

Morpho-functional correlations in RENAL AMYLOIDOSIS

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BACKGROUND

The term amyloidosis groups a number of diseases characterized by insoluble fibril deposition at the tissue level. AL amyloidosis is the most common form of the disease in the Western world and renal impairment is often the first manifestation of this pathology. The aim of our study was to evaluate the type and extension of renal histological lesions at diagnosis and correlate them with clinical parameters and with the progression of the renal disease.

METHODS

We retrospectively enrolled 18 patients affected by AL amyloidosis who underwent renal biopsy between 1996 and 2014 in two hospitals of the same city. Renal histological lesions were graded according to the score proposed by Sen and Colleagues and renal amyloid deposition at the glomerular level was determined by morphometric analysis and correlated with clinical parameters at baseline and progression of kidney disease during a one-year follow-up.

RESULTS

PATIENT CHARACTERISTICS	
Male/Female (n, %)	11, 61% / 7, 39%
Age (mean ± s.d.)	62.6 ± 13.3 (min: 38 – max: 85)
BMPG %	14.0 ± 7.7 (min: 5 – max: 25; median: 10.5)
Underlying plasma cell dyscrasia (n, %)	
MGUS	12, 66.7%
Multiple Myeloma	5, 27.8%
Lymphoma	1, 5.6%
Monoclonal component in the serum	
IgG	10, 55.6%
IgM	1, 5.6%
IgA	2, 11.1%
Free light chain only	5, 27.8%
Bence Jones proteins in the urine	
Undetectable	3, 16.7%
Kappa	6, 33.3%
Lambda	9, 50%
Amyloidogenic light chain	
Kappa	8, 44.4%
Lambda	10, 55.6%
Clinical presentation (n, %)	
Renal failure	14 (77.8%)
Nephrotic syndrome	11 (61.1%)
Non-nephrotic proteinuria	7 (38.9%)

CLINICAL DATA AT DIAGNOSIS		
	Mean value ± s.d.	Range (min-max)
Creatinine (mg/dL)	2.2 ± 1.89772	0.60 – 8.2
eGFR (mL/min)	46.68 ± 31.05038	6.00 – 106.0
24h Urine Protein (g/24h)	6.8 ± 6.00509	0.12 – 24.0
Total serum proteins (g/dL)	5.5 ± 1.54874	3.30 – 9.9
Albumin (g/dL)	2.5 ± 0.88666	1.20 – 4.3
Hemoglobin (g/dL)	12.3 ± 1.76365	9.70 – 15.8

GRADE OF RENAL AMYLOIDOSIS (n, %)	
Early renal amyloidosis	1 (5.6%)
Late renal amyloidosis	8 (44.4%)
Advanced renal amyloidosis	9 (50%)
Total	18 (100%)

SUPPORTIVE TREATMENT	
Use of diuretics (n, %)	11, 61%
Use of ACE-I (n, %)	6, 33%
Use of ARB (n, %)	5, 28%
Dialysis (n, %)	
HD	3, 17%
Peritoneal dialysis	0, 0%

HISTOLOGICAL SCORE	
Glomerular amyloid pattern (GAP)	
Class I: minimal amyloid deposition	1, 5.6%
Class II: mesangial minimal amyloid deposition	3, 16.7%
Class III: focal mesangiocapillary deposition	3, 16.7%
Class IV: diffuse mesangiocapillary deposition	6, 33.3%
Class V: membranous amyloid deposition	3, 16.7%
Class VI: advanced amyloidosis	2, 11.1%
Glomerular amyloid quantity (GAQ)	
GAQ 1: 5, 27.8%	VA0: 2, 11.1%
GAQ 2: 4, 22.2%	VA1: 5, 27.8%
GAQ 3: 4, 22.2%	VA2: 4, 22.2%
GAQ 4: 5, 27.8%	VA3: 4, 22.2%
	VA4: 3, 16.7%
Interstitial amyloid deposition (IA)	
IA0: 2, 11.1%	Ifib0: 2, 11.1%
IA1: 4, 22.2%	Ifib1: 3, 16.7%
IA2: 7, 38.9%	Ifib2: 5, 27.8%
IA3: 4, 22.2%	Ifib3: 5, 27.8%
IA4: 1, 5.6%	Ifib4: 3, 16.7%
Interstitial inflammatory infiltrate (Iif)	
Iif0: 4, 22.2%	GS0: 10, 55.6%
Iif1: 9, 50.0%	GS1: 0, 0%
Iif2: 3, 16.7%	GS2: 4, 22.2%
Iif3: 1, 5.6%	GS3: 2, 11.1%
Iif4: 1, 5.6%	GS4: 4, 11.1%
RAPS	15.5 (7 – 28)

