Clinical Kidney Journal, 2025, vol. 18, no. 9, sfaf268

https://doi.org/10.1093/ckj/sfaf268
Advance Access Publication Date: 26 August 2025
Original Article

ORIGINAL ARTICLE

Predicting prognosis in ANCA-associated vasculitis with kidney involvement

Christian Maalouli[1,*], Selda Aydin[2,3,*], Alix Collard[4], Jean-Francois Cambier[5], Agnes Dejardin[6], Benoit Georges[7], Gaelle Gillerot[8], Benedicte Vanderperren[9], Ann-Karolien Vandooren[10], Michel Jadoul[3,11], Johann Morelle[12,13] and Nathalie Demoulin[1,11]; UCLouvain Kidney Disease Network

[1]Division of Nephrology, Centre Hospitaliser de Wallonie Picarde, Tournai, Belgium, [2]Department of Pathology, Cliniques universitaires Saint-Luc, Brussels, Belgium, [3]Institut de Recherche Expérimentale et Clinique, UCLouvain, Brussels, Belgium, [4]Statistical Support Unit, Cliniques universitaires Saint-Luc, Brussels, Belgium, [5]Department of Nephrology, Grand Hôpital de Charleroi, Gilly, Belgium, [6]Department of Nephrology, Cliniques de l'Europe, Brussels, Belgium, [7]Department of Nephrology, Centre Hospitalier Régional Sambre et Meuse, Namur, Belgium, [8]Department of Nephrology, Clinique Saint-Pierre, Ottignies, Belgium, [9]Department of Nephrology, Centres Hospitaliers Universitaires HELORA, Jolimont, Belgium, [10]Department of Nephrology, Centre Hospitalier de Mouscron, Mouscron, Belgium, [11]Division of Nephrology, Cliniques universitaires Saint-Luc, Brussels, Belgium, [12]Divsion of Nephrology, University Hospitals Namur (CHU UCL Namur), Namur, Belgium and [13]de Duve Institute, UCLouvain, Brussels, Belgium

*Both authors contributed equally.
Correspondence to: Nathalie Demoulin; E-mail: nathalie.demoulin@saintluc.uclouvain.be

ABSTRACT

Background. The ANCA Renal Risk Score was updated in 2023 to the ANCA Kidney Risk Score (AKRiS) to improve clinicopathological prognostication in patients with anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) and kidney involvement. Our study aimed to assess whether incorporating recently identified predictors of kidney survival in AAV could further refine the prognostic accuracy of AKRiS in our multicentric cohort.

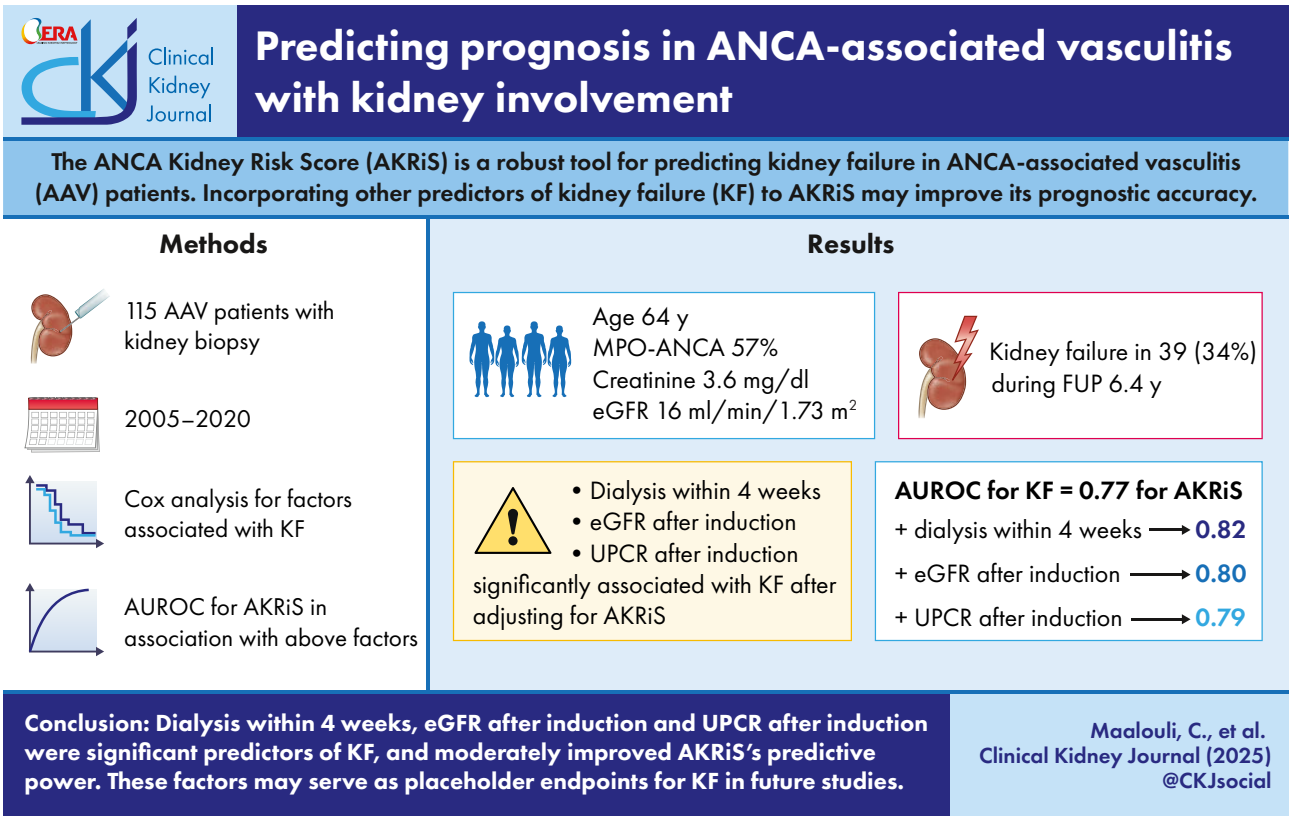
Methods. We retrospectively reviewed all incident AAV with kidney biopsy from 2005 to 2020. Cox regression analysis examined factors [AKRiS, dialysis within 4 weeks, urine protein–creatinine ratio (UPCR) and hematuria at baseline, C3 deposits, renal arteritis on biopsy, estimated glomerular filtration rate (eGFR), UPCR and hematuria after induction] associated with kidney failure. These factors in combination with AKRiS were analyzed using the area under the receiver operating characteristic curve (AUROC) for prediction of kidney failure.

