Allocating Deceased Donor Kidneys to High PRA Patients: A Simulation

Howard M. Gebel* Bert Kasiske Sally Gustafson Eugene Shteyn Ajay Israni Jon Snyder John Friedewald Dorry Segev

SCIENTIFIC REGISTRY OF TRANSPLANET-RECIPIENTS

*Presenter

Howard M. Gebel, Ph.D. Professor of Pathology Emory University Hospital Atlanta, GA

• I have no financial relationships to disclose within the past 12 months relevant to my presentation.

AND

- My presentation does not include discussion of off-label or investigational use.
- I do not intend to reference unlabeled/unapproved uses of drugs or products in my presentation.



KI 1.1 Adult patients waiting for a kidney transplant





KI 1.4 Distribution of adult patients waiting for a kidney transplant



		2001		2011
Level	N	%	N	%
<20%	33,414	71.6	57,954	67.0
≥20%	13,163	28.2	28,594	33.0
Unknown	72	0.2	0.0	0.0
<1 year	15,942	34.2	24,418	28.2
1-<2	11,085	23.8	19,714	22.8
2-<3	7,331	15.7	14,525	16.8
3-<4	4,668	10.0	9,629	11.1
4-<5	2,872	6.2	6,602	7.6
5+	4,751	10.2	11,660	13.5
Will not accept	8		46,418	53.6
Will accept			40,130	46.4
	Level <20% ≥20% Unknown <1 year 1-<2 2-<3 3-<4 4-<5 5+ Will not accept Will accept	Level N <20%	Level N % <20%	Level N % N <20%

KI 1.15 Characteristics of adult patients on the kidney transplant waiting list on December 31, 2001 & December 31, 2011.



Reasons Patients Removed From UNOS Wait-list Dec 1999 to Nov 2005

Current PRA%	<u>0-19%</u>	<u>20-79%</u>	<u>80-100%</u>
D D Transplant	47% (33,998)	42% (3,611)	37% (1,879)
Living Donor Transplant	20% (14,853)	12% (1,002)	5% (276)
Condition Deteriorated	4% (3,065)	7% (561)	8% (409)
Died	17% (12,290)	27% (2,292)	37% (1,906)
Other • Not clarified • Medically unsuitable • Refused Transplant • Tx'd Kid-Pan or Panc • Condition Improved	6% (4,216) 1% (401) 2% (1,221) 3% (2,302) <1% (243)	7% (595) <1% (61) 3% (235) 2% (141) <1% (24)	7% (383) 1% (55) 3% (147) 1% (55) <1% (15)



	2009	2010	2011
Patients at start of year	74,572	79,365	83,879
Patients added during year	28,645	29,216	28,131
Patients removed during year	23,820	24,662	25,463
Patients at end of year	79,397	83,919	86,547
Removal reason			
Deceased donor transplant	9,713	9,980	10,399
Living donor transplant	5,170	5,235	4,922
Tx (type not specified)	54	89	81
Patient died	5,181	5,172	5,139
Patient refused transplant	271	318	406
Improved, tx not needed	131	101	135
Too sick to transplant	1,358	1,467	1,903
Changed to kidpan. list	165	191	194
Other	1,777	2,109	2,284

KI 1.8 Kidney transplant waiting list activity among adult patients.



Distribution of cPRA at time of waitlist death

cPRA	Count	Frequency
0	2360	48.6%
1-9	441	9.1%
10-19	226	4.7%
20-29	219	4.5%
30-39	137	2.8%
40-49	106	2.2%
50-59	112	2.3%
60-67	113	2.3%
70-74	74	1.5%
75-79	61	1.3%
80-84	77	1.6%
85-89	77	1.6%
90-94	154	3.2%
95	28	0.6%
96	32	0.7%
97	51	1.1%
98	78	1.6%
99	131	2.7%
100	381	7.8%



SRTR & OPTN Annual Data Report 2010



SRTR & OPTN Annual Data Report 2010



KI 4.4 Kidney transplant rates in adult waiting list candidates, by PRA/CPRA



Why do patients with >80%PRA wait longer for offers from compatible deceased donors?

- Vast repertoire of HLA antibodies?
- Allocation system?



