

The significance of extracapillary proliferation in IgA Nephropathy



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BACKGROUND

The prognostic utility of extracapillary proliferation was not assessed in the original Oxford classification of IgA Nephropathy (IgAN), and is still controversial. **Accordingly, we aimed to evaluate the impact of crescents on renal prognosis.**

METHODS

In this retrospective cohort from two tertiary academic medical care centers we examined the renal outcome at December 31, 2014 of **121 adult patients (mean age 40.1 (37.8, 42.4) years, 69% male, eGFR 47.0 (43.0, 50.4) mL/min)** who had **biopsy proven primary IgAN** between 2003 and 2013. Patients with less than eight glomeruli on renal biopsy and insufficient clinical data were excluded from the study. **The primary endpoint was kidney survival defined as doubling of serum creatinine or end-stage renal disease (ESRD).** Renal biopsies from all patients were scored according to Oxford classification of IgAN and any grade of extracapillary proliferation was noted by one pathologist who was blinded to the clinical information.

RESULTS

Thirty-one percent of the patients had a degree of **extracapillary proliferation**. As compared to those with no crescents, they had **higher grade of inflammation, lower eGFR and increased proteinuria**. The patients with extracapillary proliferation were **more frequent in M1 and S1 classes**. Almost all of the patients received RASi agents, while half of them were on a form of immunosuppressive treatment during the observation period. There were no differences regarding the treatment between the two groups.

Thirty-nine percent of the extracapillary proliferation group reached the composite endpoint as compared to 23% in the no crescents group. **The mean kidney survival time for the entire cohort was 10.6 (9.1, 12.0) years.** In univariate time-dependent analyses, regarding the composite end point, **extracapillary proliferation was associated with impaired renal survival.** Furthermore, crescents presence had significant impact on a harder endpoint, renal replacement therapy initiation only.

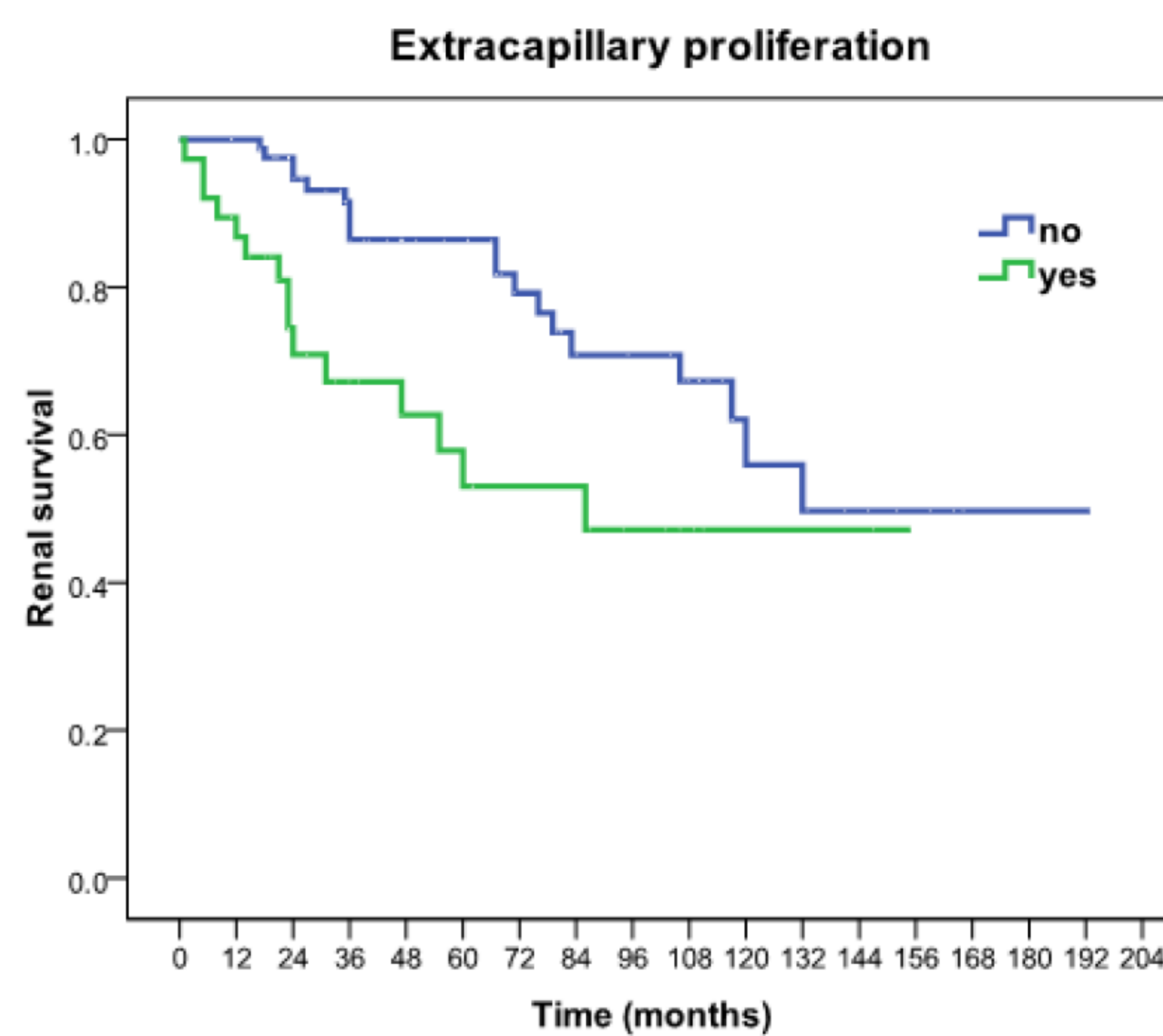
In the Cox regression model, **the only independent predictors of decreased renal survival were eGFR at time of biopsy, S1 and the presence of extracapillary proliferation.**