Results. The cohort included 115 patients (age 64 years, 55% male, 57% myeloperoxidase-ANCA, baseline creatinine 3.6 mg/dL, eGFR 16 mL/min/1.73 m^2), with 34 (30%) dialysed within 4 weeks. During a median 6.4-year follow-up, 39 (34%) patients progressed to kidney failure, and 13 (11%) died. Cox analysis identified AKRiS, dialysis within 4 weeks, C3 deposits, renal arteritis on biopsy, lower eGFR after induction and higher UPCR after induction as unadjusted risk factors for kidney failure. After adjusting for AKRiS, dialysis within 4 weeks [hazard ratio (HR) 6.20 (95% confidence interval 2.76 to 13.95), $P \leq .001$], eGFR after induction [HR 0.94 (0.89 to 0.99), $P = .03$] and UPCR after induction [HR 1.62 (1.02 to 2.58), $P = .04$] remained significantly associated with kidney outcome. The AUROC for kidney failure prediction was 0.77 for AKRiS, increasing to 0.82, 0.80 and 0.79 when adding dialysis within 4 weeks, eGFR and UPCR after induction, respectively.

Received: 10.4.2025; Editorial decision: 28.7.2025

Conclusion. Dialysis within 4 weeks, eGFR after induction and UPCR after induction are able to predict long-term kidney outcome in AAV patients. Adjusting AKRiS for these variables modestly enhances its predictive power. We propose using them as placeholder endpoints for kidney failure in future studies.

GRAPHICAL ABSTRACT



Keywords: AKRiS, ANCA Renal Risk Score, pauci-immune necrotizing glomerulonephritis

KEY LEARNING POINTS

What was known:

- The ANCA Kidney Risk Score (AKRiS) is a robust tool for predicting kidney failure in anti-neutrophil cytoplasmic antibody–associated vasculitis patients.

This study adds:

- Dialysis within 4 weeks of presentation, glomerular filtration rate (GFR) after induction and urine protein–creatinine ratio (UPCR) after induction significantly predicted the risk of kidney failure, independently of AKRiS.
- Addition of dialysis within 4 weeks, GFR after induction and UPCR after induction to AKRiS modestly improved its predictive performance.

Potential impact:

- These variables may be used as placeholder endpoints for kidney failure in future studies.

INTRODUCTION

Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) are a group of severe autoimmune disorders involving small-vessel vasculitis. They are characterized by the development of autoantibodies to neutrophil proteins myeloperoxidase (MPO) or proteinase 3 (PR3) [1]. Kidney involvement is common and often severe, with up to 20%–25% patients reaching kidney failure within a few years of diagnosis [2]. The treatment of

AAV includes an induction regimen, followed by a maintenance regimen [3, 4].

Several classification scores, essentially based on kidney function at presentation and histopathological characteristics, have been evaluated as prognostication tools in AAV [5]. Accurate prognostication allows clinicians to identify patients at higher risk of progression and may enable personalized therapeutic management and disease progression monitoring. Berden *et al*. proposed a classification based on the percentage of sclerotic, normal and cellular crescentic glomeruli on initial kidney biopsy. The focal class showed the best kidney survival, followed by the crescentic, mixed and fibrotic classes [6]. The Mayo Clinic Chronicity Score is a semi-quantitative approach to assessing global and segmental glomerulosclerosis, interstitial fibrosis and tubular atrophy (IFTA) in all kidney biopsies [7]. This chronicity score independently predicted kidney function in a cohort of AAV patients [8]. The ANCA Renal Risk Score (ARRS) was developed using a multicenter prospective cohort and included three parameters: percentage of normal glomeruli, percentage IFTA and estimated glomerular filtration rate (eGFR) at presentation. The ARRS predicted kidney failure risk as low, intermediate and high [9]. Several studies confirmed the prognostic utility of ARRS, as did a recent meta-analysis [10–17].

The ARRS was recently revised, with serum creatinine replacing eGFR and an additional risk group added (very high risk of kidney failure). This new ANCA Kidney Risk Score (AKRiS) had a strong discriminative ability in predicting kidney function outcome in a large international cohort [18]. AKRiS has the potential to become the gold standard of ANCA-associated glomerulonephritis prognostication, but more validations are needed with collaboration across centers and with comparisons of scores [19, 20]. As the prognostic yield of AKRiS decreases over time, a second calculation of AKRiS, including post-therapy kidney function, may improve its long-term performance [21, 22]. Recently, the Percentage of ANCA Crescentic Score (PACS) was developed to predict risk of kidney failure in a Japanese cohort. This score takes into account the percentage of cellular crescents, fibrocellular crescents, fibrous crescents and sclerotic glomeruli [23].

Amongst other potential predictors of kidney survival in AAV, low serum C3 and complement deposition in kidney biopsy have been associated with worse outcomes [24–28]. In addition, the incorporation of AAV-associated arteritis significantly improved the discrimination of ARRS in predicting kidney failure in a large French cohort [29]. Lastly, persistent proteinuria [urine protein–creatinine ratio (UPCR) $\geq$0.05 g/mmol] after induction therapy was associated with kidney failure or death in a post-hoc analysis of AAV patients having participated in five European randomized clinical trials [30].

We aimed to determine whether adding selected factors at presentation and after induction therapy to AKRiS could improve the prediction of kidney failure in our multicentric cohort.

MATERIALS AND METHODS

Patient cohort

We identified all incident cases of AAV with kidney involvement from our kidney biopsy registry. Kidney biopsies were performed from 1 January 2005 to 31 December 2020 in one of the hospitals of the UCLouvain Kidney Disease network (list provided in the Acknowledgments section). Inclusion criteria included age $\geq$18 years, pauci-immune glomerulonephritis, a minimum of five glomeruli per biopsy, kidney biopsy performed <1 month after start of immunosuppressive therapy and a follow-up of at least 12 months for patients who had not died within the year following kidney biopsy. Patients with (i) eosinophilic granulomatosis with polyangiitis, (ii) double-positive serology for anti-glomerular basement membrane antibodies and ANCA, or (iii) coexisting glomerular diseases [such as concomitant immunoglobulin (IgA) or lupus nephritis] were excluded. ANCA were detected using enzyme-linked immunosorbent assay for MPO and PR3 in all centers.

