60	0.373
Fibrous crescents(%)	13(0,26)	0.0(0.0,18.75)	3.3(0,21.1)	0(0,11.1)	0.552	20.0(11.1,29.2)	0.004[c]
Fibrinoid necrosis, n(%)	2(16.7)	17(24.3)	5(17.9)	8(29.6)	0.412	13(52)	0.019[c]
Bowman's capsule rupture, n%	8(66.7)	0	0	0		1(4)	<0.001[a, b]
Global glomerulosclerosis(%)	10.8(1.4,30.6)	0(0,11.5)	3.1(0,12.5)	0(0,11.1)	0.200	13.3(0,21.6)	0.007[c]
Interstitial inflammation, n(%)					0.180		0.038[a]
Absent	0(0)	2(2.9)	0	1(3.7)		0(0)	
<25%	4(33.3)	56(80)	22(78.6)	20(74.1)		18(72)	
25–50%	7(58.3)	11(15.7)	5(17.9)	6(22.2)		6(24)	
>50%	1(8.3)	1(1.4)	1(3.6)	0		1(4)	
Interstitial fibrossis, n(%)					<0.001[d]		<0.001[a, b,c]
Absent	1(8.3)	19(27.1)	2(7.1)	9(33.3)		0(0)	
<25%	7(58.3)	44(62.9)	21(75)	16(59.3)		19(76)	
≥25%	4(33.3)	7(10)	5(17.9)	2(7.4)		6(24)	
Immunofluorescence pattern, n(%)							
C3 Number of negative	1(8.3)	1(1.4)	0	0	0.041[d]	4(16.7)	<0.001[a, c]
Number of 1+	6(50)	16(22.9)	6(21.4)	4(14.8)		11(45.8)	
Number ≥ 2+	5(41.7)	53(75.7)	22(78.6)	23(85.2)		9(37.5)	
IgA Number of negative	7(58.3)	4(5.7)	0	3(11.1)	0.004[d]	19(79.2)	<0.001[a, c]
Number of 1+	3(25)	12(17.1)	0	8(29.6)		3(12.5)	
Number ≥ 2+	2(16.7)	54(77.1)	28(100)	16(59.3)		2(8.3)	
IgG Number of negative	4(33.3)	39(55.7)	25(89.3)	3(11.1)	<0.001[d]	17(70.8)	0.079
Number of 1+	5(41.7)	21(30.0)	3(10.7)	17(63)		7(29.2)	
Number ≥ 2+	3(25)	10(14.3)	0	7(25.9)		0(0)	
IgM Number of negative	8(66.7)	15(21.4)	5(17.9)	2(7.4)	0.064	12(50)	0.006[a, c]
Number of 1+	4(33.3)	38(54.3)	18(64.3)	16(59.3)		8(33.3)	
Number ≥ 2+	0(0)	17(24.3)	5(17.9)	9(33.3)		4(16.7)	
C1q Number of negative	11(91.7)	36(51.4)	23(82.1)	1(3.7)	<0.001[d]	18(72)	<0.001[a, b,c]
Number of 1+	1(8.3)	15(21.4)	5(17.9)	7(25.9)		7(28)	
Number ≥ 2+	0(0)	19(27.1)	0(0)	19(70.4)		0(0)	

Note: Values for categorical variables are given as number(percentage); values for continuous variables, as mean ± standard deviation or median [interquartile range].

Abbreviations: IgAN, IgA nephropathy; LN, lupus nephritis; IgAVN, IgA vasculitis nephritis.[a]P <0.05 between typesland II; [b]P <0.05 between typesland III; [c]P <0.05 between types II and III.[d]P <0.05 between IgAN and LN.

in decreased serum C3 levels. Consistent with previous studies conducted in China, type III patients predominantly tested positive for MPO-ANCA [2, 6]. Additionally, among patients with type III, the prevalence of ANA positivity was 44%, exceeding those reported in South Asia [10]. This finding may be attributed to the elevated incidence of MPO-ANCA positivity and the older age of the patients in this study. Given that both P-ANCA and ANA are nuclear antibodies, this suggests that higher MPO-ANCA titers may correlate with increased ANA positivity [17]. Moreover, the prevalence of ANA positivity tends to rise with advancing age [18].In the LN group ($n=27$), only 7 patients demonstrated moderate to high-intensity IgG deposition. This may reflect the critical role of cellular immunity in crescent formation; as the proportion of crescents increases and uremic status worsens, humoral immunity may be relatively suppressed, leading to decreased production of autoantibodies and, consequently, lower deposition of immune complexes in renal tissue [19].

