RECIPIENT APOL1 GENOTYPE AND ALLOGRAFT OUTCOMES IN LIVE KIDNEY TRANSPLANTATION

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Background

- Apolipoprotein1 (APOL1) risk variants have emerged as a risk factor for renal disease in African Americans.

- In a study of 3438 healthy young adults, (median f/u 24.9 years), it was shown that the projected risk for CKD is significantly increased for AA with 2 APOL1 renal-risk variants

- In Transplantation, it has been shown that the well documented poor outcomes of African American (AA) deceased-donor allografts, are probably influenced by donor APOL1 risk alleles

Genovese G, et al. Science 2010; 329: 841
Reeves-Daniel AM, et al. Am J Transplant. 2011; 11:1025–1030.
Lee BT, et al.. Am J Transplant. 2012; 12:1924–1928.

Background

- The effect of APOL1 genotype of the Living Kidney Transplant Recipients (KTR) has been rarely reported.

- A retrospective analysis of 119 AA kidney transplant recipients, found that 58 (48.7%) carried two APOL1 risk variants. These did not increase the risk of allograft loss after kidney transplant

Lentine KL, Schnitzler MA, Xiao H, et al. N Engl J Med. 2010; 363:724–732.
Lee BT, et al. Am J Transplant. 2012 Jul;12(7):1924-8
Locke JE, etla. Ann Surg. 2017 Feb 9

Aim

In this study, we investigated the effect of KTR APOL1 genotype on allograft outcomes

Methods

- We reviewed prospectively collected data on 220 KTR (141 male, mean age 46.7, 18-73 years).
- Primary outcomes were:
  - Death censored allograft loss
  - Post transplant eGFR at 6, 12 and 36 months as a measure of kidney function
- Student's t-test and chi square were applied to compare continuous and non parametric variables.
- Repeated Measures, and Kaplan Meier analysis were used to investigate outcomes

Methods

- Genomic DNA was extracted from stored blood samples and three APOL1 single nucleotide polymorphisms (SNPs) were amplified using primers.

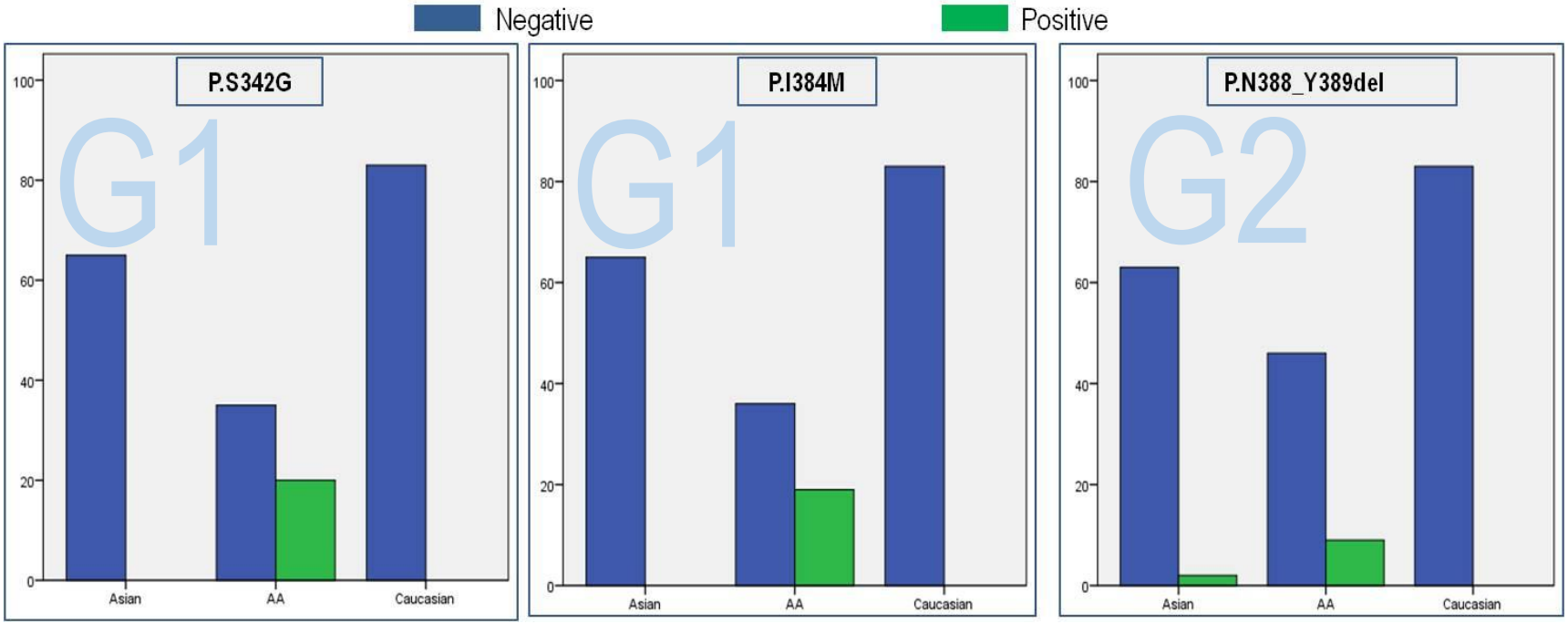
  - The variants typed were:
    - **G1 (rs73885319 and rs60910145): 2 missense mutations in the last exon of the APOL1 gene** (S342G and I384M), leading to two non-synonymous amino acid substitutions (A→G; S342G and G→T; 384M, respectively), and
    - **G2 (rs71785313): a 6 base pair deletion** leading to the deletion of two amino acids (delN388/Y389) in the last exon of the APOL1 gene.

