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

V. Gillion[1], K. Dahan[1,2*], E. Goffin[1], J-P. Cosyns[3], P. Hilbert[2*], M. Jadoul[1], M. De Meyer[4], M. Mourad[4], Y. Pirson[1], N. Kanaan[1]

Divisions of (1) Nephrology, (2*) Human Genetics, (3) Pathology, (4) Abdominal Surgery and Transplantation Cliniques Universitaires Saint-Luc, Université catholique de Louvain, Brussels, Belgium
*Center of Human Genetics, Institut de Pathologie et de Génétique, Gosselies, Belgium

BACKGROUND

Alport syndrome (AS) is caused by mutations in α3/α4/α5 (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

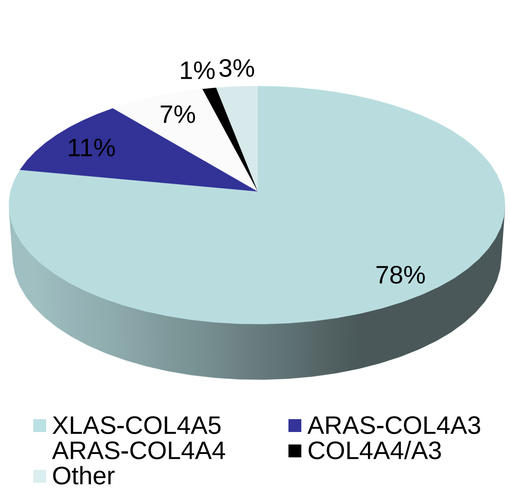
Retrospective analysis including AS patients with an identified mutation transplanted between 1971 and 2014. Severe mutations included truncating, splice-site and non-sense mutations. Missense mutations and in-frame deletions were considered non-severe.

