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Original Article

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Plasma Exchange in the Treatment of Anti-Neutrophil Cytoplasmic Antibody-Associated Vasculitis: A Retrospective Analysis

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ABSTRACT

Objective: Immunosuppressive therapy in anti-neutrophil cytoplasmic antibody-associated vasculitis is indispensable for patient and kidney survival. There is a controversy about whether the risks of plasma exchange treatment override the probability of kidney-related outcomes. Hence, the question arises in which conditions the plasma exchange will be required? In this study, we aimed to evaluate the effect of plasma exchange adding to immunosuppressive therapy in anti-neutrophil cytoplasmic antibody-associated vasculitis patients.

Methods: We retrospectively analyzed 57 patients with biopsy-proven anti-neutrophil cytoplasmic antibody-associated vasculitis. We grouped patients according to treatment options with or without plasma exchange. We investigated the 1-year and 5-year patients and kidney outcomes.

Results: Thirty-six (63.2%) of 57 patients were treated with plasma exchange besides the routine immunosuppressive treatment. Sixteen (44.5%) of 36 patients were with active pulmonary hemorrhage and the remaining 20 (55.5%) were with vasculitic pulmonary involvement. The survival rate was 80.7% and 68.8% in the first and fifth year, respectively. In the multivariate Cox regression analysis model, risk factors affecting patient survival were age >50 years (hazard ratio = 17.11 P = .034), pulmonary involvement (hazard ratio = 13.25, P =.02), positive perinuclear anti-neutrophil cytoplasmic antibody-associated vasculitis (hazard ratio = 5.93, P =.036), and lower albumin level (hazard ratio = 0.18, P =.014). It is found that C-reactive protein level and plasma exchange did not relate to better patient and kidney outcomes (P > .05).

Conclusions: In anti-neutrophil cytoplasmic antibody-associated vasculitis, although pulmonary hemorrhage and pulmonary involvement are serious complications, plasma exchange did not provide additional benefit to standard treatment.

Keywords: ANCA-associated vasculitis, kidney survival, plasma exchange, end-stage kidney disease

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INTRODUCTION

Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) involves a group of disorders which are composed of inflammation and destruction of small vessels with necrotizing inflammation, absence (pauci-immune) or presence of immune complex deposition with circulating ANCA.[1] The characteristic lesion of pauci-immune glomerulonephritis is focal necrotizing and crescentic glomerulonephritis.[2]

Treatment strategies may differ between the centers. Immunosuppressive therapy started on time alters the course of the disease, mainly patient and kidney survival.[3,4] The addition of cyclophosphamide to corticosteroid during induction increases the remission rates from 55% to 85%, while decreases the recurrence rates by 3 times.[5,6] Immunosuppressive therapy is recommended for all patients with kidney involvement unless they were with severe glomerular loss and severe tubulointerstitial injury.[7] And patients with extra-kidney organ involvement are recommended to be treated with immunosuppressive

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therapy regardless of the degree of kidney problem.[8] Many authors consider plasma exchange (PE) with corticosteroid and cyclophosphamide during remission induction in patients with severe kidney problems (need for dialysis or rapid increase in creatinine) and/or vasculitis-induced alveolar hemorrhage or with anti-GBM positivity in addition to ANCA positivity at admission.[9,10] On the contrary, some studies showed that PE was not beneficial as additional treatment in patients with serum creatinine < 5.66 mg/dL (<500 µmol/L).[11] A newly published randomized controlled study by Walsh et al[12] displayed that PE has no impact on death or end-stage kidney disease (ESKD) too. It is also not clear whether the patient with severe, moderate, or mild alveolar hemorrhage (with small focal infiltrations, mild hypoxia, or without hypoxia) will benefit from PE or not.[13,14] The main aim of our study was to explore the role of PE and other risk factors on patient and kidney survivals in patients with AAV.

