International Journal of General Medicine

Dovepress
Taylor & Francis Group

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ORIGINAL RESEARCH

Systemic Immune-Inflammation Index and Prognostic Nutritional Index as Predictors of Renal Survival in Crescentic Glomerulonephritis

Hatice Şahin[1], Fatma Ayerden Ebinç[1], Gülay Ulusal Okyay[1], Ebru Gök Oğuz[1], Ebru Şebnem Ayva[2], Arzu Sağlam Ayhan[3], Mehmet Deniz Aylı[1]

[1]Division of Nephrology, Department of Internal Medicine, Etlik City Hospital, Ankara, Turkey; [2]Department of Pathology, Etlik City Hospital, Ankara, Turkey; [3]Department of Pathology, Hacettepe University Faculty of Medicine, Ankara, Turkey

Correspondence: Hatice Şahin, Division of Nephrology, Department of Internal Medicine, Etlik City Hospital, Ankara, Turkey, Tel +9053225502180, Email haticeharmansa@hotmail.com

Purpose: Crescentic glomerulonephritis (GN) is a rapidly progressive kidney disease associated with a high risk of end-stage renal disease (ESRD). This study aimed to assess whether systemic inflammation and nutritional status, as measured by the systemic immune-inflammation index (SII) and prognostic nutritional index (PNI) at diagnosis, can predict one-year renal survival in patients with crescentic GN.

Methods: This retrospective study included 82 adult patients with biopsy-proven Type 1 or Type 3 crescentic GN. Baseline SII and PNI were calculated from pre-treatment blood samples. Clinical, laboratory, and histopathological data were collected. Patients were followed for 12 months and classified into two groups based on the development of ESRD.

Results: The cohort (63.4% male) had a mean age of 53.65 ± 15.87 years; 26 patients (31.7%) progressed to ESRD. Multivariate analysis identified elevated SII [OR: 1.79; 95% CI: 1.22–18.81; p = 0.03], low PNI [OR: 0.92, 95% CI: 0.96–0.99; p = 0.03], hypoalbuminemia [OR: 0.36, 95% CI: 0.15–0.84; p = 0.02], reduced estimated glomerular filtration rate [OR: 0.93, 95% CI: 0.88–0.98; p = 0.009], anemia [OR: 0.37; 95% CI: 0.22–0.63; p < 0.001], higher crescent ratio [OR: 1.05, 95% CI: 1.02–1.09; p = 0.02], and plasmapheresis requirement [OR: 0.074, 95% CI: 0.016–0.349; p = 0.001] as independent predictors of ESRD. Receiver operating characteristic analysis determined cutoff values of 176.38 for SII (area under the curve [AUC]: 0.679, p = 0.01) and 31.88 for PNI (AUC: 0.650, p = 0.03). Glomerulosclerosis ratio and interstitial fibrosis/tubular atrophy were not independently associated with ESRD (p = 0.13 and p = 0.14, respectively).

Conclusion: SII and PNI are independent but moderate predictors of one-year renal survival in crescentic GN. Incorporating these readily available biomarkers with histological evaluation may enhance risk stratification and help guide early, aggressive immunosuppressive therapy.

Keywords: crescentic glomerulonephritis, systemic immune-inflammation index, prognostic nutritional index, end-stage renal disease

Introduction

Rapidly progressive glomerulonephritis (RPGN) is a life-threatening kidney disorder characterized by a rapid and severe decline in renal function over weeks to months, necessitating prompt diagnosis and treatment. The hallmark histopathological feature in renal biopsy specimens is extensive extracapillary proliferation of parietal epithelial cells, forming crescents in Bowman's space and involving more than 50% of glomeruli. Based on immunofluorescence findings, crescentic GN is classified into three types: Type 1, anti-glomerular basement membrane (anti-GBM) disease; Type 2, immune complex–mediated GN; and Type 3, pauci-immune GN, most commonly associated with anti-neutrophil cytoplasmic antibodies (ANCA).[1–3]

Both anti-GBM disease and ANCA-associated glomerulonephritis (AAGN) frequently present with severe renal involvement. If left untreated, these conditions may rapidly progress to end-stage renal disease (ESRD), potentially leading to increased healthcare utilization and economic burden due to frequent hospitalizations and the need for renal replacement therapy.[4,5]

https://doi.org/10.2147/IJGM.S565960
Received: 8 September 2025
Accepted: 17 February 2026
Published: 26 February 2026

