Center-Level Variation in the Development of Delayed Graft Function Following Deceased Donor Kidney Transplantation

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Background

Delayed graft function (DGF), as defined by the need for dialysis in the first 7 days post-transplant, is collected on every kidney transplant (KT) recipient in the U.S. through the Organ Procurement and Transplantation Network (OPTN). Studies have explored the role of DGF in directing care and predicting outcomes, with variable results. Since DGF involves a subjective decision to dialyze, one possible explanation for the heterogeneity of DGF's effects between single-center reports could be heterogeneity in center-level post-transplant dialysis practice patterns. Centers that have a low threshold to dialyze a patient post-operatively will necessarily have a higher DGF rate, independent of patient factors.

Our goal was to explore and quantify center-level heterogeneity of DGF following KT, to determine whether or not center-level factors that can be ascertained from OPTN data are associated with DGF beyond patient factors, and to examine residual variability in DGF incidences across centers after accounting for patient and center level factors.

Methods

Adults undergoing non-preemptive, kidney-only deceased donor (DD) KT from 2003-2012 in the Scientific Registry of Transplant Recipients were selected for analysis.

Patient-Level Logistic Model: Multivariable logistic regression exploring patient-level associations with DGF was performed to ensure consistency with prior DGF models with donor (age, black race, BMI, blood type, diabetes mellitus, hypertension, terminal creatinine, cause of death, donation after cardiac death [DCD], expanded criteria donor [ECD] status, import from another region, and cold ischemia time [CIT]) and recipient variables (age, sex, black race, peak PRA, zero-HLA-mismatch, prior transplantation). Using a hierarchical (multi-level) model with a center-level random intercept, we calculated the expected and observed DGF incidence across centers.

Multilevel Logistic Model: To explore whether center-level characteristics were associated with DGF, independent of patient-characteristics, we fit a hierarchical model that incorporated plausible, measured center-level characteristics: total DDKT volume and the proportion of total KT comprised of the following: DDKT, DCD, ECD, transplants with CIT>30 hours, imported kidneys, donors with creatinine>1.5 mg/dL, hypertensive donors, black donors, diabetic donors, donors >age 65, recipients >age 65, and black recipients. The model also included patient-level donor and recipient variables.

Results

DGF Incidence: Of 82,143 patients, 27.0% developed DGF. The DGF incidence varied widely across 177 centers, from 3.2%-63.3%.

Table 1. Patient-Level Characteristics, By Development of DGF

	DGF (n=22,185)	No DGF (n=59,958)	P-value
Donor Characteristics			
Mean Age (SD)	41.9 (15.8)	37.7 (16.8)	<0.001
African-American	3,007 (26.3%)	8,440 (73.7%)	0.055
Hypertension	7,694 (34.0%)	14,961 (66.0%)	<0.001
Diabetes Mellitus	1,859 (32.7%)	3,826 (67.3%)	<0.001
Creatinine>1.5mg/dL	5,111 (38.1%)	8,307 (61.9%)	<0.001
DCD	4,202 (43.8%)	5,389 (56.2%)	<0.001
ECD	5,002 (33.2%)	10,042 (66.7%)	<0.001
Imported Kidney	6,577 (30.5%)	15,002 (69.5%)	<0.001
Median CIT (IQR)	19 (13.3-24.6)	16.4 (11.2-22.0)	<0.001
Recipient Characteristics			
Mean Age (SD)	52.7 (12.7)	51.7 (13.2)	<0.001
Male	14,854 (29.5%)	35,444 (70.5%)	<0.001
African-American	8,888 (32.1%)	18,775 (67.9%)	<0.001
Median PRA (IQR)	4 (0-36)	3 (0-37)	0.7
Zero-HLA-Mismatch	1,738 (20.8%)	6,597 (79.1%)	<0.001
Prior Transplant	3,113 (27.3%)	8,298 (72.7%)	0.5

