Predictors of Kidney and Patient Survival in Monoclonal Gammopathy–Associated Kidney Disease: A Single-Center Cohort from Colombia

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Introduction. Monoclonal gammopathies can induce various kidney disorders through the deposition of monoclonal immunoglobulin. Precise recognition and classification are essential for predicting outcomes and customizing treatment. However, data on prognostic factors in Hispanic and Latin American populations remain scarce. This study aimed to determine the predictors of kidney and patient survival in adults with biopsy-proven monoclonal gammopathy-associated kidney disease.

Methods. We conducted a retrospective cohort involving 98 individuals with biopsy-confirmed disease evaluated between 2011 and 2022. Kidney and patient survival were estimated using Kaplan-Meier analysis, and differences across histopathologic subtypes were assessed with the log-rank test. Predictors of end-stage kidney disease (ESKD) and mortality were identified using univariate and multivariable Cox regression after verification of the proportional hazards' assumption.

Results. Approximately one third of patients required kidney replacement therapy (KRT) at presentation. The need for KRT (hazard ratio [HR] 4.86, 95% confidence interval [CI] 2.01-11.79) and an estimated glomerular filtration rate (eGFR) < 30 mL/min/1.73 m² (HR 4.02, 95% CI 1.38-11.71) independently predicted progression to ESKD. Amyloidosis (HR 2.38, 95% CI 1.22-4.86) and age > 60 years (HR 1.96, 95% CI 1.06-3.61) were associated with higher mortality. The median follow-up was 41 months (interquartile range 24-68); 31% progressed to ESKD and 46% died.

Conclusions. Severe kidney dysfunction and the need for replacement therapy at diagnosis are strong predictors of poor renal outcomes. Amyloidosis and older age significantly affect overall survival. Early recognition of high-risk patients and access to effective, clone-directed therapy are essential to improve prognosis in resource-limited settings.

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INTRODUCTION

Monoclonal gammopathies are disorders characterized by the overproduction of monoclonal immunoglobulins by clonal plasma cells or B-lymphocytes. Their clinical relevance depends on the extent of the clonal burden and the presence

of organ damage, particularly kidney injury.[1,2] In many cases, kidney disease is the first manifestation of these disorders and may precede the diagnosis of overt hematologic malignancy.[3]

The term monoclonal gammopathy of renal significance (MGRS) refers to kidney impairment caused by a monoclonal immunoglobulin in patients who do not meet diagnostic criteria for multiple myeloma, Waldenström macroglobulinemia, or other lymphoproliferative neoplasms.[4] MGRS encompasses a spectrum of renal lesions identified by immunofluorescence and electron microscopy, including monoclonal immunoglobulin deposition disease (MIDD), proliferative glomerulonephritis with monoclonal immunoglobulin deposits (PGNMID), and AL amyloidosis.[3,5,6] Accurate identification of these lesions is crucial because their clinical course is often progressive without timely clone-directed hematologic therapy.[2,6]

The prevalence of monoclonal gammopathy of undetermined significance (MGUS)) increases with age, attaining 3.2% in individuals over 50 years, 5.3% in those over 70, and 7.5% in those over 85 years.[8] It is more prevalent among African Americans and has a 1% annual risk of progression to multiple myeloma.[9,10] Kidney biopsy studies in patients with monoclonal gammopathy show that up to 40% of cases present with MGRS-consistent lesions, while 60% exhibit lesions unrelated to monoclonal protein deposition; predictors for MGRS development include proteinuria > 1.5 g/day, hematuria, and an elevated serum free light chain ratio.[11] Prior cohorts report that roughly one-third of MGRS patients progress to end-stage kidney disease (ESKD), with higher risks in MM and lower risks in MGUS.[6,12,13]

Other series indicate that approximately one-third of patients with MGRS present with moderate chronic kidney disease at diagnosis while up to 40% present with advanced kidney dysfunction; overall survival at 24 months is near 80%, underscoring substantial renal and systemic morbidity.[6,7]

Despite these data, information from Latin American populations is scarce. In Colombia, small cohorts have reported delayed diagnosis, advanced kidney dysfunction at presentation, and limited access to novel therapies, factors that may contribute to poorer outcomes compared with high-income regions.[14-16]

Understanding the prognostic factors associated with kidney and patient survival in MGRS is essential to improve early recognition and guiding treatment approaches in underrepresented populations. This study aimed to identify prognostic factors for kidney survival and mortality in patients with monoclonal gammopathy-associated renal disease, providing insight into outcomes within a Colombian cohort.