METHODS

We retrospectively analyzed patients who were admitted to 3 nephrology centers between 2012 and 2018 with the diagnosis of glomerular diseases. Fifty-seven of 556 patients with biopsy-proven AAV were included in the study. Patients older than 18 years and with at least 5 years of follow-up were included in the study. Patients with missing data were excluded.

Informed consent was obtained from all living patients and from relatives of deceased patients. The study was performed in accordance with the Declaration of Helsinki and approved by local Ethical Committee (date: April 20, 2020; reference number: 86/02).

Treatment Protocol

All patients were treated with standard immunosuppressive treatment protocols in accordance with the Kidney Disease: Improving Global Outcomes (KDIGO) 2012 glomerulonephritis guideline and The European Vasculitis Society (EUVAS) by evaluating current laboratory results, clinical status, physical examination, and pathology findings. Pulse steroids (maximum cumulative dose 1-3 g) were given to all cases for 3 days. In maintenance therapy, the steroid dose was reduced gradually to 5 mg at the sixth month. Steroid dosage after the sixth month varied according to guidelines and physicians. In addition to steroids, cyclophosphamide (0.75 g/m^2 intravenously) was given every 3-4 weeks, the dose was decreased to 0.5 g/m^2 if the age >60 years or GFR <20 mL/min/1.73 m^2. Kidney remission was considered with the dedection of less than 5 erythrocytes in each large magnification area and disappearance of erythrocyte cylinders in urine microscopy. The patients whose kidney function did not return to normal after treatment but with normal urinary sediment, stable serum creatinine, and stable non-nephrotic proteinuria for the last 3 months were also considered in kidney remission. The cases of non-glomerular hematuria such as stone, tumor, and so on, or the use of cyclophosphamide, which is toxic for the bladder mucosa, were not considered as disease activation. While pulmonary involvement was determined by clinical and radiological evaluation, severe pulmonary involvement was considered as cases with severe hemoptysis and the oxygen saturation below 85% under oxygen therapy. Clinical remission is stated as per the recommendation of European League Against Rheumatism/EUVAS, which is zero for the Birmingham Vasculitis Activity Score.[15]

MAIN POINTS

- Anti-neutrophil cytoplasmic antibody-associated vasculitis is related to high mortality and morbidity.
- Immunosuppressive therapy started on time alters the course of the disease, mainly patient and kidney survival.
- There is a controversy about whether the risks of plasma exchange treatment override the probability of kidney-related outcomes.

Plasma Exchange

Plasma exchange was performed on an average of 7-10 times at a dose of 60 mL/kg/session. Fresh frozen plasma was used as the replacement fluid considering the risk of bleeding.

Cytoplasmic- and Perinuclear Anti-neutrophil Cytoplasmic Antibody Measurement

The enzyme-linked immunosorbent assay and immunofluorescence assay methods were used to measure the c-ANCA and p-ANCA values of the patients.

Statistical Analysis

In statistical analysis, categorical variables were given as numbers and percentages. For descriptive statistics, mean ± standard deviation (SD) and median (min-max value) were used depending on the normal distribution state of the variables. Normal distribution was evaluated with Kolmogorov–Smirnov/Shapiro–Wilk tests. Chi-square tests were used for comparison of categorical variables between groups. Student's *t*-test or Mann–Whitney *U* test was used for comparison of data sets. Survival analyses were performed by Kaplan–Meier methods and Log-rank test. Multivariate Cox regression analysis was used to determine the independent prognostic factors for overall survival (OS) or ESKD state. Variables with $P < .05$ as determined by log-rank test were entered into multivariate Cox regression analysis. The hazard ratios (HRs) with corresponding 95% CIs were used to show the factors affecting the outcomes. $P < .05$ was accepted to be statistically significant. Statistical Package for the Social Sciences version 22.0 (IBM SPSS Corp.; Armonk, NY, USA) was used for analysis.

