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ORIGINAL ARTICLE

Distinction between MPO-ANCA and PR3-ANCA-associated glomerulonephritis in Chinese patients: a retrospective single-center study

Yan Hong[1,2] · Pengxian Shi[1] · Xia Liu[3] · Liu Yang[3] · Kang Li[3] · Feng Xu[3] · Shaoshan Liang[3] · Zhengzhao Liu[3] · Haitao Zhang[3] · Yinghua Chen[3] · Weixin Hu[1,3]

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Abstract

Objectives To retrospectively investigate the clinical and histological features and outcomes of ANCA-associated glomerulonephritis (AAGN) with different ANCA serotypes.

Method A total of 467 AAGN patients were divided into MPO-AAGN (MPO) and PR3-AAGN (PR3) groups according to ANCA serotype. Clinical and histological features and renal outcomes were compared.

Results In this study, 429 (91.9%) patients tested positive for MPO-ANCA, and 38 (8.1%) for PR3-ANCA. The median age at diagnosis ($P = 0.017$) and proportion of females ($P = 0.003$) were higher in the MPO group. Joint ($P < 0.001$), ENT ($P = 0.000$), skin ($P = 0.007$), and eye ($P = 0.014$) involvements were more common in the PR3 group. Compared with that in the PR3-group, a higher proportion of patients in the MPO group had microscopic polyangiitis ($P = 0.000$), and a lower proportion of exhibited granulomatosis with polyangiitis ($P = 0.000$). Patients in the MPO group also exhibited lower BVAS scores ($P = 0.003$) and higher serum albumin levels ($P = 0.009$). Histologically, a lower proportion of MPO patients had crescentic glomerulonephritis ($P = 0.028$) and acute tubule-interstitial lesion scores ($P = 0.007$), but a higher proportion of these patients exhibited mixed class glomerulonephritis ($P = 0.032$) than in the PR3 group. The relapse rate was lower ($P = 0.020$), and the 5-year relapse-free survival rate ($P = 0.003$) was higher in the MPO group than in the PR3 group. However, the 5-year renal survival rates ($P = 0.106$) were not significantly different.

Conclusions MPO-ANCA was predominant in Chinese patients with ANCA-associated vasculitis and renal disease. The epidemiological characteristics, extra-renal involvement, and histopathological classes and outcomes were different between MPO-positive and PR3-positive patients, implying that they might be two different disease entities.

Keywords Antineutrophil cytoplasmic antibody · Glomerulonephritis · Myeloperoxidase · Proteinase 3

Introduction

Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a systemic disease characterized by inflammation and necrosis of small vessels, resulting in multiple organ damage and dysfunction. The kidney is the most frequently affected organ, leading to pauci-immune segmental necrotizing crescentic glomerulonephritis [1], which is called ANCA-associated glomerulonephritis (AAGN).

AAV is classified into four categories depending on the clinical features: microscopic polyangiitis (MPA), granulomatosis with polyangiitis (GPA), eosinophilic GPA (EGPA), and renal-limited vasculitis (RLV) [2]. Organ involvement produces many alterations in various categories of AAV, and the clinical manifestations lack specificity. ANCA is almost

✉ Yinghua Chen
cherry1109@163.com

✉ Weixin Hu
huwx@vip.163.com

[1] Jinling Clinical Medical College of Nanjing Medical University, Nanjing, China

[2] The Affiliated Wuxi No. 2 People's Hospital of Nanjing Medical University, Wuxi, China

[3] National Clinical Research Centre of Kidney Diseases, Nanjing Jinling Hospital, Nanjing University School of Medicine, Nanjing, China

always directed against myeloperoxidase (MPO) or protease 3 (PR3) [3]. Conflicts of ANCA serotypes exist between the various clinical types, but MPO-ANCA and PR3-ANCA are more common in MPA and GPA, respectively. A total of 20% of MPA patients are PR3-ANCA-positive, and 20–40% of GPA patients are MPO-ANCA-positive [4].

