Nature Reviews Nephrology **7**, 485 (2011); published online 9 August 2011; doi:10.1038/nrneph.2011.97

TRANSPLANTATION

Should we match for HLA-DR in pediatric renal transplantation?

Although the avoidance of HLA-DRB1 mismatch is associated with improved graft survival rates in children, the likelihood of finding young ABO-matched local donors without DR mismatches is very low, reports a paper published in *Archives of Surgery*.

The United Network for Organ Sharing (UNOS) organ allocation system currently takes HLA-DR matching into account for adults, but such matching is no longer a priority in children, in order to reduce waiting times and decrease time on dialysis, which is also deleterious.

"Traditionally, we have not been proponents for HLA-DR matching," says Peter Stock from the University of California at San Francisco (UCSF), an author on the recent paper. "We have been advocates for obtaining a high-quality kidney for children regardless of HLA-DR type, to minimize time on dialysis, which we felt was more important than waiting for an HLA-matched kidney. However, we wanted to check whether we were right."

Stock and colleagues designed a retrospective cohort study to determine whether HLA-DR mismatching affects rejection, graft survival and sensitization in their local allocation system that focuses on donor quality rather than HLA-DR matching for children requiring kidney transplantation. They also investigated the probability of finding a suitable donor on the basis of HLA-DR match.

The researchers included data from 178 patients aged <21 years who underwent primary kidney transplantation at UCSF between 1997 and 2006. Standard induction therapy during this time included daclizumab and corticosteroids, and standard maintenance therapy was mycophenolate mofetil and tacrolimus. Data including patient sex, age at transplantation, race/ethnicity, degree of HLA-DRB1 mismatch, cause of end-stage renal disease, duration of dialysis, and pretransplantation panel reactive antibody (PRA) level were obtained from medical records, as were donor source, age and race/ethnicity. The main outcome measures were graft failure (defined as initation of dialysis after transplantation), biopsy-proven acute rejection (humoral or cellular), and post-transplantation sensitization (conservatively defined as the detection of any HLA antigen antibodies after transplantation in a patient who had a pretransplantation PRA level of 0%).

Median follow-up duration was 49.1 months, and median age of patients at the time of transplantation was 13.8 years. Overall, 37.9% of the cohort were white, 9.6% were black, 38.4% were Hispanic, and 14.1% were of another race/ethnic group. Rejection had occurred in 35% of patients by 1 year after transplantation; after 5 years, rejection had occurred in 55%. The risk of rejection was 1.7 times higher in patients with one or two HLA-DRB1 mismatches than in those with zero HLA mismatches. Other factors associated with rejection included increasing number of total HLA antigen mismatches, older age, and pretransplantation dialysis for >24 months.

Graft survival rate was 97% at 1 year and 82% at 5 years. The researchers found that the degree of HLA-DRB1 mismatches did not influence graft survival, but that patients with a history of rejection were nearly eight times more likely to experience graft failure than patients who had never experienced rejection.

Among the 85 patients (68.5% of the cohort) for whom pretransplantation PRA level was 0% and post-transplantation serum samples were available, the frequency of sensitization was 57.6%. Almost 60% of the sensitized patients had functional grafts and the degree of HLA-DRB1 mismatch was not a risk factor for sensitization. However, the risk of sensitization was almost 10 times higher in patients with at least one episode of rejection than in those without rejection.

Stock *et al.* found that the frequency of finding an ABO-identical local donor aged <35 years with zero mismatches was very low for all ethnic groups (1–2 per 100 local donors for most groups).

"This issue is a politically charged one," notes Stock, "but moving forward, we hope that the kidney committee for UNOS will take note of our findings and consider increasing the geographic boundaries for deceased donors so that children will have a chance of receiving an HLA-DR-matched kidney without a prolonged time on dialysis." The authors note that in the absence of such a policy change, however, given the scarcity of matched organs locally in many regions most pediatric recipients would probably benefit more from the reduced dialysis time associated with accepting an HLA-mismatched kidney.

Rebecca Ireland

Original article Vu, L.T. *et al.* HLA-DR matching in organ allocation: balance between waiting time and rejection in pediatric kidney transplantation. *Arch. Surg.* **146**, 824–829 (2011)