RESULTS

The mean age of the patients was 53.9 ± 14.0 years and 28 (49.1%) of them were male. Immunosuppressive therapy was initiated for all patients after biopsy. Twenty-one patients (36.8%) received only cyclophosphamide and steroid therapy as remission induction. Thirty-six patients (63.2%) received PE

in addition to cyclophosphamide and steroid therapy. At the end of the first year, 9 patients (15.8%) were in clinical and kidney remission; there were 25 patients (43.8%) with chronic kidney disease (CKD) and 12 patients (21.1%) with ESKD. Eleven patients (19.3%) died at the end of the first year. Twenty-seven patients (47.3%) were c-ANCA positive, while the remaining 30 (52.6%) patients were p-ANCA positive. p-ANCA-positive patients were older (59.4 years vs. 47.8 years, *P* = .001).

When we grouped patients according to their remission induction treatments, in the PE-treated group, patients were with higher serum creatinine (*P* = .014) and lower estimated glomerular filtration rate (*P* = .045). Twenty-three patients (58.5%) patients were male in the same group (*P* = .004). Serum C-reactive protein (CRP) was also higher in the PE group (*P* = .006, *P* = .01). The number of patients with pulmonary involvement in the 2 groups was similar (44.4% vs. 61.9%, *P* =,.203), while all patients with pulmonary hemorrhage (16 patients (44.4%)) were in the PE group. At the end of the first year, 8 patients (22.2%) in the PE group, 3 patients (14.2%) in the without PE group died (*P* = .086). Data were summarized in Table 1.

In the survival analysis, the mean survival time was 91.6 ± 7.8 months. The 1-year survival rate was 80.7% and the 5-year

Table 1. The Comparison of the Demographic Data and Laboratory Characteristics of the Patients at the Diagnosis Time and the Clinical Outcomes According to the Treatments

N = 57	Plasma Exchange +ISt, n = 36	ISt, n = 21	*P*
Age (years), mean ± SD	52.9 ± 15.2	55.5 ± 11.9	.520[1]
Gender (male), n (%)	23 (63.9)	5 (23.8)	.004[2]
Hypertension, n (%)	17 (47.2)	11 (52.4)	.707[2]
Diabetes mellitus, n (%)	14 (38.9)	3 (14.3)	.050[2]
Pulmonary involvement, n (%)	16 (44.4)	13 (61.9)	.203[2]
Pulmonary hemorrhage, n (%)	16 (44.4)	0 (0)	
Urea (mg/dL), median (min-max)	128.0 (7.0-278.0)	71.0 (15.0-141.0)	.003[3]
Creatinine (mg/dL, SD), median (min-max)	4.0 (0.5-11.0)	2.51 (0.7-11.2)	.014[3]
eGFR (mL/min/1.73 m^2) (EPI-CKD) median (min-max)	13.5 (4.0-125.0)	23.0 (4.0-102.0)	.045[3]
Total protein (g/dL, SD), mean ± SD	6.2 ± 0.7	6.3 ± 1.0	.479[1]
Albumin (g/dL, SD), mean ± SD	3.0 ± 0.7	2.9 ± 0.6	.743[1]
<2.5 g/dL albumin, n (%)	9 (25)	4 (19)	.605[2]
Proteinuria (>150 mg/day), n (%)	36 (100)	19 (90.5)	.132[4]
White blood cell (/mm^3), median (min-max)	10 700 (1500-26 200)	11 000(6200-21 230)	.546[3]
Hgb (g/dL), mean ± SD	9.1 ± 1.5	10,0 ± 2.1	.071[1]
Plt (10^3/μL) median (min-max)	296.5 (89.0-887.0)	305.0 (36.0-616.0)	.747[3]
Plt/MPV, median (min-max)	36.0 (9.2-94,3)	44.0 (5.4-72.0)	.869[3]
CRP, mg/dL, median (min-max)	62.6 (0.5-232.0)	21.5 (0.4-123.0)	**.011[3]**
Sedimantasyon, mm/h, median (min-max)	45.5 (2.0-143.0)	72.00 (19.0-104.0)	.077[3]
c-ANCA positive n (%)	16 (44.4)	11 (52.4)	.563[2]
p-ANCA positive n (%)	20 (55.6)	10 (47.6)	.563[2]
Clinical outcomes (12th month), n (%)			.399[2]
Remission	5 (13.8)	4 (19.1)	
CKD	16 (44.4)	9 (42.9)	
ESKD	7 (19.4)	5 (23.9)	
Death	8 (22.2)	3 (14.2)	

