J Rheum Dis 2023;30(4):251-259
https://doi.org/10.4078/jrd.2023.0031
pISSN: 2093-940X, eISSN: 2233-4718

Original Article

Recovery and long-term renal outcome of patients with anti-neutrophil cytoplasmic antibody-associated vasculitis who are on dialysis at presentation

Yeo-Jin Lee, M.D.[1], Soo-Min Ahn, M.D., Ph.D.[1], Ji-Seon Oh, M.D., Ph.D.[2], Yong-Gil Kim, M.D., Ph.D.[1], Chang-Keun Lee, M.D., Ph.D.[1], Bin Yoo, M.D., Ph.D.[1], Seokchan Hong, M.D., Ph.D.[1]

[1]Department of Rheumatology, Asan Medical Center, University of Ulsan College of Medicine, [2]Department of Information Medicine, Big Data Research Center, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

Objective: Renal involvement in anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) can lead to severe renal dysfunction requiring dialysis at diagnosis. We aimed to study the clinical and pathologic characteristics of patients with AAV dependent on dialysis at presentation and the long-term renal outcomes of patients who recovered from dialysis.

Methods: This retrospective study analyzed data of patients diagnosed with AAV who were on dialysis from July 2005 to May 2021 at a single tertiary center in Korea.

Results: Thirty-four patients were included in the study (median age: 64.5 years, females: 61.8%), of which 13 discontinued and 21 continued dialysis. The proportion of normal glomeruli (p<0.001) and interstitial fibrosis (p=0.024) showed significant differences between both groups. Multivariable analysis showed that the proportion of normal glomeruli was associated with dialysis discontinuation (odds ratio=1.29, 95% confidence interval 0.99~1.68, p=0.063), although without statistical significance. Treatment modalities, including plasmapheresis, did not show significance with dialysis discontinuation. In the follow-up analysis of 13 patients who had discontinued dialysis for a median of 81 months, 12 did not require dialysis, and their glomerular filtration rate values significantly increased at follow-up time compared to when they stopped dialysis (37.5 [28.5~45.5] vs. 24.0 [18.5~30.0] mL/min/1.73 m^2; p=0.008).

Conclusion: Approximately 38% of AAV patients on dialysis discontinued dialysis, and the recovered patients had improved renal function without dialysis during longer follow-up. Patients with AAV on dialysis should be given the possibility of dialysis discontinuation and renal recovery, especially those with normal glomeruli in kidney pathology.

Keywords: Dialysis, Anti-neutrophil cytoplasmic antibody-associated vasculitis

INTRODUCTION

Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a small vessel vasculitis commonly involving the kidneys and lungs [1]. Depending on the subtype, the prevalence of renal involvement is almost 100% for microscopic polyangiitis (MPA) and greater than 70% for granulomatosis with polyangiitis [2]. Renal involvement in AAV is important due to its high frequency and association with poor prognosis. Approximately 20% or more of AAV patients with renal involve-

Received May 22, 2023; **Revised** July 19, 2023; **Accepted** August 4, 2023, **Published online** September 6, 2023

Corresponding author: Seokchan Hong, https://orcid.org/0000-0001-8722-3124
Department of Rheumatology, Asan Medical Center, University of Ulsan College of Medicine, 88 Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Korea. **E-mail:** medivineluke@gmail.com

*The abstract of this paper has been previously presented as a poster at the 2023 European Alliance of Associations for Rheumatology (EULAR) conference.

ment have been shown to have progressed to end-stage renal disease (ESRD) and were on dialysis during follow-up [3-6]. The risk of patients' survival is significantly related to impaired renal function at diagnosis, with a hazard ratio of 2.63~4.45 [7-10].

A significant proportion of patients with AAV who have severe renal dysfunction require dialysis at presentation [11,12]. However, when treatment with immunosuppressants is effective, dialysis may be discontinued in 28% to 70% of patients with AAV within 6 to 12 months [13-15]. Kidney pathologies, such as the proportion of normal glomeruli and the extent of tubular atrophy or interstitial fibrosis, have been reported to be associated with dialysis discontinuation [15]. In terms of treatment, however, the effectiveness of rituximab, cyclophosphamide, or plasmapheresis for dialysis discontinuation remains controversial [13,16-18]. Furthermore, the long-term renal prognosis of patients after recovery from dialysis in AAV is not known. Therefore, we aimed to identify the clinicopathologic characteristics of patients who required dialysis at the time of AAV diagnosis and long-term renal prognosis, including whether they can remain dialysis-free after dialysis discontinuation.

