

Graft loss from anti-GBM nephritis: a rare event in Alport syndrome, even with a severe COL4A5/A4/A3 mutation

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BACKGROUND

Alport syndrome (AS) is caused by mutations in $\alpha 3/\alpha 4/\alpha 5$ (IV) collagen genes, whose severity determines the progression of AS. Post-transplant outcome is good, though anti-GBM glomerulonephritis occurs in 3-5% of recipients, clustering in patients with a severe mutation.

AIM

To assess whether the severity of the underlying AS mutation (COL4A5/A4/A3 genes) affects graft and patient's outcome after transplantation, including the occurrence of anti-GBM nephritis.

METHODS

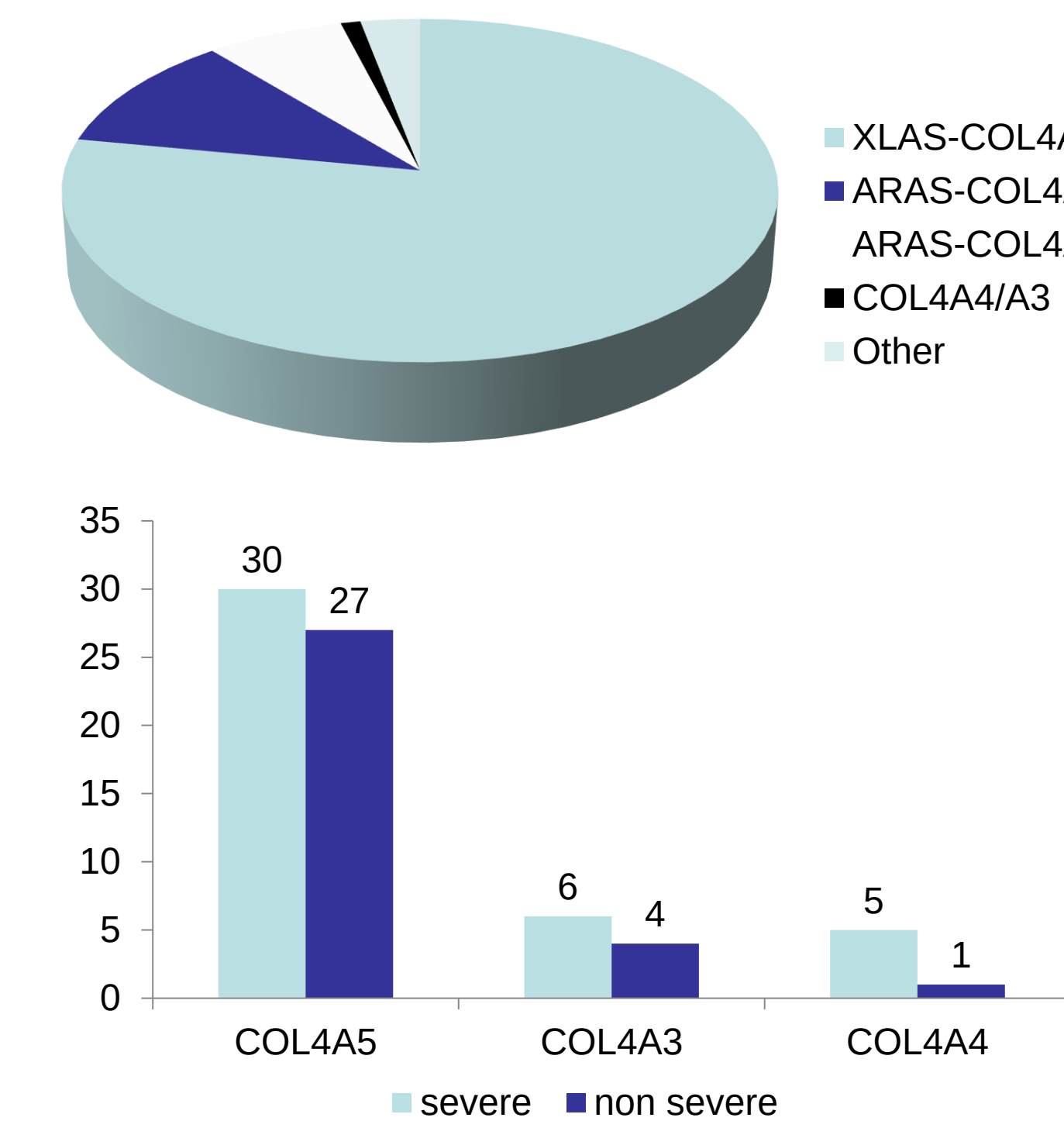
Retrospective analysis including AS patients with an identified mutation transplanted between 1971 and 2014. Severe mutations included truncating, splice-site and non-sense mutations. Missense mutations and in-frame deletions were considered non-severe.