Moreover, infection is the leading cause of mortality in patients with ANCA-associated vasculitis (AAV) within the first year.[6] These observations highlight the urgent need for reliable prognostic markers to identify high-risk patients and optimize clinical management in crescentic GN. Well-established prognostic indicators of poor renal outcome include clinical features such as pulmonary hemorrhage, oliguria, and dialysis requirement; laboratory abnormalities such as elevated serum creatinine (sCr) and positive anti-GBM antibodies; and histopathological findings such as fibrous crescents and interstitial fibrosis/tubular atrophy.[1–3,5] Recent evidence also indicates that lower baseline hemoglobin is an independent predictor of adverse renal outcomes in patients with AAV.[4] Several histopathological scoring systems, such as the International Pathology Classification,[7] the Renal Risk Score (RRS),[8] and the Mayo Clinic Chronicity Score (MCCS),[9] are widely used to improve ESRD risk prediction in AVV. In addition, systemic inflammation has emerged as a key driver in the progression of crescentic GN. Inflammatory markers such as the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) have been associated with poorer renal outcomes and increased mortality.[10–12] More recently, composite indices such as the Systemic Immune-Inflammation Index (SII) and the Prognostic Nutritional Index (PNI), which can be easily derived from complete blood count parameters, have demonstrated prognostic significance in a variety of conditions, including cancers, cardiovascular diseases, and autoimmune disorders.[13–15] Data on the prognostic value of these indices in patients with AAV remain limited,[16–18] and, to date, no studies have investigated their ability to predict renal survival in patients with Type 1 or Type 3 crescentic GN. We hypothesized that SII and PNI, readily measurable biomarkers, could improve early risk stratification beyond traditional indicators.

Consequently, this study aimed to assess whether SII and PNI, derived from pre-biopsy blood samples, could predict the one-year risk of ESRD in patients with Type 1 and Type 3 crescentic GN.

Materials and Methods

The study protocol was approved by the Institutional Review Board of Etlik City Hospital on June 10, 2025 (approval no. AEŞH-BADEK2-2025-293) and was conducted in accordance with the principles of the Declaration of Helsinki. Due to the retrospective design, the requirement for informed consent was waived. Patient confidentiality was strictly maintained throughout the study. This retrospective observational study was conducted at our nephrology clinic. All patient care and data management were supervised by the same nephrology team, ensuring consistency in clinical practice. Medical records of 97 adult patients with serologically positive ANCA or anti-GBM antibodies and a suspected diagnosis of crescentic GN based on clinical and laboratory findings were reviewed at Dışkapı Yıldırım Beyazıt Education and Research Hospital and, following the relocation of the nephrology clinic, its successor institution, Etlik City Hospital, in Ankara, Turkey, between January 1, 2015, and June 1, 2024. Inclusion criteria required patients to be ≥18 years of age with biopsy-confirmed, newly diagnosed, and treatment-naive Type 1 or Type 3 crescentic GN. Exclusion criteria were applied a priori to ensure a clinically and pathophysiologically homogeneous study cohort and included a follow-up duration shorter than 12 months or absence of renal biopsy (n = 7), the presence of a concurrent infection at diagnosis (n = 4), or previous vasculitis treatment (n = 4). None of the included patients had a history of malignancy, rheumatic disease, or other chronic kidney disorders. Following this systematic screening process, a final cohort of 82 patients was enrolled in the analysis (Figure 1). Type 2 crescentic GN was deliberately excluded, as it does not represent a single disease entity but rather a descriptive framework encompassing multiple immune complex–mediated disorders such as lupus nephritis, immunoglobulin (Ig) A nephropathy, infection-related GN, and membranoproliferative GN with distinct immunopathological mechanisms, treatment strategies, and prognostic determinants. We believed that including these heterogeneous entities would have compromised the study's internal validity and obscured the interpretation of prognostic associations within a unified mechanistic framework.

Data on patient demographics, anthropometric measurements, laboratory results, renal biopsy findings, and treatment modalities were systematically extracted from electronic hospital records and patient charts. Key variables included age, sex, presence of diabetes mellitus (DM), hypertension (HT), and episodes of haemoptysis. Serum levels of myeloperoxidase (MPO)-ANCA and proteinase 3 (PR3)-ANCA were measured using established methods: indirect immunofluorescence assays (IFA; Euroimmun, Lübeck, Germany) and direct enzyme-linked immunosorbent assays (ELISA; Inova Diagnostics, San Diego, USA). Serum anti-GBM antibody levels were detected using the Alegria device.