MATERIALS AND METHODS

Patients and data collection

We retrospectively analyzed the data of patients diagnosed with AAV who were on dialysis due to renal involvement from July 2005 to May 2021 at a single tertiary center in Seoul, Korea. Diagnosis of AAV was based on the International Chapel Hill Consensus Conference Nomenclature of Vasculitides, and kidney involvement of AAV was clinically or histologically confirmed [19]. The patients on dialysis at the time of AAV diagnosis were included in our study. Patients who stopped dialysis during follow-up were classified into the 'discontinuation of dialysis' group, and those who continued dialysis were classified into the 'on dialysis' group. This study was performed in accordance with the Declaration of Helsinki and its later amendments. The study protocol was approved by the Institutional Review Board of Asan Medical Center (Seoul, South Korea) (2021-1357). The requirement for informed consent was waived, given the retrospective nature of the study.

The following data from electronic medical records were reviewed—age, sex, body mass index (BMI), ANCA type, comorbidities, estimated glomerular filtration rate (eGFR), urine analysis, erythrocyte sedimentation rate, C-reactive protein (CRP), and treatment administered, including corticosteroid doses. eGFR was calculated using the following Modification of Diet in Renal Disease equation: $175\times[\text{serum creatinine (mg/dL)}]^{-1.154}\times(\text{age})^{-0.203}\times(0.742 \text{ if female})$. Disease activity was measured using the Birmingham vasculitis activity score (BVAS) version 3.0. [20]. The disease remission was defined as 0 or persistence as 1 BVAS within 1 year and requiring less than 7.5 mg

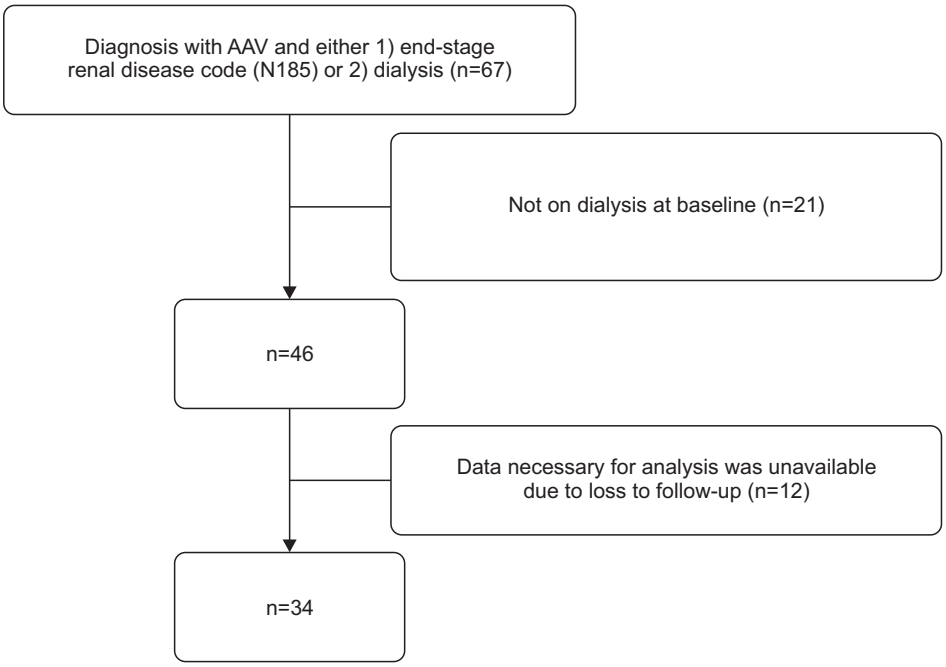

Figure 1. Patient selection flowchart. AVV: anti-neutrophil cytoplasmic antibody-associated vasculitis.

of prednisolone [21,22]. The results of kidney biopsy were collected and classified into four types, according to Berden et al. [23]. Histopathologic findings, including interstitial infiltration, fibrosis, and tubular atrophy, were marked as –, +, ++, and +++ [14,15]. Clinical characteristics, including creatinine levels and dialysis requirements after the follow-up period, were assessed.