MATERIALS AND METHODS

Study Design and Patients

This retrospective cohort included 98 adult patients with biopsy-confirmed kidney involvement secondary to monoclonal gammopathy. A consecutive non-probability sampling was used to include all patients aged ≥18 years diagnosed between 2011 and 2022 at San Vicente Fundación hospital and Alma Mater de Antioquia hospital, both tertiary referral centers in Medellín, Colombia.

Individuals already on chronic dialysis, defined as dialysis for > 3 months at presentation, were excluded; however, those with acute kidney injury (AKI) or acute need for kidney replacement therapy (KRT) during hospitalization were included and analyzed accordingly. Missing data were handled by complete-case analysis.

Kidney Pathology

Kidney biopsies were performed at the discretion of the treating nephrologist when clinical or laboratory findings suggested hematologic kidney disease (e.g., proteinuria > 500 mg/24 h, hematuria > 3-5 red blood cells per high-power field, or eGFR < 60 mL/min/1.73 m²). No protocol biopsies were performed. All samples were examined by a single expert nephropathologist using light microscopy, Congo red staining, and immunofluorescence study for kappa and lambda light chains. Electron microscopy was performed in most, but not all, cases. Inter-observer review was not performed. Diagnostic classification followed the International Kidney and Monoclonal Gammopathy Research Group (IKMG) consensus, including AL amyloidosis, monoclonal immunoglobulin deposition disease (MIDD), proliferative glomerulonephritis with monoclonal immunoglobulin deposits (PGNMID), light chain proximal tubulopathy (LCPT), cryoglobulinemic glomerulonephritis, immunotactoid and fibrillary glomerulonephritis, and C3 glomerulopathy associated with monoclonal gammopathy.[5] Amyloidosis diagnosis was based on characteristic

histological features, including Congo red positivity with apple-green birefringence under polarized light. Immunohistochemistry was performed in all amyloidosis cases to differentiate AA from AL. Mass spectrometry was not routinely available locally; selected cases were referred to the Mayo Clinic (Rochester, MN, USA) for confirmatory typing.

Variables

Demographic, clinical, laboratory, and histopathological variables were extracted from medical records. Demographic variables included age and sex. Clinical variables encompassed comorbidities (hypertension, diabetes mellitus, and where available, cardiovascular disease and hematologic complications), the diagnosis of monoclonal gammopathy, and disease staging for multiple myeloma (MM) using the International Staging System (ISS). Laboratory parameters included serum creatinine, blood urea nitrogen, hemoglobin, calcium, albumin, and serum free light chain ratio. eGFR was estimated by the CKD-EPI 2009 equation.[17] Urinalysis and 24-hour proteinuria were recorded.

Histological parameters included glomerular count, degree of sclerosis, interstitial fibrosis and tubular atrophy, immunofluorescence profile, Congo red staining, and final renal diagnosis. ESKD was defined as eGFR < 15 mL/min/1.73 m² for at least 3 months, initiation of permanent dialysis (> 3 months), or need for kidney transplantation.

Treatment data (chemotherapy exposure and hematologic response) were recorded when available; however, response variables were not uniformly captured and were therefore not included in multivariable models.

Outcomes

The primary composite outcome was the occurrence of ESKD or death from any cause during follow-up. Kidney survival was defined as the interval from biopsy to ESKD, and patient survival as the time from biopsy to death, confirmed through hospital records and the national mortality database. Mortality was reported as all-cause mortality due to incomplete cause-of-death adjudication. Transplant recipients were described but not analyzed separately due to small numbers. Participants were censored at the last recorded clinical contact.

Statistical Analysis

Continuous variables were summarized as means ± standard deviation or medians with interquartile range, depending on distribution. Normality was assessed using the Shapiro-Wilk test. Categorical variables were expressed as frequencies and percentages. Group comparisons (alive vs. deceased) were performed using Student›s t-test or Mann-Whitney U test for continuous variables and the chi-square test for categorical variables.

Survival analyses (kidney and patient) were performed using Kaplan-Meier curves, displayed with 95% confidence-interval bands; comparisons by histological category and amyloidosis status used the log-rank test. Univariate and multivariable Cox proportional hazards models were fitted to identify independent predictors of ESKD and mortality. The proportional hazards assumption was verified using Schoenfeld residuals. Variables with clinical relevance or $P < .25$ in univariate analysis were entered into the multivariable model, which was adjusted for age, eGFR, KRT at diagnosis, presence of AKI, and amyloidosis. Results are expressed as hazard ratios (HRs) with 95% confidence intervals (CIs); two-sided P-values < .05 were considered statistically significant.