The Saint-Luc Hospital's Ethical Committee approved the study (2020/28AVR/253) and the study procedures were in accordance with the Helsinki Declaration of 1975, as revised in 2013.

Data collection and outcomes

Patient characteristics were collected at baseline, including demographics, ANCA-subtype and titer, kidney function (and dialysis requirement within 4 weeks of presentation, considered as early dialysis) and pathological findings (see below). Kidney function, hematuria and proteinuria parameters were collected at 3–6 months (after induction therapy), 12 months, 24 months and at the last follow-up. GFR was estimated using the Chronic Kidney Disease Epidemiology Collaboration equation 2021.

The main outcome studied was the cumulative percentage of patients developing kidney failure, defined as the need for chronic dialysis (>3 months) or transplantation, over time, censored for death. The study was reported according to the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines.

Kidney histology and analysis

Kidney biopsies were processed using standard techniques for light microscopy and immunofluorescence (IF). Hematoxylin and eosin, periodic acid–Schiff, trichrome and Jones colorations were used. IF was systematically performed using antibodies directed against IgA, IgG, IgM, C3, C1q, kappa and lambda.

The senior pathologist (S.A.) reviewed all kidney biopsies to determine the percentage of normal, cellular crescentic, fibrocellular crescentic, fibrous crescentic and sclerotic glomeruli, presence of renal arteritis, extent of IFTA and intensity of IF C3 deposits. Renal arteritis was defined by the presence of fibrinoid necrosis of the arterial wall and/or inflammatory infiltrate affecting the media of interlobular and/or arcuate arteries [29]. Berden classification, Mayo Clinic Chronicity Score, Percentage of ANCA Crescentic Score, ARRS and AKRiS were calculated in all patients. We used the creatinine level at presentation or just before initiation of dialysis in the ARRS and AKRiS scores.

Statistical analysis

Continuous variables were summarized with the median and interquartile range and categorical values with number and percentage. Cox proportional hazards regression analysis was performed to study selected factors (among AKRiS, initiation of dialysis within 4 weeks, UPCR at baseline, hematuria at baseline, presence of C3 deposits on IF, presence of renal arteritis on biopsy, eGFR, UPCR and hematuria after induction) associated with time to kidney failure on follow-up (death-censored). Records with missing data were not taken into account in the regression analysis. Hazard ratios (HR) with 95% confidence intervals (CI) are reported. The regression analysis was repeated in a sub-group of the cohort with a minimum of 10 glomeruli on kidney biopsy. The different factors in association with AKRiS

Table 1: Characteristics at baseline.

	N*	Total cohort, N = 115	Kidney failure, N = 39	No kidney failure, N = 76
Demographics				
Age (years)	115	64 (55–71)	65 (57–71)	63 (53–70)
Gender (male)	115	63 (55)	20 (51)	43 (57)
Organ involvement				
ENT (*N*)	115	24 (21)	7 (18)	17 (22)
Lung (*N*)	115	53 (46)	18 (46)	35 (46)
Biological parameters at baseline				
Creatinine (mg/dL)	115	3.6 (2.2–6.0)	5.6 (3.6–8.5)	2.8 (1.7–4.5)
Baseline GFR	115	15.52 (7.86–29.22)	8.35 (5.42–15.09)	19.75 (12.14–37.36)
Dialysis within 4 weeks (*N*)	115	34 (30)	23 (59)	11 (14)
Baseline UPCR (g/g)	108	1.37 (0.74–2.76)	1.65 (1.01–3.28)	1.19 (0.70–2.40)
Baseline hematuria (/µL)	97	59 (24–168)	50 (34–100)	69 (22–189)
ANCA type (MPO/PR3)	115	66/42	23/14	43/28
ANCA titer (AU/L)	103	112 (56–161)	110 (44–200)	119 (75–157)
CRP (mg/dL)	115	34 (15–115)	27 (10–115)	39 (15–122)
Histological data				
Number of glomeruli (*N*)	115	14 (10–20)	12 (7–22)	14 (11–19)
Normal glomeruli (%)	115	27 (14–46)	13 (4–25)	35 (22–50)
Crescentic glomeruli (%)	115	32 (15–50)	27 (14–57)	35 (16–47)
Cellular crescentic glomeruli (%)	115	14 (6–33)	13 (6–27)	18 (7–36)
Fibrocellular crescentic glomeruli (%)	115	0 (0–14)	3 (0–17)	0 (0–11)
Fibrous crescentic glomeruli (%)	115	0 (0–6)	0 (0–9)	0 (0–6)
Sclerotic glomeruli	115	17 (7–31)	20 (9–52)	13 (6–27)
IFTA	115			
0		50 (43)	14 (36)	36 (47)
1		30 (26)	8 (21)	22 (29)
2		24 (21)	9 (23)	15 (20)
3		11 (10)	8 (21)	3 (4)
Arteritis	115	7 (6)	5 (13)	2 (3)
IF C3 deposits (≥1+)	103	45 (44)	20 (63)	25 (35)

Data presented as median (IQR) or *N* (%).
*N**, number of patients with available data.
ENT, ear, nose, throat; UPCR, urinary protein to creatinine ratio; IFTA, interstitial fibrosis and tubular atrophy; CRP, C-reactive protein.

were analyzed using the area under the receiver operating characteristic curve (AUROC) for prediction of kidney failure over the study period.

Selected baseline variables (AKRiS, initiation of dialysis within 4 weeks, UPCR and hematuria at baseline, presence of C3 deposits on IF, presence of renal arteritis on biopsy, eGFR, UPCR and hematuria after induction) were compared between patients recovering from early dialysis and those developing kidney failure, using Kruskal–Wallis for continuous variables and Fisher's exact test for categorical variables.

