

# PREDICTORS OF CLINICAL AND HISTOPATHOLOGICAL OUTCOMES FOR IGA NEPHROPATHY AND EFFECT OF TREATMENT IN AN INDIAN COHORT

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## OBJECTIVES

- To evaluate clinical and histopathological outcomes in IgA nephropathy (IgAN)
- To evaluate the effect of treatment (RAS Blockade, Immunosuppression) in IgA nephropathy

## METHODS

- Retrospective cohort of IgAN patients followed at Christian Medical College, Vellore, India from 2006 to 2011.
- We evaluated clinical and pathological predictors of renal survival (time to reach end-stage renal disease requiring dialysis) by cox proportional hazards model and effect of treatment such as renin-angiotensin system blockade and immunosuppression.

## RESULTS

### Baseline characteristics

Characteristics	Total patients - (n/mean ± SD)	Study patients - (n/mean ± SD ± (range))
IgA nephropathy patients	436	315
Demographic profiles		
Age at the time of biopsy (years)	38.5 ± 11.2 (11 - 80)	38.7 ± 11 (13 - 70)
Male: female ratio	1.9:1	1.9:1
Duration of follow-up in months	28.4 ± 21.2 (1 - 82)	29 ± 21 (3 - 82)
Laboratory profiles		
Serum creatinine (mg/dl)	2.61 ± 2.23 (0.5 - 15.2)	2.06 ± 1.33 (0.6 - 9.2)
e-GFR at the time of presentation (ml/min/1.73m <sup>2</sup> )	46.43 ± 32.24 (3.22 - 182.56)	51.02 ± 30.69 (6.81 - 182.56)
Proteinuria (mg/day)	2872 ± 2513 (40 - 17000)	2690 ± 2338 (81 - 12900)
Systolic blood pressure (mm/Hg)	134 ± 17 (94 - 200)	133 ± 17 (94 - 200)
Diastolic blood pressure (mm/Hg)	85 ± 10 (56 - 120)	84 ± 10 (56 - 120)
Mean arterial pressure MAP (mm/Hg)	101 ± 11 (49 - 143)	101 ± 12 (49 - 143)
BMI	23.5 ± 4.3 (13.8 - 44.9)	23.4 ± 4.3 (13.8 - 44.9)
Serum albumin (g/dl)	4.0 ± 2.7 (1.2 - 4.9)	4.0 ± 2.4 (1.2 - 4.9)
Serum cholesterol (mg/dl)	191 ± 63 (79 - 541)	191 ± 63 (79 - 541)
Hypertension	153(35.1)	107(34)
Dialysis requirement at the time of presentation	23(5.3)	7(2.2)

### Histology - MEST & Others

Score	M	E	S	T
0	284 (90.2)	209 (66.3)	119 (37.8)	50 (15.9)
1	31 (9.8)	106 (33.7)	196 (62.2)	135 (42.9)
2	-	-	-	130 (41.3)