Complete blood counts (CBC), including hemoglobin, white blood cell (WBC), neutrophil, lymphocyte, and platelet counts, were analyzed using a Sysmex XN-1000 hematology analyzer (Sysmex Corp., Kobe, Japan). The SII value was calculated by the equation of [Platelet ($\times 10^3/\mu L$) × Neutrophil ($\times 10^3/\mu L$)/Lymphocyte ($\times 10^3/\mu L$)].[16] Serum albumin

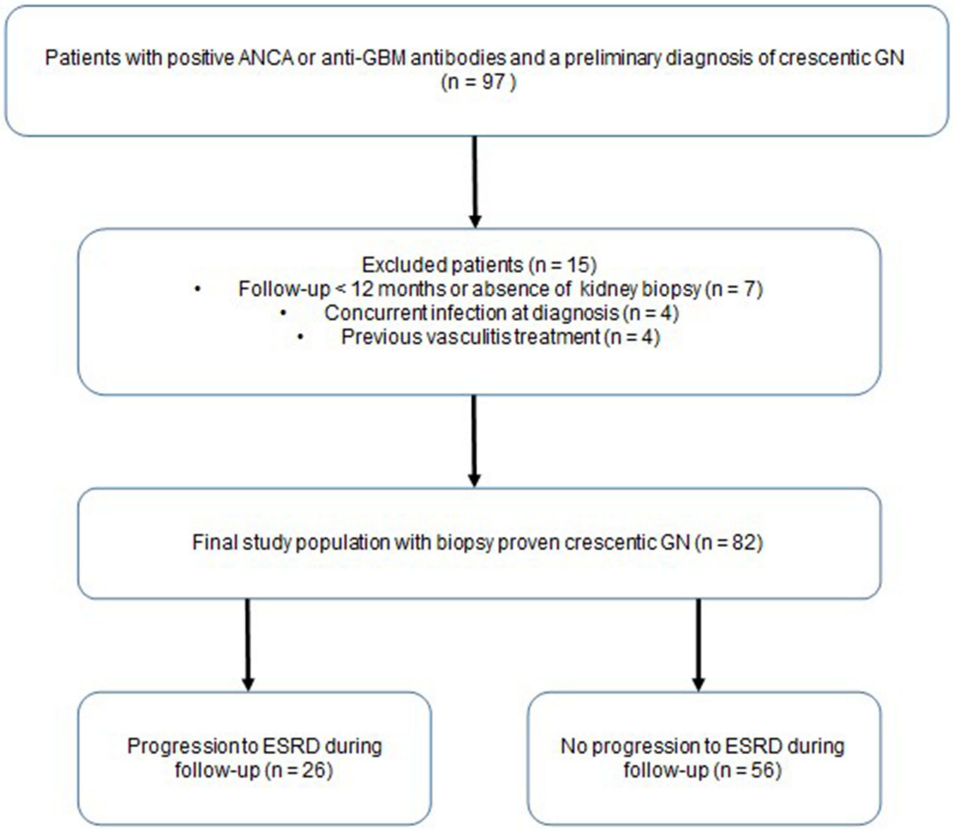

Figure 1 Flowchart of the study population.
Abbreviations: ANCA, anti neutrophilic cytoplasmic antibody; GBM, glomerular basement membrane; GN, glomerulonephritis; ESRD, end-stage renal disease.

levels were measured using a colorimetric method with bromocresol green on a Roche Cobas c702 analyzer (Roche Diagnostics GmbH, Mannheim, Germany). PNI was calculated as the following equation: [10 x serum albumin (g/dL) + 0.005 × Lymphocyte count ($\times 10^3/\mu L$)].[18] sCr levels were measured via the Jaffé method on the Roche Cobas c702 analyzer. The estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine equation.[19] C-reactive protein (CRP) levels were determined using the Architect Plus C4000 analyzer (Abbott, USA). Due to the retrospective design of the study, erythrocyte sedimentation rate (ESR) values were not available for all patients.

Following baseline data collection, all patients were monitored for 12 months. The primary endpoint was ESRD, defined as the requirement for dialysis for more than three months. At the 12-month follow-up, patients were stratified into two groups: those who progressed to ESRD and those who did not.

Renal tissue specimens were examined by light microscopy and immunofluorescence following standard protocols, and diagnoses of Type 1 and Type 3 crescentic GN were confirmed by experienced pathologists. Histopathological findings from the biopsy reports were recorded, including the percentage of global glomerular sclerosis and the presence of crescents. The crescent percentage was calculated by dividing the number of crescentic glomeruli by the total number of non-sclerosed glomeruli. Interstitial fibrosis and tubular atrophy (IF/TA) were classified semiquantitatively as follows: Grade 1 (mild), ≤25% of the tubulointerstitium affected; Grade 2 (moderate), 26–50% affected; and Grade 3 (severe), >50% involved.

All patients received standard immunosuppressive therapy in accordance with KDIGO guidelines.[20,21] Induction therapy consisted of intravenous pulse methylprednisolone administered over 3 consecutive days, with a cumulative dose of 1–3 g, followed by cyclophosphamide or rituximab, and plasmapheresis for patients meeting specific criteria.