A sensitivity analysis using logistic regression evaluated factors associated with histologic diagnosis of amyloidosis at biopsy. Potential interactions (e.g., between eGFR and amyloidosis) were not tested due to limited power. Follow-up duration was calculated from biopsy date to last recorded visit or death; the median follow-up time is reported to aid interpretation of survival estimates. All analyses were performed with STATA 16 (College Station, TX, USA).

This study was approved by the Institutional Review Boards of Hospital San Vicente Fundación and Hospital Alma Mater de Antioquia, as well as by the Research Committee of Universidad de Antioquia. The requirement for informed consent was waived due to the retrospective design and anonymized data use.

RESULTS

We analyzed 98 patients (Figure 1) with a mean age of 61 years (SD ± 11); 58% were male. Hypertension was present in 40% and diabetes mellitus in 16% of patients. MM was identified in 65.3%, mostly at advanced stages (ISS stage 3 in

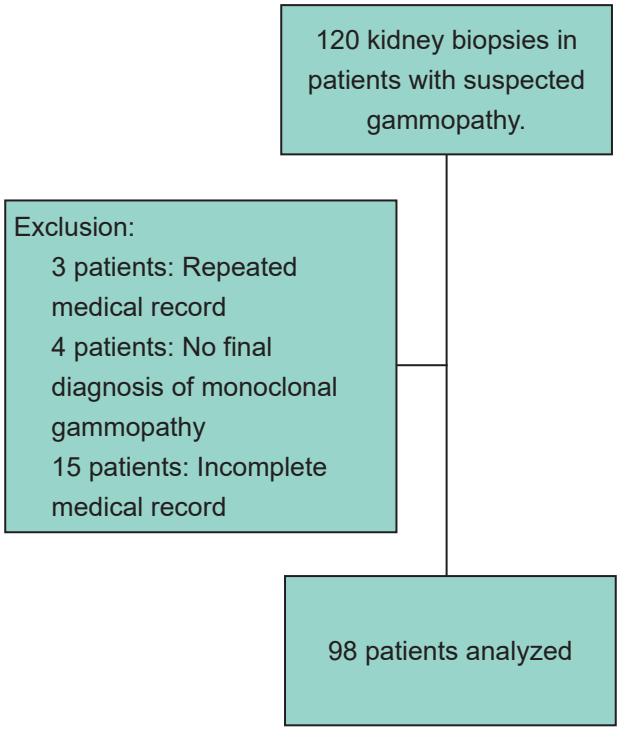

Figure 1. Inclusion and Exclusion Criteria Flowchart

64%), followed by AL amyloidosis in 31%, with two overlapping cases.

At the time of kidney biopsy, the median eGFR was 26 mL/min/1.73 m² (IQR 13-57) and the median 24-hour proteinuria was 4,556 mg (IQR 2,254-8,497). Hematuria was present in 28% and 42% had KDIGO stage 3 AKI. Comprehensive baseline characteristics are summarized in Table 1.

Histopathological analysis revealed cast nephropathy as the predominant lesion (48%). MGRS was diagnosed in 34 patients, including 28 AL amyloidosis (with lambda-chain predominance in 86%), three cases of LCPT, and one case each of MIDD, PGNMID, and crystal-storing histiocytosis. The median IFTA score was 10% (Table 2).

During a median follow-up of 41 months (IQR 24-68), kidney and patient outcomes were evaluated. Dialysis was required in 39% of patients, and 26% remained on permanent hemodialysis. Overall mortality was 46%, and 31% progressed to end-stage kidney disease (ESKD). Patients who developed ESKD exhibited significantly higher mortality (69% vs. 36%, $P = .002$) and greater need for kidney replacement therapy (KRT) at diagnosis (90% vs. 17%, $P < .001$), while proteinuria and nephrotic syndrome were not significantly different between groups (Table 3).