The distinction between GPA and MPA in the context of ANCA serotypes is flawed and underlines the discordance between disease categorization and ANCA serotype. Differences between MPO-ANCA vasculitis (MPO-AAGN) and PR3-ANCA vasculitis (PR3-AAGN) were reported in epidemiology, genetics, pathogenesis, and clinical manifestations and prognosis [5]. These differences were validated primarily in patients from Europe and the USA based on the diversity of phenotype distribution, and most of these patients present with PR3-ANCA-associated GPA. In contrast, most patients with AAV in China and other Asian countries present with MPO-ANCA-associated MPA [5, 6]. The differences between MPO-AAGN and PR3-AAGN in Asian patients are not clear. Therefore, we retrospectively analyzed the differences between MPO-AAGN and PR3-AAGN in terms of the epidemiology and clinical and histological features and outcomes in Chinese patients.

Methods

Study participants

A total of 467 patients with AAGN diagnosed at the National Clinical Research Centre of Kidney Diseases, Nanjing Jinling Hospital, from June 1998 to May 2016 were included (Fig. 1). All patients fulfilled the following criteria: (a) met the Chapel Hill diagnostic criteria [2], (b) had renal involvement, and (c) were identified as ANCA-positive by both indirect immunofluorescence assay (IIF) and enzyme-linked immunosorbent assay (ELISA). ANCAs were divided according to antigen serotypes into myeloperoxidase (MPO)-ANCA and proteinase 3 (PR3)-ANCA. The patients were allocated into an MPO-AAGN (MPO) group or a PR3-AAGN (PR3) group. Patients with any of the following conditions were excluded: (a) double-positive for MPO-ANCA and PR3-ANCA ($n = 10$); (b) secondary vasculitis, such as Henoch-Schonlein purpura, drug allergies, drug-associated AAGN, lupus vasculitis, rheumatoid vasculitis, tumor, cryoglobulinemia, and infection; (c) comorbid kidney diseases, such as IgA nephropathy, diabetic nephropathy, membranous nephropathy, and antiglomerular basement membrane nephritis; and (d) HBV, HCV, or HIV infection. This study was approved by the ethics committee of Nanjing Jinling Hospital and fulfilled the Declaration of Helsinki. All patients provided written informed consent.

Renal histology

All renal biopsy specimens were examined by light microscopy, immunofluorescence, and electron microscopy. Renal histopathology was classified as focal (≥ 50% normal glomeruli), crescentic (≥ 50% glomeruli with cellular crescents), mixed (< 50% normal, < 50% crescentic, and < 50% global sclerotic glomeruli), or sclerotic (≥ 50% sclerotic glomerulus) [7]. Global glomerulosclerosis was defined as sclerotic changes in a single glomerulus > 80%. Cellular crescents were defined as cellular components of the segmental or annular crescent > 10%.

Tubulointerstitial lesions were scored semi-quantitatively and described as mild (score of 1) for < 25% renal tubulointerstitial involvement, moderate (score of 2) for 25~50% involvement, and severe (score of 3) for > 50%