Maintenance therapy included low-dose corticosteroids in combination with azathioprine (1–2 mg/kg/day), mycophenolate mofetil (1.0–1.5 g/day), or rituximab alone.[20,21]

Statistical Analysis

Statistical analyses were performed using SPSS version 24 (SPSS Inc., Chicago, IL, USA). Categorical variables were compared using the chi-square test or Fisher's exact test, with results presented as counts and percentages. The distribution of continuous variables was assessed with the Kolmogorov–Smirnov test. Normally distributed data were compared using the Student's *t*-test and reported as mean ± standard deviation (SD), whereas non-normally distributed data were analyzed with the Mann–Whitney *U*-test and reported as median with interquartile range (IQR, 25^{th}–75^{th} percentiles). Spearman correlation analysis was performed to assess associations between ESRD and study parameters. Multivariate logistic regression was applied to identify independent predictors of ESRD. Logarithmic transformation was applied to non-normally distributed variables included in the regression models. Due to the limited number of events, multivariate models were adjusted for age and gender. Results are presented as odds ratios (OR) with 95% confidence intervals (CI). Receiver operating characteristic (ROC) curve analysis was conducted to evaluate the predictive performance of the studied parameters. A p-value < 0.05 was considered statistically significant.

Results

A total of 82 patients with Type 1 or Type 3 crescentic GN were included in the study. The baseline characteristics of the cohort are summarized in Table 1. The mean age was 53.65 ± 15.87 years, 63.4% male, and 14.6% had DM. At presentation, all patients exhibited hematuria, proteinuria, and oliguria, while 31.7% reported haemoptysis. Anti-GBM antibodies were positive in 8 patients (9.8%), PR3-ANCA in 30 patients (36.5%), and MPO-ANCA in 44 patients (53.7%). By the end of one year, 26 patients (31.7%) had reached the primary endpoint of ESRD, and no deaths were recorded. The ESRD and non-ESRD groups were comparable with respect to age, sex distribution, and the prevalence of DM, HT, and haemoptysis (Table 1). However, the ESRD group had significantly lower eGFR ($p < 0.001$), serum albumin ($p = 0.04$), and hemoglobin levels ($p < 0.001$), and higher sCr levels ($p < 0.001$) compared with the non-ESRD group.

The median SII for the entire cohort was 1647.29 (IQR 1122.98–3192.67), 1363.79 (IQR 904.48–2490.99) in the non-ESRD group, and 2444.48 (IQR 1557.93–4643.74) in the ESRD group ($p = 0.01$). The median PNI was 35.97 (IQR 27.46–46.36) overall, 36.78 (IQR 30.15–47.85) in patients without ESRD, and 29.68 (IQR 23.91–41.46) in those who developed ESRD ($p = 0.03$) (Table 1).

Table 1 General Characteristics of the Study Population and Subgroups

	All Patients (n = 82)	Non–ESRD Group (n = 56)	ESRD Group (n = 26)	P value
Age (years)	53.65 ± 15.87	53.89 ± 16.20	53.12 ± 15.29	0.840
Male sex, n (%)	52 (63.4)	36 (64.3)	16 (61.9)	0.810
Arterial hypertension, n (%)	58 (48.5)	30 (53.6)	18 (69.2)	0.230
Diabetes mellitus, n (%)	12 (14.6)	6 (10.7)	6 (23)	0.180
Haemoptysis, n (%)	26 (31.7)	15 (26.8)	11 (42.3)	0.200
ANCA–positivity, n (%)	74 (90.2)	54 (96.4)	20 (76.9)	0.320
Anti-GBM positivity, n (%)	8 (9.8)	2 (3.6)	6 (23.1)	**0.010**
Plasmapheresis, n (%)	51 (62.2)	27 (48.2)	24 (92.2)	**< 0.001**

(*Continued*)

Table 1 (Continued).