Table 1. Baseline characteristics of the study cohort

Variables	N: 98
Age (year)– mean ± SD	61.2 ± 11.1
Sex – male – n (%)	57 (58%)
Creatinine at biopsy (mg/dL) – median (IQR)	2.4 (1.2 – 4.0)
BUN (mg/dL) – median (IQR)	32 (20 – 46)
eGFR (ml/min/1.73) at biopsy – median (IQR)	26 (13 – 57)
24-hour Protein (mg) – median (IQR)	4556 (2254 – 8497)
Hematuria – yes – n (%)	27 (28%)
Nephrotic syndrome – n (%)	46 (47%)
Acute kidney injury diagnosis - n (%)	61 (62.2%)
KDIGO 1	13 (13.2%)
KDIGO 2	7 (7.1%)
KDIGO 3	41 (41.8%)
None	37 (37.7%)
Involved light chain	
Lambda	41 (42%)
Kappa	39 (40%)
Involved heavy chain	
IgA	16 (16%)
IgG	24 (24%)
IgM	1 (1%)
No heavy chain involvement	47 (47%)
Hemoglobin – median (IQR)	9.7 (8.3 – 11.3)
Hematocrit – median (IQR)	28 (24 – 33)
Serum calcium (mg/dL)– median (IQR)	8.8 (8.2 – 9.9)
Lytic bone lesions – n (%)	43 (44%)
Monoclonal peak (g/dL) – median (IQR)	3.3 (2.3 – 4.7)
Light chain ratio – median (IQR)	2 (0.2 – 27)
History of hypertension – n (%)	39 (40%)
History of diabetes mellitus – n (%)	16 (16%)
Associated neoplasm	
Multiple myeloma	64 (65,3%)
MGRS-A Organized fibrillar (AL Amyloidosis)	28 (28,6%)
MGRS-NA	6 (6,1%)
ISS – n (%)	
1	2 (3%)
2	13 (17%)
3	49 (64%)

Baseline demographic, clinical, and laboratory characteristics of 98 patients with biopsy-confirmed monoclonal gammopathy-related kidney disease. Continuous variables are expressed as mean ± standard deviation (SD) or median (interquartile range, IQR), and categorical variables as counts and percentages.
Abbreviations: AKI, acute kidney injury; AL, amyloidosis; BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate; Ig, immunoglobulin; ISS, International Staging System; KDIGO, Kidney Disease: Improving Global Outcomes; MGRS, monoclonal gammopathy of renal significance; MGRS-A, amyloidosis-related MGRS; MGRS-NA, non-amyloidosis MGRS.

Patients with amyloidosis exhibited higher levels of proteinuria (8,343 mg vs. 3,407 mg, $P = .011$) and lower serum creatinine (1.4 mg/dL vs. 2.6 mg/dL, $P < .001$) compared with those with other

Table 2. Relevant clinical and histological outcomes

Outcomes	N:98
Histological outcomes	
Light chain cast nephropathy	47 (48%)
Immunoglobulin light chain AL Amyloidosis	28 (28,5%)
AL Amyloidosis and Overt Multiple Myeloma	2 (2,04%)
Proximal tubulopathy due to light chains and overt Multiple Myeloma	15 (15,3)
Proximal tubulopathy due to light chains (LCPT)	3 (3,06%)
Other patterns (MIDD, monoclonal immunoglobulin deposition disease; PGNMID, proliferative glomerulonephritis and monoclonal immunoglobulin deposits, crystal-storing histiocytosis)	3 (3%)
Clinical outcomes	
Dialysis requirement at any point	38 (39%)
Death	45 (46%)
End-stage kidney disease	30 (31%)
eGFR < 15 ml/min/1.73 m^2 for more than 3 months without dialysis	5 (5%)
Permanent dialysis	25 (26%)
Bone marrow transplant	5 (5%)

Summary of histological diagnoses and main clinical outcomes in 98 patients with biopsy-confirmed monoclonal gammopathy-related kidney disease. Percentages were calculated using the total number of patients as the denominator.
Abbreviations: AL, amyloidosis; eGFR, estimated glomerular filtration rate; LCPT, light chain proximal tubulopathy; MIDD, monoclonal immunoglobulin deposition disease; PGNMID, proliferative glomerulonephritis with monoclonal immunoglobulin deposits; ESKD, end-stage kidney disease.

histologic diagnoses.

In the multivariate Cox regression, adjusted for age, sex, hypertension, and diagnosis, acute KRT requirement at diagnosis was associated with an increased risk of ESKD or death (HR 4.86; 95% CI 2.01-11.79). eGFR < 30 mL/min/1.73 m^2 predicted a higher risk of ESKD (HR 4.02; 95% CI 1.38-11.71). Age > 60 years and amyloidosis were independently associated with higher mortality (HR 1.96; 95% CI 1.06-3.61; HR 2.38; 95% CI 1.22-4.86, respectively) (Table 4).

Kaplan-Meier analysis with 95% confidence-interval bands demonstrated that eGFR < 30 mL/min/1.73 m^2 was linked to worse kidney survival (56%, 54%, and 45% at 1, 5, and 9 years, respectively) compared with 89% in those with higher eGFR (P = .001) (Figure 2A). KRT at diagnosis was associated with both poorer kidney (P < .001) and patient survival (P = .01) (Figures 2B-2D). Among histological subtypes, LCPT showed the most favorable prognosis, whereas amyloidosis demonstrated the least favorable kidney survival (Figure 2E).