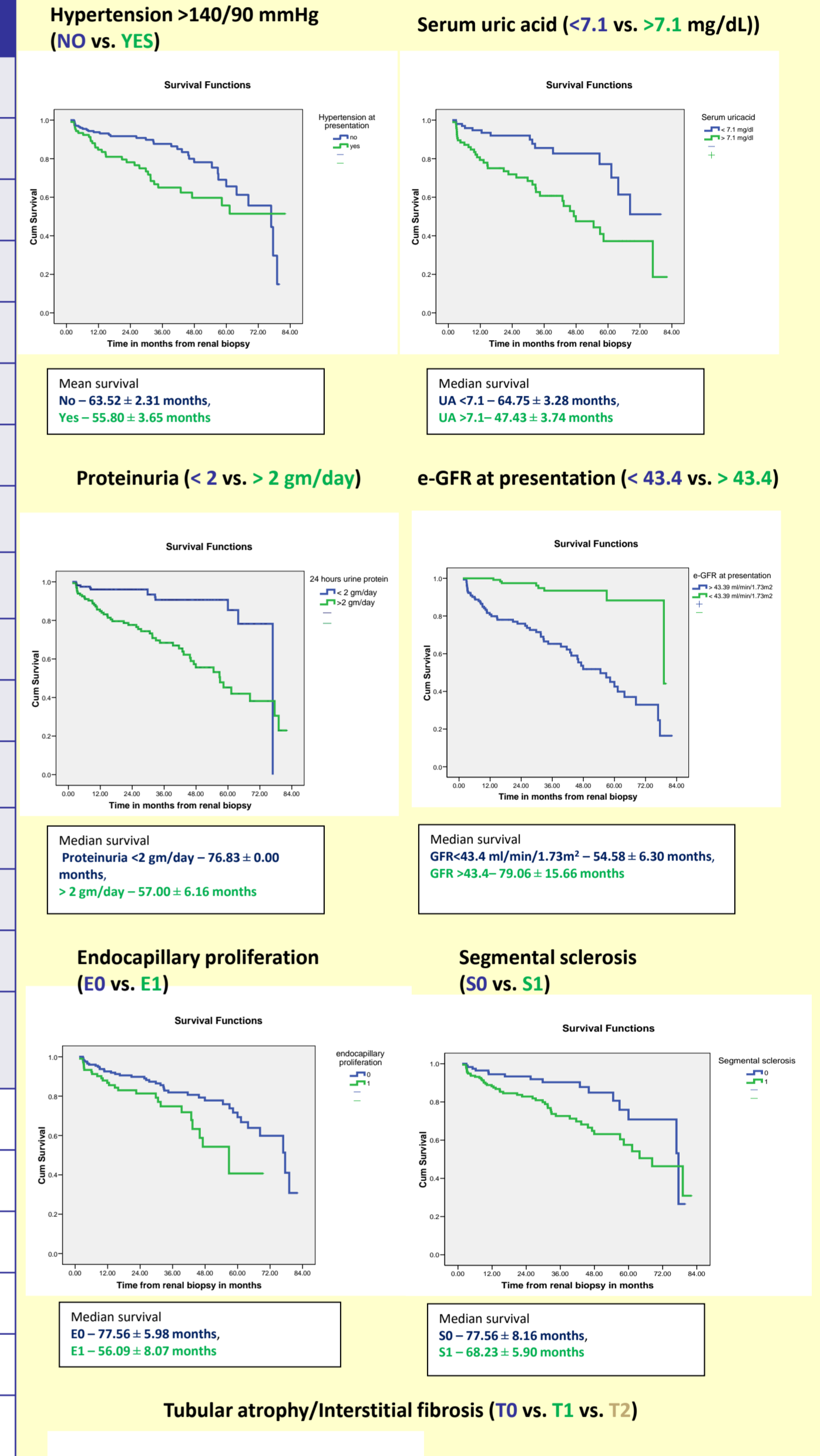
### Treatment details

Treatment details (Total no. of patients - 315)	
Immunosuppressant drugs (%)	223 (70.8)
Prednisone alone (%)	82 (36.8)
Prednisone and MMF (%)	89 (39.9)
RAS blockade (ACEI/ARB) (%)	232 (73.7)

Study patients (315 biopsies)-n (%)	
Crescents	33(10.5)
Co-deposition with C3	109(34.6)
Co-deposition with IgG	31(9.8)
Capillary wall IgA deposits	36(11.4)