CRP, C-reactive protein; c-ANCA, cytoplasmic anti-neutrophil cytoplasmic antibody; CKD; chronic kidney disease; eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease; Hgb, hemoglobin; ISt, immunosuppressive treatment (cyclophosphamide + corticosteroid); MPV, mean platelet volume; plt, platelet; p-ANCA, perinuclear anti-neutrophil cytoplasmic antibody; SD, standard deviation.
[1]Student's *t*-test, [2]Chi-squared test, [3]Mann-Whitney U-test, [4]Fisher's exact test.

Table 2. The OS Rates According to the Factors

Total N = 57	Log Rank Test *P*	Overall Survival, Months Mean ± Standart Error*	1-Year Survival Rate, %	5-Year Survival Rate, %
All Patients		91.6 ± 7.8	80.7	68.8
Sex	.959			
Female		62.3 ± 7.0	82.8	68.8
Male		91.4 ± 11,1	78.6	68.8
Age	**.031**			
<50 years		114.8 ± 9.4	95.0	87.7
≥50 years		54.2 ± 6.6	73.0	58.9
Pulmonary involvement	**.030**			
No		76.3 ± 11.5	92.9	81.3
Yes		57.3 ± 4.4	69.0	56.8
ANCA	**.042**			
c-ANCA+		108.3 ± 9.4	92.6	82.2
p-ANCA+		52.4 ± 7.4	70.0	56.9
Creatinine	**.040**			
Cr ≥ 4.39 (mg/dL)		38.9 ± 6.8	70.0	51.3
Cr < 4.39 (mg/dL)		103.4 ± 8.6	86.5	78.6
Plasma exchange	.919			
Only ISt		60.8 ± 8.5	85.7	65.5
Plasma exchange + ISt		92.9 ± 9.6	77.8	70.4
Diabetes mellitus	.132			
Yes		47.3 ± 9.1	64.7	56.6
No		98.5 ± 8.8	87.5	73.9

*Since the median survival rate could not be reached, the data are presented as the mean ± standard error.
c-ANCA, cytoplasmic anti-neutrophil cytoplasmic antibody; ISt, immunosuppressive treatment (cyclophosphamide + corticosteroid); OS, overall survival p-ANCA, perinuclear anti-neutrophil cytoplasmic antibody.

survival rate was 68.8%. Gender (*P* = .959), PE (*P* = .919), and diabetes mellitus (*P* = .132) did not affect survival according to the results of our study. Data were summarized in Table 2. Kaplan–Meier graphs were shown for age (Figure 1) and pulmonary involvement (Figure 2). Risk factors related to the survival of the patients were evaluated with the multivariate Cox regression analysis model. According to multivariate Cox regression analysis, the patients younger than 50 years (HR = 17.11, *P* = .034), with pulmonary involvement (HR = 13.25, *P* = .02), having positive p-ANCA (HR = 5.93, *P* = .036), having serum creatinine level above 4.39 mg/dL (HR = 4.45, p = 0.018), and having serum albumin level lower than 2.5 g/dL (HR = 0.18, *P* = .014) had increased risk of death. C-reactive protein, PE, and the presence of diabetes were not found to be significant risk factors for mortality (*P* > .05) (Table 3).

The mean time between clinical admission and ESKD development was 49.2 ± 4.5 months. None of the parameters like gender, age, ANCA positivity, or diabetes were related to ESKD (*P* > .05). Plasma exchange was also not related to ESKD (*P* = .554).