Statistical analysis

Categorical variables were described as percentages (%) and continuous variables as median (interquartile ranges [IQR]) or mean values (standard deviation). Parametric and nonparametric data were compared using the t-test and Mann–Whitney U test, respectively. Categorical variables were compared using the Chi-squared test and Fisher's exact test. Logistic regression was performed with the discontinuation of dialysis as the dependent variable for the univariable and multivariable analysis. When performing multivariable analysis, factors with a p-value >0.2 in univariate analysis were excluded to favor the criterion of par-

Table 1. Baseline characteristics of patients with or without the discontinuation of dialysis

	All (n=34)	Discontinuation of dialysis (n=13)	On dialysis (n=21)	p-value
Age (yr)	64.5 (60.0~72.3)	64.0 (60.0~69.5)	67.0 (60.0~75.5)	0.467
Female	21 (61.8)	7 (53.8)	14 (66.7)	0.455
Body mass index (kg/m^2)	23.2±3.1	22.8±3.3	23.4±3.0	0.567
BVAS	20.3±5.6	21.3±5.0	19.7±6.0	0.415
Duration of follow up (mo)	35.5 (16.8~93.0)	81.0 (21.5~105.5)	28.0 (12.5~71.0)	0.132
Time from symptom onset to treatment (day)	33.0 (18.5~51.5)	29.0 (16.0~35.0)	34.0 (22.5~56.5)	0.279
Achievement of remission	24 (70.6)	10 (76.9)	14 (66.7)	0.704
Duration from symptom onset to treatment ≤1 mo	19 (55.9)	5 (38.5)	14 (66.7)	0.107
ANCA-associated vasculitis type				0.313
MPA	25 (73.5)	9 (69.2)	16 (76.2)	
GPA	8 (23.5)	3 (23.1)	5 (23.8)	
ANCA type by ELISA				0.434
Anti-PR3	7 (20.6)	2 (15.4)	5 (23.8)	
Anti-MPO	25 (73.5)	9 (69.2)	16 (76.2)	
Both anti-PR3 and anti-MPO	1 (2.9)	1 (7.7)	0 (0.0)	
Manifestations at enrollment				
Pulmonary involvement	24 (70.6)	9 (69.2)	15 (71.4)	0.891
Alveolar hemorrhage	6 (17.6)	1 (7.7)	5 (23.8)	0.370
Ear, nose, and throat	3 (8.8)	3 (23.1)	0 (0.0)	0.048*
Neurologic involvement	5 (14.7)	3 (23.1)	2 (9.5)	0.348
Comorbidity				
Hypertension	14 (41.2)	8 (61.5)	6 (28.6)	0.058
Diabetes mellitus	4 (11.8)	3 (23.1)	1 (4.8)	0.274
Chronic kidney disease	4 (11.8)	2 (15.4)	2 (9.5)	0.627
Coronary artery disease	1 (2.9)	0 (0.0)	1 (4.8)	>0.999
Renal profiles at baseline				
eGFR (mL/min/1.73 m^2)	8.0 (6.8~10.3)	10.0 (9.0~13.0)	7.0 (5.5~8.5)	<0.001*
Hematuria (>10/HPF)†	23 (74.2)	9 (75.0)	14 (73.7)	0.437
Proteinuria (dipstick, > +1)	19 (55.9)	5 (38.5)	14 (66.7)	0.067
Laboratory data				
ESR, (mm/h)	61.39±39.83	70.0±41.0	54.8±39.2	0.376
CRP (mg/dL)	7.6 (2.5~3.5)	9.5 (4.0~12.9)	5.4 (1.2~13.8)	0.507

Values are median (interquartile range), number (%), or mean±standard deviation. BVAS: Birmingham Vasculitis Activity Score, ANCA: antineutrophil cytoplasmic antibody, MPA: microscopic polyangiitis, GPA: granulomatosis polyangiitis, Anti-PR3: anti-proteinase 3, Anti-MPO: anti-myeloperoxidase, eGFR: estimated glomerular filtration rate, HPF: high-power field, ESR: erythrocyte sedimentation rate, CRP: C-reactive protein. *Statistically significant (p<0.05). †The value of microscopic hematuria had three missing values.

simony. All statistical analyses were performed using SPSS software, version 21.0 (IBM Corp., Armonk, NY, USA). A p-value of <0.05 was considered statistically significant.

RESULTS

Baseline characteristics

A total of 34 patients with AAV who were on dialysis at baseline were included in the present study (Figure 1). Of these patients, 13 discontinued dialysis after treatment for AAV, and the remaining 21 continued to be dialysis-dependent. The baseline characteristics of total patients and a comparison of the two groups according to dialysis dependency are shown in Table 1. The median age was 64.5 years (IQR, 60.0~72.3 years), and the proportion of female patients was 61.8% (21/34). The mean BVAS score was 20.3±5.6 at baseline, which was not significantly different between the two groups. The duration from symptom onset to treatment was 33.0 days (IQR, 18.5~51.5 days). There was no significant difference between the two groups with respect to the clinical features, including AAV subtypes, co-morbidities, and organ involvement, except ear-nose-throat manifestation. In terms of renal parameters, the baseline eGFR value of the dialysis-discontinued group was 10.0 mL/min/1.73 m^2 (IQR 9.0~13.0 mL/min/1.73 m^2), which was significantly higher than that of the dialysis-dependent group (7.0 mL/min/1.73 m^2 [IQR 5.5–8.5 mL/min/1.73 m^2]; p<0.001).