At one and five years, survival rates were 87% and 55% in patients without amyloidosis, compared with 59% and 29% in those with amyloidosis (P = .02). The five-year survival was 29% for amyloidosis, 49% for myeloma kidney, and 79% for LCPT (P = .05).

In the sensitivity analysis, eGFR > 60 mL/min/1.73 m^2 and presence of nephrotic syndrome were associated with biopsy-proven amyloidosis, while hematuria and age > 60 years were not significant predictors (Table 5).

In a subset with available hematologic response data (n = 23), 21 patients achieved a response to first-line therapy-10 complete responses and 11 partial responses and two patients progressed during treatment. Only five patients underwent hematopoietic stem-cell transplantation; no kidney transplants were performed during follow-up. For clarity, complete hematologic response (CR) was defined as negative serum and urine immunofixation with a normal serum free light chain (FLC) ratio, and partial response (PR) as a ≥50% reduction in serum M-protein or urine light-chain excretion, or a ≥50% decrease in the involved FLC level when measurable; progressive disease (PD) required a ≥50% increase from nadir in M-protein or FLC (with reappearance of a monoclonal band if relapsing from CR).

DISCUSSION

This retrospective cohort identified key prognostic factors influencing kidney and patient survival in Latin American adults with biopsy-confirmed monoclonal gammopathy-related kidney disease. The findings emphasize the prognostic value of baseline kidney function and the need for acute KRT at diagnosis, as well as the poorer outcomes associated with amyloidosis and older age.

The requirement for KRT at presentation emerged as the strongest predictor of adverse outcomes, markedly increasing the risk of both ESKD and mortality (HR 4.86, 95% CI 2.01-11.79). This aligns with prior reports indicating that initiation of KRT reflects advanced kidney injury and systemic disease burden.[5-7,14] Likewise, eGFR < 30 mL/min/1.73 m^2 independently predicted progression to ESKD (HR 4.02, 95% CI 1.38-11.71), supporting its role as a reliable indicator of irreversible kidney damage and worse prognosis.[6,7,14-15] These results underscore the importance of early risk stratification

Table 3. Baseline comparison of patients with and without end-stage kidney disease (ESKD)

Variables	ESKD n = 30	NO ESKD n = 66	*P*
Age (year)– mean ± SD	60.3 ± 10.6	61.2 ± 11.2	.707
Male Sex – n (%)	18 (60%)	38 (58%)	.823
Creatinine at biopsy (mg/dl) – median (IQR)	3.8 (2.5 – 7.3)	1.8 (0.9 – 3.3)	< .001
BUN (mg/dl) – median (IQR)	43 (37 – 64)	28 (16 – 38)	< .001
GFR at biopsy (ml/min/1.73) – median (IQR)	15 (7 – 20)	40 (18 – 69)	< .001
24-hour Proteins (mg) – median (IQR)	5830 (3392 – 10642)	4130 (2003 – 8384)	.149
Light chain involved – n (%)			
Lambda	10 (33%)	31 (47%)	.348
Kappa	13 (43%)	26 (39%)	
Heavy chain involved – n (%)			
IgA	6 (20%)	10 (15%)	.018
IgG	2 (7%)	22 (33%)	
IgM	1 (3%)	0	
No data	21 (70%)	34 (52%)	
Serum Calcium – median (IQR)	8.5 (8.3 – 9.1)	9.0 (8.2 – 10.3)	.044
Lytic bone lesions – n (%)	13 (43%)	30 (45%)	.797
Acute kidney injury diagnosis – n (%)			
KDIGO 1	5 (17%)	8 (12%)	.013
KDIGO 2	1 (3%)	6 (9%)	
KDIGO 3	19 (63%)	22 (33%)	
None	5 (17%)	30 (45%)	
Nephrotic syndrome – n (%)	17 (57%)	28 (42%)	.195
Amyloidosis	11 (37%)	19 (27%)	.477
ISS – n (%)			
1	0	2 (3%)	.127
2	1 (3%)	12 (18%)	
3	17 (57%)	34 (52%)	
Outcomes			
Death – n (%)	20 (69%)	24 (36%)	.002
Dialysis requirement at any point before ESKD – n (%)	27 (90%)	11 (17%)	< .001

Baseline demographic, laboratory, and histological characteristics comparing patients who progressed to end-stage kidney disease (ESKD) with those who did not. Continuous variables are shown as mean ± SD or median (IQR) and compared using *t*-test or Mann-Whitney U test as appropriate; categorical variables are expressed as counts (%) and compared using χ^2 or Fisher›s exact test.
Abbreviations: AKI = acute kidney injury; BUN = blood urea nitrogen; eGFR = estimated glomerular filtration rate; ESKD = end-stage kidney disease; Ig = immunoglobulin; ISS = International Staging System; KDIGO = Kidney Disease: Improving Global Outcomes.

and expedited, clone-directed therapy in patients presenting with severe renal dysfunction.