	All Patients (n = 82)	Non–ESRD Group (n = 56)	ESRD Group (n = 26)	P value
Laboratory results at admission				
White blood cell (10^3/μL)	9.75 (7.697–13.4)	9.62 (7.692–12.625)	10.30 (7.825–14.527)	0.390
Neutrophil (10^3/μL)	7.335 (5.652–10.405)	7.145 (5.510–9.210)	8.300 (6.135–12.582)	0.153
Lymphocyte (10^3/μL)	1.265 (8.325–1.725)	1.285 (0.845–1.930)	1.125 (0.810–1.530)	0.161
Hemoglobin (g/dL)	9.4 (8.5–10.43)	9.70 (8.92–10.80)	8.5 (7.1–9.4)	**< 0.001**
Platelet (10^3/μL)	305 (222.75–388)	294 (220.50–361)	314.50 (235–411.2)	0.455
Serum creatinine (mg/dL)	4.43 (2.29–6.44)	3.44 (1.86–5.23)	6.47 (4.49–9.28)	**< 0.001**
eGFR (mL/min/1.73 m^2)	13.0 (8.0–26.0)	15.5 (9.25–36.75)	8 (5–13)	**< 0.001**
Albumin (g/dL)	3.19 (2.6–3.51)	3.23 (2.71–3.59)	2.87 (2.24–3.34)	**0.040**
C-reactive protein (mg/dL)	63.5 (18.83–111.36)	61.76 (15.00–105.27)	87.64 (24–158)	0.130
SII ($x10^3$)	1647.29 (1122.98–3192.67)	1363.79 (904.48–2490.99)	2444.48 (1557.93–4643.74)	**0.010**
PNI	35.97 (27.46–46.36)	36.78 (30.15–47.85)	29.68 (23.91–41.46)	**0.030**
Histopathological findings				
Number of glomeruli (n)	25 (14–37.5)	25 (14–36)	20 (14–39)	0.746
Crescentic glomeruli ratio (%)	59 (41.5–75.25)	55 (35.62–69.25)	75 (53–88.5)	**0.003**
Glomerulosclerosis ratio (%)	19.4 (2.88–35.0)	17.5 (0.5–33.0)	19.75 (5.8–41.25)	0.218
Interstitial fibrosis/tubular atrophy				0.268
• Grade 1: ≤25%	60 (73.2)	44 (78.6)	16 (61.5)	
• Grade 2: 26–50%	13 (15.7)	7 (12.5)	6 (23.1)	
• Grade 3: > 50%	9 (10.8)	5 (8.9)	4 (15.4)	

Notes: Normally distributed continuous data are expressed as mean ± standard deviation. Abnormally distributed data are expressed as median and interquartile range. Categorical variables are expressed as numbers and percentages. Statistically significant parameters are shown in bold.
Abbreviations: ESRD, end-stage renal disease; ANCA, anti neutrophilic cytoplasmic antibody; GBM, glomerular basement membrane; eGFR, estimated glomerular filtration rate (according to Chronic Kidney Disease Epidemiology Collaboration formula); PNI, prognostic nutritional index; SII, systemic immune-inflammation index.

The development of ESRD was significantly correlated with serum albumin (r = −0.230; p = 0.037), hemoglobin (r = −0.440; p < 0.001), SII (r = 0.288; p = 0.009), PNI (r = −0.241; p = 0.029), and the crescentic glomeruli ratio (r = 0.328; p = 0.003) (Table 2). In univariate logistic regression analysis, albumin, CRP, hemoglobin, eGFR, need for plasmapheresis, crescentic glomeruli ratio, SII, and PNI were significantly associated with the development of ESRD. In multivariate logistic regression analysis, low serum albumin [OR: 0.36, 95% CI: 0.15–0.84; p = 0.02], elevated CRP [OR: 1.007, 95% CI: 1.001–1.013; p = 0.03], low hemoglobin [OR: 0.37, 95% CI: 0.22–0.63; p < 0.001], low eGFR [OR: 0.93, 95% CI: 0.88–0.98; p = 0.009], requirement for plasmapheresis [OR: 0.074, 95% CI: 0.016–0.349; p = 0.001], high crescent ratio [OR: 1.05, 95% CI: 1.02–1.09; p = 0.01], high SII [OR: 1.79, 95% CI: 1.22–18.81; p = 0.03], and low PNI [OR: 0.92, 95% CI: 0.96–0.99; p = 0.02] remained independent predictors of ESRD (Table 3).

ROC analyses were conducted to determine the optimal cutoff values of SII and PNI for predicting one-year ESRD. The ROC curve for SII showed an area under the curve (AUC) of 0.679 (95% CI: 0.557–0.800; p = 0.01), with a cutoff value of 1763.83, corresponding to a sensitivity of 65% and specificity of 62%. Similarly, the ROC curve for PNI showed an AUC of 0.650 (95% CI: 0.523–0.776; p = 0.03), with a cutoff value of 31.88, yielding a sensitivity of 62% and specificity of 69% (Figure 2).

Table 2 Spearman's Rho Correlation Between ESRD and Different Research Parameters

	ESRD	
	r	**p**
Age (year)	−0.038	0.737
Albumin (g/dL)	−0.230	**0.037**
C-reactive protein (mg/dL)	0.166	0.136
White blood cell	0.095	0.395
Lenfosit	−0.156	0.163
Nötrofil	0.159	0.154
Platelet	0.083	0.458
Hemoglobin	−0.440	**< 0.001**
SII	0.288	**0.009**
PNI	−0.241	**0.029**
Crescentic glomeruli ratio (%)	0.328	**0.003**

Abbreviations: ESRD, end-stage renal disease; SII, systemic immune-inflammation index; PNI, prognostic nutritional index. Statistically significant parameters are shown in bold.