### Clinical and pathological predictors of renal survival

Parameters	Median/ Mean survival ± SE	p-value
Age (years)	≤39 56.94 ± 3.00 >39 64.49 ± 2.76	0.109
Sex	Male 60.82 ± 2.46 Female 55.78 ± 2.67	0.898
BMI	≤23.1 57.62 ± 3.04 >23.1 63.68 ± 2.63	0.101
Hypertension	No 63.52 ± 2.31 Yes 55.80 ± 3.65	0.015*
MAP (mmHg)	≤99 76.83 ± 14.50 >99 68.29 ± 5.26	0.125
Macroscopic hematuria	No 60.41 ± 2.15 Yes 59.44 ± 4.45	0.291
Serum uric acid (mg/dl)	≤7.1 64.75 ± 3.28 >7.1 47.43 ± 3.74	0.000*
Serum cholesterol (mg/dl)	≤182 60.99 ± 3.45 >182 61.47 ± 3.08	0.638
e-GFR at presentation (ml/min/1.73m <sup>2</sup> )	≤43.39 54.58 ± 6.30 >43.39 79.06 ± 15.66	0.000*
24 hours proteinuria (mg/day)	≤2000 76.83 ± 0.00 >2000 57.00 ± 6.16	0.000*
Before biopsy RAS blockade	No 76.83 ± 7.65 Yes 68.28 ± 5.21	0.598
Before biopsy Immunosuppressant drugs	No 60.91 ± 2.18 Yes 55.03 ± 3.55	0.689
Mesangial proliferation	M0 76.83 ± 6.20 M1 59.97 ± 9.27	0.978
Endocapillary hypercellularity	E0 77.56 ± 5.98 E1 56.09 ± 8.07	0.009*
Segmental sclerosis	S0 77.56 ± 8.16 S1 68.23 ± 5.90	0.006*
Tubular atrophy/interstitial fibrosis	T0 60.26 ± 1.14 T1 70.35 ± 2.51 T2 47.17 ± 3.07	0.000*
Crescents	No 76.83 ± 4.79 Yes 56.81 ± 0.00	0.164
Co-deposition with C3	No 57.33 ± 2.40 Yes 66.20 ± 3.25	0.094
Co-deposition with IgG	No 77.56 ± 10.41 Yes 76.83 ± 0.00	0.431
Capillary wall IgA	No 76.83 ± 4.82 Yes 56.81 ± 0.00	0.818
Treatment with RAS blockade	No 47.15 ± 12.56 Yes 79.07 ± 8.66	0.000*
Treatment with Immunosuppressant drugs	No 50.83 ± 4.25 Yes 64.08 ± 2.14	0.000*



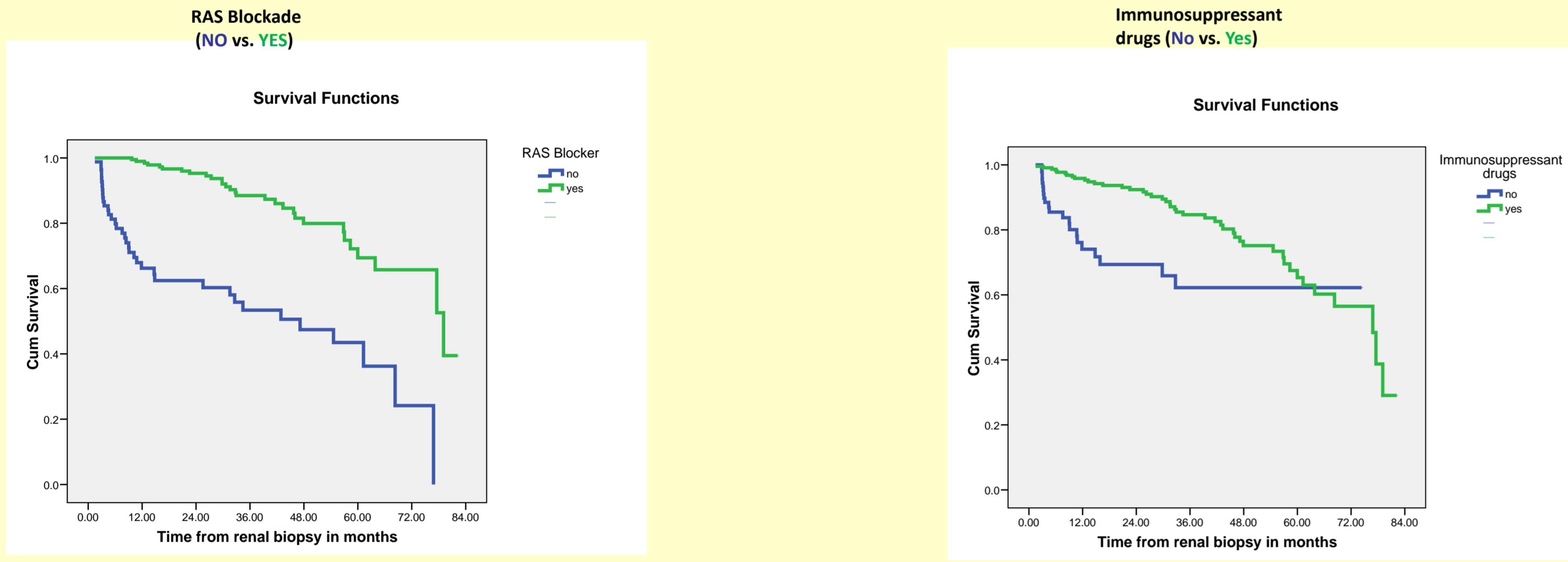
### Cox proportion Hazard ratio model for independent risk factor for renal survival