Current Deceased Donor Kidney Allocation Policy

- 3.5.6 Geographic Sequence of Deceased Kidney Allocation. In general, kidneys are to be allocated locally first, then regionally, and then nationally.
- 3.5.6.1 Local Allocation. With the exception of kidneys that are 1) shared as a result of a zero antigen mismatch, 2) offered as payback as defined in Policy 3.5.5 or 3) are allocated according to a voluntary organ sharing arrangement as provided in Policy 3.4.6, all kidneys will be allocated first to candidates within the local unit where the kidneys are procured.
 3.5.6.2 Regional Allocation. If a standard donor kidney is not accepted by any of the local transplant centers for local candidates, the kidney is to be allocated next via the regional list consisting of all candidates listed on the Waiting Lists of other Members within the same Region as the Member which procured the kidney. When a standard donor kidney is allocated regionally, it is to be offered to Members for specific candidates in the region according to the point system described in
 - Policy 3.5.11 in descending point order beginning with the candidate in the region who has been assigned the highest number of points



Simulation Model

- Patients: All sensitized candidates on the waitilist at the end of 2010 with <u>>80%</u> cPRA listed for a kidney (only). No other recipients were considered.
- Unacceptable antigens: The actual HLA-A, B, C, DRB1 and DQB1 antigens that had been entered into UNET as unacceptable for each of the above patients.
- Allocation scheme: Deceased donor kidneys were offered exclusively to this group of patients. Simulation priority was first to candidates with cPRA=100, then 99,98 etc.



Current Allocation vs Simulated Allocation

cPRA	Waiting List (n)	Actual Transplants (2010)	Potential Transplants (based on simulation)
80-84	1700	375 (22.1)	580 (34.1)
85-89	1929	325 (16.8)	1506 (78.1)
90-94	2562	322 (12.6)	2456 (95.9)
95	659	71 (10.8)	629 (95.4)
96	860	84 (9.8)	813 (94.5)
97	1010	83 (8.2)	946 (93.7)
98	1455	89 (6.1)	1343 (92.3)
99	2618	93 (3.6)	2258 (86.2)
100	5436	75 (1.4)	2587 (47.6)



Looks good-BUT

- Not all kidneys acceptable for all patients
- Not all HLA antibodies considered (HLA-DP, DQA)
- Physical crossmatches not performed.
- Logistics
- Policy changes
- Philosophies



It can work!

The Acceptable Mismatch Program as a Fast Tool for Highly Sensitized Patients Awaiting a Cadaveric Kidney Transplantation: Short Waiting Time and Excellent Graft Outcome

Frans H. J. Claas,^{1,2} Marian D. Witvliet,¹ René J. Duquesnoy,³ Guido G. Persijn,⁴ and Ilias I. N. Doxiadis^{1,2,5}

There are many highly sensitized patients on the kidney waiting lists of organ exchange organizations because it is difficult to find a crossmatch negative cadaver kidney for these patients. Recently, several protocols have been developed to remove the donor-specific human leukocyte antigen (HLA) antibodies from the serum of these patients before transplantation. These approaches, including the use of intravenous immunoglobulins, plasmapheresis and immunoglobulins (plasmapheresis-cytomegalovirus-immunoglobulin), and immunoabsorption, seem to lead to a certain success rate, although the additional immunosuppression necessary to remove and control the production of donorspecific alloantibodies may have its impact on the short-term (infections) and long-term (incidence of cancer) immune surveillance. Furthermore, some of these therapies represent a considerable financial burden for patients and society. In the present report, we advocate selection of crossmatch negative donors on the basis of the Acceptable Mismatch Program, as the first and best option for highly sensitized patients to undergo transplantations. No additional immunosuppression is necessary, and graft survival in this group of "difficult" patients is identical to that of nonsensitized recipients. Because the nature of the HLA polymorphism does not allow all patients to profit from this approach, removal of circulating HLA antibodies can be considered as a rescue therapy for those patients for whom the Acceptable Mismatch Program does not give a solution.

Key Words: Highly sensitized patients, kidney transplantation, acceptable mismatches.

(Transplantation 2004;78: 190-193)



KI 1.5 Distribution of adult patients *newly listed* for a kidney transplant

Resetting the bar!



17

SCIENTIFIC REGISTRY OF TRANSPLANT RECIPIENTS

Conclusions

- Highly sensitized patients wait longer for compatible kidneys then their less sensitized or unsensitized counterparts.
- Although these patients are highly sensitized, HLA antibodies DO NOT APPEAR TO BE the major factor that denies allocation of a compatible deceased donor organ to most of these recipients.
- Based on this simulated model, it appears that allocation (and, hopefully, transplantation) of deceased donor organs to the majority of highly sensitized patients on the UNOS waitlist is feasible.