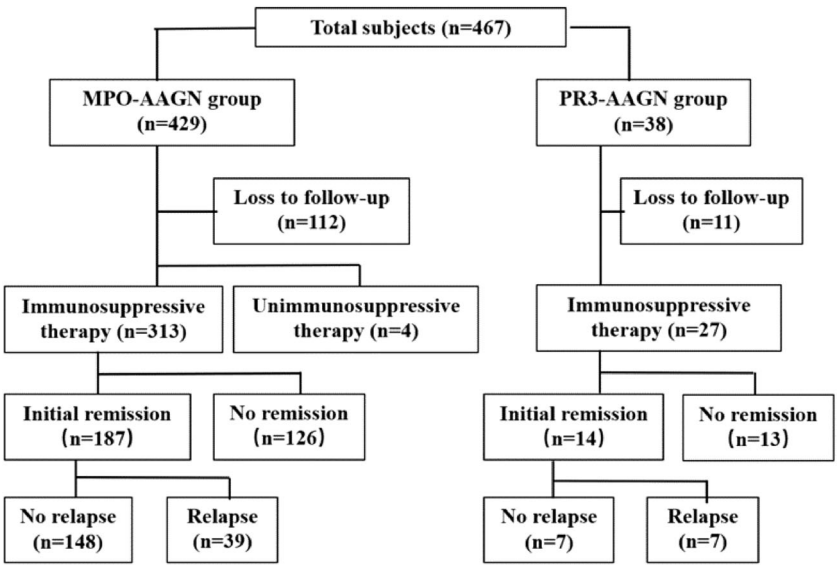

Fig. 1 Study recruitment process and patient outcomes

involvement. All renal biopsies were read independently by two experienced renal pathologists who were blinded to the clinical data.

Treatment

According to the recommended treatment, induction therapy typically included corticosteroids plus cyclophosphamide (CTX) [8] or mycophenolate mofetil (MMF) [9]. A small number of patients were treated with multiple target therapy (corticosteroids, MMF, and tacrolimus) [10]. Patients with severe renal damage or pulmonary hemorrhage received staphylococcal protein A immunoadsorption (IA) [11] or double filtration plasmapheresis (DFPP) [12]. Maintenance therapy included glucocorticoids plus azathioprine or MMF.

Clinical assessment

AAV activity was assessed by the Birmingham Vasculitis Activity Score (BVAS). AAV remission was defined as no new, worse, or persistent symptoms of vasculitis activity and a BVAS = 0 for consecutive 28 days. Renal remission was defined as no active urine sediment and stable or decreased Scr. Relapse was defined as an increase in the BVAS of 1 or more points. Renal relapse was defined as recurrence of hematuria with or without increased proteinuria or an increase in the Scr in patients who achieved remission.

Follow-up

The patients were followed until death, progression to end-stage renal disease (ESRD), or the final follow-up date (June 30, 2017). The estimated glomerular filtration rate (eGFR) was calculated using the CKD-EPI collaboration equation. ESRD was defined as eGFR < 15 ml/(min·1.73 m^2) or maintenance of renal replacement therapy for more than 3 months.

Statistical analyses

Categorical variables are expressed as numbers (percentage), and results were compared using Fisher's exact test. Quantitative variables are expressed as means ± SD (for data that were normally distributed) or medians (interquartile range, IQR) (for data that were not normally distributed) and compared using Student's *t* test or the Mann–Whitney *U* test. Kaplan–Meier survival analysis was used to estimate renal survival, and the log-rank test was used to compare differences between the survival curves. The Cox proportional hazards model was established to analyze the risk factors of recurrence. Statistical analysis was performed using SPSS version 19.0. $P < 0.05$ (two-sided) was considered significant.

Results

Clinical features

A total of 429 (89.9%) of the 467 patients were positive for MPO-AAGN, and 38 (8%) patients were positive for PR3-AAGN. A total of 415 (88.9%) patients were diagnosed as MPA, 37 (7.9%) patients were GPA, and 15 (3.2%) patients were EGPA. MPA (90.7%) was predominant in the MPO group, and GPA accounted for only 6.3%. MPA accounted for 68.4% in the PR3 group, and GPA accounted for 26.3%. The median age (57 years vs. 46 years, $P = 0.017$) and proportion of women (59.9% vs. 34.2%, $P = 0.003$) were significantly higher in the MPO group than in the PR3 group. The median BVAS was significantly lower in the MPO group than in the PR3 group (17 vs. 21, $P = 0.003$). The incidences of arthralgia (6.3% vs. 44.7%, $P = 0.000$), ENT symptoms (1.6% vs. 18.4%, $P = 0.000$), and skin rash (4.0% vs. 15.8%, $P = 0.007$) were significantly lower in the MPO group than in the PR3 group. Extra renal involvement of joint (18.4% vs. 47.4%, $P < 0.001$) and eyes (7.9% vs. 21.1%, $P = 0.014$) was lower in the MPO group than in the PR3 group. There were no differences in the duration of AAV, renal disease, or other organ involvements between the groups (Table 1).