RESULTS

Baseline characteristics

The cohort included 115 patients with AAV and kidney involvement (Table 1). The median age was 64 [interquartile range (IQR) 55–71] years and 55% of patients were males. The patients presented with ear, nose and throat (ENT) and lung involvement in 21% and 46% of cases, respectively. At baseline, median creatinine level was 3.6 (IQR 2.2–6.0) mg/dL and C-reactive protein 34 (IQR 15–115) mg/L. ANCA titer was 112 (IQR 56–161) AU. Median hematuria was 59 (IQR 24–168)/µL and UPCR 1.37 (IQR 0.74–2.76) g/g. Thirty-four patients (30%) required hemodialysis within 4 weeks of initial presentation. Kidney biopsies contained a median of 14 (IQR 10–20) glomeruli, of which 27 (IQR 15–46) % were normal, 32 (IQR 15–50) % crescentic, 14 (IQR 6–33) % cellular crescentic, 0 (IQR 0–14) % fibrocellular crescentic, 0 (IQR 0–6) % fibrous crescentic, and 17 (IQR 7–31) % sclerotic. Renal arteritis and C3 staining (≥1+ intensity) were present in 6% and 44% of biopsies, respectively.

Induction and maintenance therapy

Ninety-seven (84%), 12 (10%) and 6 (5%) patients received intravenous cyclophosphamide/steroid, rituximab/steroid and steroid only based induction therapy, respectively. Additionally, seven patients underwent plasma exchanges (Table 2).

Maintenance therapy was given to 88/111 patients (79%) (azathioprine 75, rituximab 8, ± low-dose steroids). Maintenance therapy was stopped in 43/85 patients after a median duration of 2.4 years.

Kidney function data after induction and kidney failure outcome

Eleven of 34 patients (32%) who required hemodialysis within 4 weeks of presentation were weaned off dialysis (time to recovery: 40 days) (Fig. 1). After induction therapy, median eGFR, UPCR and hematuria levels were 38 (IQR 23–55) mL/min/1.73 m^2, 0.60 (IQR 0.26–1.37) g/g and 5 (IQR 2–16)/µl (Table 2). eGFR increased and UPCR decreased during the first 24 months of follow up, whilst hematuria disappeared between 3 and 6 months. ANCA titers decreased until approximately 6 months of follow-up (Supplementary data, Fig. S1).

Table 2: Induction therapy and subsequent kidney parameters.

	N*	Total cohort, N = 115	Kidney failure, N = 39	No kidney failure, N = 76
Induction with cyclophosphamide and steroids (N)	115	97 (84)	33 (85)	64 (84)
Induction with rituximab and steroids (N)	115	12 (10)	2 (5)	10 (13)
Induction with steroids alone	115	6 (5)	4 (10)	2 (3)
eGFR after induction (mL/min/1.73 m^2)	85	38 (23–55)	20 (18–32)	39 (26–59)
UPCR after induction (g/g)	83	0.60 (0.26–1.37)	1.26 (0.60–1.80)	0.55 (0.25–1.30)
Hematuria after induction (/μL)	83	5 (2–16)	18 (6–30)	3 (1–12)

Data are presented as median (IQR) or N (%).
N*, number of patients with available data.

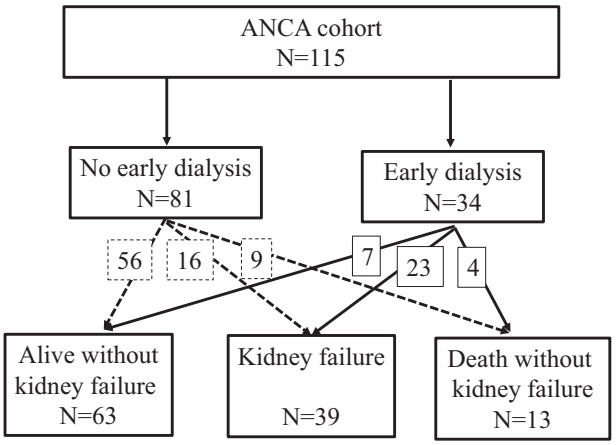


Figure 1: Patient outcome according to early dialysis status (within 4 weeks of presentation).

During a median follow up was 6.4 years (IQR 5.7–7.5), 39 (34%) patients progressed to kidney failure and 63 (55%) were alive without kidney failure [eGFR 42 (IQR 27–62) mL/min/1.73 m^2] (Fig. 1). Thirty-three patients (29%) relapsed at a median of 2 years after presentation. Thirteen (11%) died before reaching kidney failure [5, 3, 2, 2 and 1 death(s) attributed to cardiovascular complications, vasculitis, infection, cancer and other causes, respectively].

Histopathological and clinical risk scores

The Berden classification, Mayo Clinic Chronicity Score, Percentage of ANCA Crescentic Score, ARRS and AKRiS are shown in Table 3 for the total cohort and according to kidney failure outcome; 36%, 31%, 25% and 8% of patients were classified as low, medium, high and very high risk according to AKRiS, respectively. Patients in the AKRiS low, medium, high and very high risk groups progressed to kidney failure in 4/41 (10%), 12/36 (33%), 15/29 (52%) and 8/9 (89%) cases, respectively (Table 3).

Factors associated with kidney failure outcome and recovery from early dialysis

Cox proportional hazards analysis revealed that AKRiS, initiation of dialysis within 4 weeks, presence of C3 deposits on IF, presence of renal arteritis on biopsy, lower eGFR after induction and higher UPCR after induction were associated with kidney failure (Table 4). The results of the analysis repeated in the sub-group of the cohort with a minimum of 10 glomeruli on kidney biopsy are shown in Supplementary data, Table S1. Figure 2 shows kidney survival of AAV patients according to AKRiS risk group.

Using a bivariate analyses model for each variable, after adjustment for AKRiS, dialysis within 4 weeks, eGFR after induction and UPCR after induction remained significantly associated with progression to kidney failure (Table 4). Notably, C3 deposits, renal arteritis on biopsy and hematuria after induction were not associated with kidney outcome after adjusting for AKRiS. The AUROC for kidney failure prediction was 0.77 for AKRiS and increased to 0.82, 0.80 and 0.79 when adding dialysis at presentation, eGFR after induction and UPCR after induction, respectively (Fig. 3). In comparison, AUROC for kidney failure prediction were 0.61, 0.61, 0.68 and 0.74 for Berden classification, Mayo Clinic Chronicity Score, Percentage of ANCA Crescentic Score and ARRS respectively (curves not shown).

Among patients dialysed within 4 weeks, the percentage of normal glomeruli and absence of C3 deposits on biopsy were associated with recovery from dialysis on univariate analysis ($P = .009$ and $P = .009$, respectively) (Table 5).