Treatment of total patients with or without the discontinuation of dialysis

Thirty-two patients were treated with intravenous or oral cyclophosphamide as an induction therapy for AAV (Table 2). Rituximab was administered as first-line induction therapy in two patients. During induction therapy, 50% of the patients were administered pulse (≥500 mg/day) corticosteroids, and high- and medium-dose corticosteroids were used in 41.2% and 8.8% of the patients, respectively. Plasmapheresis was performed in 11 patients (32.4%). As maintenance therapy, azathioprine and mycophenolate mofetil were used in 52.9% and 5.9% of the patients, respectively. There was no significant difference between the two groups in terms of immunomodulatory therapy, including plasmapheresis, for AAV.

Histopathologic findings of renal biopsy of patients with AAV

Of the 34 patients, a kidney biopsy was performed in 24 patients, and the histopathologic results were compared between patients who continued dialysis and those who discontinued dialysis (Table 3). The median number of total glomeruli present in the biopsy specimens was 16.0 (IQR, 11.0~20.5), and the number of normal glomeruli was 2.0 (IQR 0.3~5.0). Interestingly, patients in the dialysis discontinuation group had significantly higher numbers (5.0 [2.5~11.5] vs. 1.0 [0.0~3.0]; p=0.002) and percentages (46.7% [18.0%~69.2%] vs. 8.2% [0.0%~12.8%], p<0.001) of normal glomeruli than those in the dialysis-dependent group. While eight patients had interstitial fibrosis of 2+ or

Table 2. Treatment of patients with or without the discontinuation of dialysis

	All (n=34)	Discontinuation of dialysis (n=13)	On dialysis (n=21)	p-value
Induction therapy				
IV cyclophosphamide	7 (20.6)	3 (23.1)	4 (19.0)	0.781
PO cyclophosphamide	26 (76.5)	10 (76.9)	16 (76.2)	0.962
Rituximab	2 (5.9)	1 (7.7)	1 (4.8)	0.728
Plasmapheresis	11 (32.4)	3 (23.1)	8 (38.1)	0.370
Steroid doses during induction				0.984
Medium (≥0.5 mg/kg/day)	3 (8.8)	2 (15.4)	1 (4.8)	
High (≥1 mg/kg/day)	14 (41.2)	4 (30.8)	10 (47.6)	
Pulse (≥ 500 mg/day)	17 (50.0)	7 (53.8)	10 (47.6)	
Maintenance therapy				
Azathioprine	18 (52.9)	10 (76.9)	8 (38.1)	0.055
Mycophenolate mofetil	2 (5.9)	2 (15.4)	0 (0.0)	0.068

Values are presented as number (%). IV: intravenous, PO: per oral.

Table 3. Histopathologic findings of patients with or without the discontinuation of dialysis

	All (n=24)	Discontinuation of dialysis (n=9)	On dialysis (n=15)	p-value
Total glomeruli (n)	16.0 (11.0~20.5)	13.0 (10.5~22.0)	18.0 (12.0~21.0)	0.482
Normal glomeruli (n)	2.0 (0.3~5.0)	5.0 (2.5~11.5)	1.0 (0.0~3.0)	0.002*
Normal glomeruli (%)	12.2 (4.7~36.4)	46.7 (18.0~69.2)	8.2 (0.0~12.8)	<0.001*
Fibrinoid necrosis (n)	2.0 (0.0~3.0)	0.0 (0.0~2.5)	2.0 (0.0~3.0)	0.410
Fibrinoid necrosis (%)	4.1 (0.0~20.7)	0.0 (0.0~21.6)	7.3 (0.0~21.1)	0.741
Cellular crescents	7.3 (0.0~37.8)	9.1 (0.0~46.5)	5.6 (0.0~35.7)	0.976
Fibrous crescents	0.0 (0.0~0.0)	0.0 (0.0~0.0)	0.0 (0.0~0.0)	0.795
Fibrocellular crescents	14.3 (0.0~36.0)	0.0 (0.0~29.4)	20.0 (11.1~49.0)	0.101
Glomerulosclerosis	3.0 (3.0~3.0)	3.0 (3.0~3.0)	3.0 (3.0~3.0)	0.646
Interstitial infiltration (–/+/++/+++)	7/9/4/4	4/4/1/0	3/5/3/4	0.061
Interstitial fibrosis (–/+/++/+++)	8/9/4/5	5/4/1/0	3/5/3/5	0.024*
Tubular atrophy (–/+/++/+++)	6/10/4/4	3/5/0/1	3/5/4/3	0.168
Arteriosclerosis (–/+)	11/13	4/5	7/8	0.918
Type				0.525
Sclerotic	3 (12.5)	0 (0.0)	3 (20.0)	
Focal	4 (16.7)	4 (44.4)	0 (0)	
Crescentic	14 (58.3)	4 (44.4)	10 (66.7)	
Mixed	3 (12.5)	1 (11.1)	2 (13.3)	