Results

220 KTR, with a mean follow up 69+27 months, were included:

- 77 Asian (48 male, mean age 45.9, 20-69 years),
- 66 AA (37 male, mean age 47.7, 20-71 years), and
- 77 Caucasian (47 male, mean age 46.65, 18-74 years)

Results



Two APOL1 risk alleles were found in 28 (42.4%) AA, 1 (1.3%) Asian and none of the Caucasian KTR's. ($p<0.001$)

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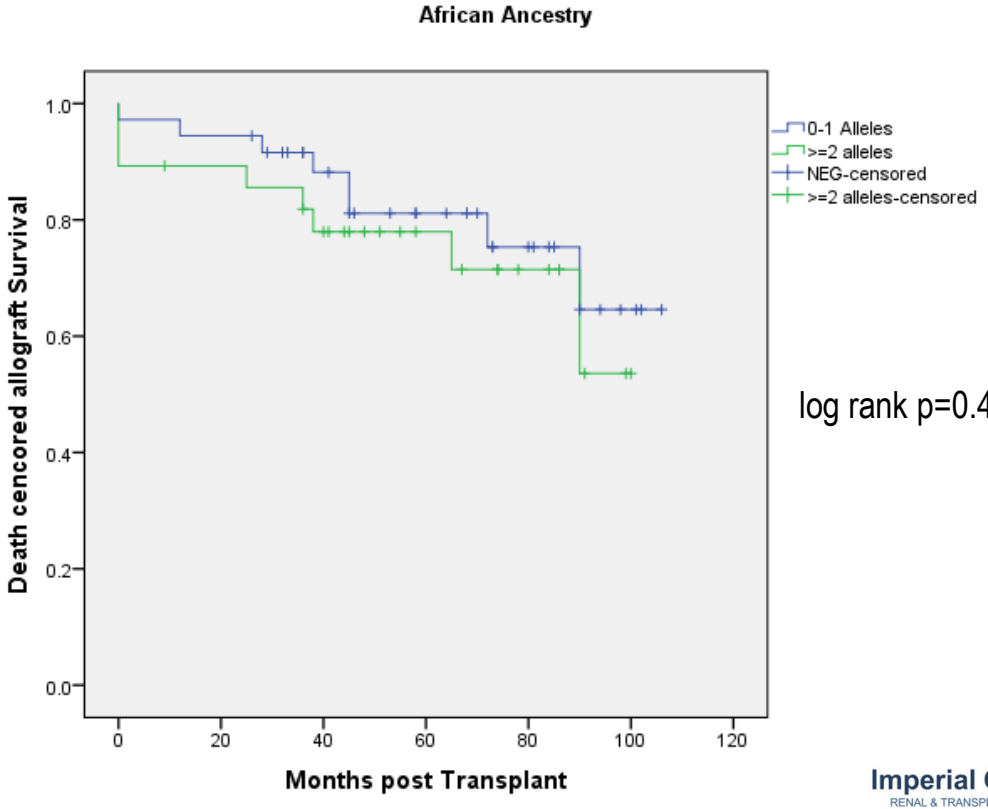
Results