Table 3 Logistic Regression Analysis to Evaluate Possible Risk Factors for the Development of ESRD

	Univariate Analysis		Multivariate Analysis	
	OR (95% CI)	**p**	**OR (95% CI)**	**p**
Age	0.99 (0.96–1.02)	0.830	–	
Gender	1.12 (0.43–2.94)	0.810	–	
Albumin	0.40 (0.18–0.89)	**0.030**	0.36 (0.15–0.84)	**0.020**
CRP	1.007 (1.001–1.012)	**0.031**	1.007 (1.001–1.013)	**0.031**
Hemoglobin	0.42 (0.26–0.66)	**< 0.001**	0.37 (0.22–0.63)	**< 0.001**
eGFR	0.93 (0.88–0.98)	**0.010**	0.93 (0.88–0.98)	**0.009**
Haemoptysis	0.50 (0.19–1.32)	0.160	2 (0.76–5.36)	0.160
Plasmapheresis	0.08 (0.02–0.36)	**0.010**	0.074 (0.016–0.349)	**0.001**
Glomerulosclerosis ratio	1.02 (0.99–1.04)	0.160	1.02 (0.99–1.05)	0.130
Interstitial fibrosis/tubular atrophy	1.62 (0.84–3.16)	0.150	1.69 (0.84–3.41)	0.140
Crescentic glomeruli ratio (%)	1.05 (1.02–1.06)	**0.004**	1.05 (1.02–1.09)	**0.010**
SII	4.38 (1.16–16.47)	**0.030**	1.79 (1.22–18.81)	**0.030**
PNI	0.96 (0.93–0.99)	**0.030**	0.92 (0.96–0.99)	**0.020**

Notes: The results are presented with odds ratios (OR) and 95% confidence intervals (CI). Multivariate Models, adjusted by age and gender (variables are restricted with total number of three). Statistically significant parameters are shown in bold.
Abbreviations: ESRD, end-stage renal disease; CRP, C-reactive protein; eGFR, estimated glomerular filtration rate; SII, systemic immune-inflammation index; PNI, prognostic nutritional index.

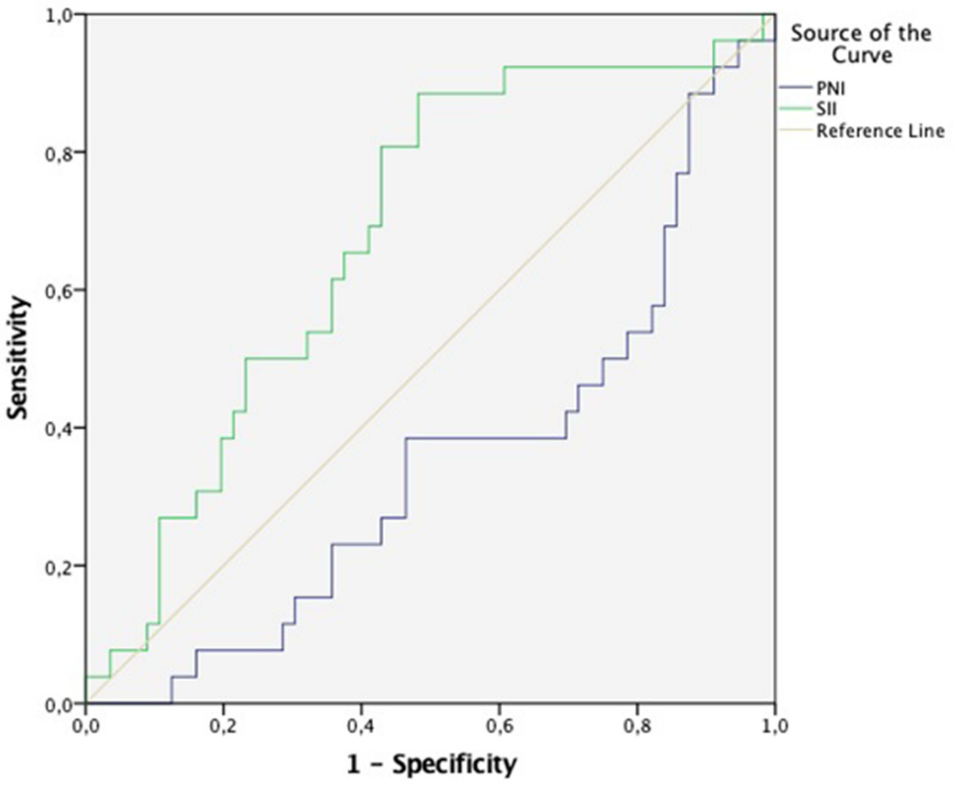

Figure 2 ROC curve of SII and PNI for predicting ESRD showed an AUC of 0.679 (p = 0.01; 95% CI: 0.557–0.800) for SII and 0.650 (p = 0.02; 95% CI: 0.523–0.776) for PNI.
Abbreviations: ROC curve, receiver operator characteristic curve; SII, systemic immune-inflammation index; PNI, prognostic nutritional index; ESRD, end-stage renal disease; AUC, area under the curve; CI, confidence interval.