There is no literature reporting the clinical manifestations and prognosis of different diseases in type II patients. In this study, we analyzed the three most common diseases in type II patients and discovered that the 5-year kidney survival rate was lower in IgA nephropathy compared to IgA vasculitis nephritis and lupus nephritis. The baseline creatinine and proportion of fibrous crescents were higher in IgA nephropathy compared to the

Table 3 Treatment and outcomes of follow-up queue patients

Item	Type I(*n* = 12)	Type II(*n* = 63)				Type III(*n* = 23)	*P* value
		Total(*n* = 63)	IgAN(*n* = 26)	LN(*n* = 25)	*P* value		
In-hospital dialysis, n(%)	10(83.3)	15(23.8)	3(11.5)	8(32)	0.162	12(52.2)	<0.001[a, c]
Plasma exchange, n(%)	8(66.7)	5(7.9)	0	4(16)	0.054	3(13.0)	<0.001[a, b]
GC + CTX	11(91.7)	49(77.8)	19(73.1)	21(84)		20(87.0)	
GC + MMF	0	6(9.5)	2(7.7)	3(12)		1(4.3)	
GC + LEF	0	2(3.2)	1(3.8)	0		0	
GC	1(8.3)	4(6.3)	4(15.4)	0		2(8.7)	
Follow-up(months, means ± SD)	28.8 ± 31.1	41.2 ± 36.3	36.6 ± 34.0	37.9 ± 33.3	0.085	25.1 ± 23.3	0.107
Status at last follow-up							
Scr,μmol/L	524(367,949)	105(73,503)	108(75,346)	86(73,572)	0.819	451(313,522)	<0.001[a, c]
eGFR, mL/min/1.73m^2	8(5,17)	62(13,95)	63(15,98)	79(9,94)	0.720	10(8,16)	<0.001[a, c]
dialysis, n(%)	9(75)	21(33.3)	10(38.5)	7(28)		17(73.9)	<0.001[a, c]
6 months renal survival rate	33.3 ± 13.6	84.1 ± 4.6	84.6 ± 7.1	88.0 ± 6.5	0.966	52.2 ± 10.4	<0.001[a, c]
3-year renal survival rate	33.3 ± 13.6	70.2 ± 6.2	65.6 ± 10.1	72.1 ± 9.9	0.552	27.9 ± 10.8	<0.001[a, c]
5-year renal survival rate	0	57.5 ± 7.7	51.6 ± 11.9	64.1 ± 11.6	0.600	18.6 ± 10.4	<0.001[a, c]

Note: Values for categorical variables are given as number(percentage); values for continuous variables, as mean ± standard deviation or median [interquartile range].

Abbreviations: GC, Glucocorticoid; CTX, Cyclophosphamide; MMF, Mycophenolate Mofetil; LEF, Leflunomide; eGFR, estimated glomerular filtration rate; Scr, serum creatinine; IgAN, IgA nephropathy; LN, lupus nephritis. [a]*P* <0.05 between typesland II; [b]*P* <0.05 between typesland III; [c]*P* <0.05 between types II and III.[d]*P* <0.05 between IgAN and LN.