Values are median (interquartile range) or number (%). *Statistically significant (p<0.05).

Table 4. Uni- and multi-variate analysis of predictors associated with the discontinuation of dialysis

Predictor	Univariate		Multi-variate	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age	0.97 (0.91~1.03)	0.370		
Sex, male	0.58 (0.14~2.41)	0.583		
ANCA type	0.71 (0.11~4.44)	0.715		
Duration between symptom and treatment	1.00 (0.98~1.01)	0.714		
BVAS	1.06 (0.93~1.20)	0.406		
Percentage of normal glomeruli	1.23 (0.99~1.54)	0.059	1.29 (0.99~1.68)	0.063
Presence of interstitial fibrosis	0.31 (0.05~1.94)	0.212		
Presence of tubular atrophy	0.50 (0.08~3.27)	0.469		
Steroid, high dose compared with pulse	0.57 (0.13~2.58)	0.467		
Maintenance therapy	4.44 (0.94~21.00)	0.060	9.41 (0.25~356.54)	0.227
Plasma exchange	0.49 (0.10~2.33)	0.367		
Achievement of remission	1.67 (0.34~8.07)	0.526		
Duration from symptom onset to treatment ≤ 1 mo	0.31 (0.07~1.32)	0.113		
eGFR (mL/min/1.73 m^2)	1.12 (0.95~1.32)	0.192	0.97 (0.81~1.16)	0.736

OR: odds ratio, CI: confidence interval, ANCA: antineutrophil cytoplasmic antibody, BVAS: Birmingham Vasculitis Activity Score, eGFR: estimated glomerular filtration rate.

higher in the group who continued dialysis, interstitial fibrosis was found in only one patient in the group who discontinued dialysis. There was, however, no significant difference in certain types of histopathologic findings according to the four different classifications (sclerotic, focal, crescentic, and mixed) [23].

Predictors associated with discontinuation of dialysis

To determine the clinicopathologic factors related to the discontinuation of dialysis in patients who were under dialysis at the time of AAV diagnosis, we performed a logistic regression analysis (Table 4). Clinical features, including age, sex, and BVAS, did not show a significant association with dialysis discontinuation. In addition, treatment modality and baseline eGFR were not associated with recovery from dialysis. In the pathologic findings, the percentage of normal glomeruli tended to be associated with dialysis discontinuation at follow-up (odds ratio=1.29, 95% confidence interval 0.99~1.68, p=0.063), although this association did not reach statistical significance.

Table 5. Long-term follow-up of patients who discontinued the dialysis

	All (n=13)
Age (yr)	64.0 (60.0~69.5)
Female	7 (53.8)
Duration of follow up (mo)	81.0 (21.5~105.5)
Duration of dialysis (day)	36.0 (33.5~126.5)
Remission	10 (76.9)
Renal profile at the time of dialysis discontinuation	
Creatinine (mg/dL)	2.60 (2.05~3.16)
eGFR (mL/min/1.73 m²)	24.0 (18.5~30.0)
Induction therapy	
IV cyclophosphamide	3 (23.1)
PO cyclophosphamide	10 (76.9)
Rituximab	1 (4.8)
Maintenance therapy	
Azathioprine	10 (76.9)
Mycophenolate mofetil	2 (15.4)
Duration of therapy (day)	594.0 (119.5~2,160.5)
Steroid doses	
Duration of therapy (day)	1,067.0 (427.5~1,825.5)
Cumulative dose (g)	10.23 (8.74~12.70)
Renal profile at last follow-up	
Creatinine (mg/dL)	1.85 (1.34~2.02)
eGFR (mL/min/1.73 m²)	36.0 (27.5~45.0)
On re-dialysis	1 (7.7)
BVAS at last follow-up	
0	9 (69.2)
1 (persistent)	2 (15.4)
4	1 (7.7)
6	1 (7.7)

Values are presented as median (interquartile range) or number (%). eGFR: estimated glomerular filtration rate, IV: intravenous, PO: per oral, BVAS: Birmingham Vasculitis Activity Score.