DISCUSSION

AKRiS demonstrated a strong discriminative ability in predicting the risk of kidney failure in patients with AAV in our cohort, aligning with the findings of three recent studies [18, 19, 21]. AKRiS outperformed the Berden classification, the Mayo Clinic Chronicity Score and the Percentage of ANCA Crescentic Score, and showed similar predictive performance to ARRS in predicting kidney survival in our cohort. Additional key clinical variables, including dialysis at presentation, eGFR after induction and UPCR after induction also significantly predicted risk of kidney failure, after adjusting for AKRiS.

Dialysis at presentation of AAV often indicates more severe disease and/or a higher degree of chronic kidney damage. However, in our cohort, 32% of patients who began dialysis recovered autonomous kidney function, consistent with previous studies [31, 32]. These have shown that despite advanced lesions on renal biopsy at diagnosis, patients requiring dialysis at presentation have a chance of renal recovery exceeding that of therapy-related death [31]. Notably, 8/21 (38%) patients who were initially dialyzed and had a high AKRiS risk score recovered autonomous kidney function. As with other prognostic scores, AKRiS can help clinicians assess prognosis when discussing risks and potential benefits of therapies, but cannot be used to rule out immunosuppressive therapy.

In our cohort, both eGFR and UPCR measured after induction were significant predictors of kidney failure risk. Benichou *et al.* showed that persistent proteinuria at the end of induction was associated with a greater risk of death/kidney failure and kidney relapse [30]. In our study, incorporation of post-induction eGFR or UPCR into the ARKiS model modestly improved its predictive performance, as reflected by a slight increase in AUROC. A recent study by Sandino-Bermudez *et al.* reported that the

Table 3: Prognostic risk scores.

	N*	Total cohort, N = 115	Kidney failure, N = 39	No kidney failure, N = 76
Berden classification	115			
Focal		26 (23)	3 (8)	23 (30)
Crescentic		23 (20)	11 (28)	12 (16)
Mixed		50 (43)	15 (38)	35 (46)
Sclerotic		16 (14)	10 (26)	6 (8)
Mayo Clinic Chronicity Score	107			
Minimal		38 (36)	11 (31)	27 (38)
Mild		39 (36)	8 (22)	31 (44)
Moderate		19 (18)	11 (31)	8 (11)
Severe		11 (10)	6 (17)	5 (7)
Percentage of ANCA Crescentic Score		58 (42–71)	67 (50–82)	54 (38–67)
ARRS	115			
Low risk		35 (30)	3 (8)	32 (42)
Medium risk		60 (52)	18 (46)	42 (55)
High risk		20 (17)	18 (46)	2 (3)
AKRiS	115			
Low risk		41 (36)	4 (10)	37 (49)
Medium risk		36 (31)	12 (31)	24 (32)
High risk		29 (25)	15 (38)	14 (18)
Very high risk		9 (8)	8 (21)	1 (1)

Data are presented as median (IQR) or N (%).
N*, number of patients with available data.

Table 4: Predictors of kidney failure—survival analysis.

		Unadjusted			Adjusted[a]		
	N	HR	95% CI	P	HR	95% CI	P
AKRiS	115						
Low risk (1)		1.00 (ref)					
Medium risk (2)		4.04	1.30–12.53	.02			
High risk (3)		8.36	2.76–25.30	<.001			
Very high risk (4)		17.56	5.25–58.76	<.001			
Dialysis within 4 weeks	115	7.50	3.87–14.55	<.001	6.20	2.76–13.95	<.001
Presence of C3 deposits	103	2.57	1.25–5.26	.01	1.76	0.83–3.73	.14
Presence of renal arteritis	115	3.65	1.41–9.46	.008	2.25	0.84–6.06	.11
UPCR at baseline	108	1.20	1.02–1.41	.03	1.00	0.83–1.21	.96
Hematuria at baseline	97	1.00	1.00–1.00	.689	1.00	1.00–1.00	.50
eGFR after induction	85	0.93	0.89–0.98	.002	0.94	0.89–0.99	.03
UPCR after induction	83	1.90	1.25–2.89	.003	1.62	1.02–2.58	.04
Hematuria after induction	83	1.01	1.00–1.02	.14	1.01	1.00–1.03	.09

[a]Adjusted for AKRiS.
N, number of patients with data.

predictive performance of AKRiS declined with longer follow-up intervals, but was significantly improved by adding the peak eGFR attained post-therapy [21]. The difference in the magnitude of AKRiS improvement between our study and that of Sandino-Bermudez may be attributed to differences in cohort characteristics. Our cohort was older, had a higher proportion of MPO-ANCA positive patients, and showed more severe kidney involvement at baseline. Importantly, predictive scores that incorporate both baseline and post-induction therapy variables are only applicable to patients who remain free of kidney failure following induction therapy, and are therefore challenging to compare statistically with scores used at baseline. In addition, proteinuria after induction therapy may result from active glomerulonephritis or chronic kidney damage. In this sense, kidney biopsies may be useful in AAV patients with persistent proteinuria after induction therapy to adapt immunosuppressive therapy [33].

Complement activation is emerging as a key contributor to poor renal outcome in AAV. Complement C3 staining (≥1+ intensity) was observed in 44% of patients in our cohort, which is consistent with the findings of Oba *et al*. (39.4%) [25]. Although C3 deposition was not significantly associated with kidney failure in multivariate analysis in our cohort, previous studies have shown its correlation with worse long-term outcomes [24–28]. Similarly, renal arteritis was identified in 6% of our patient biopsies and associated with kidney failure in univariate analysis. This concurs with Boudhabhay *et al*., who suggested that AAV patients with renal arteritis represented a distinct subtype, often characterized by older age, a more pronounced inflammatory syndrome and significantly poorer renal survival [29]. The

