A Novel Application of SRTR Data to Interrogate the Effects of HLA-DQ Mismatches in Kidney Transplantation

Dylan Isaacson[1,2], Michael W. Gmeiner[3], Vasilis Kosmoliaptsis[4], Hannah C. Copley[4], Jesse D. Schold[5], Anat R. Tambur[1]

[1]Comprehensive Transplant Center, Department of Surgery, Northwestern University, Chicago IL; [2]Department of Urology, Northwestern University; [3]Department of Economics, London School of Economics, London, UK; [4]Department of Surgery, University of Cambridge, Cambridge, UK; [5]Department of Quantitative Health Sciences, Cleveland Clinic, Cleveland, OH

Background

- Single-center studies demonstrate *de novo* HLA-DQ donor-specific antibodies (DSA) are the most common and pathogenic
- HLA-DQ is not accounted for in many kidney allocation schemes
- Scientific Registry of Transplant Recipients (SRTR) data do not include DSA or antibody-mediated rejection: not amenable to directly study DQ DSA and transplant outcomes
- SRTR HLA typing data: low-resolution, serologic-equivalent only
- Our solution: Examine patients in the SRTR who returned to the kidney waitlist after a failed transplant with new HLA unacceptable antigens (UA) corresponding to donor HLA typing (DS-UA) (Fig. 1)
- Presence of new DS-UA at relisting implicates *de novo* DSA in graft failure

Methods

- Adult patients in the SRTR receiving a primary kidney transplant Jan 2010 – Mar 2020, relisted after graft loss
- Data: donor/recipient HLA typing, UA data at all HLA loci, cPRA pre- and post-transplant
- Linear regression applied to evaluate:
  - Probability of developing a new HLA DS-UA given an HLA mismatch
  - Maximal increase in cPRA given a new DS-UA
  - The magnitude of these effects for HLA-DQ compared to other HLA loci
- Controlled for effects of other HLA mismatches, DS-UA at other loci, waitlist time, time between graft failure/relisting, pre-transplantation cPRA

Results

- Fig 2: Each HLA-DQ mismatch increased probability of new DQ DS-UA by:
  - 25.2% in deceased donor recipients
  - 28.9% in living donor recipients
  - DQ effect significantly greater than all other HLA loci ($p<0.05$)
- Fig 3: Each HLA-DQ DS-UA increased cPRA by:
- 23.5% in deceased donor recipients
- 27.9% in living donor recipients
- DQ effect greater than all other HLA loci except HLA-A in deceased donor recipients (23.1%) ($p<0.05$)

Conclusions

- First study applying registry data to evaluate HLA mismatches, DSA and sensitization after graft loss
- HLA-DQ mismatches: highest probability of producing DS-UA, DQ DS-UA associated with largest cPRA increases
- These findings implicate DQ DSA in graft loss and provide additional justification for HLA-DQ matching in kidney allocation

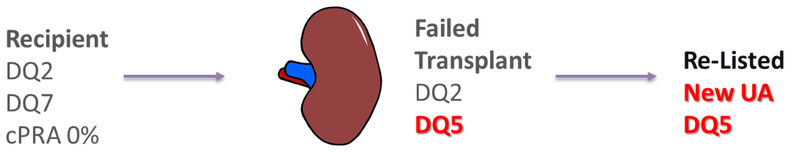

Figure 1: Example scenario – Initially unsensitized patient, transplanted with an HLA-DQ mismatched kidney. Upon graft failure and re-listing, a new HLA-DQ UA is declared, implying the presence of a new HLA-DQ DSA

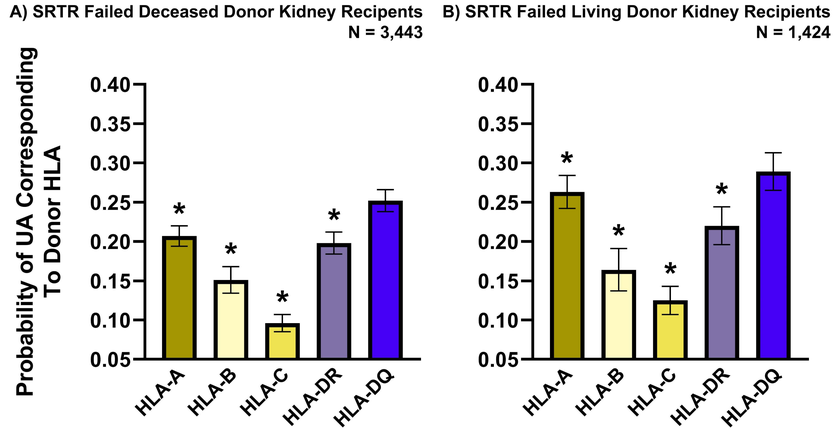

Figure 2: Probabilities of new DS-UA at relisting for each additional donor/recipient HLA mismatch. Asterisk (*) indicates significantly lower probability for an HLA locus as compared to HLA-DQ ($p<0.05$)

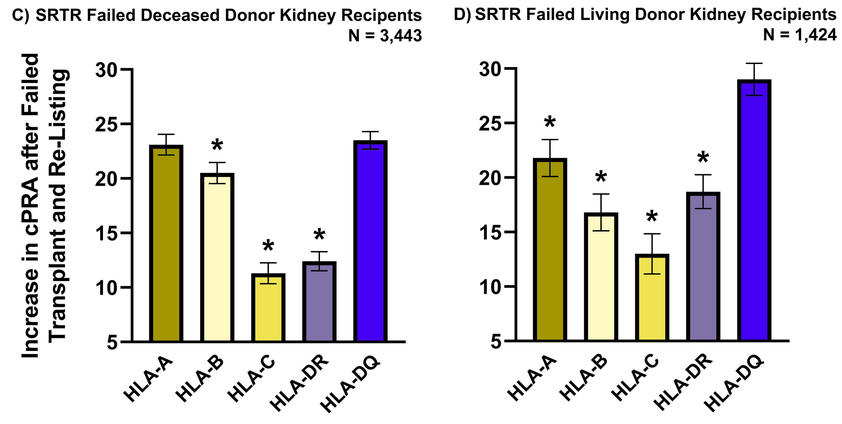

Figure 3: Average increases in cPRA after relisting given presence of a new DS-UA. Asterisk (*) indicates significantly lower cPRA increase for an HLA locus as compared to HLA-DQ ($p<0.05$)

Northwestern Medicine®
Feinberg School of Medicine

Contact: dylan.isaacson@northwestern.edu