Table 2. Transplant Center-Level Characteristics

	Minimum	25th Percentile	Median	75th Percentile	Maximum
DGF Incidence	3.2%	18.7%	27.3%	33.8%	63.3%
Center Volume	151	275	421	633	1797
DD Transplants	18.1%	57.0%	64.6%	74.1%	97.5%
DCD	0.0%	6.1%	11.5%	16.0%	40.4%
ECD	1.7%	11.6%	17.0%	22.9%	47.8%
Imported Kidneys	8.7%	16.4%	21.0%	29.5%	77.5%
CIT>30 Hours	0.0%	3.2%	6.5%	17.6%	91.3%
Donor Creatinine>1.5 mg/dL	2.3%	10.6%	13.6%	18.7%	41.2%
Preemptive Transplant	0.4%	4.8%	6.7%	10.6%	24.2%
Diabetic Donors	1.7%	4.6%	6.4%	8.3%	14.5%
Hypertensive Donors	11.4%	22.2%	26.7%	31.8%	52.6%
Donor Age >65	0.0%	1.2%	2.4%	4.6%	14.6%
Recipient Age >65	4.2%	12.1%	15.3%	19.1%	34.4%
African-American Donors	1.1%	6.8%	11.9%	17.6%	36.4%
African-American Recipients	0.4%	14.0%	29.9%	43.5%	91.6%

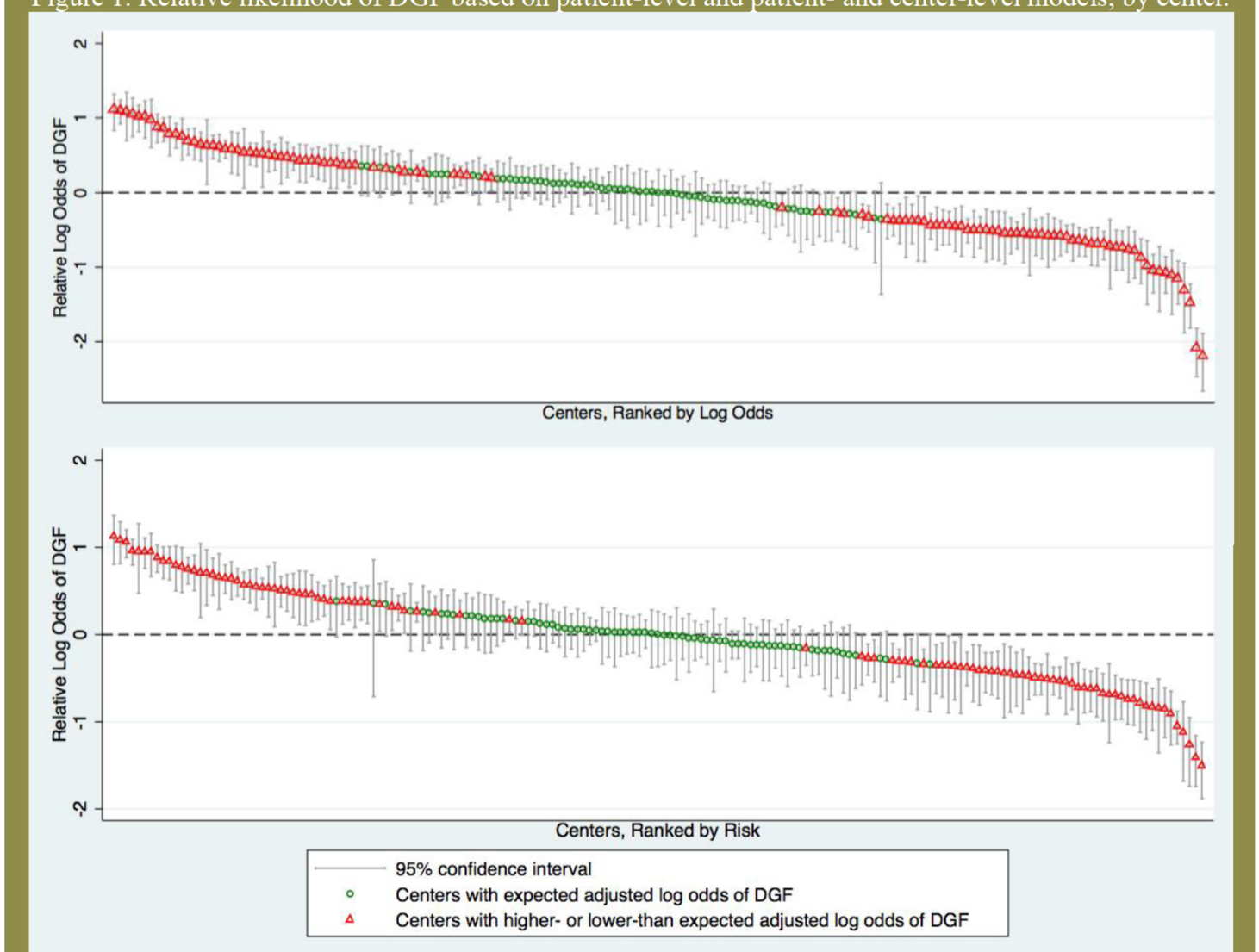
Table 3. Adjusted Odds Ratio for the Development of DGF