Renal morphology

Renal biopsies were performed in 330 patients: 300 patients in the MPO group and 30 patients in the PR3 group. Immunofluorescence revealed no or little glomerular staining for immunoglobulins or complement in MPO-AAGN and PR3-AAGN. The proportion of crescentic class (18.3% vs. 36.7%, $P = 0.028$) and acute tubulointerstitial lesion scores (1.0 (1.0–2.0) vs. 2.0 (1.0–2.5), $P = 0.007$) were significantly lower in the MPO group than in the PR3 group. However, the proportion of mixed class was higher in the MPO group than in the PR3 group (44.7% vs. 23.3%, $P = 0.032$) (Fig. 2). There were no significant differences in the proportions of crescent, glomerulosclerosis, glomerular capillary necrosis, chronic interstitial vascular necrosis, or tubulointerstitial lesion score between groups (Table 2).

Treatment and outcomes

A total of 112 patients in the MPO group and 18 patients in the PR3 group were lost to follow-up, and 4 patients in the MPO group did not receive immunosuppressive therapy. The remaining 340 patients were included in observations of the treatment efficacy, including 313 cases in the MPO group and 27 in the PR3 group (Fig. 1). There were no differences between the two groups in terms of extracorporeal circulation or immunosuppressive treatment (Table 3).

Table 1 Clinical features of ANCA-associated glomerulonephritis in different ANCA serotypes

	MPO-AAGN ($n = 429$)	PR3-AAGN ($n = 38$)	P value
Age (year)	57 (45–65)	46 (32–64)	0.017
Male/female	172/257	25/13	0.003
Duration of vasculitis (month)	3.0 (1.0–10.0)	3.0 (1.0–9.8)	0.883
Duration of renal disease (month)	2.0 (1.0–4.0)	1.0 (0.5–2.3)	0.096
Clinical classification, *n* (%)			
MPA	389 (90.7)	26 (68.4)	< 0.001
GPA	27 (6.3)	10 (26.3)	< 0.001
EGPA	13 (3.0)	2 (5.3)	0.349
Initial symptoms, *n* (%)			
Hematuria	99 (23.1)	4 (10.5)	0.100
Arthralgia	27 (6.3)	17 (44.7)	0.000
Cough	108 (25.2)	10 (26.3)	0.847
Hemoptysis	104 (24.2)	13 (34.2)	0.176
Pulmonary nodules	47 (11.0)	5 (13.2)	0.597
ENT symptoms	7 (1.6)	7 (18.4)	< 0.001
Skin rash	17 (4.0)	6 (15.8)	0.007
Extra-renal involvement, *n* (%)			
Respiratory system	315 (73.4)	30 (79.0)	0.565
ENT	219 (51.1)	25 (65.8)	0.091
Joint	79 (18.4)	18 (47.4)	< 0.001
Eye	34 (7.9)	8 (21.1)	0.014
Skin	37 (8.6)	6 (15.8)	0.145
Digestive system	36 (8.4)	5 (13.2)	0.363
Nervous system	51 (11.9)	5 (13.2)	0.795
Cardiovascular	21 (4.9)	1 (2.6)	1.000
BVAS	17(15–21)	21 (16–23)	0.003
Hypertension, *n* (%)	206 (48.0)	16 (42.1)	0.503
Initial RRT, *n* (%)	172 (40.1)	18 (47.4)	0.394
Nephrotic syndrome, *n* (%)	25 (5.8)	3 (7.9)	0.489
Urinary protein (g/24 h)	1.7 (1.1–3.1)	2.0 (1.1–3.0)	0.956
Urine red blood cell count (10^4/ml)	400 (112–1000)	288 (31–833)	0.192
Serum creatinine (μmol/L)	398 (191–595)	415 (221–776)	0.264
Serum albumin (g/L)	34.3 (5.1)	32.0 (5.5)	0.009
Hemoglobin	83.0 (71.5–96.0)	79.0 (67.8–91.5)	0.299
Anemia, *n* (%)	389 (90.7)	35 (92.1)	1.000
Serum complement 3, (g/L)	0.8 (0.8–1.0)	0.9 (0.8–1.0)	0.972
C reactive protein, (mg/L)	6.8 (0.8–40.2)	17.7 (3.2–69.6)	0.061

