

AA AMYLOIDOSIS WITH RENAL INVOLVEMENT: RETROSPECTIVE REVIEW OF 121 PATIENTS

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Objectives:

AA amyloidosis is a multisystemic, progressive and fatal disease. The kidney is one of the most frequent sites of amyloid deposition. Renal involvement occurs early in the course of disease. The aim of this retrospective study was to investigate the etiology, clinical and laboratory features, and outcome of patients with biopsy-proven AA amyloidosis with renal involvement.

Methods:

All records of patients who were treated in our in/outpatient clinic of nephrology between January of 2001 and May of 2013 were reviewed for the presence of biopsy proven AA amyloidosis with renal involvement. Other forms of amyloidosis were excluded. The creatinine clearance was calculated MDRD-4 formula. Renal disease was classified according to K/DOQI-NKF guideline. Date of onset and type of dialysis and causes of death were recorded, if identified. Deaths were recorded as unknown whenever the exact cause was not reported.

Table 1. The demographic features and laboratory findings of the patients at the time of diagnosis.

	All (n=121)	FMF (n=45)	Tbc (n=30)	P
Age (years)	42.6±14.4	35.0±13.1	42.9±10.0	0.007
Gender (F/M)	37/84	16/29	9/21	NS
BMI (kg/m ²)	21.7±2.63	21.3±2.1	21.8±3.6	NS
Follow-up time (months)	38.2±37.2	47.3±37	37.1±37.0	NS
Serum urea (mg/dl)	65.3±56.2	56.2±63.3	62.4±42.5	NS
Serum creatinine (mg/dl)	2.3±2.1	1.77±1.78	2.12±1.80	NS
Creatine clearance (ml/min)	69.4±57.4	81.3±47.3	61.4±40	NS
Serum albumin (g/dl)	2.7±1.0	3.02±1.1	2.31±0.80	0.005
Hemoglobin (g/dl)	12.1±2.1	12.36±1.95	11.9±1.98	NS
Serum sodium (mmol/l)	139±4	139.3±4.1	137.7±3.7	NS
Serum calcium (mg/dl)	8.4±0.93	8.56±0.91	8.36±0.84	NS
Serum phosphorus (mg/dl)	4.9±1.6	4.80±1.79	5.04±1.47	NS
Ferritin (ng/ml)	185±20	130.9±164.5	237.3±265.6	0.035
intact Parathormone (pg/ml)	119±119	118.8±136	129.5±121.5	NS
Proteinuria (g/24 h)	6.7±5.3	5.52±4.98	9.01±5.86	0.007

Table 2. The demographic features and laboratory findings of the patients according to dialysis requirement.

	Dialysis (-) (n: 53)	Dialysis (+) (n: 68)	P
Age (years)	39.0±13.0	45.5±14.9	0.014
Gender (F/M)	21/32	16/52	NS
BMI (kg/m ²)	22.2±3.0	21.3±2.2	NS
Follow-up time (months)	41.0±39.4	36±35.5	NS
Serum urea (mg/dl)	47.5±52.7	79.2±55.3	0.002
Serum creatinine (mg/dl)	1.22±0.83	3.05±2.38	0.001
Creatine clearance (ml/min)	89.1±41.0	46.2±38	0.001
Serum albumin (g/dl)	2.94±1.11	2.49±0.89	0.015
Hemoglobin (g/dl)	12.6±2.01	11.6±2.03	0.013
Serum sodium (mmol/l)	139.3±3.5	138.2±3.8	NS
Serum calcium (mg/dl)	8.72±0.77	8.15±0.97	0.001
Serum phosphorus (mg/dl)	4.30±0.84	5.35±1.93	0.001
Ferritin (ng/ml)	144.7±164.8	215.7±224.1	NS
intact Parathormone (pg/ml)	81.2±107.4	148.6±120.0	0.002
Proteinuria (g/24 h)	5.16±3.91	7.93±5.95	0.004

Table 3. Renal survival time according to etiology and renal failure stage.