DISCUSSION

We found that there was no difference in terms of ESKD, mortality, and clinical outcome in patients who received PE and those who did not. The baseline level of the CRP, which is marker of inflammation, was not found to be associated with the outcomes. In multivariate Cox regression analysis, risk factors affecting patient survival were age >50 years, pulmonary involvement, positive p-ANCA, serum creatinine level >4.39 mg/dL, and lower albumin level.

Anti-neutrophil cytoplasmic antibody-associated vasculitis is related to high mortality and morbidity. Therefore, effective and reliable treatments are needed. Treatment is generally planned according to the 2012 Kidney Disease Improving

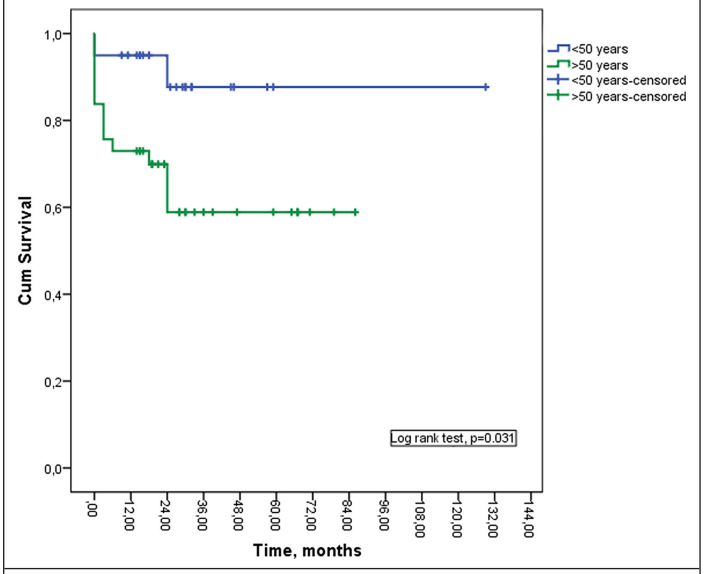

Figure 1. The relationship between the age and overall survival.

Global Outcomes (KDIGO) nephritis guide.[16] We prefer steroid and cyclophosphamide as remission induction, and in some cases, PE was added to this standard therapy. In the updated report of EUVAS on AAV, as in the 2012 KDIGO guide, PE treatment is recommended in the presence of rapidly progressing kidney failure and severe pulmonary hemorrhage for the treatment of AAV.[15] However, in these international guidelines, it should be noted that PE has been recommended for the treatment of AAV with pulmonary hemorrhage based on observational studies involving fewer than 100 patients.[17,18] Besides, it has been seen that the patients are in the form of case series in the post-guideline studies on this subject, and these studies

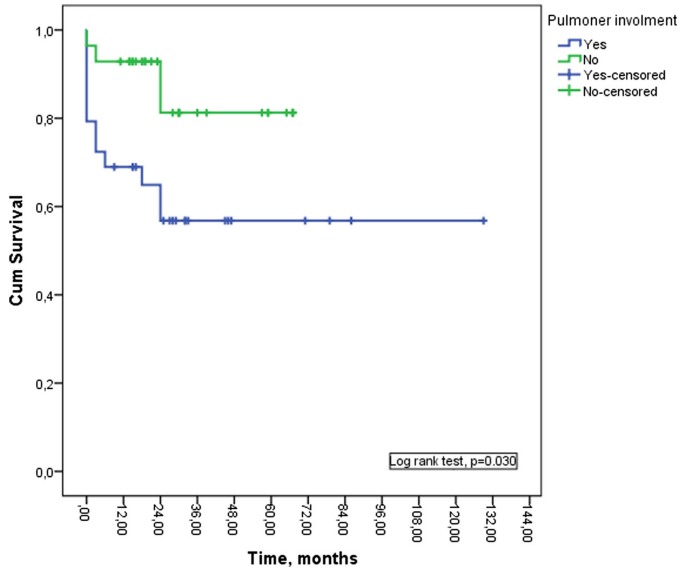

Figure 2. The relationship between pulmonary involvement and overall survival.