Cast nephropathy was the predominant lesion on kidney biopsy, consistent with prior series identifying myeloma kidney and amyloidosis as the most frequent patterns of renal involvement in monoclonal gammopathies.[18,21] Cast nephropathy-characterized by intratubular light-chain precipitation-drives AKI and rapid loss of kidney function if not promptly treated.[6,7,26] The high AKI frequency at diagnosis in our cohort reinforces the need for early detection and supportive measures (e.g., light-chain reduction, avoidance of nephrotoxins).[6,20,23-25]

Amyloidosis and MM showed distinct clinical and prognostic profiles. Patients with amyloidosis had worse survival and higher mortality (HR 2.38), consistent with literature highlighting systemic involvement-particularly cardiac amyloidosis-as a determinant of poor outcomes.[15,28-29] In contrast, MM-related kidney disease (cast nephropathy) can improve with effective hematologic response.[6,7,26] These differences argue for phenotype-tailored management pathways within the MGRS spectrum.

Patients with LCPT demonstrated the most favorable kidney survival, likely reflecting its predominantly tubular pattern of injury with minimal glomerular involvement and a more indolent course.[7,8,26] This trajectory, together with potential reversibility under early clone-directed therapy, helps explain the comparatively better prognosis versus amyloidosis or cast nephropathy.

Table 4. Cox proportional hazards regression analysis for death and end-stage kidney disease (ESKD)

All-cause Mortality						
	Univariate			Multivariate		
Variable	**HR**	**IC**	***P***	**HR**	**IC**	***P***
Age ≥ 60 years	2.38	1.22-4.62	0.010	2.44	1.22-4.86	0.011
Need for RRT	2.13	1.17-3.87	0.013	1.7	0.77-3.75	0.187
Presence of Amyloidosis	1.99	1.09-3.63	0.024	1.96	1.06-3.61	0.03
eGFR < 30 ml/min/1.73m^2	1.30	0.37-4.53	0.675	1.31	0.57-2.96	0.51
End-Stage Kidney Disease (ESKD)						
	Univariate			Multivariate		
Variable	**HR**	**IC**	***P***	**HR**	**IC**	***P***
Age ≥ 60 years	1.20	0.57-2.53	0.622	0.99	0.45-2.17	0.998
eGFR < 30 ml/min/1.73m^2	4.87	1.84-12.85	0.001	4.02	1.38-11.71	0.011
Presence of Amyloidosis	1.32	0.62-2.78	0.461	1.83	0.82-4.09	0.138
Acute Kidney Injury per KDIGO	3.41	1.29-8.97	0.013	1.94	0.65-5.78	0.231
Combined Death and ESKD						
	Univariate			Multivariate		
Variable	**HR**	**IC**	***P***	**HR**	**IC**	***P***
Age ≥ 60 years	1.58	0.88-2.85	0.125	1.36	0.73-2.56	0.325
eGFR < 30 ml/min/1.73m^2	3.53	1.90-6.54	0.000	1.21	0.48-3.04	0.682
Presence of Amyloidosis	1.08	0.61-1.92	0.768	1.28	0.70-2.34	0.417
Need for KRT at diagnosis	5.63	3.10-10.24	0.000	4.86	2.01-11.79	0.000

Cox proportional hazards regression analysis showing univariate and multivariate predictors of all-cause mortality, end-stage kidney disease (ESKD), and the combined outcome of death or ESKD. Multivariate models were adjusted for age, baseline eGFR, amyloidosis, and need for kidney replacement therapy (KRT) at diagnosis.
Abbreviations: CI = confidence interval; eGFR = estimated glomerular filtration rate; ESKD = end-stage kidney disease; HR = hazard ratio; KDIGO = Kidney Disease: Improving Global Outcomes; KRT = kidney replacement therapy.