Parameter	Sig.	Exp(B)	95.0% CI for Exp(B)
Age	.004	.941	.903 .980
Hypertension	.0036	1.049	1.003 1.097
Macroscopic hematuria	.015	.154	.034 0.692
e-GFR at presentation	.000	.925	.892 .959
Endocapillary proliferation E1	.000	4.534	2.006 10.246
Segmental sclerosis S1	.058	2.651	.968 7.258
Tubular atrophy T2	.041	2.891	0.927 13.578
Treatment with RAS blockade	.026	0.353	0.141 0.883
Treatment with Immunosuppressant drugs	.000	0.163	0.065 0.405

- In clinical parameters, the independent predictors of poor renal survival were young age, hypertension, baseline renal dysfunction,
- Whereas macroscopic hematuria was found to have good prognosis.

### Effect of treatment in IgA nephropathy

Treatment with immunosuppression and renin-angiotensin blockade had better renal survival.

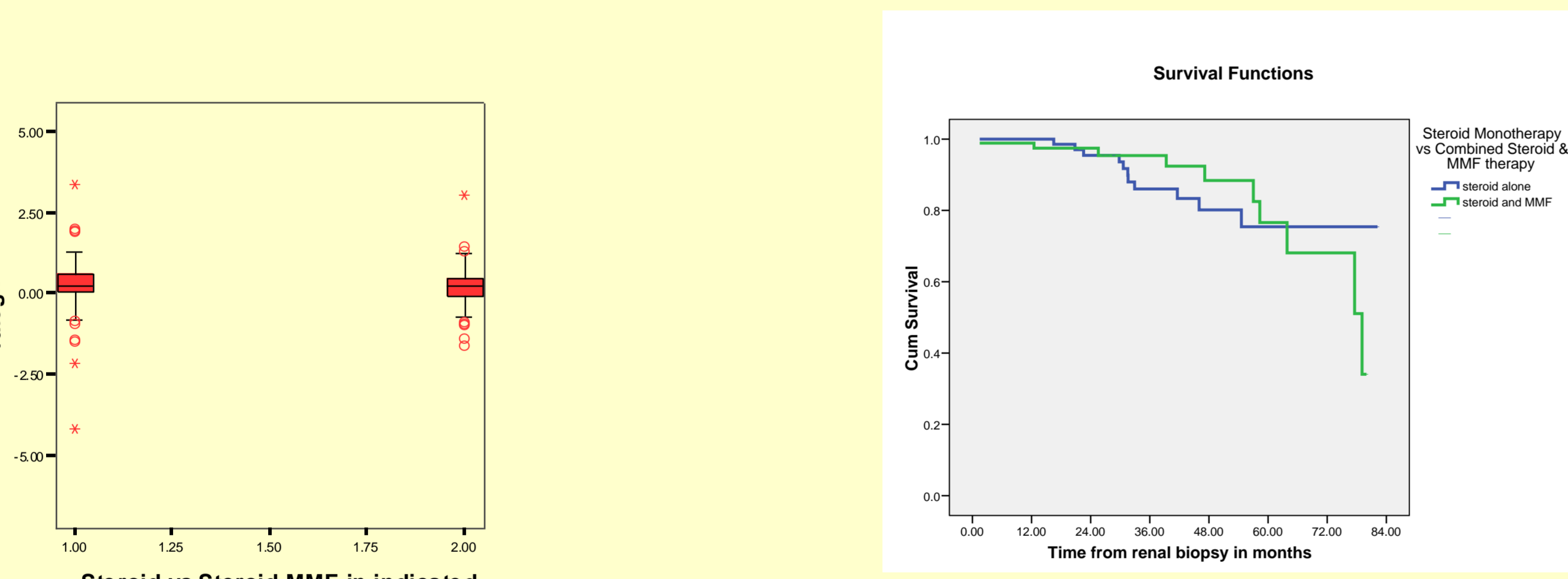


Median survival  
No RAS Blocker - 47.15 ± 12.56 months,  
RAS Blocker - 79.07 ± 8.66 months

Mean survival  
No IMS - 50.83 ± 4.25 months,  
IMS - 64.08 ± 2.14 months

### Effect of combined steroid and MMF therapy on rate of decline in GFR

KM survival curve - Steroid alone vs. along with MMF



Spearman rho -0.092, p 0.230

Mean survival  
Steroid monotherapy - 71.02 ± 3.02 months,  
Combined steroid & MMF therapy - 69.91 ± 2.89 months

### Effect of combined steroid & MMF therapy on secondary outcomes

Percentage reduction	Steroid alone	Steroid & MMF	p-value
ΔProteinuria (%)	-41.41 ± 104.30	-49.51 ± 79.73	0.570
ΔMAP (%)	-5.18 ± 11.51	-3.64 ± 12.27	0.401

- Combined steroid and MMF therapy did not have any improvement in outcome (such as better renal survival, proteinuria reduction, BP control) over steroid monotherapy.

### Rate of decline in GFR

Parameters	Univariate analysis		Multivariate analysis	
