

Protective Effect of Non-HLA IgG2 and Detrimental Effect of Non-HLA IgG1 & IgG3 Against Angiotensin II Type 1 Receptor (AT1R) in Kidney Transplantation

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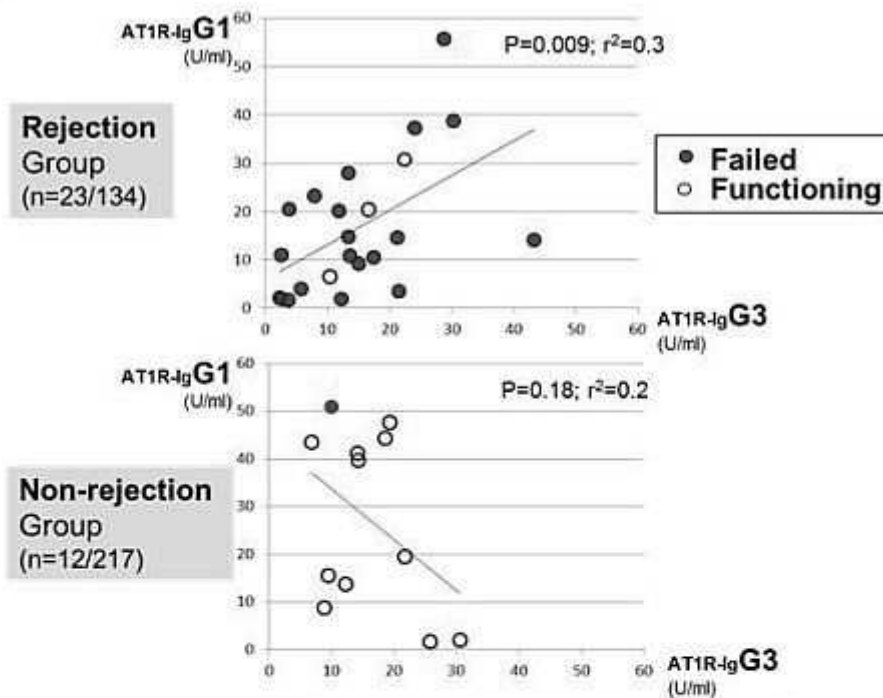
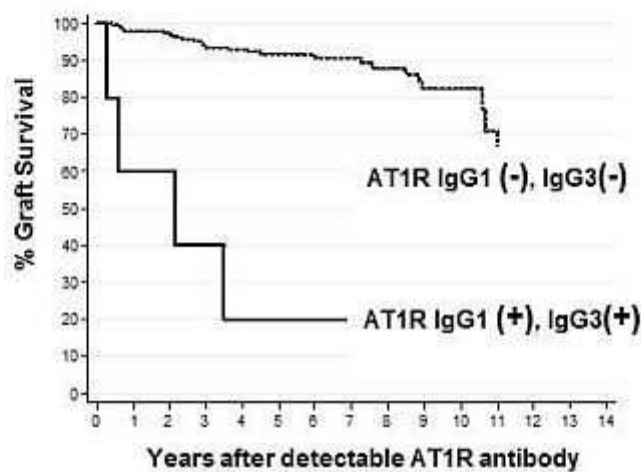
Abstract number: 530

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A longitudinal study on non-HLA antibodies (abs) showed a higher risk of graft failure (gf) in the presence of AT1R abs. The aim of the present study was to further differentiate AT1R abs by AT1R-IgG subclasses for their impact on graft outcomes.

Methods: The study enrolled 351 patients (pts) who received kidney transplants between 1999-2009, in which 134 pts had histopathologic diagnoses (rejection group [RG]) whereas 217 pts did not (non-rejection group [NRG]). Serial sera were tested for AT1R-IgG subclasses with ELISA (CellTrend GmbH, Germany).

Results: The RG had a significantly higher rate of AT1R abs than the NRG (17% vs. 6%, $P=0.001$). Further examination of AT1R abs revealed that AT1R-IgG2 level was significantly higher in the NRG than in the RG (Wilcoxon $P=0.001$), resulting in a higher rate of AT1R abs with no AT1R-IgG2 in the RG than in the NRG (16% vs. 2%, $P<0.001$). Only RG pts developed AT1R-IgG1 in significant positive correlation with AT1R-IgG3 ($P=0.009$; $r^2=0.3$) (Fig A). Serum creatinine levels (sCr) during histopathologic diagnosis in the presence of AT1R abs were significantly higher in the pts with both AT1R-IgG1 and IgG3 than in the pts without it (5.2 ± 6.4 mg/dL vs. 2.9 ± 2.5 mg/dL, $P=0.02$). Longitudinal analysis showed that the HLA-abs negative pts who developed AT1R-IgG1 + IgG3 with no AT1R-IgG2 had a significantly lower graft survival ($P<0.001$) with a higher risk of gf (HR: 5.8, $P=0.006$) than those who didn't (Fig B).

A**Correlation between AT1R- IgG1 and IgG3****B****Graft Survival by AT1R IgG1 & IgG3 in the absence of IgG2**

Conclusions: This is the first study to suggest that AT1R-IgG2 may have a protective role from graft injuries. It may explain why some AT1R abs were detectable in the pts without histopathologic evidence. On the other hand, AT1R-IgG1 + IgG3 have a negative impact on long-term graft survival.

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