Long-term follow-up of patients who discontinued dialysis

Thirteen patients with AAV who had discontinued the dialysis were further followed up for a median of 81 months (21.5~105.5 months). The total duration of dialysis was a median of 36.0 days (IQR, 33.5~126.5 days), and all patients stopped dialysis within 278 days after dialysis initiation (Table 5). At the time of dialysis discontinuation, the median creatinine level of patients was 2.60 mg/dL (2.05~3.16 mg/dL), and the median eGFR value was 24.0 mL/min/1.73 m² (18.5~30.0 mL/min/1.73 m²). During follow-up, only one patient restarted dialysis due to acute kidney injury with septic shock at 2,337 days after discontinuation. The remaining 12 patients were independent of dialysis, with a median eGFR value of 37.5 mL/min/1.73 m² (28.5~45.5 mL/min/1.73 m²) at the last follow-up. Notably, eGFR values were significantly higher at the last follow-up than at the time of dialysis discontinuation (Figure 2). At the last follow-up, 11 patients were still in remission based on the BVAS (0 or persistent 1).

DISCUSSION

In the present study, the data of 34 patients on dialysis at the time of AAV diagnosis were analyzed. We found that 38.2% of patients (n=13) were able to discontinue dialysis after treatment for AAV. The patients who discontinued dialysis had significantly higher numbers and proportions of normal glomeruli than those who depended on dialysis, and there was a trend, although not statistically significant, between the proportion of normal glomeruli and dialysis discontinuation. Upon analysis of follow-up data of patients with dialysis discontinuation, we

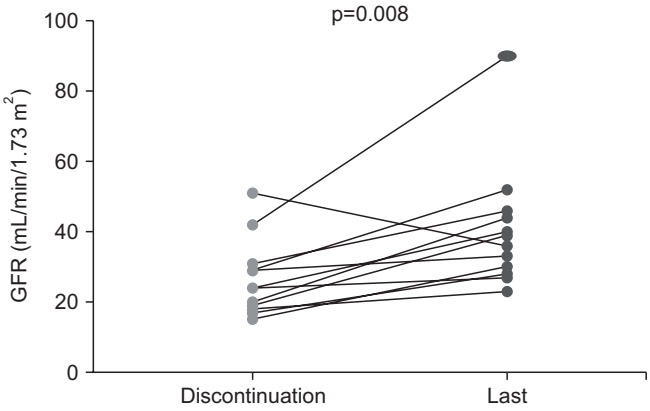

Figure 2. The comparison of values of estimated glomerular filtration rate (eGFR) of patients (n=12) with dialysis discontinuation between the time of dialysis discontinuation and time after the follow-up period.

found that most patients remained dialysis-free with an improvement in renal function.

The present study demonstrated that in the long-term follow-up of patients who discontinued dialysis, most patients remained off dialysis. Previous studies mainly focused on short-term outcomes of whether dialysis could be discontinued in AAV patients after induction treatment [14,15]. A previous study with data of patients on dialysis from the Plasma Exchange for Renal Vasculitis (MEPEX) trial aimed to identify risk factors associated with the chances of dialysis independence over death after 12 months of treatment [14]. This study showed that recovery from dialysis dependence was related to histological features, including the proportion of normal glomeruli and the extent of tubular atrophy. In a study of a similar design from a single Chinese center, histological features (such as, the proportion of normal glomeruli, extent of tubular atrophy, and extent of interstitial fibrosis) but not clinical factors (such as, age and sex) were independently associated with dialysis discontinuation 6 months after diagnosis [15]. Similar to these previous studies, we found that the proportion of normal glomeruli in the kidney tissue was related to recovery from dialysis in the present study. Considering that kidney biopsies are not routinely performed when AAV patients are already on dialysis but were performed in 70.6% (24/34) of the patients in our study, indicates that kidney biopsies can be more actively utilized to predict renal prognosis even in patients with severe renal dysfunction.