Values are given as the mean (standard deviation) or median (interquartile range). *AAGN* antineutrophil cytoplasmic antibody–associated glomerulonephritis; *ANCA* antineutrophil cytoplasmic antibody; *MPO* myeloperoxidase; *PR3* protease 3; *MPA* microscopic polyangiitis; *GPA* granulomatosis with polyangiitis; *EGPA* eosinophilic granulomatosis with polyangiitis; *ENT* ears, nose, and throat; *BVAS* Birmingham vasculitis activity score; *RRT* renal replacement therapy

During the treatment, 187 cases (59.7%) in the MPO group and 14 cases (51.9%) in the PR3 group achieved remission. There was no significant difference in the remission rates between groups ($P = 0.424$).

The median follow-up time was 21 months. Thirty-nine (20.9%) patients in the MPO group relapsed. Seven (50%) patients in the PR3 group relapsed. The relapse rate of the MPO group was significantly lower than the PR3 group ($P = 0.020$). There were no differences between the two groups in median relapse time (22 months vs. 18 months, $P = 0.183$). The 5-year relapse-free renal survival rate of AAGN was 74.9%, and it was significantly higher in the MPO group than in the PR3 group (77.6% vs. 41.3%, $P = 0.003$) (Fig. 3a). Adjusting for baseline clinical data on

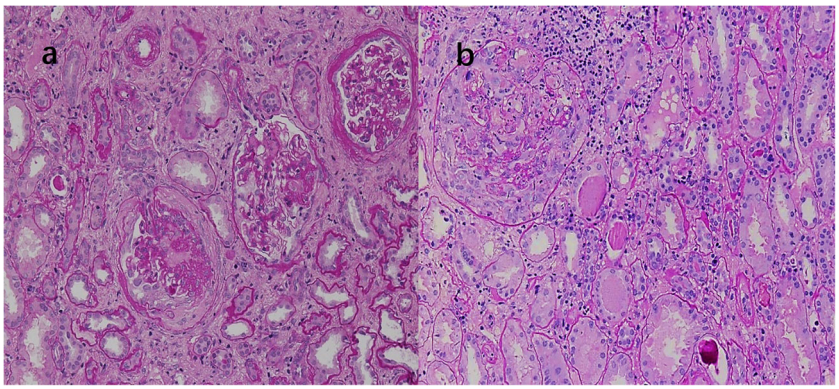

Fig. 2 Renal histological comparisons between two types of ANCA-associated glomerulonephritis. Renal biopsies show glomerular fibrous crescents and segmental glomerulosclerosis with chronic tubulointerstitial fibrosis from a patient in MPO group (**a**, PAS × 200) and glomerular circular cellular crescent with prominent acute tubulointerstitial inflammation from a patient in PR3 group (**b**, PAS × 200)

patients with remission, multivariate Cox regression analysis revealed that PR3-ANCA was significantly associated with a higher risk of relapse (HR 3.570, $P = 0.011$) (Table 4).

Of the 467 patients, 52 were lost to follow-up, and the remaining 415 were included in the renal survival analysis. A total of 382 patients were in the MPO group, and 33 patients were in the PR3 group. The median follow-up time was 16 months (2–49 months), and 207 patients (49.9%) ultimately progressed to ESRD. The 5-year renal survival rate was 46.9%. The incidence of ESRD tended to be higher in the PR3 group (20, 60.6%) than in the MPO group (187, 49.0%, $P = 0.210$), and the 5-year renal survival rate tended to be lower in the PR3 group than in the MPO group (28.9% vs. 48.4%, $P = 0.106$). Neither difference was statistically significant (Fig. 3b).