Accurate recognition of amyloidosis on kidney biopsy remains critical for prognosis. Amyloid deposits appear as eosinophilic material on Hematoxylin and Eosin (H&E) staining and are confirmed by Congo red positivity with apple-green birefringence under polarized light.[2,6,28,34] Predictors include nephrotic-range proteinuria, marked glomerular involvement, and systemic features, particularly cardiac manifestations.[2,7,8,28] However, in routine practice, incomplete EM assessment or limited access to mass spectrometry may lower diagnostic yield and precision; moreover, the absence of inter-observer variability assessment can affect reproducibility in subtle entities such as PGNMID or LCPT.[19,25,26,34]

Age > 60 years was independently associated with higher mortality (HR 1.96), in keeping with broader CKD and monoclonal gammopathy literature, where advanced age portends worse outcomes due to comorbid burden, reduced physiologic reserve, and delays in diagnosis/treatment.[16,28-31]

The poorer prognosis observed in this Colombian cohort likely reflects delayed diagnosis, limited access to kidney biopsy and novel agents (e.g., daratumumab, lenalidomide), and broader health-care disparities relative to high-income settings. These regional constraints, documented in local real-world MM data and expert commentary, highlight the need to strengthen early diagnostic pathways, biopsy access, and availability of clone-directed therapies in Latin America.[14-16,23,31,33,35] Prospective, multicenter studies that incorporate hematologic staging, treatment response, and longer follow-up are warranted to validate these prognostic indicators and inform context-appropriate care models.

This study has limitations. The retrospective design limits causal inference and may introduce missing-data bias. Biopsy-based inclusion can select for more severe cases, potentially underrepresenting patients not biopsied due to frailty or comorbidity. Subgroup sample sizes (e.g., amyloidosis, LCPT) reduce power and widen CIs. Therapy details and hematologic response were incompletely captured, limiting model adjustment. Mortality was analyzed as all-cause mortality (without subclassification as infectious, cardiovascular, renal, or hematologic), restricting disease-specific interpretation. Finally, incomplete EM and absent inter-observer review could have influenced histologic classification. Despite these constraints, our work provides real-