In terms of treatment, data on patients with AAV on dialysis was limited. There have been conflicting results on the efficacy of plasmapheresis as adjuvant therapy in severe AAV. While early data in the MEPEX trial showed a benefit of plasmapheresis in reducing the requirement of dialysis at 12 months, recent studies, including the PEXIVAS (plasma exchange and glucocorticoid dosing in the treatment of antineutrophil cytoplasm antibody associated vasculitis) trial conducted in patients with severe AAV including dialysis, demonstrated that plasmapheresis did not reduce the incidence of death or ESRD in patients with AAV [16-18]. In contrast, in a recent study involving 66 patients under dialysis at baseline, the use of plasmapheresis in patients receiving cyclophosphamide was associated with a higher dialysis-free rate at 12 months [13]. In the present study, there were no significant differences in therapeutic modalities, including induction therapy, plasmapheresis, and corticosteroid dosage between the dialysis-discontinuation and dialysis-dependent groups. Further studies are needed to identify the subgroups of patients with AAV on dialysis who would benefit from particular types of therapy.

Our study is notable in that it showed that dialysis was no longer required in the group that stopped dialysis for a follow-up of a median of 81 months. Additionally, except for one patient who restarted dialysis due to acute kidney injury with septic shock, patients who discontinued dialysis showed stable or even improving kidney function during follow-up. In the dialysis-discontinuation group, dialysis was required for a median of 36 days (IQR 33.5~126.5 days) and a maximum of 278 days. Thus, these findings suggest that long-term follow-up is necessary to determine the possibility of discontinuing dialysis. Furthermore, this study provides robust evidence regarding the long-term outcomes of renal AAV patients in South Korea.

The present study has several limitations. First, this study was conducted in a single center and included a small number of patients. Thus, it is difficult to generalize our results to the overall population. However, to the best of our knowledge, this is the first study covering the long-term data of patients after dialysis discontinuation. Second, although histologic findings in a kidney biopsy can be important, it was not performed in all patients.

In conclusion, 13 of 34 (38.2%) patients who required dialysis at the time of AAV diagnosis were able to discontinue dialysis. The higher proportion of normal glomeruli in kidney pathology and cessation of dialysis were positively correlated. Importantly, analysis of follow-up data of patients who discontinued dialysis showed that most patients had improved renal function without re-dialysis. Our findings suggest that patients with AAV on dialysis should be given the possibility of dialysis discontinuation and renal recovery, especially those with normal glomeruli in kidney pathology.

FUNDING

This study was supported by a grant (2022IP0062-1) from the Asan Institute for Life Sciences, Asan Medical Center, Seoul, Korea.

ACKNOWLEDGMENTS

None.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

AUTHOR CONTRIBUTIONS

Conceptualization: S.H., B.Y. Data curation or/and Analysis: Y.J.L. and J.S.O. Writing - original draft: Y.J.L., S.M.A. Writing - Review & Editing: Y.J.L., Y.G.K., C.K.L., and S.H. All authors read and approved the final manuscript.

ORCID

Yeo-Jin Lee, https://orcid.org/0000-0002-1050-673X
Soo-Min Ahn, https://orcid.org/0000-0002-9213-9768
Ji-Seon Oh, https://orcid.org/0000-0002-0205-6492
Yong-Gil Kim, https://orcid.org/0000-0002-8029-7355
Chang-Keun Lee, https://orcid.org/0000-0003-3653-7515
Bin Yoo, https://orcid.org/0000-0002-1836-5273
Seokchan Hong, https://orcid.org/0000-0001-8722-3124