AA KTR Characteristics

		Number of alleles		
		0	>=2	*P*
Gender	M	25	12	***0.06***
	F	13	16	
Recipient Age		48 (20-71)	47.3 (22-68)	***0.83***
Primary Diagnosis	Diab Neph	10	3	***0.1***
	GN	10	11	
	Other	12	13	
	Unknown	6	1	
Induction im/on	IL2	9	11	***0.2***
	Alemtuzumab	29	17	
Donor Type	LRTx	28	20	***0.52***
	LURtx	10	8	
Donor age		41.3(18-68)	36.9 (22-56)	***0.11***

Results

In the AA cohort, Kaplan Meier analysis showed no significant difference in allograft survival in KTR'S with ≥2 and 0-1 risk alleles.



log rank p=0.49

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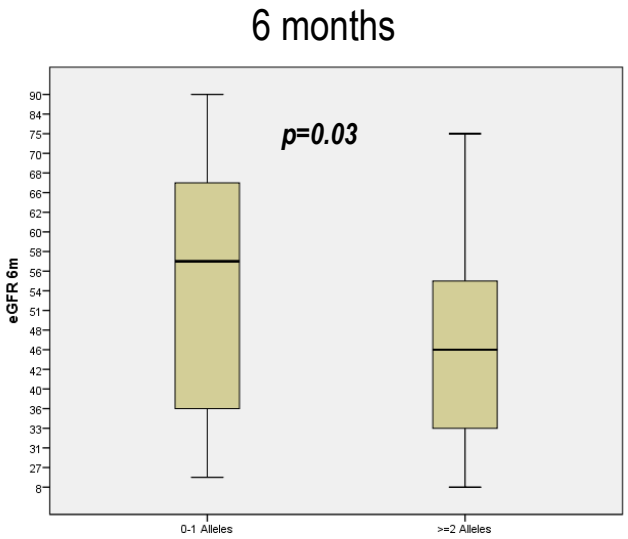
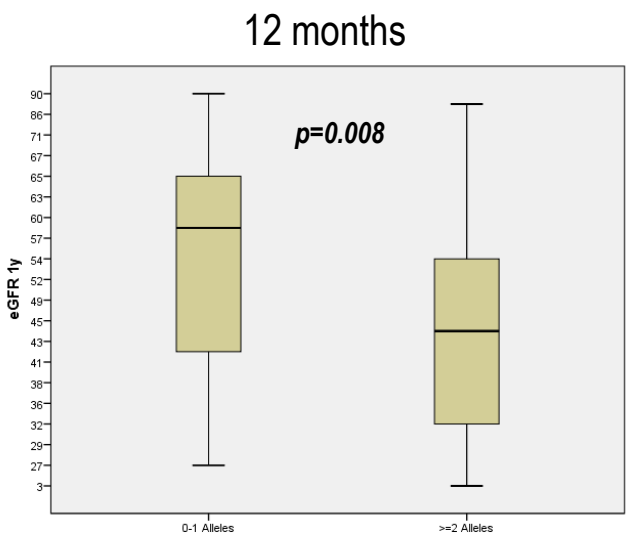
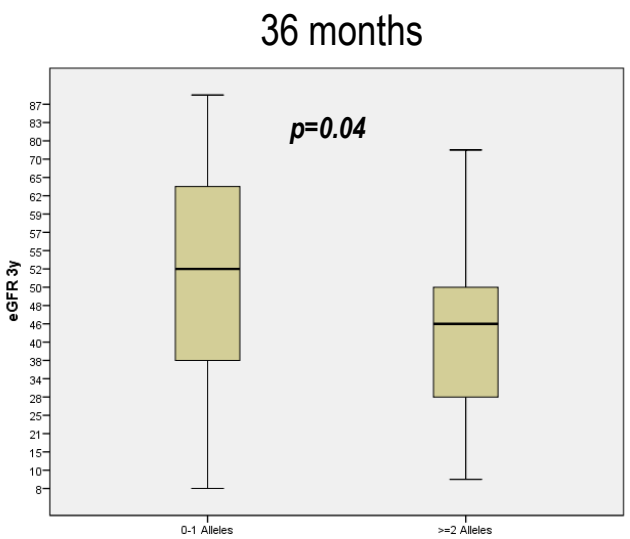
Results







KTR with ≥2 risk alleles were found to have lower eGFR at 6m (54.7±18.1 vs 45.3±15.3, p=0.03), 1y (56,7±17.5 vs 44±17.4, p=0.008) and 3y (51.5±21.7 vs 40.9±17.1, p=0.04).