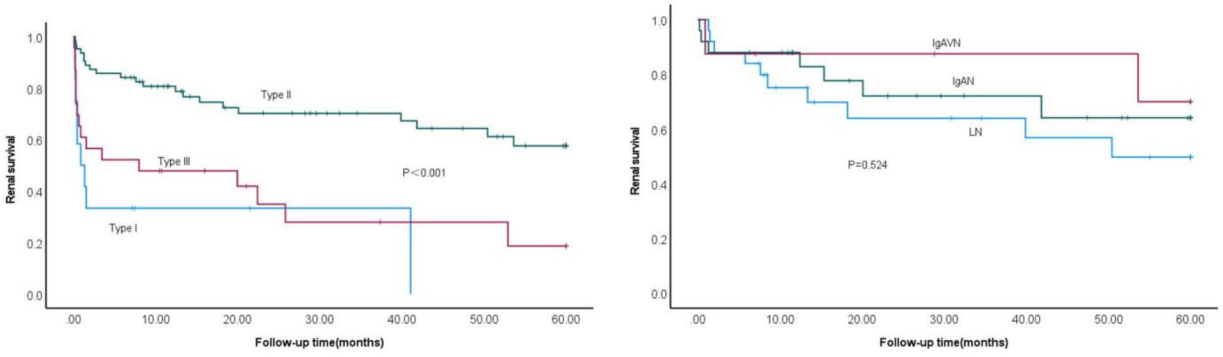

Fig. 2 **A**: Renal survival in patients by diffuse crescentic glomerulonephritis type based on histopathologic criteria. **B**: Renal survival rate of patients with IgA nephropathy, lupus nephritis, and IgA vasculitis nephritis. IgAN: IgA nephropathy, LN: lupus nephritis, IgAVN, IgA vasculitis nephritis

other two diseases. We attribute this to the presence of extrarenal diseases, which makes the diagnosis of IgA vasculitis nephritis and lupus nephritis easier in the early stages, allowing for earlier treatment [20]. In contrast, IgA nephropathy patients have no clinical symptoms, and kidney biopsies are performed at any stage of disease progression. This can explain the poorer renal function at the time of diagnosis. Therefore, our study supports early kidney biopsy for patients with abnormal kidney function to establish a definitive diagnosis.

The study's findings suggested a significant correlation between DCGN classification and renal prognosis, with patients diagnosed with Type II diffuse crescentic glomerulonephritis (DCGN) exhibiting the highest kidney survival rates, and those with Type I DCGN experiencing the lowest kidney survival rates. However, there are discrepancies in the prognosis of different types of DCGN among different studies. The results from studies conducted in southern China and India are similar to ours [2, 10]. However, a study by Su et al., which included 109 cases of crescentic glomerulonephritis, demonstrated

Table 4 Potential prognostic factors for kidney outcome by multivariate Cox's regression analyses

Variables	Univariate Analysis		Multivaria Analysis	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Type	0.196(0.087,0.439)	<0.001	1.593(0.660,3.844)	0.301
eGFR	0.952(0.931,0.973)	<0.001	0.971(0.951,0.991)	0.004
MAP(mmHg)	1.015(0.999–1.031)	0.074		
Initial KRT	7.904(4.056–15.403)	<0.001	3.272(1.525,7.019)	0.002
Hemoglobin, < 90 g/L	1.774(0.990–3.179)	0.054		
Proteinuria, g/d	1.010(0.938–1.088)	0.793		
Urine RBC count,×104/mL	1.000(1.000–1.000)	0.093		
TAIF, moderate to severe	1.903(1.051–3.447)	0.034		
Global glomerulosclerosis(%)	1.046(1.027–1.065)	<0.001	1.052(1.025,1.080)	<0.001
Crescent(%)	1.033(1.012–1.055)	0.002	1.022(0.997,1.048)	0.089
Cellular crescent(%)	0.995(0.980,1.010)	0.502		
Fibrous crescent(%)	1.023(1.006,1.041)	0.007		
Fibrocellular crescent(%)	1.007(0.988,1.025)	0.482		

The clinical and pathological factors with a p-value < 0.05 on univariate analysis were included in the multivariable analysis.TAIF: Tubular Atrophy and Interstitial Fibrosis; KRT: kidney replacement therapy; MAP, mean arterial pressure; eGFR, estimated glomerular filtration rate.

that Type II had the best renal prognosis, while Type III had the poorest prognosis [5]. On the other hand, Wu et al. proposed that Type III had the best renal prognosis, while Type I had the poorest prognosis [15]. Further confirmation of these comparisons may require larger research cohorts in the future. Furthermore, our current study shows that 46 patients (46.9%) developed end-stage kidney disease (ESKD) at the end of follow-up. The poor renal prognosis in the enrolled patients may be associated with higher creatinine levels and crescent proportions at the time of presentation. A study with similar findings to ours reported that 89 patients (45%) in an Indian population developed ESKD within a median follow-up of 9.4 months [10]. Another study involving 72 patients from Saudi Arabia showed that 26% of patients required dialysis at the end of follow-up [13]. In contrast, Su et al.'s study revealed that 67% of patients died or developed ESKD during long-term follow-up, indicating severe kidney involvement as a characteristic of their patient cohort [5].