Table 3. The Multivariate COX Regression Analysis According to the Factors for the OS

	Multivariate Cox Regression Analysis Model for OS (n = 3228)	
	Adjusted HR (95% CI)	*P*
Age		.034
<50 years	Reference	
≥50 years	17.11 (1.23-88,58)	
Pulmonary involvement		.002
Yes	13.25 (2.52-39.46)	
No	Reference	
ANCA		.036
c-ANCA+	Reference	
p-ANCA+	5.93 (1.13-31.26)	
Creatinine		.018
Cr ≥ 4.39 (mg/dL)	4.45 (1.29-15.31)	
Cr < 4.39 (mg/dL)	Reference	
Albumin (g/dL)	0.18 (0.05-0.71)	.014
CRP (mg/dL)	0.99 (0.96-1.01)	.994
Diabetes mellitus		.613
Yes	0.68 (0.15-3.07)	
No	Reference	
Plasma exchange		.637
Only ISt	0.69 (0.16-3.12)	
Plasma exchange + ISt	Reference	

CRP, C-reactive protein; c-ANCA, cytoplasmic anti-neutrophil cytoplasmic antibody; HR, hazard ratio; ISt, immunosuppressive treatment (cyclophosphamide + corticosteroid); OS, overall survival p-ANCA, perinuclear anti-neutrophil cytoplasmic antibody.

have a low level of evidence and have conflicting results regarding its effectiveness.[19,20]

The Plasma Exchange and Glucocorticoid Dosing in the Treatment of Anti-Neutrophil Cytoplasm Antibody-Associated Vasculitis study investigating the appropriate treatment options for AAV is the large-scale, multicenter, and randomized controlled study in the literature. In the study published by Walsh et al.[12] they investigated the effects of PE primarily on the patient outcomes in the cases with severe AAV (severe definition: GFR <50 mL/min or diffuse pulmonary hemorrhage). The primary outcomes of this study were determined as all-cause mortality or ESKD. This study included 704 patients at 95 centers in 16 countries and the patients were followed for up to 7 years. As a result, it has been shown that plasmapheresis in addition to standard treatment does not provide additional benefit for severe AAV. Similarly, in our local patient population, we have shown that PE in the patients with ANCA-associated

vasculitis did not result in lower death or less incidence of ESKD than in the patients treated without PE.

Some other previous studies in the literature have shown the critical benefits of PE to reduce the need for dialysis in the first year in patients with severe kidney disease.[21,22] These studies have also suggested that PE affects ESKD without any benefit for survival. Contrary to these studies, Walsh et al[12] have shown that PE is not related to kidney survival, supporting the findings of our study. In 2020, a meta-analysis of 1235 AAV patients from 10 studies including Walsh's study was published. Plasma exchange was not associated with lower rates of either mortality at third and twelfth months or ESKD at third and twelfth months. The present meta-analysis does not support a wider use of PE for the management of AAV in routine clinical practice.[23]

The factors affecting mortality were age, pulmonary involvement, creatinine level above 4.39 mg/dL, and lower albumin level. These findings are compatible with the literature.[24,25] And the highest HR related to mortality was age (17.11; 1.23-88.58, *P* = .034) and pulmonary involvement (13.25; 2.52-39.46, *P* = .002). It has been detected that the baseline level of the CRP, which is marker of inflammation, did not determine the prognosis. C-reactive protein did not show disease activity, response to treatment, and disease recurrence.[26] In the literature, the prognosis of ANCA-negative vasculitis and c-ANCA-positive vasculitis was worse.[15,27] In our study group, mortality was higher in p-ANCA-positive patients. On the other hand, the incidence of being over the age of 50 and decreased level of serum albumin, which are findings of poor prognosis, are higher in these patients than the c-ANCA positive ones.