	Spearman's correlation coefficient	p-value	ExpB (95% CI)	p-value
Age (years)	-0.138	0.014	-	-
Sex (Female)	0.011	0.848	-	-
BMI	-0.134	0.017	-	-
Hypertension	-0.021	0.712	-	-
MAP (mmHg)	-0.015	0.789	-	-
Macroscopic hematuria	-0.044	0.436	-	-
Serum uric acid	-0.012	0.863	-	-
Serum cholesterol (mg/dl)	0.101	0.122	-	-
e-GFR at presentation (ml/min/1.73m <sup>2</sup> )	0.030	0.596	-	-
24 hours proteinuria (mg/day)	0.219	0.000	-	-
Before biopsy RAS blockade	32(20)	0.335	-	-
Before biopsy Immunosuppressant drugs	17(10.8)	0.461	-	-
Mesangial proliferation (M1)	-0.029	0.612	-	-
Endocapillary hypercellularity (E1)	0.060	0.287	-	-
Segmental sclerosis (S1)	0.063	0.268	-	-
Tubular atrophy/interstitial fibrosis (T0 & T1 vs. T2)	0.159	0.005	2.166(0.019 - 0.386)	0.031
Crescents	-0.039	0.489	-	-
Co-deposition with C3	-0.106	0.060	-	-
Co-deposition with IgG	0.001	0.985	-	-
Capillary wall IgA	0.095	0.093	-	-
Treatment with RAS blockade	-0.123	0.029	-	-
Treatment with Immunosuppressant drugs	-0.078	0.167	-	-

By linear regression by using backward method, using the following dependent variables age, BMI, 24 hours proteinuria, MEST, treatment with RAS blockade were analyzed.

## CONCLUSION

- In the Indian cohort, apart from clinical parameters such as young age, baseline hypertension and renal dysfunction, Oxford histological score E1, S1, T2 had poor renal survival and aid in predicting prognosis.
- Treatment with immunosuppression had better renal survival in Indian patients in contradictory with other studies.
- Combined steroid and MMF therapy did not have any improvement in outcome

•Keywords: IgA nephropathy (IgAN), Oxford classification, MEST score (Mesangial hypercellularity, Endocapillary proliferation, Segmental sclerosis, Tubular atrophy/interstitial fibrosis)