Low renal survival was associated with low eGFR levels, glomerulosclerosis, and initial KRT at presentation, as demonstrated by the results of this study. As reported in most of the previous studies, high serum creatinine level was considered as a predictor of low renal survival in patients with diffuse crescentic nephritis. However, our study found that global glomerulosclerosis and initial KRT were also significant risk factors for poor renal survival, which was rarely mentioned in previous studies.

Historically, the severity of glomerular inflammation was often reflected by the high proportion of crescents observed. Recently, Su et al. analyzed 109 patients with crescentic glomerulonephritis and observed that all patients with a crescent proportion over 90% reached the primary outcome [5]. However, to date, there is a relatively limited investigation on the impact of crescent type on kidney survival rates. Our study included patients with global glomerulosclerosis and found it to have higher predictive value. Our study adds to the literature and emphasizes the importance of performing renal biopsies for definitive diagnosis and early treatment for improving patient prognosis. During 2022, Ge et al. conducted a prognostic analysis involving 76 patients with antiglomerular basement membrane nephritis and determined that the initial KRT could function as an indicator of an unfavorable renal outcome in these patients [21]. In contrast, the correlation between initial KRT and renal survival was not investigated in other studies involving patients with diffuse crescentic nephritis. Therefore, the current study contributes to the limited body of research by confirming the association between initial KRT and renal prognosis. This study provides evidence that renal function recovery is challenging for patients undergoing initial kidney replacement therapy (KRT).

Plasma exchange therapy has been proven beneficial for patients with ANCA-associated vasculitis or crescentic glomerulonephritis caused by anti-GBM antibodies [22, 23]. However, Wang et al. suggested that plasma exchange therapy does not improve the prognosis of patients with crescentic IgA nephropathy on top of conventional immunosuppressive therapy [24]. Within our follow-up cohort, a total of 16 patients underwent combination therapy involving plasma exchange, glucocorticoids, and cyclophosphamide. At the conclusion of the follow-up period, 11 patients (69%) had progressed to end-stage kidney disease. Therefore, we believe that for Type I diffuse crescentic glomerulonephritis patients, occasional recovery of renal function may occur with combination therapy, while plasma exchange therapy seems to have limited benefits for Type II and Type III patients. Additionally, the presence of crescents has been widely recognized as an indicative factor for the severity

of glomerular inflammation over a significant period of time. In our cohort, all patients with 100% involvement of crescents in the glomeruli reached ESKD, while only 10 cases with more than 75% crescents in the glomeruli had any remaining viable glomeruli, despite receiving glucocorticoids and immunosuppressive therapy. In summary, for patients with more than 75% crescentic involvement in the glomeruli, the value of intensified treatment is extremely limited [5].

This study report has several limitations that should be acknowledged. To begin with, This retrospective study was conducted at a single center, potentially leading to selection bias. Secondly, because of the compromised renal function in patients with Type I diffuse crescentic glomerulonephritis at the time of presentation, renal biopsies were not conducted, leading to a relatively small number of cases included in the study. Lastly, the sample size in this study was limited, and the follow-up duration was insufficient. Additionally, certain types of Type II patients were not included (e.g., C3 nephropathy, membranous nephropathy). Future multicenter and prospective cohort studies are planned to further validate these findings.

In conclusion, our study showed that type II DCGN was the most prevalent type in DCGN, and favors better renal prognosis than type I and III DCGN. IgA nephropathy exhibited the highest incidence in Type II and had a less favorable prognosis compared to lupus nephritis and IgA vasculitis nephritis. In addition, baseline eGFR, initial KRT and global glomerulosclerosis were predictive factors for ESKD in DCGN.