It was reported that kidney survival was higher in female patients. The risk for the development of ESKD was higher in the patients with low GFR levels and a low percentage of normal glomerulus in biopsy at the time of diagnosis.[28] We found that gender, CRP, or PE had no progression effect to ESKD.

There are several limitations to our study. The retrospective design of the study is the main limitation of the study. Different treatment options suggested by the guidelines could be chosen differently by doctors. The number of patients in our study is also low. However, we think that our study will have a contribution to the literature by showing local patient data even if the number of patients with this rare disease is low.

CONCLUSION

In AAV, PE did not provide additional benefit to standard treatment. CRP at the time of diagnosis was not found useful in determining prognosis. Instead, pulmonary involvement even with or without pulmonary hemorrhage and age might be used as clinical surrogates of worse outcomes.

Ethics Committee Approval: Ethical committee approval was received from the Ethics Committee of Dışkapı Yıldırım Beyazıt Education and Research Hospital (Date: April 20, 2020, Decision No: 86/02).

Informed Consent: Informed consent was obtained from the patients who participated in this study.

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REFERENCES

1. Binda V, Moroni G, Messa P. ANCA-associated vasculitis with renal involvement. *J Nephrol*. 2018;31(2):197-208. [CrossRef]
2. Xiao H, Hu P, Falk RJ, Jennette JC. Overview of the pathogenesis of ANCA associated vasculitis. *Kidney Dis (Basel)*. 2016;1(4): 205-215. [CrossRef]
3. Yamagata K, Usui J, Saito C, et al. ANCA-associated systemic vasculitis in Japan: clinical features and prognostic changes. *Clin Exp Nephrol*. 2012;16(4):580-588. [CrossRef]
4. Geetha D, Jefferson JA. ANCA-associated vasculitis: core curriculum 2020. *Am J Kidney Dis*. 2020;75(1):124-137. [CrossRef]
5. Hogan SL, Falk RJ, Chin H, et al. Predictors of relapse and treatment resistance in antineutrophil cytoplasmic antibody-associated small vessel vasculitis. *Ann Intern Med*. 2005;143(9):621-631. [CrossRef]
6. Nachman PH, Hogan SL, Jennette JC, Falk RJ. Treatment response and relapse in antineutrophil cytoplasmic autoantibody-associa ted microscopic polyangiitis and glomerulonephritis. *J Am Soc Nephrol*. 1996;7(1):33-39. [CrossRef]
7. Ford SL, Polkinghorne KR, Longano A, et al. Histopathologic and clinical predictors of kidney outcomes in ANCA-associated vasculitis. *Am J Kidney Dis*. 2014;63(2):227-235. [CrossRef]
8. Moiseev S, Novikov P, Jayne D, Mukhin N. End-stage renal disease in ANCA-associated vasculitis. *Nephrol Dial Transplant*. 2017;32(2): 248-253. [CrossRef]
9. Padmanabhan A, Connelly-Smith L, Aqui N, et al. Guidelines on the use of therapeutic apheresis in clinical practice evidence-based approach from the writing committee of the American Society for Apheresis: the eighth special issue. *J Clin Apher*. 2019;34(3):171-354. [CrossRef]
10. Klemmer PJ, Chalermskulrat W, Reif MS, Hogan SL, Henke DC, Falk RJ. Plasmapheresis therapy for diffuse alveolar hemorrhage in patients with small-vessel vasculitis. *Am J Kidney Dis*. 2003;42(6): 1149-1153. [CrossRef]
11. Jayne DR, Gaskin G, Rasmussen N, 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):2180-2188. [CrossRef]

