

Supplemental Material

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Appendix A: Data quality description

At the onset of the study in 2010, investigators from five transplant centers (University of Pennsylvania, Barnabas Health, Mount Sinai Recanati/Miller Transplantation Institute, Harper Hospital, and Yale-New Haven Hospital) collaborated to perform retrospective chart reviews of the respective recipients of kidneys at their centers from the donors that were enrolled by each of the five participating organ procurement organizations (Gift of Life Donor Program in Philadelphia, Gift of Life Michigan, LiveOnNY, NJ Sharing Network, and New England Donor Services). With funding renewal from the National Institutes of Health in 2016, recipient chart abstraction was expanded by recruiting the additional centers that had transplanted the greatest numbers of kidneys from enrolled donors. A total of 132 different centers had transplanted at least one kidney from enrolled donors, and 13 of the top centers agreed to participate with data for this analysis. Trained study participants at each site recorded recipient data on standardized case report forms using a secure, online database (OnCore). Outcomes were adjudicated by site investigators, and extensive data quality control checks were performed by study monitors from Yale University. Study monitors validated data abstraction processes via secondary review of submitted paper charts and then continuously reviewed all data points following form completion by site coordinators to confirm data quality and accuracy.

This study utilized various methods such as rigorous study documentation, in-depth coordinator training, independent data monitoring, and principal investigator (PI) involvement to increase the quality of the data collected. A detailed protocol and a manual of operations were created to facilitate consistency in data collection practices across all participating research centers. Coordinators were required to attend two separate web-based trainings provided by a co-investigator, a study monitor (hired from the Yale Center for Clinical Investigation – separate from our department), and a project coordinator. The trainings demonstrated how to use

OnCore and provided detailed explanation of important data variables and key practices to utilize during chart abstraction.

Research centers were all required to send the first five completed charts to the study monitor for data verification from source documents. All of the remaining charts were validated remotely by following defined guidelines for data quality developed by the Data Coordinating Center. Queries were used for quality control checks to identify potential data anomalies such as missing data or forms, out-of-range or erroneous data, and inconsistent data. Statisticians also conducted separate back-end data checks. For instance, if the baseline form indicated a biopsy report was available at 3 month, the statistician would check to see if the biopsy details were provided in the 3-month follow-up form. If it was not, sites would be queried to enter the information. Participants who met the study stopping criteria were verified by each site PI. Monthly PI and coordinator calls were utilized to inform sites about timelines and any other updates that required their attention.

Appendix B: Participating transplant center BKV testing protocols

Site	1	2	3	4	5	6	7	8	9	10	11	12	13
Screening frequency	Urine at month 1 and 3, then every 3 months for 2 years (usually plasma testing after initial urine)	Plasma at month 1, 3, 6 and 12; then yearly	Urine at 1, 2, 3, 6, 9 and 12 months	Plasma monthly first 6 months; then at month 9 and 12; then yearly	Plasma for cause after rise in serum creatinine	Plasma at month 1, 2, 3, 4, 5, 6, 9 and 12; then yearly	Plasma at month 4 and 12; then yearly	Plasma at month 1, 3, 6, 9 and 12	Urine at month 1 and 3, then every 3 months for 2 years (usually plasma testing after initial urine)	Plasma starting at month 3, then monthly to 1 year; then yearly	Plasma monthly to 1 year; then at month 18 and 24	Plasma, frequency not available	Plasma, frequency not available
Lower limit of detection, copies/mL	3000	500	250	100	7000 until year 2012, then 1500 thereafter	500	400	1000	500	100	30	Not available	Not available

Supplemental Table S1. Donor (kidney) and recipient characteristics by inclusion/exclusion in the DDS cohort