Abbreviations

DCGN	Diffuse crescentic glomerulonephritis
IgAN	IgA nephropathy
IgAVN	IgA vasculitis nephritis
MAP	Mean arterial pressure
LN	Lupus nephritis
RBC	Red blood cell
Scr	Serum creatinine
BMI	Body Mass Index
MAP	Mean arterial pressure
CRP	C-reactive protein
UA	Uric acid
BUN	Blood urea nitrogen
ANCA	Antineutrophil cytoplasmic antibody
C3	Complement 3
C4	Complement 4
GBM	Glomerular basement membrane
MPO	Myeloperoxidase
PR3	Proteinase3
ANCA	Antineutrophil cytoplasmic antibody
GC	Glucocorticoid
CTX	Cyclophosphamide
MMF	Mycophenolate Mofetil
LEF	Leflunomide
TAIF	Tubular Atrophy and Interstitial Fibrosis
KRT	Kidney replacement therapy

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12882-024-03923-1.

Supplementary Material 1

Acknowledgements

We gratefully acknowledge all the participants who contributed to this study.

Author contributions

Data collection was conducted by S.W., S.C., P.Z., Y.L., and W.W. The study design was developed by S.W., S.C., W.W., and G.L. Statistical analyses were performed by S.W., S.C., and W.W. The writing of the manuscript was completed by S.W., S.C., and W.W. All authors contributed to the revision of the manuscript and approved the final version for submission.

Funding

The National Natural Science Foundation of Sichuan Province provided support for this study (No. 23NSFSC0600).

Data availability

The dataset used in this study is available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

All procedures in this study were performed in accordance with the ethical standards of the relevant institutional and/or national research committees, adhering to the principles outlined in the Declaration of Helsinki. The study was approved by the Ethics Committee of Sichuan Provincial People's Hospital (Ethical approval number: 2024 – 617). We confirm that informed consent to participate was obtained from the parents or legal guardians of all participants under the age of 16, as well as from all adult participants.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Received: 8 July 2024 / Accepted: 19 December 2024
Published online: 14 January 2025

References

1. Tang Z, Wu Y, Wang Q, Zeng C, Yao X, Hu W, Chen H, Liu Z, Li L. Clinical spectrum of diffuse crescentic glomerulonephritis in Chinese patients. Chin Med J (Engl). 2003;116(11):1737–40.
2. Chen S, Tang Z, Xiang H, Li X, Chen H, Zhang H, Hu W, Zeng C, Liu Z. Etiology and outcome of Crescentic Glomerulonephritis from a single Center in China: a 10-Year review. Am J Kidney Dis. 2016;67(3):376–83.
3. Chen Z, Xu J, Wu J, Xue C, Ruan M, Mei C, Mao Z. Prognostic analysis of crescentic glomerulonephritis with acute kidney injury: a single-center cohort with 5-year follow-up. Int Urol Nephrol. 2022;54(9):2375–83.
4. Gupta A, Agrawal V, Kaul A, Verma R, Jain M, Prasad N, Pandey R. Etiological Spectrum and clinical features in 215 patients of Crescentic Glomerulonephritis: is it different in India? Indian J Nephrol. 2021;31(2):157–62.
5. Su X, Song R, Li S, Guo W, Guo X, Qiao X, Wang L. Outcomes and risk factors in patients with crescentic glomerulonephritis: a multicenter cohort study. J Nephrol. 2023;36(4):1027–35.
6. Lin W, Chen M, Cui Z, Zhao MH. The immunopathological spectrum of crescentic glomerulonephritis: a survey of 106 patients in a single Chinese center. Nephron Clin Pract. 2010;116(1):c65–74.
7. Jennette JC. Rapidly progressive crescentic glomerulonephritis. Kidney Int. 2003;63(3):1164–77.

