

Pauciimmune vasculitis

Experience of a single center

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INTRODUCTION AND AIMS

Recent data suggest different pathogenic pathways for MPO- and PR3- vasculitis, resulting in distinct phenotypes. Although ANCA-vasculitis is a systemic disease, kidney is frequently affected and the severity of kidney lesions has a major impact on outcome.

OBJECTIVES

To evaluate the clinical and evolutive characteristics, factors associated with treatment response and outcome (defined as patient and kidney survival) in patients with pauci-immune vasculitis, according to ANCA pattern.

METHODS

A retrospective, single-center study on patients admitted in a big tertiary (nephrology) center from 1997 to 2013, monitored using Birmingham Vasculitis Activity Score (BVAS) and treated according to a standardized protocol: induction (pulse-therapy with cyclophosphamide every 2/4 weeks, and pulse then oral corticosteroids, until remission) followed by long-term maintenance therapy (azathioprine and low dose oral corticosteroids).

RESULTS

- 104 patients (57F/43M, median age 60.5 [17-79] years); follow-up period 6 (3-19.5) months.
- 53% pANCA(+), 23% cANCA(+) and 24% ANCA(-).
- Features at presentation: renal involvement (100%) [macroscopic hematuria (43%), renal failure 100%], pulmonary and skin involvement (47% and 10%, respectively), general symptoms (78%).
- Laboratory data at presentation: mean hemoglobin 8.4 2g/dL; inflammation (ESR 99 [63-120]mm/H; fibrinogen 620 [510-780]mg/dL; serum albumin 3.3 0.7g/dL; renal failure (serum creatinine 6.2 3.9mg per dL; BVAS 19 3) and pulmonary infiltrates 43%.
- 24 patients (14/100 patients-years) required hemodialysis at presentation, half becoming dialysis independent thereafter; plasmapheresis was prescribed only in 6 patients.

As compared to pANCA(+) and ANCA(-), which seem to have similar characteristics, cANCA (+) patients were younger, predominately male, had more severe inflammation, more frequent macroscopic hematuria and required more often hemodialysis at presentation (Table I).

Table I. Patients' characteristics according to ANCA type

Parameter	cANCA(+)	pANCA(+)	ANCA(-)	p†
Patients number	24	55	25	
Age (years)	51.7	62.5	65.6	<0.001
Gender (male %)	79%	33%	32%	<0.001
Hemoglobin (g/dL)	7.5	8.8	8.9	0.01
Thrombocytes (no/mm ³)	345,000	307,000	260,000	<0.001
Albumin (g/dL)	3.0	3.4	3.5	0.04
Macroscopic hematuria (%)	67%	31%	39%	0.01
Hemodialysis (%)	46%	16%	16%	0.009

* median; † cANCA(+) vs pANCA(+) and ANCA(-)

- Complete renal remission** (absence of hematuria) was achieved by 58 patients (34.7/100 patients-years); mean time to response was 3.7±2.1 months. Patients not needing dialysis at presentation had two times more chances to respond, although age over 65 years and kidney damage (lower proteinuria) were also kept in the Cox model. ANCA type was not related to remission (Table II).

Table II. Predictors of response to therapy (Cox regression analysis)

Variables	B	S.E.	Exp. (B)	95% CI	Sig.*
Age >65 years (No)	-0.37	0.30	0.69	0.38 1.25	0.22
Ln (Proteinuria)	-0.17	0.12	0.84	0.66 1.07	0.16
Temporary dialysis (No)	0.53	0.27	1.70	1.00 2.89	0.05

*-2 Log Likelihood 350; Chi square 11; df. 3; p=0.01

- Relapses** were rare in this cohort (8 patients, 4.3/100 patients-years) and most occurred in the first year of observation (63%); the median time to relapse was 11.3 [9.2; 19.9] months.

CONCLUSIONS

In this cohort with severe vasculitis affecting mostly the kidney and requiring hemodialysis at admission in 14/100 patients-years of cases, complete renal remission was obtained in more than half and relapses were rare. The need of hemodialysis at presentation, reflecting the degree of renal damage, was the main determinant of treatment response and of event-free (dialysis/death) survival. cANCA(+) patients differed from those pANCA(+) and ANCA(-) by younger age, male predominance, and by more severe inflammation and kidney disease. They also appear to have more chances of dialysis-free survival.

- The main determinant of outcome** (patient and kidney survival) was the intensity of kidney damage at presentation. Those not needing dialysis at presentation had nine times more chances of dialysis-free survival in Cox regression analysis (Table III).