Discussion

Our retrospective study provides novel evidence that inflammatory and nutritional indices, specifically higher SII and lower PNI are independent predictors of renal outcomes in crescentic GN, with moderate discriminative ability. Additionally, baseline characteristics including reduced eGFR, anemia, elevated CRP, greater crescent formation, and the requirement for plasmapheresis were associated with adverse outcomes. To our knowledge, this is the first study to concurrently assess SII and PNI as prognostic markers in patients with Type 1 and Type 3 crescentic GN, underscoring their potential utility for early risk stratification.

Despite advances in the diagnosis and treatment of crescentic GN, persistent systemic inflammation remains central to its pathogenesis. Traditional acute-phase reactants, such as ESR and CRP, are widely used to assess inflammatory activity, and our findings confirm that elevated CRP at diagnosis independently predicts adverse renal outcomes. However, single-parameter markers may not fully capture the complexity of the immune response. Composite indices, such as the SII and PNI, have recently emerged as promising objective markers. SII was first introduced by Hu et al[22] as a prognostic indicator in hepatocellular carcinoma, and subsequent studies linked it to poor prognosis, tumor recurrence, and metastasis in various malignancies.[13,23] The rationale for SII lies in the interaction of immune cells in crescentic GN. Experimental models indicate that neutrophils are key effectors in Type 3 crescentic GN,[24] while AAV can induce lymphopenia by recruiting peripheral T cells to inflamed tissues.[25] Pro-inflammatory cytokines, including IL-6 and IL-8, further exacerbate this imbalance by reducing lymphocyte counts and increasing neutrophil and platelet activity.[16,26,27] By integrating neutrophil, lymphocyte, and platelet counts, SII may provide a more comprehensive measure of inflammatory burden than individual markers. Our findings support this, showing that elevated SII at diagnosis is significantly associated with ESRD risk. This aligns with previous reports in AAV patients, where high SII predicted poor kidney outcomes.[16] However, contrasting evidence exists; a Chinese study suggested that higher SII might indicate a lower ESRD risk in MPO-AAV, although it remained positively correlated with CRP and ESR.[17] Differences in genetics, ethnicity, and treatment strategies may account for these discrepancies. Overall,

these findings suggest that SII, together with CRP, provides complementary information reflecting the severity of systemic inflammation and predicting renal outcomes in crescentic GN.

The Prognostic Nutritional Index, first described by Onodera et al, was initially used to predict outcomes in malnourished cancer patients undergoing surgery.[28] Calculated from serum albumin and lymphocyte counts, PNI reflects both nutritional status and immune competence.[18,29] Low PNI may result from hypoalbuminemia, lymphopenia, or both. Albumin has anti-inflammatory, anticoagulant, and antiplatelet properties, and stabilizes circulating inflammatory cytokines, while its levels decline in systemic inflammation, malnutrition, and proteinuria, explaining the protective effect of higher albumin.[18,29] PNI has been linked to prognosis in malignancies, chronic diseases, and autoimmune disorders such as systemic lupus erythematosus.[30–33] Although data in AAV are limited, existing evidence indicates that PNI at diagnosis correlates with disease activity, relapse risk, and prognosis, often more strongly than albumin or lymphocyte counts alone. Ahn et al reported that patients with AAV and renal involvement had lower PNI, and that low PNI was associated with higher disease activity.[18] In our cohort, patients with crescentic GN who progressed to ESRD within one year had significantly lower baseline PNI. Multivariate analysis identified low PNI as an independent predictor of ESRD, highlighting its potential as a marker of substantial glomerular inflammatory burden. Validation in larger, multicenter studies is warranted to confirm its generalizability.

Conflicting evidence exists in the literature concerning the prognostic significance of specific renal pathologies in GN. While some studies report no significant correlation between the extent of glomerular sclerosis, IF, or crescents[34,35] and adverse renal outcomes, others have underscored their prognostic value.[3,4,7,36–38] In another study multivariate analyses have yielded mixed results regarding tubular atrophy's role as an independent predictor of ESRD, despite its frequent association with IF.[39] Specifically, in ANCA-associated GN patients, some studies have found no correlation between IF or TA and ESRD risk using predefined cutoffs.[40,41] As Berden et al have emphasized, the potential for renal recovery is largely determined by the reversibility of active lesions rather than chronic changes like glomerulosclerosis or IF.[7] This suggests that chronic lesions alone may not comprehensively reflect a patient's long-term prognosis. In our cohort, no significant differences were observed in the percentages of glomerulosclerosis, IF, or TA between patients who progressed to ESRD and those who did not. A crucial finding from our analysis was that a higher crescent ratio, which reflects the burden of active inflammatory lesions, was an independent predictor of ESRD. These findings suggest that treatment decisions should not be based solely on chronic histopathological markers such as glomerulosclerosis or IF and TA. Instead, the extent of active lesions, particularly crescents, appears to be a more reliable indicator of ongoing inflammatory activity and thus, a better predictor of prognosis. Accordingly, early and aggressive immunosuppressive therapy should be considered in patients with extensive crescent formation to improve long-term renal outcomes.