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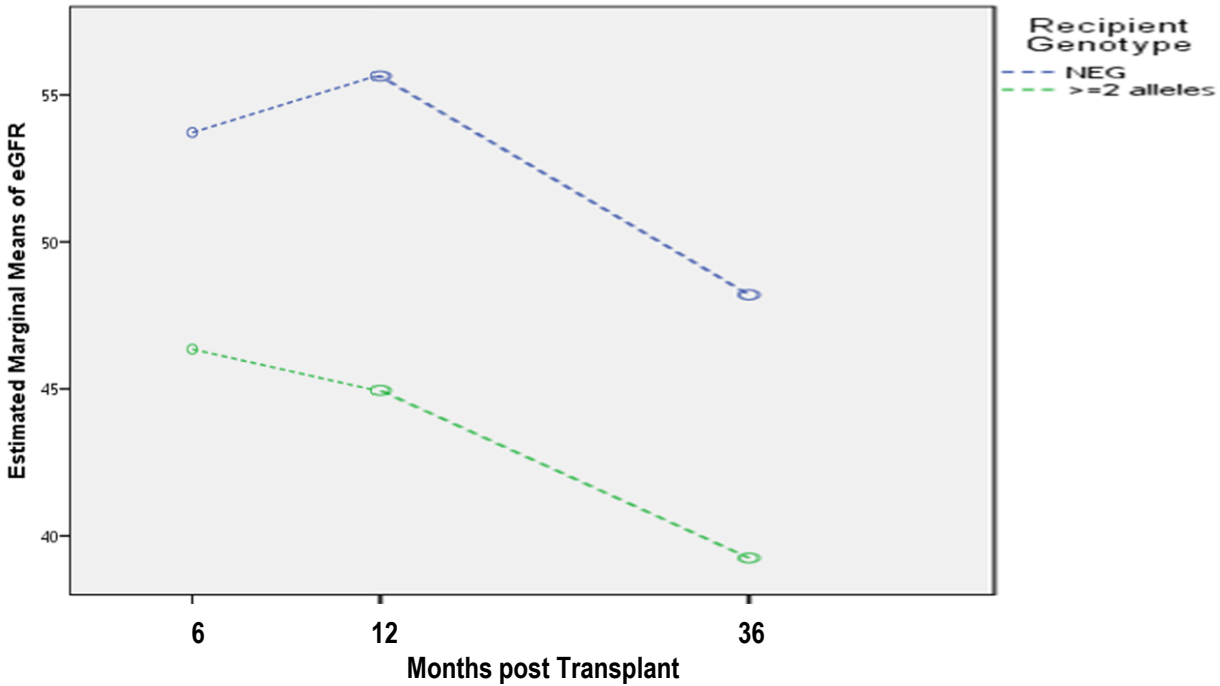
However, repeated measures analysis showed no significant difference in the rate of eGFR decline between groups. (p=0.6)



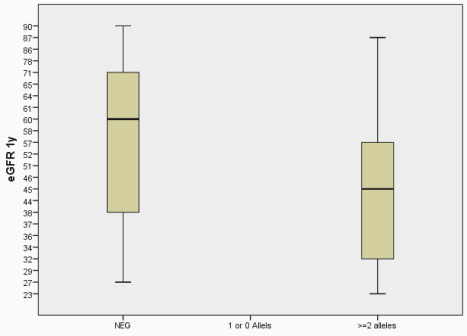
Results

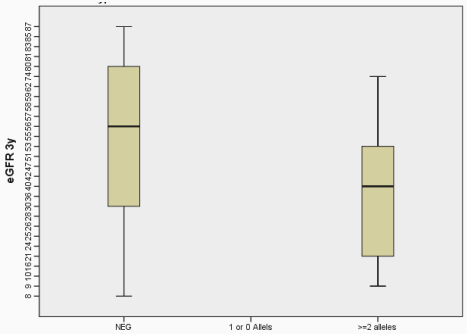
What about the Donors?