Discussion

The present study compared the clinical and histological features and outcomes of two ANCA serotypes in Chinese patients. We found that MPO-AAGN was predominant and presented more commonly in females. The prevalence of MPO-AAGN was tenfold greater than that of PR3-AAGN. An epidemiological study of 426 AAVs in China also confirmed that MPO-AAGN was dominant [6]. Although this disease is widely recognized to be prevalent in middle-aged and older people, the issue of age differences between MPO-AAGN and PR3-AAGN remains controversial. The present study found that the median age of the MPO-AAGN group was 11 years older than that of the PR3-AAGN group, which suggests a more insidious onset of MPO-AAGN [13, 14].

The clinical phenotype of AAV correlates with ANCA specificity. However, this correlation is not absolute, and some bias exists. MPA was the major type in the present study, and it accounted for 88.9%. A total of 6.3% of patients in the MPO group were diagnosed as GPA, and 68.4% of the patients in the PR3 group were MPA, which is 2.6-fold higher than GPA. A previous study also found that the incidence of MPO-ANCA positive MPA was approximately 80% [6], and 60% of GPA patients also exhibited MPO-ANCA positivity [4, 15, 16]. An overlap between the two types of classification exists for various reasons.

Table 2 Renal pathological features of different ANCA-associated glomerulonephritis

	MPO-AAGN ($n = 300$)	PR3-AAGN ($n = 30$)	P value
Pathological type, *n* (%)			
Sclerotic class	70 (23.3)	7 (23.3)	1.000
Focal class	41 (13.7)	5 (16.7)	0.587
Crescentic class	55 (18.3)	11 (36.7)	0.028
Mixed class	134 (44.7)	7 (23.3)	0.032
Pathological changes			
Cellular crescent ratio (%)	31 (14–46)	43 (19–53)	0.178
Fibrous crescent ratio (%)	0 (0–8)	0 (0–8)	0.994
Glomerulosclerosis ratio (%)	28 (10–48)	31 (7–49)	0.924
Glomerular capillary necrosis, *n* (%)	211 (70.3)	16 (53.3)	0.064
Acute tubule-interstitial lesion score	1.0 (1.0–2.0)	2.0 (1.0–2.5)	0.007
Chronic tubule-interstitial lesion score	2.0 (1.0–2.0)	1.3 (1.0–2.0)	0.069
Vascular necrosis, *n* (%)	47 (15.7)	6 (20.0)	0.600

Values are given as the median (interquartile range). *AAGN* antineutrophil cytoplasmic antibody–associated glomerulonephritis; *MPO* myeloperoxidase; *PR3* protease 3

Table 3 Initial induction treatment of different ANCA-associated glomerulonephritis

	MPO group ($n = 313$)	PR3 group ($n = 27$)	P value
IA, *n* (%)	28 (8.9)	1 (3.7)	0.716
DFPP, *n* (%)	44 (14.1)	4 (14.8)	1.000
PE, *n* (%)	8 (2.6)	0 (0.0)	1.000
P + CTX, *n* (%)	129 (41.2)	14 (51.9)	0.313
P + MMF, *n* (%)	95 (30.4)	8 (29.6)	1.000
MT, *n* (%)	7 (2.2)	1 (3.7)	0.488
P, *n* (%)	82 (26.2)	4 (14.8)	0.251

AAGN antineutrophil cytoplasmic antibody–associated glomerulonephritis; *ANCA* antineutrophil cytoplasmic antibody; *MPO* myeloperoxidase; *PR3* protease 3; *IA* immunoadsorption; *DFPP* double filtration plasmapheresis; *PE* plasma exchange; *P* prednisone; *CTX* cyclophosphamide; *MMF* mycophenolate mofetil; *MT* multiple target therapy

Overall, the genetic background is heterogeneous, and regional differences in the incidence of AAV are well known. MPA is more common in southern Europe, Asia, and the Pacific, and GPA is more common in northern parts of the world [17–23]. Genomics studies have confirmed that major histocompatibility complex (MHC) polymorphisms are the primary cause of these distinctions [24–26].

