

Introduction

- Serological double positivity for both ANCA and anti-GBM antibodies is described in patients presenting with rapidly progressive glomerulonephritis.
- The clinical significance of this serological pattern remains unclear, as does the prevalence, clinical features and natural history of this condition.
- Jayne et al¹ have suggested that 30% of patients with anti-GBM disease have ANCA, and 7.5% of those with ANCA vasculitis have anti-GBM antibodies.
- Levy et al² later found that 5% of their cohort with ANCA-positive sera had detectable anti-GBM antibodies, while 32% of those with anti-GBM positive sera had detectable ANCA.
- Outcomes in patients with severe disease have been reported as being poor³. In some series no renal recovery was shown in those who were dialysis-dependent at presentation², therefore behaving prognostically like anti-GBM disease rather than ANCA-associated vasculitis.
- However some researchers have suggested that patients with anti-MPO antibodies and anti-GBM respond better to therapy than those with anti-GBM alone⁴.

Aim

- The Rare Kidney Disease (RKD) Registry and Biobank is a collaborative effort between the network of clinical research facilities across Ireland, which enables clinical studies of rare kidney diseases where cases are scattered sporadically throughout hospitals in the country.
- Our aim was to define the prevalence of double positivity in the RKD Registry and Biobank and to examine the clinical and histological characteristics of affected patients.

Methods and Materials

- Data were collected on all patients with ANCA-associated vasculitis (AAV) and anti-GBM disease in the RKD Registry and Biobank.
- The cohort that was positive for both ANCA and anti-GBM was identified and their demographic, clinical and histological features, as well as outcomes, were recorded.
- Data were collated using Microsoft Excel and were exported to Minitab Version 17 for statistical analysis.
- Results were expressed in frequencies (percentages) and median & interquartile ranges (IQR).

Variable	Result	Variable	Result
ANCA vasculitis with anti-GBM	3%	Anti-GBM disease with ANCA	43%
Age (range)	67 (49-81)	Current/former smokers	6 (60%)
Men	5 (50%)	MPO-positive	6 (60%)
Renal involvement	10 (100%)	Dialysis-dependent	3 (30%)
Renal recovery if dialysis-dependent	0	Pulmonary haemorrhage	3 (30%)

Table 1: Clinical characteristics of the double-positive cohort

Results

- Of 302 ANCA-associated vasculitis cases, 10 (3%) were also positive for anti-GBM. Therefore, of 23 anti-GBM disease cases, 10 (43%) were also positive for ANCA.
- All 10 patients (100%) had renal involvement at presentation, with a median serum creatinine of 300 $\mu\text{mol/L}$ (204-672 $\mu\text{mol/L}$). 6 (60%) had a serum creatinine <500 $\mu\text{mol/L}$ at presentation, none of whom required dialysis later. 3 (30%) required dialysis at presentation; none of these patients recovered independent renal function. 3 (30%) had pulmonary haemorrhage.
- Data were available on 8/10 biopsies. 5 (50%) had > 50% crescents on renal biopsy, while 1 (10%) had > 50% sclerosis, 1 (10%) had a mixed Berden score and 1 (10%) had a focal Berden score.
- 6 (60%) had linear IgG deposition, 4 (40%) had granular C3 deposition, 2 (20%) had granular IgM deposition. None were pauci-immune.
- All patients received induction and maintenance immunosuppression. 8 (80%) underwent plasmapheresis with a median of 7 exchanges (5-26).
- 2 (20%) patients suffered leucopaenia during treatment, 3 (30%) patients had infectious complications. 1 patient died due to pneumocystis jiroveci pneumonia.