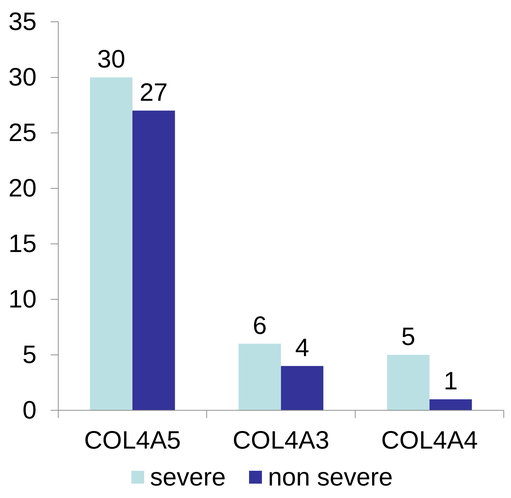
RESULTS

Patients characteristics

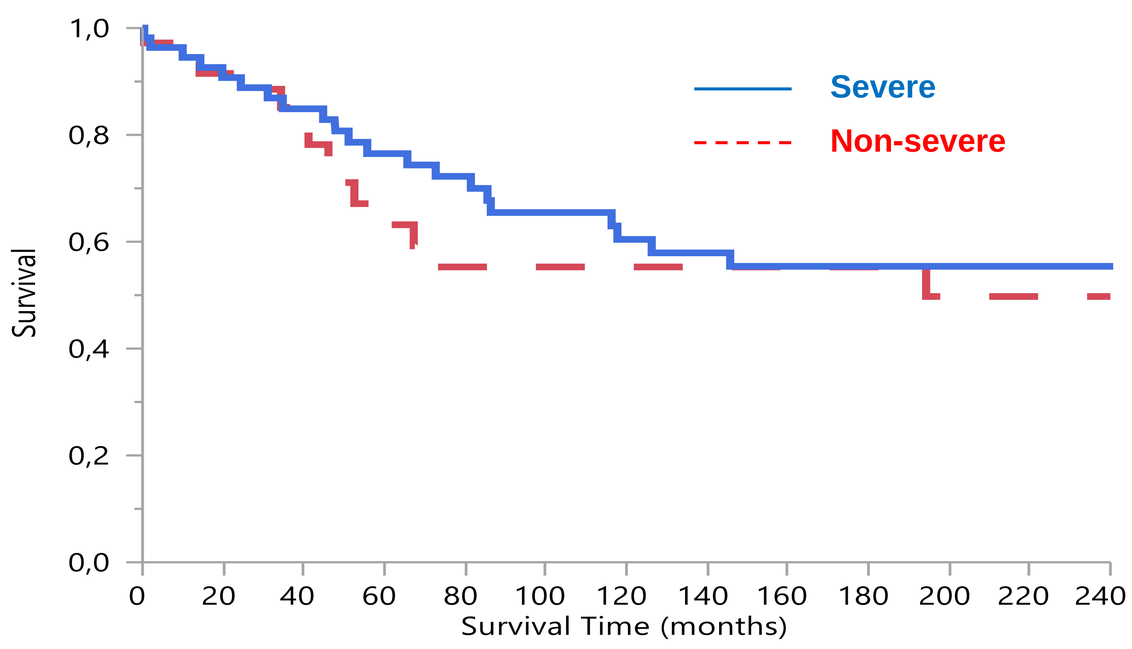
Sex (male/female) (N)	**59/14**
Race (caucasian) (%)	**99**
Age (years) at ESRD (median (min-max))	**26 (11-71)**
Time on dialysis (months, median (min-max))	**33 (1-190)**
Ocular abnormalities (N)	**20**
Lenticonus	**15**
Corneal erosions/macular spots	**4/1**
Deafness (N)	**48**
age (years) at hearing 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





Graft survival according to mutation severity



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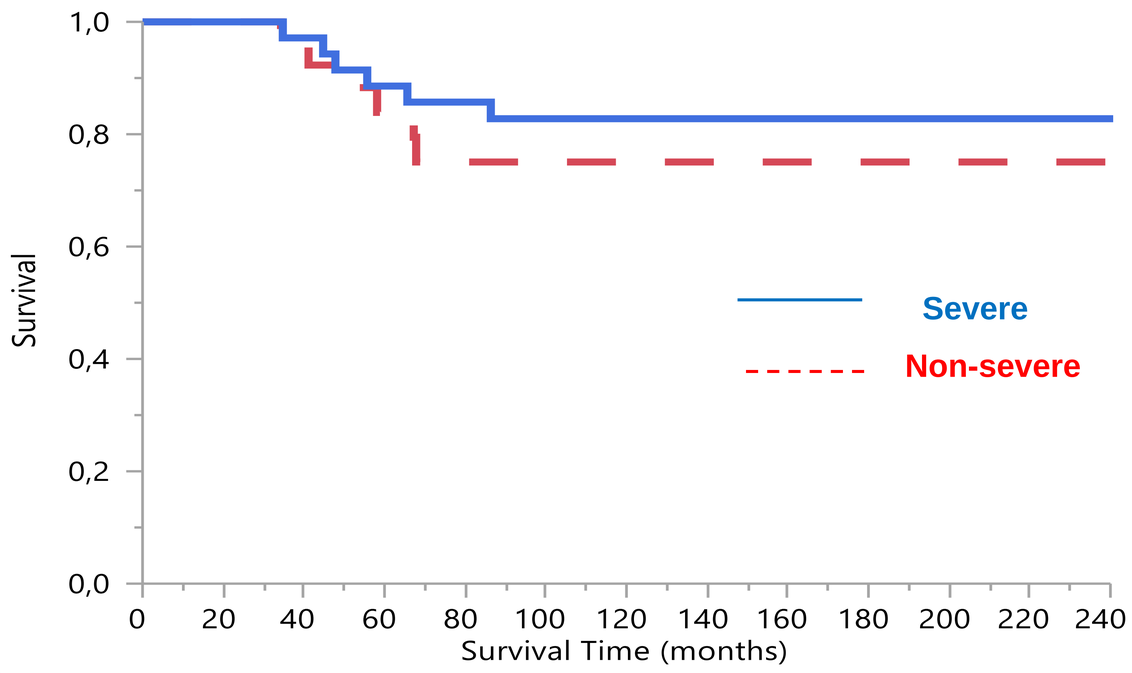

Recurrence

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.

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.

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