RESULTS

Patients characteristics

Sex (male/female) (N)	59/14
Race (caucasian) (%)	99
Age (years) at ESRD (median (min-max))	26 (11-71)
Time on dialysis (months, median (min-max))	33 (1-190)
Ocular abnormalities (N)	20
Lenticonus	15
Corneal erosions/macular spots	4/1
Deafness (N)	48
age (years) at hearing aid (median (min-max))	24 (6-55)
Age (years) at first TP (median (min-max))	28 (12-73)
Duration of post-TP follow-up (years) (median (min-max))	16 (1-42)
Living/deceased donor (N)	13/80
Number of TP (N)	93
2nd / 3rd	16/2
Immunosuppressive regimen (%)	
Induction	100
Cyclosporine	69
Tacrolimus	31
Mycophenolate	25
Azathioprine	73
Sirolimus	1
Corticosteroids	98

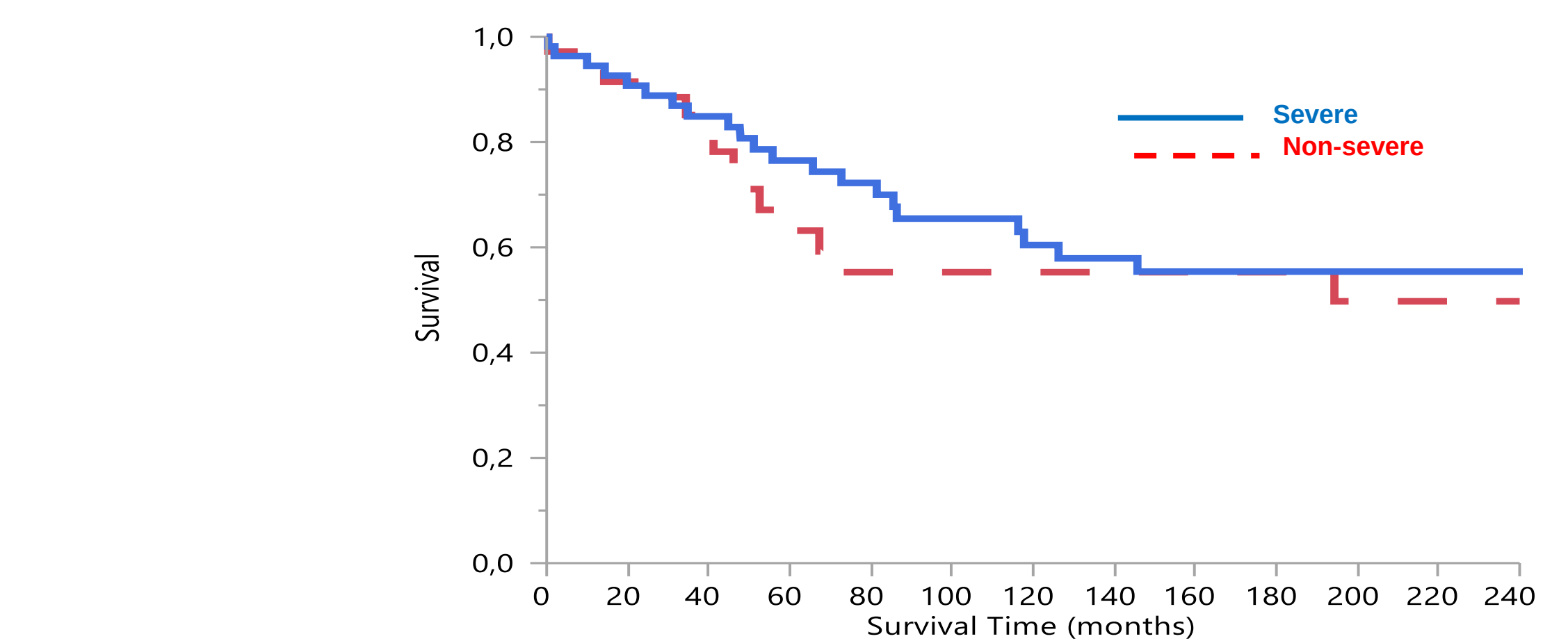
Genetic characteristics



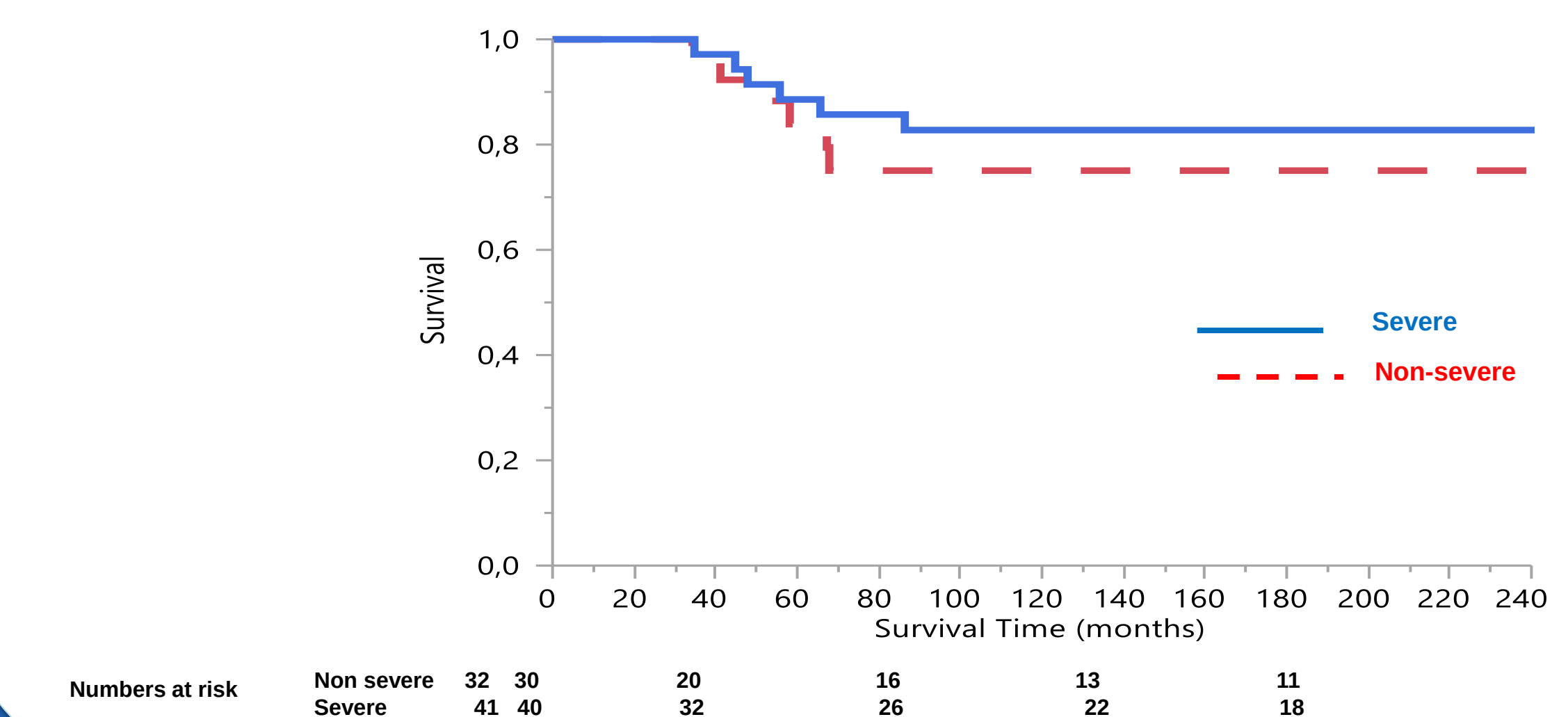
Recurrence

Anti-GBM glomerulonephritis occurred in one patient with truncating COL4A5 mutation 6 years after transplantation, with crescents and linear IgG deposits leading rapidly to graft loss. Three years after retransplantation, recurrence of anti-GBM nephritis led again to graft loss. Out of 48 grafts biopsies, linear IgG deposits without glomerular lesion were observed in 4 grafts.

Graft survival according to mutation severity



Patient survival according to mutation severity



CONCLUSION

Anti-GBM nephritis occurred in only 1,4 % of AS patients and in 2.4 % of the subgroup with a severe mutation, which is lower than generally thought.

Anti-GBM nephritis may manifest later than previously reported and recurs in a subsequent graft.