	n	Mean Renal Survival (months)	%95 Confidence Interval		One year survival rate	Two year survival rate	Five year survival rate	P
			Lower	Upper				
Renal	1(38)	123.9±13	93.3	149.5	%97.4	%93.3	%78.6	0.001
Failure	2(23)	54±8.8	36.6	71.4	%82.1	%65.7	%48.7	
Stage	3(25)	44.6±8.3	28.3	60.9	%87.2	%58.3	%26.5	
Stage	4(19)	46±11.3	23.8	68.2	%61.1	%48.1	%32.1	NS
Stage	5(16)	25.7±6.3	13.3	38.1	%56.3	%37.5	%12.5	
FMF	45	81.3±11.2	59.2	103.5	%92.9	%85.3	%65.5	NS
Tbc	30	59.4±10	39.6	79.2	%82.2	%61.4	%40.9	NS
Overall	121	64.7±6.3	52.3	77.1	%81.7	%67.3	%46.1	

Table 4. Patient survival time according to etiology, dialysis requirement and renal failure stage.

	n	Mean Patient Survival (months)	%95 Confidence Interval		One year survival rate	Two year survival rate	Five year survival rate	P
			Lower	Upper				
Renal	1(38)	141.2±10.6	120.2	162.1	%94.7	%91.8	%85.7	0.001
Failure	2(23)	47.6±8.5	30.8	64.4	%73.4	%53.7	%38.1	
Stage	3(25)	66.5±11.3	44.3	88.7	%78.8	%67.5	%42.2	
Stage	4(19)	51.5±12.3	27.3	75.7	%65.9	%49.7	%33.3	0.001
Stage	5(16)	29.9±6.9	16.2	43.6	%61.9	%41.3	%17.2	
Dialysis(-)	53	119.1±7.6	104	134.1	%89.2	%85.3	%82.7	0.001
Dialysis(+)	68	61.3±8.5	44.5	78.1	%74.3	%57.5	%33.7	
Survival on dialysis	68	32.1±6.1	20.0	44.2	%44.7	%40.0	%22.0	
FMF	45	105.6±12.1	81.8	129.3	%82.9	%82.9	%62.2	NS
Tbc	30	66.2±11.6	43.3	89.1	%75.8	%63.1	%41.5	NS
Overall	121	88.7±7.8	73.4	104.1	%80.7	%68.2	%51.3	

Table 5. Multivariate logistic regression analysis of the factors that predicts ESRD.

Predictor of ESRD	P	ODDS	% 95 CI	
			Lower	Upper
Age (years)	0.002	1.028	1.010	1.046
Serum creatinine (mg/dl)	0.001	1.476	1.287	1.691
Serum albumin (g/dl)	0.001	0.623	0.465	0.834

Table 6. Multivariate logistic regression analysis of the factors that predicts mortality.

Predictor of death	P	ODDS	% 95 CI	
			Lower	Upper
Serum creatinine (mg/dl)	0.034	0.764	0.595	0.980
Serum albumin (g/dl)	0.038	0.557	0.321	0.968
Time to dialysis (month)	0.009	0.970	0.948	0.993
Dialysis requirement (+)	0.001	5.143	2.312	11.438
Stage of renal disease	0.001	9.696	3.430	27.410

Figure 1. Patients survival according to serum albumin level.