REFERENCES

1. Almaani S, Fussner LA, Brodsky S, Meara AS, Jayne D. ANCA-associated vasculitis: an update. J Clin Med 2021;10:1446.
2. Sinico RA, Di Toma L, Radice A. Renal involvement in anti-neutrophil cytoplasmic autoantibody associated vasculitis. Autoimmun Rev 2013;12:477-82.
3. Day CJ, Howie AJ, Nightingale P, Shabir S, Adu D, Savage CO, et al. Prediction of ESRD in pauci-immune necrotizing glomerulonephritis: quantitative histomorphometric assessment and serum creatinine. Am J Kidney Dis 2010;55:250-8.
4. Rhee RL, Hogan SL, Poulton CJ, McGregor JA, Landis JR, Falk RJ, et al. Trends in long-term outcomes among patients with antineutrophil cytoplasmic antibody-associated vasculitis with renal disease. Arthritis Rheumatol 2016;68:1711-20.
5. Mohammad AJ, Segelmark M. A population-based study showing better renal prognosis for proteinase 3 antineutrophil cytoplasmic antibody (ANCA)-associated nephritis versus myeloperoxidase ANCA-associated nephritis. J Rheumatol 2014;41:1366-73.
6. Booth AD, Almond MK, Burns A, Ellis P, Gaskin G, Neild GH, et al. Outcome of ANCA-associated renal vasculitis: a 5-year retrospective study. Am J Kidney Dis 2003;41:776-84.
7. Mukhtyar C, Flossmann O, Hellmich B, Bacon P, Cid M, Cohen-Tervaert JW, et al. Outcomes from studies of antineutrophil cytoplasm antibody associated vasculitis: a systematic review by the European League Against Rheumatism systemic vasculitis task force. Ann Rheum Dis 2008;67:1004-10.
8. Sánchez Álamo B, Moi L, Bajema I, Faurschou M, Flossmann O, Hauser T, et al. Long-term outcomes and prognostic factors for survival of patients with ANCA-associated vasculitis. Nephrol Dial Transplant 2023;38:1655-65.
9. Bourgarit A, Toumelin PL, Pagnoux C, Cohen P, Mahr A, Guern VL, et al. Deaths occurring during the first year after treatment onset for polyarteritis nodosa, microscopic polyangiitis, and Churg-Strauss syndrome: a retrospective analysis of causes and factors predictive of mortality based on 595 patients. Medicine (Baltimore) 2005;84:323-30.
10. Flossmann O, Berden A, de Groot K, Hagen C, Harper L, Heijl C, et al. Long-term patient survival in ANCA-associated vasculitis. Ann Rheum Dis 2011;70:488-94.
11. Lionaki S, Hogan SL, Jennette CE, Hu Y, Hamra JB, Jennette JC, et al. The clinical course of ANCA small-vessel vasculitis on chronic dialysis. Kidney Int 2009;76:644-51.
12. Weidner S, Geuss S, Hafezi-Rachti S, Wonka A, Rupprecht HD. ANCA-associated vasculitis with renal involvement: an outcome analysis. Nephrol Dial Transplant 2004;19:1403-11.
13. Morel P, Karras A, Porcher R, Belenfant X, Audard V, Rafat C, et al. Management of severe renal disease in anti-neutrophil-cytoplasmic-antibody-associated vasculitis: the place of rituximab and plasma exchange? Rheumatology (Oxford) 2022;61:4056-64.
14. de Lind van Wijngaarden RA, Hauer HA, Wolterbeek R, Jayne DR, Gaskin G, Rasmussen N, et al. Chances of renal recovery for dialysis-dependent ANCA-associated glomerulonephritis. J Am Soc Nephrol 2007;18:2189-97. Erratum in: J Am Soc Nephrol 2007;18:3206.
15. Li ZY, Gou SJ, Chen M, Zhao MH. Predictors for outcomes in patients with severe ANCA-associated glomerulonephritis who were dialysis-dependent at presentation: a study of 89 cases in a single Chinese center. Semin Arthritis Rheum 2013;42:515-21.
16. Jayne DR, Gaskin G, Rasmussen N, Abramowicz D, Ferrario F, Guillevin L, et al. Randomized trial of plasma exchange or high-dosage methylprednisolone as adjunctive therapy for severe renal vasculitis. J Am Soc Nephrol 2007;18:2180-8.
17. Casal Moura M, Irazabal MV, Eirin A, Zand L, Sethi S, Borah BJ, et al. Efficacy of rituximab and plasma exchange in antineutrophil cytoplasmic antibody-associated vasculitis with severe kidney disease. J Am Soc Nephrol 2020;31:2688-704.
18. Walsh M, Merkel PA, Peh CA, Szpirt WM, Puéchal X, Fujimoto S, et al. Plasma exchange and glucocorticoids in severe ANCA-associated vasculitis. N Engl J Med 2020;382:622-31.
19. Jennette JC, Falk RJ, Bacon PA, Basu N, Cid MC, Ferrario F, et al. 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. Arthritis Rheum 2013;65:1-11.
20. Mukhtyar C, Lee R, Brown D, Carruthers D, Dasgupta B, Dubey S, et al. Modification and validation of the Birmingham Vasculitis Activity Score (version 3). Ann Rheum Dis 2009;68:1827-32.
21. Hellmich B, Flossmann O, Gross WL, Bacon P, Cohen-Tervaert JW, Guillevin L, et al. EULAR recommendations for conducting clinical studies and/or clinical trials in systemic vasculitis: focus on anti-neutrophil cytoplasm antibody-associated vasculitis. Ann Rheum Dis 2007;66:605-17.

22. Kemna MJ, Damoiseaux J, Austen J, Winkens B, Peters J, van Paassen P, et al. ANCA as a predictor of relapse: useful in patients with renal involvement but not in patients with nonrenal disease. J Am Soc Nephrol 2015;26:537-42.

23. Berden AE, Ferrario F, Hagen EC, Jayne DR, Jennette JC, Joh K, et al. Histopathologic classification of ANCA-associated glomerulonephritis. J Am Soc Nephrol 2010;21:1628-36.