	aOR (95% CI)	P-value
Donor Factors		
Age (per 5 years)	1.07 (1.07-1.08)	<0.001
Hypertension	1.40 (1.34-1.46)	<0.001
DCD	2.73 (2.57-2.91)	<0.001
Serum Creatinine >1.5 mg/dL	1.94 (1.85-2.02)	<0.001
CIT (per 5 hours)	1.18 (1.16-1.19)	<0.001
Recipient Factors		
Age (per 5 years)	1.00 (0.99-1.00)	0.2
Male	1.49 (1.43-1.55)	<0.001
Peak PRA (per 5%)	1.00 (1.00-1.00)	<0.001
Zero HLA Mismatch	0.73 (0.68-0.78)	<0.001
Prior Transplant	0.99 (0.93-1.05)	0.7
Center-Level Factors (in 5% increments)		
Proportion of Preemptive Transplants	0.83 (0.74-0.93)	0.001
Proportion of DCD Donors	1.12 (1.03-1.17)	<0.001
Proportion of Kidneys with CIT>30 Hours	0.95 (0.92-0.98)	0.001
Proportion of Imported Kidneys	1.06 (1.03-1.10)	<0.001

Patient-Level Factors: Males, recipients of grafts from donors with elevated serum creatinine, diabetes, and hypertension were more likely to experience DGF, as were recipients of imported grafts and recipients of grafts from DCD donors and ECD (Table 1).

Transplant Center Factors: Transplant center-level characteristics are described in Table 2, and the percentages represent the proportion of transplants at a center that fit the corresponding characteristic.

Figure 1. Relative likelihood of DGF based on patient-level and patient- and center-level models, by center.



Patient-Level Model: After adjusting for patient-level factors, 38.4% of centers had predicted DGF incidences consistent with the national median (Fig. 1A). 28.8% had predicted DGF incidences above the national median and 32.7% had predicted incidences below it. The adjusted relative odds of DGF across centers ranged from 0.11-3.02 (IQR: 0.64-1.37).

Center-level model: After adjusting for patient-level factors, there were a number of statistically significant center-level factors associated with DGF (Table 3). After adjusting for patient and center-level factors, 41.8% of centers had predicted DGF incidences consistent with the national median (Fig. 1B). 28.2% had predicted DGF incidences above the national median and 29.9% had predicted incidences below it. The adjusted relative odds of DGF across centers ranged from 0.22 to 3.08 (IQR: 0.71-1.41).

Discussion

In this national study of center-level factors and DGF, we found significant heterogeneity in a patient's likelihood of DGF based on the center at which the transplant is performed, even after adjusting for patient and center characteristics. Center-level factors associated with less DGF included a center's proportion of preemptive transplants and its proportion of kidneys with CIT>30 hours. Increased use of imported kidneys and DCD donors were associated with increased DGF. To our knowledge, this is the first study to report on center-level effects in DGF. Study strengths include its sample size and its inclusion of most U.S. centers. Limitations include its retrospective, observational nature and the difficulty in drawing causal inferences from such databases. We tested mechanistically plausible and *measurable* center-level factors. Other patient- or center-level effects not captured by this database might influence a patient's likelihood of DGF. In conclusion, there is significant heterogeneity in the incidence of DGF across centers, even after patient and center-level adjustment. Further study is needed to parse out the causes of this variability.

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