Therefore, the clinical classification is inaccurate. The 2012 CHCC categorized the disease primarily based on clinical features, and this classification was more subjective. Patients will be misclassified as MPA when important evidence (e.g., granuloma, asthma, or eosinophil aggregation) is not found at the time of diagnosis. Some unclassified AAVs are often included in the MPA category. Therefore, the classification method based on ANCA is more objective and accurate than clinical classification.

AAV is a systemic disease that often involves the lung, ENT, skin, joint, eye, and skeletal muscle. There was no difference in lung involvement between the two serotypes of AAGN in the present study. However, the incidences of joint, ENT, skin, and eye involvements were lower in the MPO-AAGN group than in the PR3-AAGN group. These results indicated that the extra-renal symptoms of MPO-AAGN were not as significant as these symptoms in PR3-AAGN. However, the incidence of pulmonary manifestations, such as pulmonary hemorrhage, pulmonary nodules, and interstitial pneumonia, were inconsistent [27–32]. ENT and eye involvement are common in PR3-AAV patients. There were no differences in the incidences of central nervous system, skin, or heart involvement between groups [29, 33–35]. Patients with small vasculitis, including those that are ANCA-negative or without renal involvement, were observed in previous studies. Our study observed Chinese AAV patients with renal involvement, which may lead to a different observation. Although there were no differences in clinical manifestations, serum creatinine, urine protein levels, or the proportion of initial renal replacement therapy between the groups, the renal pathological changes differed. Crescentic class and acute tubulointerstitial lesions were more common in the PR3 group, and the proportion of cell crescents and BVAS scores were higher than those in the MPO group. Together, these results illustrate that the disease was more active in patients with PR3-ANCA positivity. Previous studies suggested that MPO-ANCA-associated vasculitis patients exhibited more renal interstitial fibrosis and chronic lesions [36]. In the past decade, with the popularity of renal biopsy, typical manifestations of active stages were found more easily, while PR3-AAGN showed a rapid course with many extra-renal manifestations. We suggest that MPO-AAGN and PR3-AAGN exhibit fundamentally different pathogeneses and are completely different diseases.

Most patients achieve remission with immunosuppressive therapy, but 22.9% of patients experienced relapse in the present study, which is lower than a previous report in China [37]. The lower relapse rate might be related to the higher proportion of MPO-AAGN patients in our study. We found that patients with PR3-AAGN exhibited a 3.57-fold higher risk for relapse than MPO-AAGN patients, which is consistent with other findings that the risk of relapse was associated with the ANCA serotype. PR3-ANCA was 1.6–3.2-fold higher for relapse [38, 39], and 2.93-fold higher in patients of Hispanic ethnicity [40].

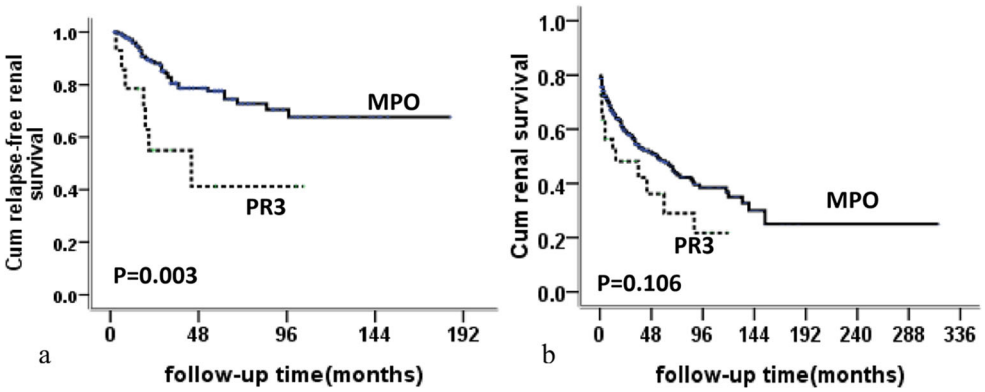

Fig. 3 Response to treatment and renal survival. **a** The relapse-free renal survival rate of different AAGNs. **b** The renal survival rates of different ANCA-associated glomerulonephritis