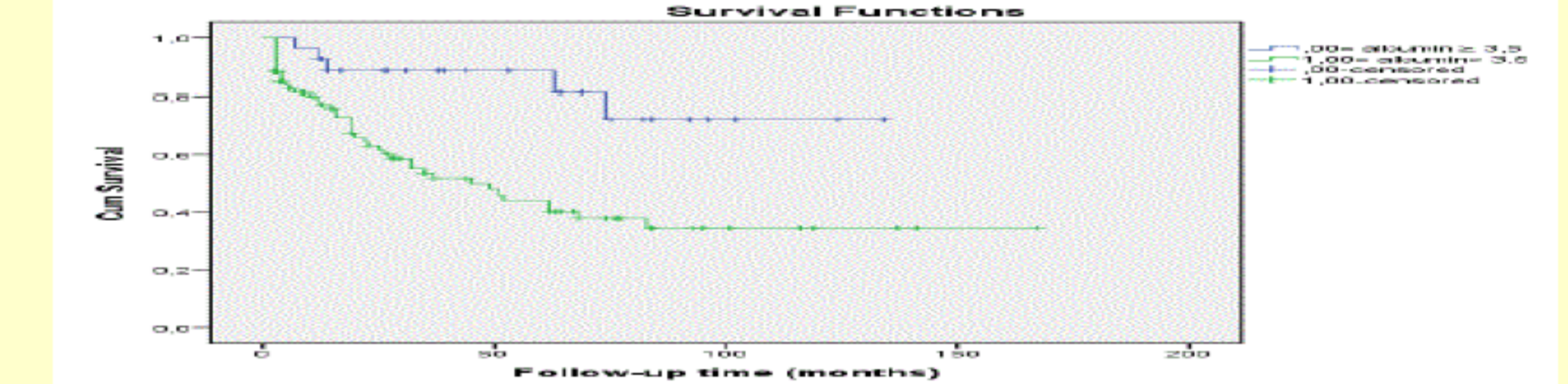
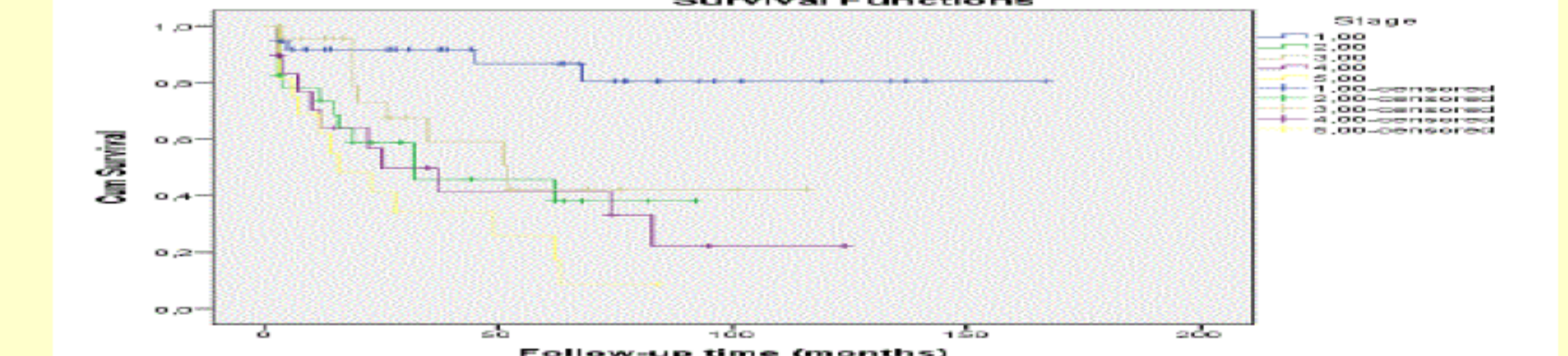


Figure 2. Patients survival according to stage of renal disease.



Results:

One hundred and twenty-one patients (Male/Female: 84/37, mean age 42.6±14.4 years) were analyzed retrospectively. Familial Mediterranean Fever (37.2%) and tuberculosis (24.8%) were the most frequent causes of amyloidosis. Mean serum creatinine and proteinuria at diagnosis were 2.3±2.1 mg/dl and 6.7±5.3 g/day, respectively. Stage I, II, III, IV and V renal disease were present in 31.4%, 19.1%, 20.6%, 15.7%, and 13.2% of the patients, respectively. Sixty-eight (56.2%) of 121 patients were started dialysis treatment during the follow-up period. Mean duration of renal survival was 64.7±6.3 months. One, two and five year renal survival rates were 81.7%, 67.3% and 46.1%, respectively. Age, serum creatinine and albumin levels were found as predictors of end stage renal disease (ESRD) in logistic regression analysis. Fifty patients (%41.3) died during the follow-up period. The mean survival of patients was 88.7±7.8 months (median: 63±13.9). One, two and five year survival rates of patients were 80.7%, 68.2% and 51.3%, respectively. Older age, male gender, lower levels of BMI, GFR, serum albumin, Ca, and higher levels of P, iPTH and proteinuria were associated with a higher mortality. Serum creatinine, albumin, dialysis requirement and short time to dialysis were predictors of mortality in logistic regression analysis.

Conclusions:

The outcome of patients with AA amyloidosis and renal involvement is poor, particularly in those who had massive proteinuria, severe hypoalbuminemia and dialysis requirement at the outset. Early diagnosis and treatment of underlying causes may improve prognosis.

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