12. Walsh M, Merkel PA, Peh CA, et al. Plasma exchange and glucocorticoids in severe ANCA-associated vasculitis. *N Engl J Med*. 2020; 382(7):622-631. [CrossRef]
13. Cole E, Cattran D, Magil A, et al. A prospective randomized trial of plasma exchange as additive therapy in idiopathic crescentic glomerulonephritis. The Canadian Apheresis Study Group. *Am J Kidney Dis*. 1992;20(3):261-269. [CrossRef]
14. Derebail VK, Falk RJ. ANCA-associated vasculitis - refining therapy with plasma exchange and glucocorticoids. *N Engl J Med*. 2020; 382(7):671-673. [CrossRef]
15. Yates M, Watts RA, Bajema IM, et al. EULAR/ERA-EDTA recommendations for the management of ANCA-associated vasculitis. *Ann Rheum Dis*. 2016;75(9):1583-1594. [CrossRef]
16. Cattran DC, Feehally J, Cook HT, et al. Kidney disease: improving global outcomes (KDIGO) glomerulonephritis work group. KDIGO clinical practice guideline for glomerulonephritis. *Kidney Int Suppl*. 2012;2(2):139-274.
17. Schwartz J, Winters JL, Padmanabhan A, et al. Guidelines on the use of therapeutic apheresis in clinical practice-evidence- based approach from the Writing Committee of the American Society for Apheresis: the sixth special issue. *J Clin Apher*. 2013;28(3):145-284. [CrossRef]
18. Gallagher H, Kwan JT, Jayne DR. Pulmonary renal syndrome: a 4-year, single center experience. *Am J Kidney Dis*. 2002;39(1):42-47. [CrossRef]
19. Chen Y, Yang L, Li K, et al. Double filtration plasmapheresis in the treatment of antineutrophil cytoplasmic autoantibody associated vasculitis with severe renal failure: A preliminary study of 15 patients. *Ther Apher Dial*. 2016;20(2):183-188. [CrossRef]
20. Al Hamzi HA, Al-Mayouf SM, Al Shaikh AA, et al. Early and late effects of therapeutic plasma exchange in patients with systemic lupus erythematosus and antineutrophil cytoplasmic antibody-associated vasculitis: a single-center experience. *Saudi J Kidney Dis Transpl*. 2019;30(4):775-780. [CrossRef]
21. Walsh M, Catapano F, Szpirt W, et al. Plasma exchange for renal vasculitis and idiopathic rapidly progressive glomerulonephritis: a meta-analysis. *Am J Kidney Dis*. 2011;57(4):566-574. [CrossRef]
22. Walters GD, Willis NS, Craig JC. Interventions for renal vasculitis in adults. A systematic review. *BMC Nephrol*. 2010;11(1):12. [CrossRef]
23. Bellos I, Michelakis I, Nikolopoulos D. The role of plasma exchange in antineutrophil cytoplasmic antibody-associated vasculitis: a meta-analysis. *Clin Rheumatol*. 2020;9:1-10.
24. Wu T, Peng J, Meng T, et al. Clinicopathological features and prognostic analysis of 49 cases with crescentic glomerulonephritis. *Exp Ther Med*. 2019;18(5):3984-3990. [CrossRef]
25. de Joode AA, Sanders JS, Stegeman CA. Renal survival in proteinase 3 and myeloperoxidase ANCA-associated systemic vasculitis. *Clin J Am Soc Nephrol*. 2013;8(10):1709-1717. [CrossRef]
26. Grayson PC, Monach PA, Pagnoux C, et al. Value of commonly measured laboratory tests as biomarkers of disease activity and predictors of relapse in eosinophilic granulomatosis with polyangiitis. *Rheumatol (Oxf Engl)*. 2015;54(8):1351-1359. [CrossRef]
27. Lee T, Gasim A, Derebail VK, et al. Predictors of treatment outcomes in ANCA-associated vasculitis with severe kidney failure. *Clin J Am Soc Nephrol*. 2014;9(5):905-913. [CrossRef]
28. Salmela A, Törnroth T, Poussa T, Ekstrand A. Prognostic factors for survival and relapse in ANCA-associated vasculitis with renal involvement: a clinical long-term follow-up study. *Int J Nephrol*. 2018;2018:6369814. [CrossRef]