Number of alleles		
0		>=2
LRTx	28	20
LURtx	10	8

LRT

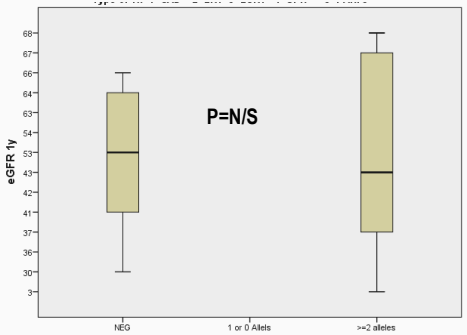
12 months

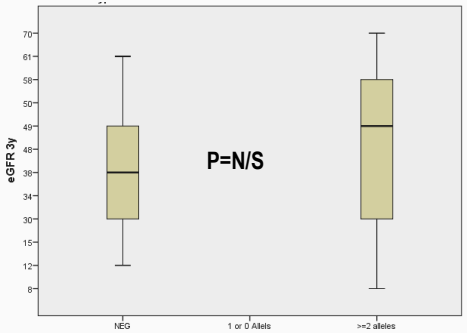




LURT

36 months





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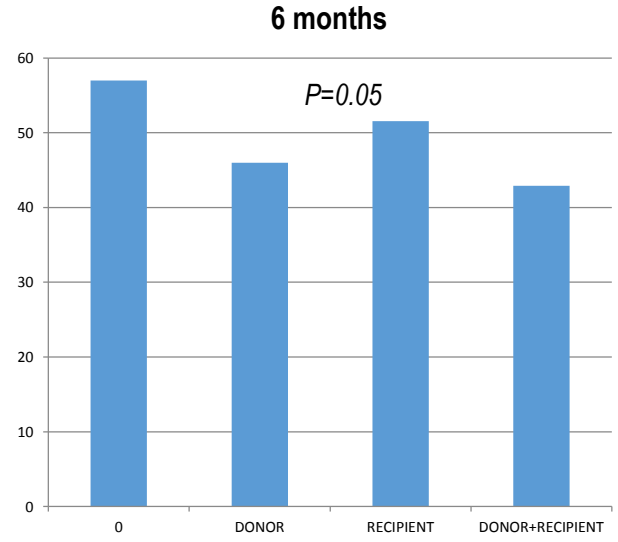
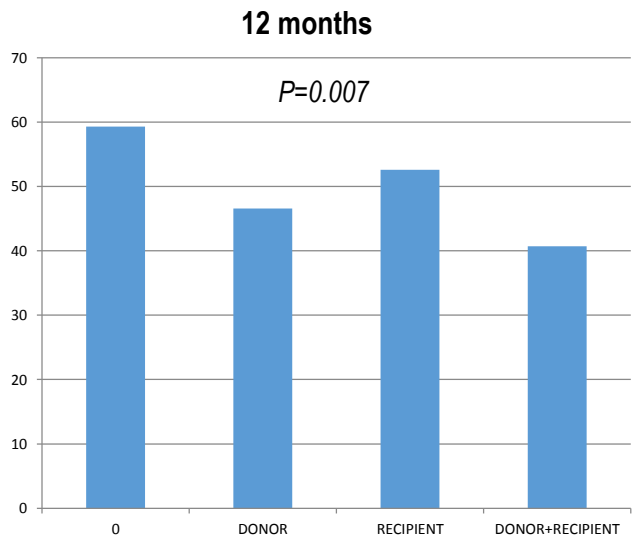
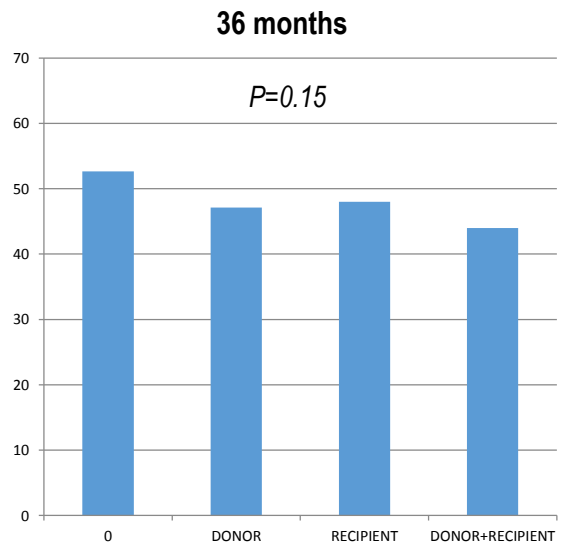
Results

Donor and recipient genotype







>=2 alleles	Neither	31
	DONOR	7
	RECIPIENT	10
	DONOR+RECIPIENT	18

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Conclusion

- Our results confirm the presence of APOL1 risk alleles in a European cohort of KTR of African Ancestry

- In this single center study, with short term follow up, the presence of APOL1 risk alleles did not affect allograft loss

- KTR with ≥2 risk alleles appear to have lower eGFR for the first 3 years post transplant, a finding which could be related to the Donor genotype

Acknowledgments

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