CONCLUSIONS

In our study, extracapillary proliferation in any degree had renal prognostic significance. Thus, we suggest that the presence of crescents should be included in the Oxford classification.

	All N=121	Crescents N=38	No crescents N=83	p
Age (years)	40.1 (37.8,42.4)	37.5 (31, 45)	39 (36, 44)	0.7
Male gender (%)	69	72	63	0.3
Hypertension (%)	58	61	57	0.6
Hemoglobin (g/dL)	13.3 (13.2, 13.8)	12.2 (11.3, 13.7)	13.8 (13.4, 14.4)	<0.001
ESR (mm/h)	29 (25, 35)	34 (24, 54)	27.5 (23, 35)	0.04
Fibrinogen (mg/dL)	417 (391, 455)	514 (440, 583)	390 (361, 422)	0.001
eGFR (mL/min)	47 (43, 50.4)	37.2 (21.3, 49.1)	47.6 (44.7, 53.7)	0.05
Proteinuria (g/24h)	2 (1.7, 2.3)	2.9 (2, 3.8)	1.8 (1.3, 2.2)	<0.01
Hematuria (h/mm ³)	128 (95, 167)	140 (90, 210)	126 (80, 160)	0.5
Oxford classif. (%)				
M1	72	84	66	0.04
E1	23	32	19	0.1
T1	79	79	78	0.9
S1	71	87	64	<0.01
Endpoint (%)				
HD	20	37	12	0.001
Double creatinine	12	11	12	0.8
Composite endpoint	28	39	23	0.05
Treatment (%)				
RASi	98	97	98	0.9
Immunosuppression	49	53	47	0.5

Kaplan Meier



No crescents versus crescents:
11.4 (9.7, 13.0) vs. 7.5 (5.6, 9.5) years, p=0.007

Cox proportional hazard model

Variables	HR (95% CI)	p
Age (per 1 year of age)	0.97 (0.94, 1.01)	0.18
Male gender vs. Female	1.42 (0.57, 3.52)	0.44
IgG deposition vs. absence	1.25 (0.51, 3.06)	0.62
Hypertension vs. absence	0.49 (0.18, 1.31)	0.15
Proteinuria (per 0.5 g/day)	0.97 (0.86, 1.09)	0.64
eGFR (per 10mL/min)	0.67 (0.53, 0.86)	0.001
Hematuria (per 10 h/mm ³)	0.98 (0.94, 1.02)	0.41
M1 vs. M0	1.62 (0.65, 4.03)	0.29
E1 vs. E0	1.01 (0.34, 2.99)	0.98
S1 vs. S0	0.24 (0.06, 0.91)	0.03
T1 vs. T0	0.86 (0.18, 4.08)	0.85
Extracapillary proliferation yes vs no	0.25 (0.09, 0.65)	0.004
Immunosuppression vs. absence	2.12 (0.85, 5.29)	0.10

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