MORPHOMETRIC ANALYSIS DATA		
	Mean ± s.d.	Range (min – max)
Mean glomerular surface area (GSA) – μm^2	25856.1209 ± 9909.95356	9428.51 – 50278.23
Mean glomerular amyloid area (GAA) – μm^2	963.2739 ± 850.80491	21.65 – 3365.11
Mean glomerular amyloid percentage (GA%)	3.4084 ± 2.06233	0.11 – 6.88

SIGNIFICANT CORRELATIONS AT DIAGNOSIS			
		r	p
Vascular Amyloid vs *	Creatinine	0.550	0.018
	eGFR	-0.60	0.009
Interstitial Fibrosis And Tubular Atrophy vs *	Creatinine	0.780	<0.001
	eGFR	-0.765	<0.001
	Hemoglobin	-0.419	0.083
Interstitial Inflammatory Infiltrate vs *	Creatinine	0.502	0.034
	eGFR	-0.536	0.022
Renal Amyloid Prognostic Score vs *	Creatinine	0.488	0.040
	eGFR	-0.560	0.016
Grade Of Renal Amyloidosis vs *	Creatinine	0.481	0.043
	eGFR	-0.491	0.039
	Hemoglobin	-0.505	0.032

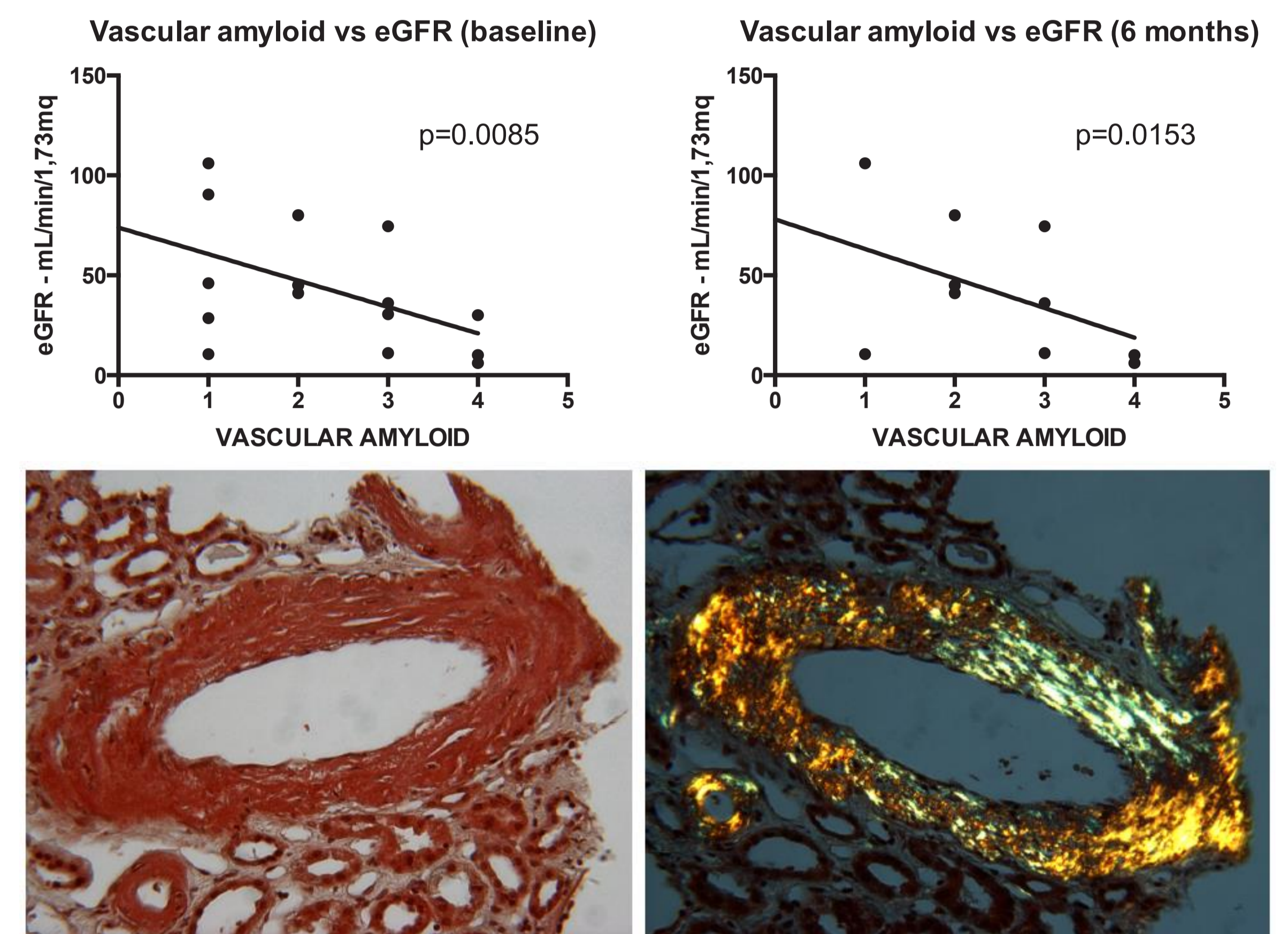


Figure 1. A more severe degree of vascular amyloid deposition was associated with a lower renal function at diagnosis and at six months.

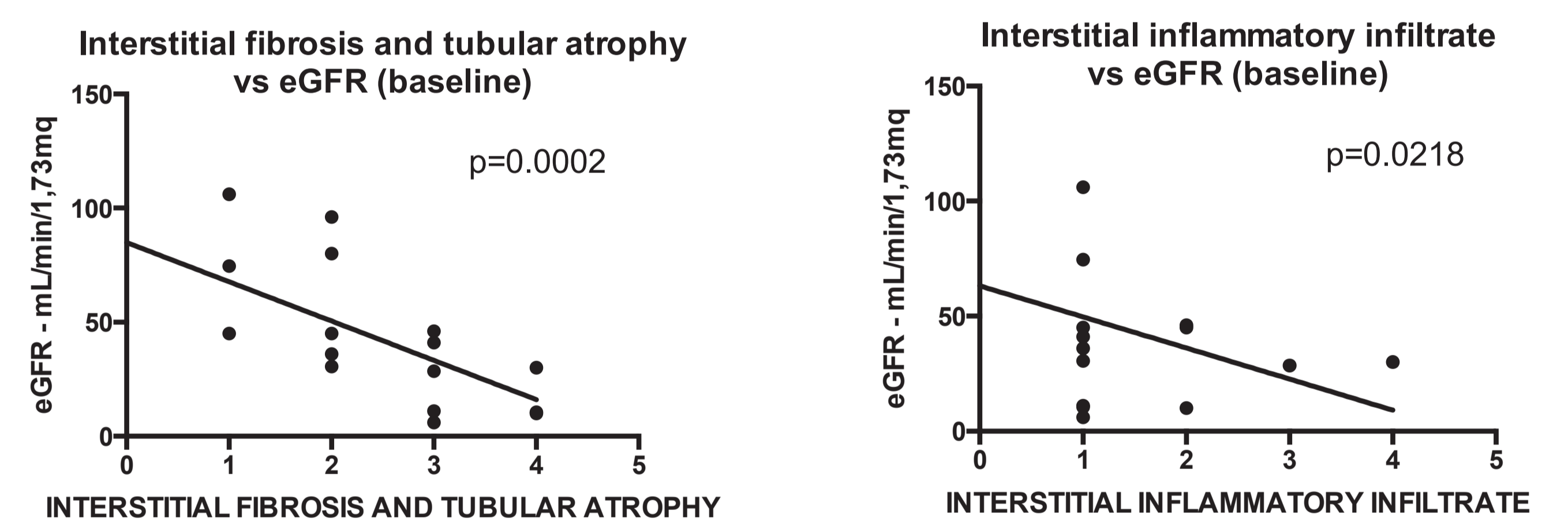


Figure 2. Interstitial fibrosis and tubular atrophy correlated negatively with estimated GFR at the time of biopsy as well as interstitial inflammatory infiltrate.