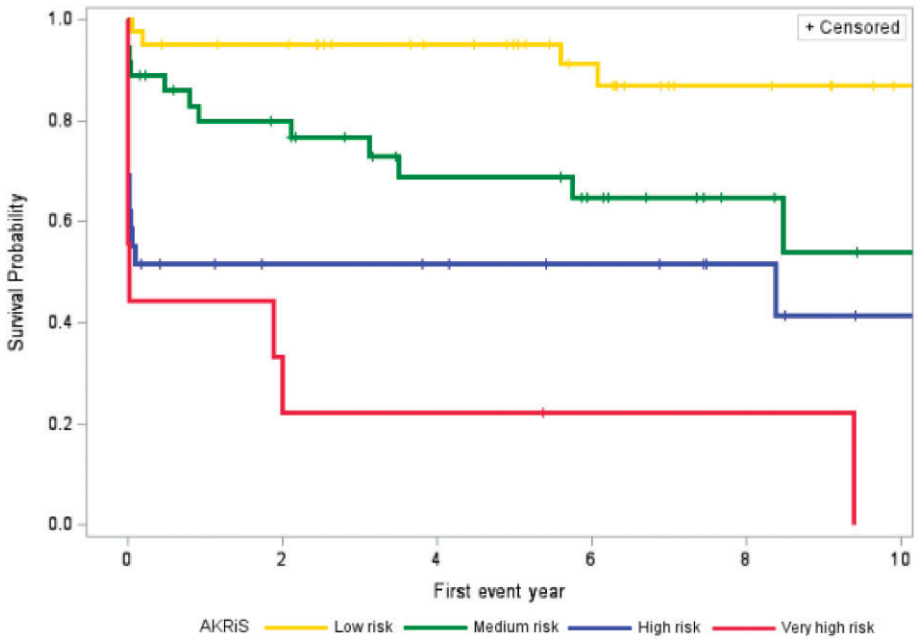


Figure 2: Kidney survival according to AKRiS classification. Kapan–Meier curve showing development of kidney failure of patients with AAV according to AKRiS risk class (low, moderate, high and very high). $P < .001$.

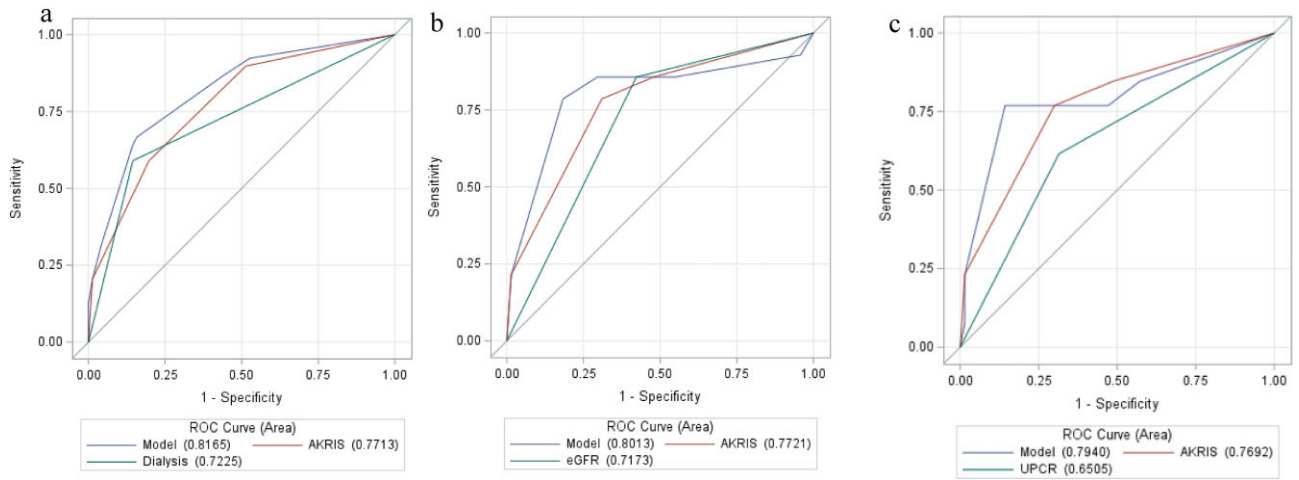


Figure 3: ROC curve for (**a**) early dialysis, AKRiS and both parameters ($N = 115$), (**b**) eGFR after induction, AKRiS and both parameters ($N = 85$), and (**c**) UPCR after induction, AKRiS and both parameters ($N = 83$).

moderate number of biopsies in our cohort may explain the lack of significant association between C3 staining and renal arteritis, and kidney failure.

Altogether, dialysis within 4 weeks of presentation, eGFR after induction and UPCR after induction were significant predictors of kidney failure risk after adjustment for AKRiS. Adding these parameters to the AKRiS model moderately improved its predictive performance (AUROC). It is worth noting that AKRiS incorporates creatinine levels, which may overlap with the information provided by dialysis within 4 weeks of presentation and eGFR after induction. Also, AUROC may not be sensitive to modest improvements in model performance, especially when adding new markers to a model that includes standard risk factors [34, 35]. A larger cohort would be necessary to reliably establish whether these additional variables improve the AKRiS model. Among patients who required dialysis within 4 weeks, the percentage of normal glomeruli was associated with recovery from dialysis on univariate analysis. This percentage, included in the AKRiS model, is known to be a very strong predictor of kidney survival in AAV [18, 31].

This study's strengths include the use of a well-defined multicentric cohort and comprehensive histopathological analysis. However, there are some limitations. The moderate sample size may have reduced the power to detect associations with features such as renal arteritis and C3 deposits. Another limitation is the review of kidney biopsies by only one senior pathologist [5].

In conclusion, AKRiS is a valuable tool for predicting kidney failure in AAV patients, although it should not be used in

Table 5: Characteristics at baseline of patients requiring early dialysis according to kidney function recovery.

