Multistate Model To Investigate the Relationship between Pre-Graft Level of Angiotensin II Type 1 Receptor (AT1R) Antibodies and Kidney Transplant Recipients Outcome, A

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Antibodies reactive with non-HLA target-angiotensin II type 1 receptor (AT1R) have been found during acute rejection with vascular involvement in kidney transplants recipients (KTR). We developed a multistate model to assess the relationship between the pre-formed non-HLA immunisation (before the transplantation) against AT1R (AT1R-Abs) and the transplantation outcome on a large population of kidney recipients from the DIVAT cohort (www.divat.fr)

599 patients who consecutively received kidney transplantations in Nantes University Hospital between 1998 and 2007 and for whom a pre-transplantation serum sample was available were included in the study. Anti-AT1R-Abs were detected by a quantitative assay using extracts of cell overexpressing the human AT1R as a solid phase. A threshold of AT1R-Ab levels was statistically determined at 10 Units based on the time to graft failure. Outcomes were the transition probabilities between 4 states: graft without any acute episode rejection (ARE), graft with at least one ARE, return to dialysis and patient death. We used a parametric Semi-Markov model.

The 599 KTR had a mean follow-up time of 6.9 years ($\pm$3.4). At the time of the study, 403(67%) patients had a functional graft without ARE whereas 105(15%) returned to dialysis, 64(11%) had an ARE and 50(8%) died with a functional graft. The multistate model showed that a high pre-graft level of AT1R-Abs ($>$10U) was associated with a higher risk of ARE ($p<0.05$). In addition, the model showed that a pre-graft level of AT1R-Abs$>$10U did not influence the risk of graft failure within the first 3 years following the transplantation ($p=0.83$), whereas a higher risk of graft failure appeared significantly from 3 years post transplantation onwards ($p=0.043$). Finally, the association between the pre-graft level of AT1R-Abs and time to death was not significant.

Our multistate semi-Markov model showed that a pre-graft level of AT1R-Abs$>$10U is significantly associated with the probability of ARE and also with the time-to-return to dialysis by itself, independently to the risk of ARE, but only after 3 years of follow up