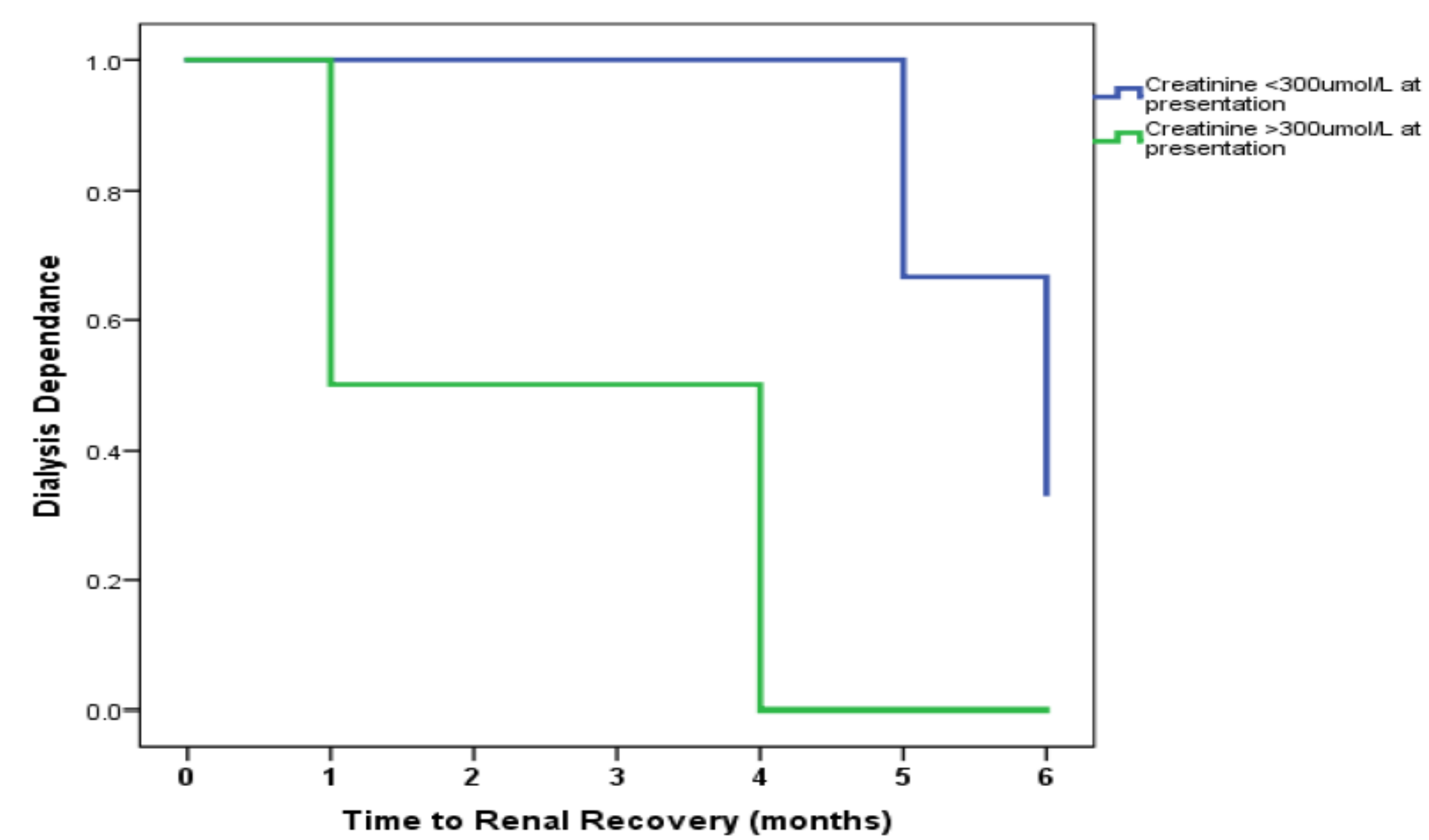


Figure 1: Cumulative probability of renal recovery according to initial serum creatinine

Discussion

- These results lend credence to previous research which has suggested that double positive patients behave like those with anti-GBM disease, both clinically and histologically.
- We did not however observe a difference in outcome according to ANCA specificity, but this may have been a function of the small cohort size.
- The mechanism for double positivity may result from glomerular damage from an ANCA-related illness leading to a secondary immune response to exposed and damaged components of the glomerular basement membrane, though this does not account for the development of ANCA after anti-GBM mediated renal injury.

Conclusions

- Serological double positivity is common in patients with anti-GBM disease but may also be observed in a minority of ANCA-positive patients with rapidly progressive glomerulonephritis.
- In keeping with prior studies, patients in our cohort who required dialysis at presentation had a poor prognosis.
- Linear IgG deposition was the most common immunofluorescent finding at renal biopsy, indicating that these patients behave more like anti-GBM patients than pauci-immune AAV.

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References

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