	Initial dialysis without recovery, N = 23	Initial dialysis with recovery, N = 11
Demographics		
Age (years)	64 (55–70)	64 (56–71)
Gender (male)	14 (61)	8 (73)
Organ involvement		
ENT (*N*)	5 (22)	2 (18)
Lung (*N*)	14 (61)	6 (55)
Biological parameters at baseline		
Baseline UPCR (g/g)	1.49 (0.75–2.08)	1.73 (1.00–3.90)
Baseline hematuria (/µL)	80 (48–250)	191 (91–332)
ANCA type (MPO/PR3)	11/10	4/6
ANCA titer (AU/L)	126 (75–200)	101 (88–134)
CRP (mg/dL)	38 (23–131)	102 (22–231)
Histological data		
Number of glomeruli (*N*)	12 (7–20)	13 (10–17)
Normal glomeruli (%)	13 (2–17)	25 (17–50)
Crescentic glomeruli (%)	45 (22–64)	42 (35–60)
Cellular crescentic glomeruli (%)	19 (8–32)	33 (17–60)
IFTA		
0	9	7
1	5	2
2	5	1
3	4	1
Vasculitis	4 (17)	1 (9)
IF C3 deposits (≥1+)	13 (54)	1 (9)
Risk scores		
Berden classification		
Focal	1	3
Crescentic	8	4
Mixed	11	4
Sclerotic	3	0
Mayo Clinic Chronicity Score		
Minimal	7	6
Mild	5	4
Moderate	7	0
Severe	1	1
Percentage of ANCA Crescentic Score	67 (50–82)	56 (44–67)
ARRS		
Low risk	1	1
Medium risk	8	10
High risk	14	0
AKRiS		
Low risk	1	1
Medium risk	4	2
High risk	13	8
Very high risk	5	0

Data are presented as median (IQR) or *N* (%).
*N**, number of patients with available data.
ENT, ear, nose, throat; CRP, C-reactive protein.

isolation to guide therapeutic decisions. Its predictive accuracy may be limited in patients requiring dialysis at presentation. Dialysis at presentation, eGFR after induction and UPCR after induction are strong predictors of kidney failure. Incorporating these factors into the AKRiS model moderately improves its predictive performance, and they may serve as practical placeholder endpoints for kidney failure. The potential for recovery, even in patients with severe kidney involvement, underscores the importance of timely and personalized treatment strategies.

SUPPLEMENTARY DATA

Supplementary data are available at *Clinical Kidney Journal* online.

ACKNOWLEDGEMENTS

We wish to thank members of the UCLouvain Kidney Disease Network for referral of kidney biopsies: Valentine Gillion (Cliniques universitaires Saint-Luc), Elliott Van Regemorter (Cliniques universitaires Saint-Luc), Miguel Guillen (EpiCURA, Hornu, Belgium), Philippe Leroy (CHR Mons-Hainaut, Mons, Belgium), Lionel Mazzoleni (CHU Ambroise Paré, Mons, Belgium), Marie Rommelaere (Hopital de Marche, Marche, Belgium), Dominique Vandervelde (Hopitaux Iris Sud, Brussels, Belgium). We also wish to thank Frederic Houssiau, Farah Tamirou, Antoine Froidure, Lucie Pothen and Halil Yildiz (Cliniques universitaires Saint-Luc), for the care of patients, and Christophe de

Terwangne (Cliniques universitaires Saint-Luc), for statistical support.

AUTHORS' CONTRIBUTIONS

C.M., S.A., J.M. and N.D. designed the study and wrote the manuscript. S.A. analysed all the kidney biopsies. A.C. performed the statistical analyses. All authors apart from A.C. were taking care of the patients and collected data at baseline and follow-up. All authors discussed the results and contributed to the final manuscript.

DATA AVAILABILITY STATEMENT

The data underlying this article will be shared on reasonable request to the corresponding author.

CONFLICT OF INTEREST STATEMENT

None declared.