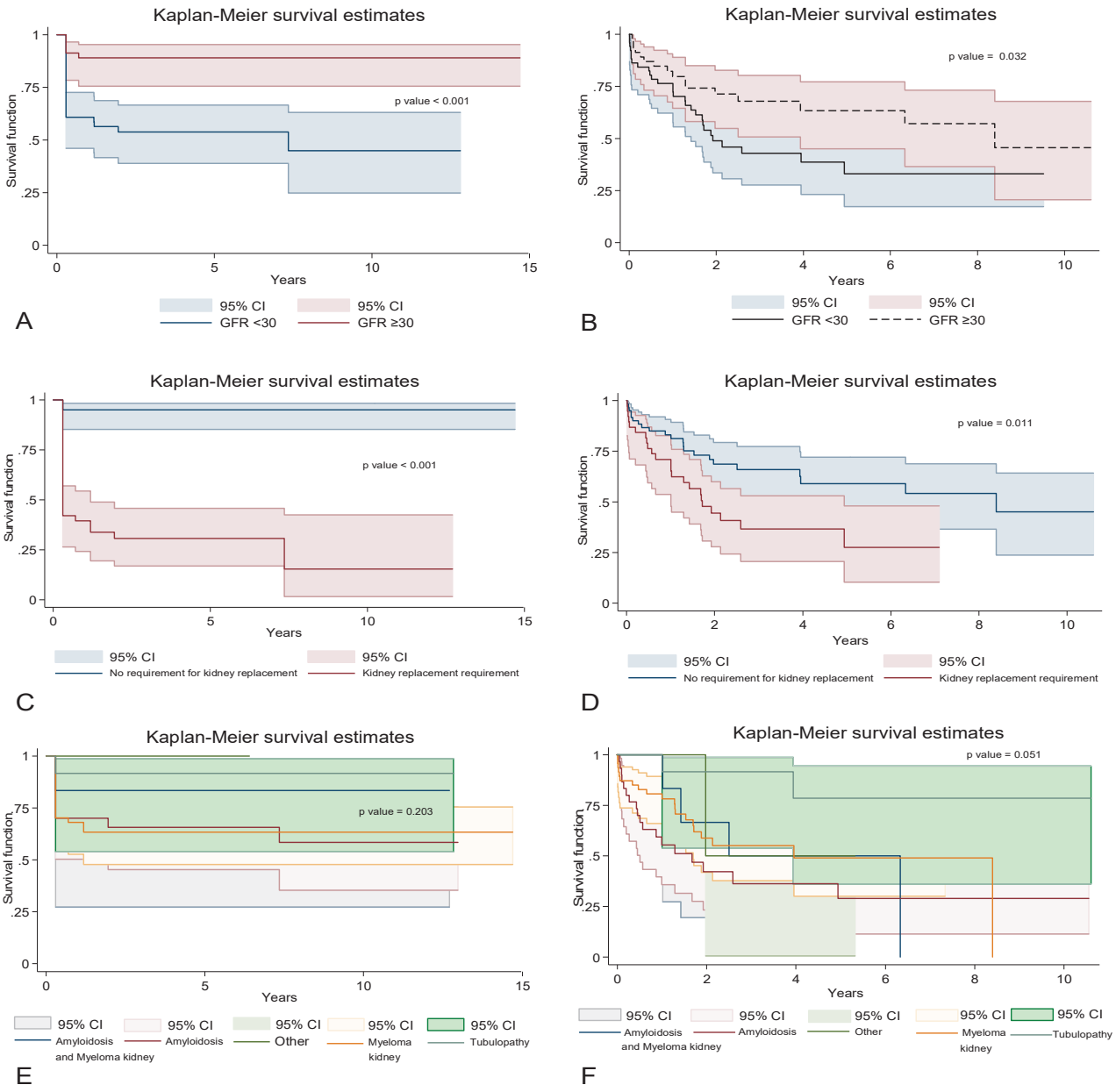

Figure 2. Kaplan-Meier kidney and patient survival with 95% confidence-interval bands. (A) Kidney survival by eGFR (< 30 vs ≥ 30 mL/min/1.73 m^2). (B) Patient survival by eGFR (< 30 vs ≥ 30 mL/min/1.73 m^2). (C) Kidney survival by KRT at diagnosis (yes vs no). (D) Patient survival by KRT at diagnosis (yes vs no). (E) Kidney survival by histologic diagnosis (AL amyloidosis, cast nephropathy, LCPT, and others).
P values from log-rank tests.
Abbreviations: eGFR, estimated glomerular filtration rate; KRT, kidney replacement therapy; LCPT, light chain proximal tubulopathy.

Table 5. Logistic regression analysis for factors associated with amyloidosis in kidney biopsy.

	Univariate			Multivariate		
Variable	**OR**	**IC**	***P***	**OR**	**IC**	***P***
Age > 60 years	1.05	0.43-2.52	0.913	1.94	0.57-6.55	0.285
eGFR > 60	4.58	1.60-13.1	0.005	5.62	1.46-21.5	0.012
Hematuria	0.33	0.10-1.11	0.074	0.33	0.88-1.24	0.102
Nephrotic Syndrome	4.01	1.59-10.1	0.003	7.49	2.24-24.9	0.001

Binary logistic regression analysis showing univariate and multivariate predictors of amyloidosis on kidney biopsy. Variables with *P* < .05 in the univariate analysis were included in the multivariate model.
Abbreviations: CI = confidence interval; eGFR = estimated glomerular filtration rate; OR = odds ratio.

world evidence from an underrepresented region and delineates clinically actionable risk markers that can guide prioritization of diagnostic and therapeutic resources.

In conclusion, this single-center cohort identifies key prognostic factors for kidney and patient survival in Latin American adults with biopsy-proven monoclonal gammopathy-related kidney disease (MGRS). The need for kidney replacement therapy (KRT) at diagnosis and a baseline eGFR < 30 mL/min/1.73 m² were the strongest predictors of progression to end-stage kidney disease (ESKD), whereas amyloidosis and age > 60 years independently predicted higher mortality. These findings underscore the importance of early recognition of kidney involvement and timely, clone-directed therapy-particularly in high-risk patients-to improve long-term survival and preserve renal function. Given the limited regional data, this study provides actionable evidence to inform prognosis and clinical management of MGRS in Latin America.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest related to this work.

AUTHORS› CONTRIBUTIONS

Research idea and study design: JRC, LAR; data acquisition: SGJ, SCR, JCQ; data analysis and interpretation: JRC, SGJ, SCR, JCQ, LAR; statistical analysis: JRC; pathology evaluation: LAR; manuscript drafting, review, and editing: JRC, SGJ, SCR, JCQ, LAR; supervision and mentorship: JRC, LAR. All authors contributed intellectually to the conception, drafting, and critical revision of the manuscript and approved the final version for publication.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This retrospective study was conducted using medical records without any direct intervention. It was classified as a no-risk investigation according to Colombian regulations (Resolutions 8430 of 1993 and 2378 of 2008, Ministry of Health). Ethical approval was obtained from the Research and Ethics Committees (REC) of the participating institutions, including Hospital San Vicente Fundación-Medellín and Hospital Alma Mater de Antioquia. Individual informed consent was waived due to the retrospective design. All data were anonymized, ensuring compliance with national ethical standards and the principles outlined in the Declaration of Helsinki.

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIAL

The datasets generated or analyzed during the current study are available from the corresponding author upon reasonable request via email.

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