Table 4 Risk factors of renal relapse in ANCA-associated glomerulonephritis

	P	HR (95%CI)
Gender (male = 0, female = 1)	0.845	1 (3.7)
Age (< 65 years old = 0, ≥ 65 years old = 1)	0.947	4 (14.8)
Initial RRT (no = 0, yes = 1)	0.499	0 (0.0)
Lung involvement (no = 0, yes = 1)	0.449	14 (51.9)
BVAS (< 20 = 0, ≥ 20 = 1)	0.629	8 (29.6)
Hb (< 110 g/L = 0, ≥ 110 g/L = 1)	0.756	1 (3.7)
Alb (< 35 g/L = 0, ≥ 35 g/L = 1)	0.758	4 (14.8)
Scr (< 176.8 umol/L)	Reference	
Scr (176.8–442 umol/L)	0.186	0.406 (0.107–1.545)
Scr (> 442 umol/L)	0.885	0.928 (0.338–2.552)
ANCA (PR3 = 0, MPO = 1)	0.011	3.570 (1.343–9.487)
Treatment regimens (glucocorticoids = 0, glucocorticoids combined with immunosuppressant = 1)	0.401	0.676 (0.270–1.688)

AAGN antineutrophil cytoplasmic antibody–associated glomerulonephritis; *RRT* renal replacement therapy; *BVAS* Birmingham vasculitis activity score; *Hb* hemoglobin; *Alb* albumin; *Scr* serum creatinine; *ANCA* antineutrophil cytoplasmic antibody; *PR3* protease 3; *MPO* myeloperoxidase

The prognosis of AAGN is poor. Nearly 50% of the patients in the present study advanced to ESRD, and the 5-year renal survival rate was less than 50%. The renal survival of AAGN was inconsistent. Some studies reported no differences between the two AAGNs with different ANCAs [40, 41], and other studies found lower renal survival rates in MPO-AAGN [42]. The incidence of ESRD in the PR3-AAGN group in the present study was 12% higher than that in the MPO-AAGN group, and the 5-year renal survival rate was 20% lower in the PR3-AAGN group than that in the MPO-AAGN group. Patients exhibited more crescentic class in renal biopsies and higher relapse rates during follow-up, which might be associated with the undesirable therapeutic responses and poor prognosis. Rituximab was more effective than cyclophosphamide in the treatment of patients with relapsing AAGN [43]. However, only a few patients with relapsing disease received rituximab in this study, which may have affected the long-term renal survival.

Our study included the largest cohort of AAGN investigated to date, but it has several limitations. First, all of the patients included in the study were of Chinese ethnicity, and this was a single-center study. Therefore, our results may not be generalizable to other ethnicities. Second, the sample size of PR3-AAGN patients was small, which may affect the statistical power for differences between MPO-AAGN and PR3-AAGN. Third, the follow-up time was limited. Therefore, the conclusions of this study require further validation.

In conclusion, MPO-ANCA was the predominant type of ANCA-associated vasculitis and renal disease in Chinese patients. The epidemiological characteristics, extra-renal involvement, and histological classes and outcomes were significantly different between these two AAGNs. MPO-AAGN and PR3-AAGN should be distinguished as two different diseases.

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Compliance with ethical standards Ethical approval of the study was obtained from the ethics committee of Nanjing Jinling Hospital, Nanjing, China. This study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. All patients gave their informed consent prior to their inclusion in the study.

Disclosures None.

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