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

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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 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, 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

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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)