		All (N=1132)	Excluded (N=107)	Included (N=1025)	P-value ¹
Donor (kidney) characteristics					
Age, years		41 ± 15	43 ± 14	41 ± 15	0.25
Male		698 (62%)	65 (61%)	633 (62%)	0.84
Black race		183 (16%)	16 (15%)	167 (16%)	0.72
BMI, kg/m ²		28 ± 7	29 ± 9	28 ± 7	0.66
DCD		217 (19%)	24 (23%)	193 (19%)	0.34
ECD		235 (21%)	23 (22%)	212 (21%)	0.81
Hypertension		351 (31%)	38 (36%)	313 (31%)	0.26
Diabetes		116 (10%)	8 (8%)	108 (11%)	0.33
Cause of death	Head trauma	304 (27%)	24 (23%)	280 (28%)	0.72
	Anoxia	410 (37%)	41 (39%)	369 (36%)	
	Stroke	389 (35%)	39 (37%)	350 (35%)	
	Other	16 (1%)	1 (1%)	15 (1%)	
Hepatitis C seropositive		30 (3%)	7 (7%)	23 (2%)	0.008
KDRI		1.31 ± 0.43	1.35 ± 0.39	1.31 ± 0.43	0.12
KDPI		49% ± 27%	53% ± 27%	49% ± 27%	0.12
Admission serum creatinine, mg/dl		1.11 ± 0.63	1.11 ± 0.8	1.11 ± 0.61	0.71
Terminal serum creatinine, mg/dl		1.21 ± 0.93	1.19 ± 0.76	1.21 ± 0.95	0.82
No AKI		827 (73%)	73 (69%)	754 (74%)	0.48
Stage 1 AKI		184 (16%)	18 (17%)	166 (16%)	
Stage 2 AKI		69 (6%)	10 (9%)	59 (6%)	
Stage 3 AKI		51 (5%)	5 (5%)	46 (4%)	
Recipient characteristics					
Age, years		54 ± 13	53 ± 14	54 ± 13	0.77
Male		690 (61%)	61 (58%)	629 (61%)	0.44
Black race		527 (47%)	51 (48%)	476 (46%)	0.74
BMI, kg/m ²		28 ± 6	28 ± 6	28 ± 6	0.51
Cause of ESRD	Diabetes	355 (31%)	29 (27%)	326 (32%)	0.47
	Hypertension	319 (28%)	30 (28%)	289 (28%)	
	Glomerulonephritis	183 (16%)	14 (13%)	169 (16%)	
	Graft failure	91 (8%)	11 (10%)	80 (8%)	
	Other or unknown	183 (16%)	22 (21%)	161 (16%)	

Peak panel reactive antibody	0%	726 (64%)	65 (61%)	661 (64%)	0.61
	1-20%	86 (8%)	7 (7%)	79 (8%)	
	21-80%	146 (13%)	18 (17%)	128 (12%)	
	>80%	173 (15%)	16 (15%)	157 (15%)	
ESRD duration, months		48 ± 37	55 ± 40	47 ± 36	0.046
Pre-emptive transplant		117 (10%)	7 (7%)	110 (11%)	0.18
Previous kidney transplant		161 (14%)	17 (16%)	144 (14%)	0.58
Private insurance		318 (28%)	27 (25%)	291 (28%)	0.49
HLA mismatches		4.4 ± 1.3	4.4 ± 1.3	4.4 ± 1.3	0.54
Cold ischemia time, hours		16.3 ± 7.06.9	17.1 ± 7.5	16.3 ± 6.9	0.19
Kidney biopsied		591 (52%)	53 (50%)	538 (52%)	0.63
Kidney pumped		541 (48%)	46 (43%)	495 (48%)	0.34

Supplemental Table S2. Available information about BKV DNAemia viral loads in the DDS cohort

BKV DNAemia results in the 1 st year		Non-missing values	Peak (highest observed) value						
			Min	25th Pctl	50th Pctl	75th Pctl	Max	Mean	Std Dev
"Positive"	Blood Quant Copies/mL	256	3.5	408	1300	7150	136,000,000	642,620	8,516,737
	Blood Quant Log Score	256	2.5	3.3	4.3	5.5	500	23.5	66.3
"Negative"	Blood Quant Copies/mL	769	0	0	0	0	0	0	0
	Blood Quant Log Score	769	0	0	0	0	0	0	0

Note, the likely impossible maximum copy number and log score shown here were considered reporting errors; however, the patient had other positive blood BK polyomavirus (BKV) tests in the first year suggesting true DNAemia.