In crescentic GN, renal outcomes are strongly influenced by the severity of kidney failure at diagnosis. Previous studies by Ozturk, Wu, and Ford et al[2,3,36] reported that higher serum creatinine at presentation predicts poor prognosis and progression to ESRD. More recent evidence confirms that lower baseline eGFR is a significant predictor of adverse outcomes.[4,40] Consistent with these findings, our analysis showed that lower initial eGFR was significantly associated with ESRD.

We also observed that low hemoglobin at diagnosis was more common among patients who developed ESRD, including those with Type 3 crescentic GN. This aligns with prior reports, such as Chen et al,[42] which identified low hemoglobin as an independent risk factor for maintenance dialysis in AAGN, and another AAV study highlighting baseline anemia as a negative prognostic factor.[4] The association between anemia and poor renal prognosis likely reflects multiple mechanisms: chronic inflammation suppresses erythropoietin and bone marrow responsiveness; tissue hypoxia from severe anemia exacerbates kidney injury and fibrosis; and low hemoglobin may result from advanced kidney disease due to insufficient erythropoietin production. Collectively, these findings indicate that readily available markers such as eGFR and hemoglobin provide essential prognostic information to guide early clinical decision-making.

In our study, plasmapheresis was performed according to KDIGO guidelines, which recommend it for RPGN patients with severe renal insufficiency, pulmonary hemorrhage, or ANCA/anti-GBM positivity. Although the PEXIVAS trial[43] reported no additional benefit of plasmapheresis in severe AAV, we observed a distinct clinical pattern: patients who progressed to ESRD had a significantly higher rate of plasmapheresis at diagnosis. Multivariate analysis confirmed that the requirement for plasmapheresis independently predicted ESRD. This suggests that the need for plasmapheresis at presentation, rather than the procedure itself, reflects a more severe disease phenotype and a higher risk of adverse renal

outcomes. Thus, the requirement for plasmapheresis may serve as a valuable prognostic indicator for identifying patients at very high risk of ESRD.

This study has several limitations. Its retrospective, single-center design and relatively small sample size, predominantly consisting of patients with Type 3 crescentic GN, may limit generalizability and introduce selection bias. The small sample size inherent to this rare disease may also have contributed to imprecision in some estimates, including wider confidence intervals. Furthermore, the relatively homogeneous geographic background of the study population may restrict the study's external validity. We were unable to track longitudinal changes in SII and PNI, as these indices were measured only at baseline, and the follow-up period was relatively short. Additional clinical data, including body mass index, serum cholesterol levels, Birmingham Vasculitis Activity Score, and 24-hour proteinuria, were incomplete and could not be analyzed. Moreover, changes in treatment practices over the study period, including limited use of rituximab, may have influenced prognostic assessments.

Despite these limitations, the study has notable strengths. The single-center design ensured uniformity in biopsy indications, therapies, follow-up protocols, and pathological assessment. Importantly, all SII and PNI values were measured on admission before immunosuppressive therapy, eliminating confounding effects from drug-induced myelosuppression or steroid-related changes. The availability of SII and PNI at the time of diagnosis and their association with short-term renal outcomes support their potential role as adjunctive markers of early disease severity, complementing conventional clinical and histopathological assessment. Beyond clinical risk stratification, these findings may reflect broader immunoinflammatory and metabolic pathways involved in crescent formation and progression to irreversible kidney injury.

Given the limited number of studies examining readily accessible inflammatory and nutritional indices in crescentic GN, our results provide novel insight into this emerging field and may inform future prognostic frameworks or clinical decision algorithms following further validation. Finally, SII and PNI are easily and cost-effectively derived from routine blood counts, making them highly accessible for clinical use.

Conclusion

In conclusion, our study underscores the critical role of systemic inflammation and nutritional status in determining renal outcomes in crescentic GN. Elevated SII, low PNI emerged as independent predictors of progression to ESRD, while a high crescent ratio was a key histological determinant, and chronic lesions were less informative. These findings highlight the value of integrating accessible serum biomarkers with histopathology for refined risk stratification. Clinically, SII and PNI may offer actionable insights beyond traditional measures, supporting early and aggressive immunosuppressive therapy. Prospective, multicenter studies are warranted to validate the prognostic utility of these indices and ultimately improve renal survival.

Funding

No funding was received for this research.

Disclosure

The authors disclose that they have no competing interests for this work.

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