REFERENCES

1. Kitching AR, Anders HJ, Basu Nc *et al*. ANCA-associated vasculitis. *Nat Rev Dis Primers* 2020;**6**:71. https://doi.org/10.1038/s41572-020-0204-y.
2. Moiseev S, Novikov P, Jayne D *et al*. End-stage renal disease in ANCA-associated vasculitis *Nephrol Dial Transplant* 2017;**32**:248–53. https://doi.org/10.1093/ndt/gfw046.
3. Chalkia A, Jayne D. ANCA-associated vasculitis-treatment standard. *Nephrol Dial Transplant* 2024;**39**:944–55. https://doi.org/10.1093/ndt/gfad237.
4. Kidney Disease: Improving Global Outcomes (KDIGO) ANCA Vasculitis Work Group. KDIGO 2024 Clinical Practice Guideline for the Management of Antineutrophil Cytoplasmic Antibody (ANCA)–Associated Vasculitis. *Kidney Int* 2024;**105**:S71–116. https://doi.org/10.1016/j.kint.2023.10.008.
5. Bajema IM, Hagen EC, Hansen BE *et al*. The renal histopathology in systemic vasculitis: an international study survey of inter- and intra-observer agreement. *Nephrol Dial Transplant* 1996;**11**:1989–95. https://doi.org/10.1093/ndt/11.10.1989.
6. Berden AE, Ferrario F, Hagen EC *et al*. Histopathological classification of ANCA-associated glomerulonephritis. *J Am Soc Nephrol* 2010;**21**:1628–36. https://doi.org/10.1681/ASN.2010050477.
7. Sethi S, D'Agati VC, Nast CC *et al*. A proposal for standardized grading of chronic changes in native kidney biopsy specimens. *Kidney Int* 2017;**91**:787–9. https://doi.org/10.1016/j.kint.2017.01.002.
8. Casal Moural M, Fervenza FC, Specks U *et al*. Kidney biopsy chronicity grading in antineutrophil cytoplasmic antibody-associated vasculitis. *Nephrol Dial Transplant* 2022;**37**:1710–21. https://doi.org/10.1093/ndt/gfab250.
9. Brix SR, Noriega M, Tennstedt P *et al*. Development and validation of a renal risk score in ANCA-associated vasculitis. *Kidney Int* 2018;**94**:1177–88. https://doi.org/10.1016/j.kint.2018.07.020.
10. van Daalen EE, Wester Trejo MAC, Göçeroglu A *et al*. Developments in the histopathological classification of ANCA-associated glomerulonephritis. *Clin J Am Soc Nephrol* 2020;**15**:1103–11. https://doi.org/10.2215/CJN.14561119.
11. Mejía-Vilet JM, Martín-Nares E, Cano-Verduzco ML *et al*. Validation of a renal risk score in a cohort of ANCA-associated vasculitis patients with severe kidney damage. *Clin Rheumatol* 2020;**39**:1935–43. https://doi.org/10.1007/s10067-020-04936-5.
12. Tan PG, O'Brien J, Pusey CD *et al*. Validation of the ANCA renal risk score in a London cohort: potential impact of treatment on prediction outcome. *Kidney Int* 2021;**99**:488–9.
13. Dp MG, Lees JS, Traynor JP *et al*. Outcomes in ANCA-associated vasculitis in Scotland: validation of the Renal Risk Score in a complete national cohort. *Kidney Int Rep* 2023;**8**:1648–56. https://doi.org/10.1016/j.ekir.2023.05.029.
14. Xia M, U R, Zhen Z *et al*. Meta-analytical accuracy of ANCA Renal Risk Score for prediction of renal outcome in patients with ANCA-associated glomerulonephritis. *Front Med* 2021;**8**:736754.
15. Saito M, Saito A, Abe F *et al*. Evaluation of a newly proposed renal risk score for Japanese patients with ANCA-associated glomerulonephritis. *Clin Exp Nephrol* 2022;**26**:760–9. https://doi.org/10.1007/s10157-022-02217-w.
16. Sanchez-Alamo B, Moi L, Bajema I *et al*. Long-term outcomes of kidney function in patients with ANCA-associated vasculitis. *Nephrol Dial Transplant* 2024;**39**:1483–93. https://doi.org/10.1093/ndt/gfae018.
17. Christodoulou M, Moysidou E, Lioulios G *et al*. The prognostic value of two histopathologic classification models of ANCA-associated glomerulonephritis: a prospective study. *J Nephrol* 2024;**37**:941–50. https://doi.org/10.1007/s40620-023-01855-x.
18. Bate S, McGovern D, Costigliolo F *et al*. The improved kidney risk score in ANCA-associated vasculitis for clinical practice and trials. *J Am Soc Nephrol* 2024;**35**:335–46. https://doi.org/10.1681/ASN.0000000000000274.
19. Scurt FG, Hirschfield V, Ganz MJ *et al*. ANCA kidney risk score performance in a German cohort of patients with histologically confirmed ANCA-associated renal vasculitis. *Kidney360* 2024;**5**:886–94. https://doi.org/10.34067/KID.0000000000000459.
20. Bate S. Will the ANCA Kidney Risk Score become the gold standard for prognostication in ANCA-associated GN? *Kidney360* 2024;**5**:789–90.
21. Sandino-Bermudez MJ, Hernandez-Andrade A, Hinojosa-Azaola M-NE *et al*. Performance of clinical and histological prognostic scores for kidney survival in ANCA-associated vasculitis. *Rheumatology (Oxford)* 2025;**64**:1981. https://doi.org/10.1093/rheumatology/keae336.
22. Boud'hors C, Riou J, Fage N *et al*. Adding 6-month parameters for the prediction of kidney prognosis in ANCA-associated glomerulonephritis. *Clin Kidney J* 2023;**16**:2530–41. https://doi.org/10.1093/ckj/sfad157.
23. Takeda R, Takahashi K, Kronbichler A *et al*. Development of a kidney prognostic score in a Japanese cohort of patients with antineutrophil cytoplasmic autoantibody vasculitis. *Kidney Int Rep* 2024;**9**:611–23. https://doi.org/10.1016/j.ekir.2024.01.007.
24. Lionaki S, Marinaki S, Liapis G *et al*. Hypocomplementemia at diagnosis of pauci-immune glomerulonephritis is associated with advanced histopathological activity index and high probability of treatment resistance. *Kidney Int Rep* 2021;**6**:2425–35. https://doi.org/10.1016/j.ekir.2021.05.043.
25. Oba R, Kanzaki G, Sasaki T *et al*. Long-term renal survival in antineutrophil cytoplasmic antibody-associated glomerulonephritis with complement C3 deposition. *Kidney Int Rep* 2021;**6**:2661–70. https://doi.org/10.1016/j.ekir.2021.08.005.

26. Villacorta J, Diaz-Crespo F, Acevedo M *et al*. Glomerular C3d as a novel prognostic marker for renal vasculitis. *Hum Pathol* 2016;**56**:31–9. https://doi.org/10.1016/j.humpath.2016.05.015.
27. Chen M, Xing GQ, Yu F *et al*. Complement deposition in renal histopathology of patients with ANCA-associated pauci-immune glomerulonephritis. *Nephrol Dial Transplant* 2009;**24**:1247–52. https://doi.org/10.1093/ndt/gfn586.
28. Hilhorst M, van Paassen P, van Rie H. Complement in ANCA-associated glomerulonephritis. *Nephrol Dial Transpl* 2017;**32**:1302–13. https://doi.org/10.1093/ndt/gfv288.
29. Boudhabhay I, Delestre F, Coutance G *et al*. Reappraisal of renal arteritis in ANCA-associated vasculitis: clinical characteristics, pathology, and outcome. *J Am Soc Nephrol* 2021;**32**:2362–74. https://doi.org/10.1681/ASN.2020071074.
30. Benichou N, Charles P, Terrier B *et al*. Proteinuria and hematuria after remission induction are associated with outcome in ANCA-associated vasculitis *Kidney Int* 2023;**103**:1144–55. https://doi.org/10.1016/j.kint.2023.02.029.
31. De Lind van Wijngaarden RAF, Hauer HA, Wolterbeek *et al*. Clinical and histological determinants of renal outcome in ANCA-associated vasculitis: a prospective analysis of 100 patients with severe renal involvement. *J Am Soc Nephrol* 2006;**17**:2264–74. https://doi.org/10.1681/ASN.2005080870.
32. Lee YJ, Ahn SM, Oh JS *et al*. Recovery and long-term renal outcome of patients with anti-neutrophil cytoplasmic antibody-asscociated vasculitis who are on dialysis at presentation *J Rheum Dis* 2023;**30**:251–9.
33. Aqeel F, Xu L, Geetha D. Repeat kidney biopsies in anti-neutophil cytoplasmic autoantibody-asscociated vasculitis: clinical and histological progression. *Kidney Int Rep* 2023;**8**:2146–9. https://doi.org/10.1016/j.ekir.2023.07.021.
34. Biwas S, Arun B, Parmigiani G. Reclassification of predictions for uncovering subgroup specific improvement. *Statist Med* 2014;**33**:1914–27. https://doi.org/10.1002/sim.6077.
35. Spitz MR, Amos CI, D'Amelio A Jr *et al*. Discriminatory accuracy from single-nucleotide polymorphisms in models to predict breast cancer risk. *J Natl Cancer Inst* 2009;**101**:1731–2. https://doi.org/10.1093/jnci/djp394.

Received: 10.4.2025; Editorial decision: 28.7.2025