Supplemental Table S3. Donor (kidney) and recipient characteristics by graft failure attributed to BKV in the OPTN cohort

		All (N=76,953)	No graft failure due to BKV (N=76,681)	Graft failure due to BKV (N=272)	P-value ¹
Donor (kidney) characteristics					
Age, years		39 ± 14	39 ± 14	42 ± 15	0.08
Male		47,283 (61%)	47,140 (61%)	143 (53%)	0.003
Black race		10,579 (14%)	10,535 (14%)	44 (16%)	0.24
BMI, kg/m ²		28 ± 7	28 ± 7	28 ± 7	0.95
DCD		10,855 (14%)	10,819 (14%)	36 (13%)	0.68
ECD		10,622 (14%)	10,557 (14%)	65 (24%)	<0.001
Hypertension		28,447 (32%)	28,348 (32%)	99 (36%)	0.13
Diabetes		5,275 (7%)	5,262 (7%)	13 (5%)	0.18
Cause of death	Head trauma	28,244 (37%)	28,166 (37%)	78 (29%)	<0.001
	Anoxia	23,770 (31%)	23,695 (31%)	75 (28%)	
	Stroke	22,714 (30%)	22,602 (29%)	112 (41%)	
	CNS tumor	327 (0%)	327 (0%)	0 (0%)	
	Other	1,898 (2%)	1,891 (2%)	7 (3%)	
Hepatitis C seropositive		2,172 (3%)	2,171 (3%)	1 (0%)	0.01
KDRI		1.2 ± 0.37	1.2 ± 0.37	1.31 ± 0.43	<0.001
KDPI		42% ± 26%	42% ± 26%	49% ± 29%	<0.001
Admission serum creatinine, mg/dl		1.03 ± 0.43	1.03 ± 0.43	1.02 ± 0.42	0.48
Terminal serum creatinine, mg/dl		1.17 ± 0.95	1.17 ± 0.95	1.13 ± 1.33	0.60
No AKI		54,416 (71%)	54,210 (71%)	206 (76%)	0.08
Stage 1 AKI		14,909 (19%)	14,858 (19%)	51 (19%)	
Stage 2 AKI		4,719 (6%)	4,708 (6%)	11 (4%)	
Stage 3 AKI		2,909 (4%)	2,905 (4%)	4 (1%)	
Recipient characteristics					
Age, years		51 ± 15	51 ± 15	52 ± 15	0.55
Male		632 (61%)	477 (62%)	155 (60%)	0.76
Black race		24,701 (32%)	24,582 (32%)	119 (44%)	<0.001
BMI, kg/m ²		28 ± 6	28 ± 6	28 ± 6	0.87
Cause of ESRD	Diabetes	23,916 (31%)	23,839 (31%)	77 (28%)	0.03
	Hypertension	17,052 (22%)	16,970 (22%)	82 (30%)	
	Glomerulonephritis	12,452 (16%)	12,411 (16%)	41 (15%)	
	Graft failure	6014 (8%)	5994 (8%)	20 (7%)	
	Other or unknown	17,519 (23%)	17,467 (23%)	52 (19%)	
Peak panel reactive	0%	47,446 (62%)	47,261 (62%)	185 (68%)	0.16

antibody	1-20%	5917 (8%)	5897 (8%)	20 (7%)	
	21-80%	11,762 (15%)	11,727 (15%)	35 (13%)	
	>80%	11,828 (15%)	11,796 (15%)	32 (12%)	
ESRD duration, months		52 ± 41	53 ± 41	57 ± 41	0.054
Pre-emptive transplant		9,201 (12%)	9,179 (12%)	22 (8%)	0.049
Previous kidney transplant		9,460 (12%)	9,429 (12%)	31 (11%)	0.65
Private insurance		18,733 (24%)	18,676 (24%)	57 (21%)	0.19
HLA mismatches		4.1 ± 1.5	4.1 ± 1.5	4.6 ± 1.3	<0.001
Cold ischemia time, hours		16.7 (8.8)	16.7 (8.8)	16.3 (9.1)	0.33
Kidney biopsied		35,240 (46%)	35,109 (46%)	131 (48%)	0.43
Kidney pumped		33,369 (43%)	33,252 (43%)	117 (43%)	0.91

Values are mean ± SD or n (%). BKV, BK polyomavirus; OPTN, Organ Procurement and Transplantation Network; BMI, body mass index; DCD, donation after circulatory death; ECD, expanded-criteria donor; CNS, central nervous system; KDRI, kidney donor risk index; KDPI, kidney donor profile index; AKI, acute kidney injury; ESRD, end-stage renal disease; HLA, human leukocyte antigen.

1. Kruskal-Wallis test for continuous variables and Chi-Square test for categorical variables