8. López-Gómez JM, Rivera F. Renal biopsy findings in acute renal failure in the cohort of patients in the Spanish Registry of Glomerulonephritis. Clin J Am Soc Nephrol. 2008;3(3):674–81.
9. Rampelli SK, Rajesh NG, Srinivas BH, Harichandra Kumar KT, Swaminathan RP, Priyamvada PS. Clinical spectrum and outcomes of crescentic glomerulonephritis: a single center experience. Indian J Nephrol. 2016;26(4):252–6.
10. Alexander S, Yusuf S, Rajan G, Elias John E, Roy S, Annamalai VC, Thomas A, Joseph Eapen J et al. A TV, George David V : Crescentic glomerulonephritis: what's different in South Asia? A single center observational cohort study. *Wellcome Open Res* 2020, 5:164.
11. Ozlu SG, Caltik A, Aydog O, Bulbul M, Demircin G, Cakici E, Arda N, Oner A. Crescentic glomerulonephritis in children: a single centre experience. World J Pediatr. 2016;12(2):225–30.
12. Mayer U, Schmitz J, Brasen JH, Pape L. Crescentic glomerulonephritis in children. Pediatr Nephrol. 2020;35(5):829–42.
13. Oudah N, Al Duhailib Z, Alsaad K, Qurashi S, Ghamdi G, Flaiw A, Hejaili F, Farooqui M, Al Sayyari A. Glomerulonephritis with crescents among adult Saudi patients outcome and its predictors. Clin Exp Med. 2012;12(2):121–5.
14. El-Husseini AA, El-Agroudy AE, Moustafa FE, Fouda MA, Sobh MA. Impact of clinical and histopathological factors on outcome of Egyptian patients with crescentic glomerulonephritis. Int Urol Nephrol. 2003;35(4):543–51.
15. Wu T, Peng J, Meng T, Liu Q, Ao X, Lin W, Yin H, Chen J, Pu J, Peng Z, et al. Clinicopathological features and prognostic analysis of 49 cases with crescentic glomerulonephritis. Exp Ther Med. 2019;18(5):3984–90.
16. Gupta R, Singh L, Sharma A, Bagga A, Agarwal SK, Dinda AK. Crescentic glomerulonephritis: a clinical and histomorphological analysis of 46 cases. Indian J Pathol Microbiol. 2011;54(3):497–500.
17. Nasr SH, D'Agati VD, Park HR, Sterman PL, Goyzueta JD, Dressler RM, Hazlett SM, Pursell RN, Caputo C, Markowitz GS. Necrotizing and crescentic lupus nephritis with antineutrophil cytoplasmic antibody seropositivity. Clin J Am Soc Nephrol. 2008;3(3):682–90.
18. Satoh M, Chan EK, Ho LA, Rose KM, Parks CG, Cohn RD, Jusko TA, Walker NJ, Germolec DR, Whitt IZ, et al. Prevalence and sociodemographic correlates of antinuclear antibodies in the United States. Arthritis Rheum. 2012;64(7):2319–27.
19. Chen S, Tang Z, Zhang Y, Liu Z, Zhang H, Hu W, Liu Z. Significance of histological crescent formation in patients with diffuse proliferative lupus nephritis. Am J Nephrol. 2013;38(6):445–52.
20. Pillebout E. IgA Vasculitis and IgA Nephropathy: same disease? J Clin Med 2021, 10(11).
21. Ge Y, Liu K, Yang G, Yu X, Sun B, Zhang B, Yuan Y, Zeng M, Wang N, Xing C, et al. Clinicopathological characteristics and outcome predictors of anti-glomerular basement membrane glomerulonephritis. Ren Fail. 2022;44(1):2037–45.
22. Jayne DR, Gaskin G, Rasmussen N, Abramowicz D, Ferrario F, Guillevin L, Mirapeix E, Savage CO, Sinico RA, Stegeman CA, et al. Randomized trial of plasma exchange or high-dosage methylprednisolone as adjunctive therapy for severe renal vasculitis. J Am Soc Nephrol. 2007;18(7):2180–8.
23. Levy JB, Turner AN, Rees AJ, Pusey CD. Long-term outcome of anti-glomerular basement membrane antibody disease treated with plasma exchange and immunosuppression. Ann Intern Med. 2001;134(11):1033–42.
24. Wang Z, Zhang JJ, Zuo L, Wang Y, Li WG, Cheng H, Cai GY, Pei HY, Wang LH, Zhou XJ, et al. [Efficacy of plasma exchange in severe crescentic IgA nephropathy: a multicentered, cohort study]. Beijing Da Xue Xue Bao Yi Xue Ban. 2022;54(5):1038–46.

Publisher's note