Increase in Renal Transplantation of Sensitized Recipients Following the Introduction of Virtual Crossmatching: One Center's Experience

Michael J. Moritz MD
Lehigh Valley Health Network, Michael.Moritz@lvhn.org

Lynsey S. Biondi MD
Lehigh Valley Health Network, Lynsey_S.Biondi@lvhn.org

Patricia Kimble BS
Lehigh Valley Health Network, Patricia.Kimble@lvhn.org

Robert Cirocco PhD
Lehigh Valley Health Network, Robert.Cirocco@lvhn.org

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Increase in Renal Transplantation of Sensitized Recipients Following the Introduction of Virtual Crossmatching: One Center's Experience

Michael J Moritz, MD[1], Lynsey A Biondi, MD[1], Patricia Kimble, BS[2] and Robert Cirocco, PhD[2]

[1]Dept. of Surgery and [2]HLA Laboratory, Lehigh Valley Health Network, Allentown, Pennsylvania, United States

Abstract:

Single Antigen Bead (SAB) technology provides more accurate identification of anti-HLA antibodies. Thus the Virtual (predicted) Crossmatch (XM) should be more accurate. We implemented both in 2009 while abandoning a limit on the number of HLA mismatches. We followed transplantation of sensitized patients (cPRA>50%), biopsy proven rejection (BPAR) and the number of deceased donor (DD) XM's. Sensitized patients transplanted rose from 9% (11 of 124, 2007-2008) to 20% (37 of 187, 2009-2011). The mean cPRA in the earlier group was 57% and was 85% in the latter. The rejection incidence did not change despite the higher degree of sensitization transplanted. Conclusions: 1) The Virtual XM enabled an increase in the number of renal transplants in sensitized recipients; 2) The degree of sensitization for this group has risen. 3) The rejection rate has not risen in sensitized recipients. 4) Post transplant IVIG prophylaxis appears to lower the incidence of AMR.

Introduction:

Sensitive XM's led to an increasing pool of high PRA, sensitized patients. Between 2002 to 2008, PRA>20% increased from 17% to 21% of the national wait list. For new registrants, PRA>20% increased from 10% to 18%. The poor success rate (~50%) in predicting compatible XM's in sensitized patients delayed allocation and led us to mandate a degree of matching for highly sensitized patients.

Methods:

In 2009, our HLA laboratory adopted SAB. Flow XM technique remained standard. This study observed the numbers of DD XM's, transplants performed, and patients' PRA to determine the impact of SAB. Post transplant, ACR (acute cellular rejection), AMR (antibody mediated rejection), and graft loss were followed.

All kidney only transplants from 2006 through 2011 were included. All transplants were XM compatible; no desensitization. Standard immunosuppression for all was rATG induction (4-6mg/kg in 3-4 doses), methylprednisolone on days 0 and 1 followed by steroid-free 2 drug maintenance with tacrolimus and mycophenolate. Protocol biopsies were at 1, 6, and 12 months. Biopsy proven acute rejection (BPAR) was defined as ACR in the first year post transplant, and includes subclinical rejection (i.e. protocol biopsy) and clinical rejection. Highly sensitized was defined as current PRA>50%.

Results:

For the following time periods, the % of transplants in highly sensitized patients was: 2006, 4%; 2007-08, 9%; and 2009-11, 20%. As the number of sensitized patients transplanted rose, mean cPRA and BPAR did not change. The ratio of subclinical to clinical rejection did not change at 1:1.

Kidney Transplantation: Highly Sensitized Patients By year

Year	Sensitized Patients Transplanted (n)	Kidney Transplants (n)	Sensitized Transplants	cPRA (mean)	BPAR* (%)	Wait List (n)	DD XM's (n)
2006	3	68	3%	99%	NA	NA	NA
2007	5	54	9%	57%	18.0	214	NA
2008	6	70	9%	75%	18.9	228	202
2009	15	75	20%	80%	21.6	263	188
2010	11	65	17%	85%	18.1	316	152
2011	11	57	19%	86%	18.0	335	132

DD XM's Total number of candidates XM'ed, NA not available

The incidence of AMR rose. In 2006, 1of 3 highly sensitized recipients had early graft loss from AMR. In 2007-08, 11 highly sensitized recipients had 4 AMR's with 1 graft loss. Between 2009-2/2010, 16 recipients had 6 AMR's, with 2 graft losses. IVIG prophylaxis was initiated in 3/2010 for recipients with PRA>80% (adapted from Ref. 2). The next 21 have had 2 AMR episodes, neither with graft loss.

Kidney Transplants in Sensitized Recipients: Effect of Prophylaxis Against AMR

Era	Prophylactic IVIG?	Transplants in Highly Sensitized Patients	AMR	AMR Causing Graft Loss	ACR (in the first year)	+DSA (in the first year)	# and Causes of Graft Loss (in the first Year)
2006	None	3	2	1	0	NA	1:AMR
2007-2008	None	11	4	1	0	4	2: 1 AMR, 1: Coag
2009-2/2010	None	16	6	3	5	8	2: 1 AMR, 1 AMR/NC
3/2010-2011	0.5gm/kg monthly x3 months	21	2	0	2 (1 with Graft Loss)	6	2: ACR/NC, TMA

Coag.-coagulopathy with biopsy complication; NC-non-compliance; CHF-congestive heart failure; TMA-thrombotic microangiopathy

Patient and graft survival in the highly sensitized (n=51) has been similar to the non-sensitized. Graft survival at 1 year is 44 of 51 (86%). Patient survival at 1 year is 50 of 51 (98%). Our last SRTR report showed overall 1 year graft and patient survival of 92% and 98%.

Discussion:

SAB dramatically improves anti-HLA antibody definition. It was hoped that this would result in more accurate Virtual XM, predicting compatible final XM's, despite very sensitive flow XM's. The data support better Virtual XM with a higher transplant rate and fewer XM's (Ref. 1).

The number of kidney transplants to highly sensitized recipients has risen, and approximates their proportion of candidates, restoring equilibrium. This has been accomplished with fewer XM's, increasing laboratory efficiency. We have seen no decrement in outcome compared to non-sensitized recipients. IVIG prophylaxis against AMR appears to be effective.

Priority for the highly sensitized has been difficult to balance for 2 major reasons. One, the greater the priority, the more final XM's to be performed. Two, sensitization was associated with poorer outcomes. Lack of enthusiasm for these transplants led to center-based obstacles such as mandating a level of matching. Our data show that these center-based hurdles are no longer necessary, either for logistic (reason #1) or outcome (reason #2) rationales. Final XM's have a ~95% agreement with Virtual XM, and recipient outcomes (with steroid-free immunosuppression and AMR prophylaxis) appear not different from non-sensitized recipients.

Conclusions:

1. Virtual XM'ing enabled an increase in the number of renal transplants in sensitized recipients.
2. The degree of sensitization transplanted has risen.
3. The rejection rate has not risen in sensitized recipients.
4. Post transplant IVIG prophylaxis appears to lower the incidence of AMR.

Abbreviations:

SAB-single antigen bead, cPRA-calculated Panel Reactive Antibody, DD-deceased donor, ACR-acute cellular rejection in the first year, AMR-antibody mediated rejection in the first year, rATG-rabbit anti-thymocyte globulin, BPAR-biopsy proven acute rejection, IVIG-intravenous immune globulin, DSA-donor specific antibody.

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