Table III. Predictors of event-free (death or dialysis) survival

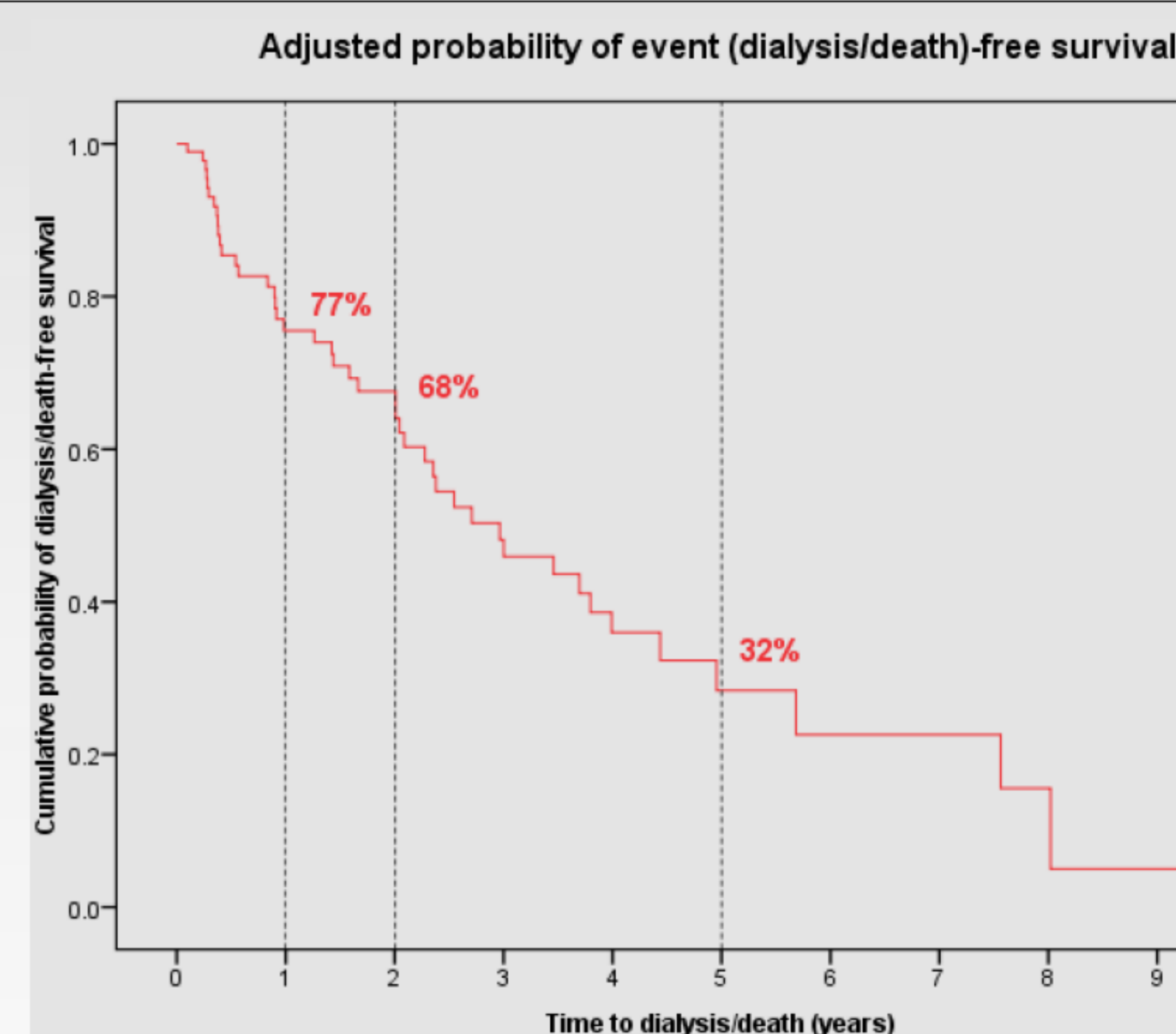
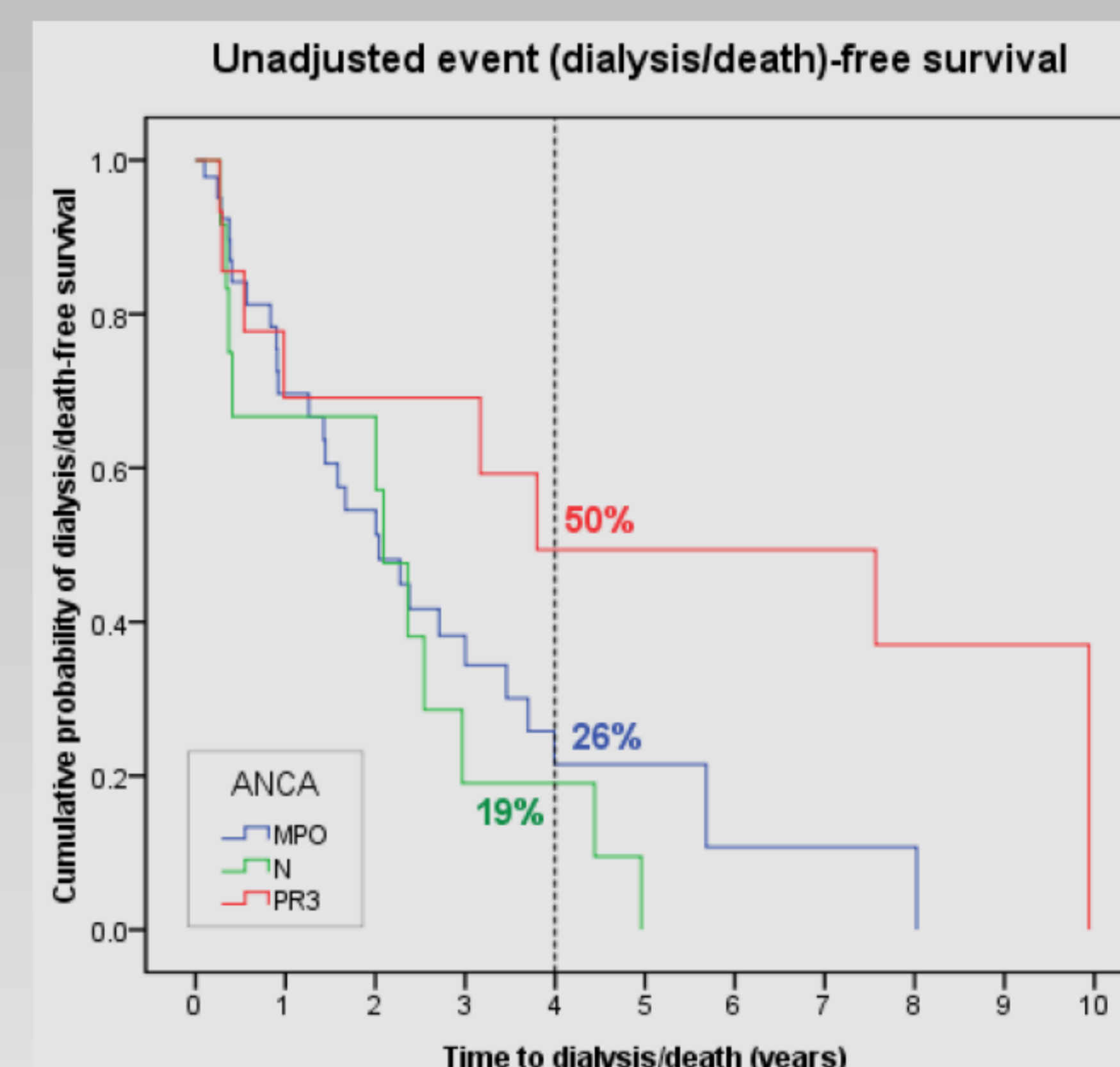
Variables	B	S.E.	Exp. (B)	95% CI	Sig.*
Ln [Serum albumin]	0.49	0.35	1.64	0.82 3.27	0.16
Temporary dialysis (No)	2.24	1.03	9.36	1.25 70.07	0.03

*-2 Log Likelihood 272; Chi-square 10; df 2; p=0.006

- Nor BVAS neither ANCA type were predictors of event-free survival, although PR3-ANCA patients showed a better prognosis in Kaplan Meier analysis.

	Median event-free survival (months)
MPO-ANCA	24.5 (13.4-35.6)
N-ANCA	25.1 (18.6-31.6)
PR3-ANCA	45.6 (0.0-115.5)
All	27.3 (21.0-34.5)

Log Rank (Mantel-Cox) 6 p=0.05



- The adjusted probability to survive (patient and kidney) for 1 year was 77%, but for 2 and 5 years decreased to 68% and to 32%, and was not different in function of ANCA type.