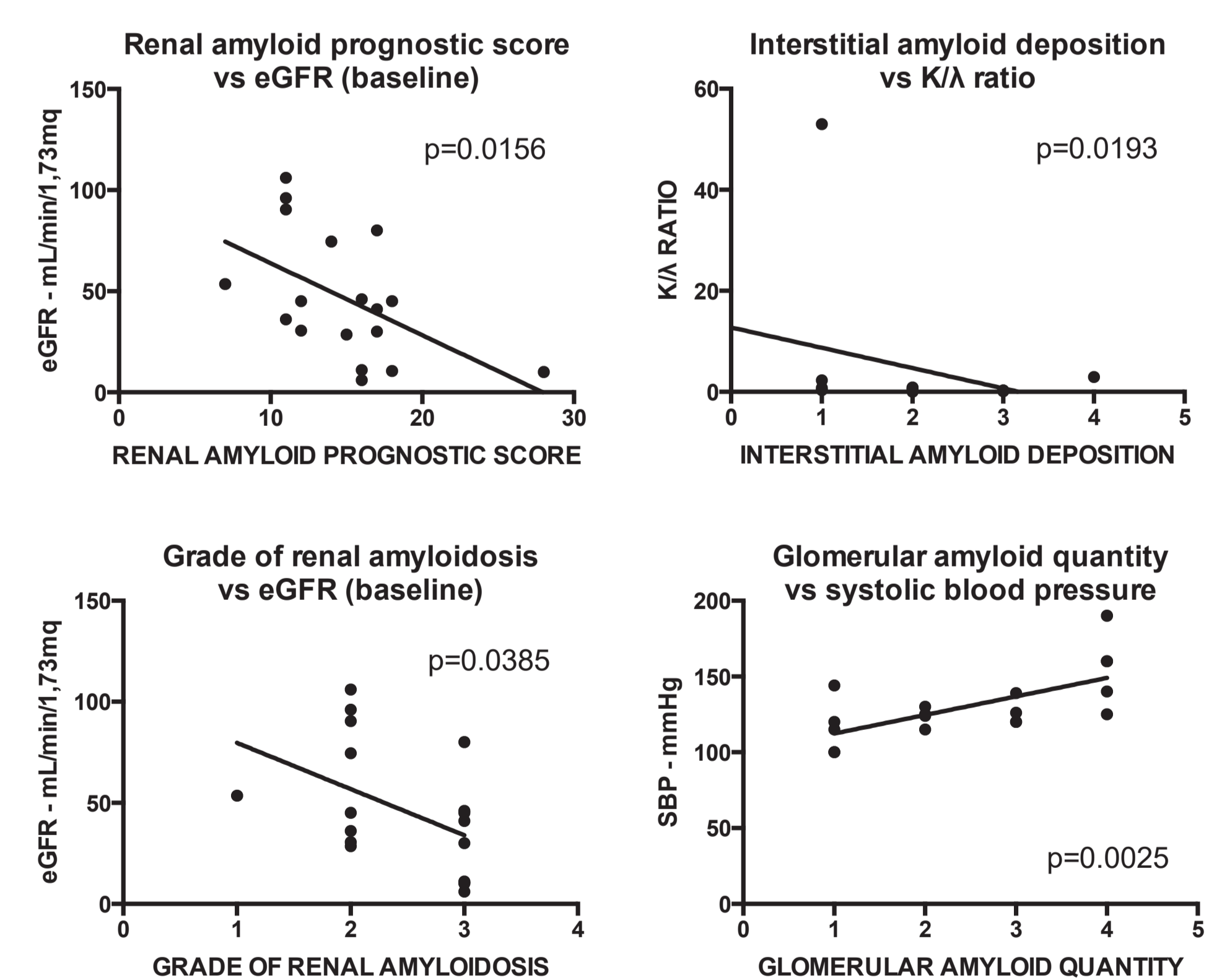


Figure 3. Renal Amyloid Prognostic Score (RAPS) and the grade of renal amyloidosis negatively correlated with renal function at baseline. The K/λ ratio correlated with interstitial amyloid deposition while an increased glomerular involvement was associated with a higher systolic blood pressure.

CONCLUSIONS

In our cohort of patients affected by renal AL amyloidosis the vascular amyloid score and the degree of interstitial fibrosis and tubular atrophy were the major determinants of renal function at the time of biopsy. Furthermore, the RAPS - calculated by the sum of all the histological lesions - and the grade of renal amyloidosis appeared to be a good estimator of the degree of renal failure. No significant correlation was established between the amyloid deposits present at glomerular level and the degree of proteinuria, possibly confirming that the toxic role of circulating free light chains is predominant compared to the role of local deposits.

