Published in final edited form as:

Transplantation. 2015 December ; 99(12): 2617–2624. doi:10.1097/TP.0000000000000773.

Association between Organ Procurement Organization Social Network Centrality and Kidney Discard and Transplant Outcomes¹

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Disclosures: The authors declare no conflicts of interest.

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Abstract

Background—Given growth in kidney transplant waitlists and discard rates, donor kidney acceptance is an important problem. We used network analysis to examine whether organ procurement organization (OPO) network centrality affects discard and outcomes.

Methods—We identified 106,160 deceased-donor kidneys recovered for transplant from 2000–2010 in SRTR. We constructed the transplant network by year with each OPO representing a node and each kidney-sharing relationship between OPOs representing a directed tie between nodes. Primary exposures were the number of different OPOs to which an OPO has given a kidney or from which an OPO has received a kidney in year preceding procurement year. Primary outcomes were discard, cold-ischemia time, delayed graft function, and 1-year graft loss. We used multivariable regression, restricting analysis to the 50% of OPOs with highest discard and stratifying remaining OPOs by kidney volume. Models controlled for kidney donor risk index, waitlist time, and kidney pumping.

Results—An increase in one additional OPO to which a kidney was given by a procuring OPO in a year was associated with 1.4% lower likelihood of discard for a given kidney (odds ratio, 0.986; 95% confidence interval, 0.974–0.998) among OPOs procuring high kidney volume, but 2% higher likelihood of discard (OR:1.021, CI:1.006, 1.037) among OPOs procuring low kidney volume, with mixed associations with recipient outcomes.

Conclusions—Our study highlights the value of network analysis in revealing how broader kidney sharing is associated with levels of organ acceptance. We conclude interventions to promote broader inter-OPO sharing could be developed to reduce discard for a subset of OPOs.

Introduction

Kidney transplantation is widely recognized as the treatment of choice for many patients with end-stage renal disease (1). However, the kidney recipient waiting list is growing at a rate that far outstrips the growth in kidney supply (2), which limits the ability of many to receive this life-saving treatment. As a greater number of lower quality kidneys have been procured over the past decade, the discard rate of deceased donor kidneys has increased steadily (2), indicating that deceased donor kidney acceptance has become an increasingly important problem. In an effort to address systems-level problems that may be exacerbating the dearth of available organs for transplant, in 2013, the United Network of Organ Sharing (UNOS) Board made substantial changes to the kidney allocation policy to be implemented in 2014, which will require sharing of many kidneys on a wider-tiered geographic basis (3). On the eve of this change in kidney allocation, it becomes important to describe the sharing behavior of organ procurement organizations (OPOs) and examine the effect of kidney sharing across geographic areas on allocation and transplant outcomes in order to chart progress of the new policy and benchmark the status quo for comparison.

Kidney sharing occurs within the organ transplant network. This network facilitates the transplantation of thousands of organs each year (4) although there is substantial geographic

variation in practices (5). The evolution of this network has resulted in a complex sharing behavior guided by national and regional allocation policies, behavior of individual OPOs, their relationships with transplant centers, and individual patient-surgeon preference (2).

The burgeoning field of network science offers valuable tools to analyze kidney sharing across this complex kidney transplant network. Network analysis has proven useful in the development of insight in a variety of fields within medicine(6–8), and in health services research in particular (9–12). However, there has been little work applying these powerful tools to the kidney transplant network in the United States.

This study examined how network centrality characteristics influence outcomes in kidney transplantation. We analyzed interconnectedness among OPOs based on sharing of kidneys for transplant and changes in network characteristics over time. We then examined whether OPO network properties such as out-degree centrality (the number of different OPOs to which an OPO has given a kidney) and in-degree centrality (the number of different OPOs from which an OPO has received a kidney) had an effect on likelihood of kidney discard and patient outcomes. Such analysis can introduce techniques to better characterize the social network of organ sharing and generate scientific and operational insights into ways to improve the organ transplant network, which can ultimately inform both OPO sharing behavior and national policy to improve patient outcomes.

Materials and Methods

Participants

This study used data from the Scientific Registry of Transplant Recipients (SRTR), which has been described elsewhere.(13)

Figure 1 depicts our sample construction. We included all 134,747 kidneys recovered for transplant from deceased donors in the United States between January 1, 2000 and December 31, 2010. We sequentially excluded 9,643 kidneys used in multi-organ transplants, 14,552 kidneys used in 0-HLA-mismatch transplants, and 4,392 kidneys given to recipients under 18 years, given their systematically altered allocation practices. Our final sample included 106,160 kidneys.

Constructing the kidney transplant network

In order to calculate OPO-level network metrics, we constructed the kidney transplant network for each year between 2000 and 2010 by further limiting our sample to the 15,588 kidneys transplanted during this period that had a different donor and recipient OPO, indicating they were shared across OPOs. Each OPO represented a node in our network in a particular year. We attributed activities of transplant centers within each OPO's designated service area (such as receipt of kidneys) to that OPO's node, given that OPOs often facilitate this process. Each kidney shared across OPOs in a particular year represented a directed connection between 2 OPO nodes. We calculated for each year the network density, a summary statistic across all OPOs defined as the number of different connections present divided by the number of possible different connections between nodes. We additionally calculated out-degree centrality and in-degree centrality for each node. Out-degree is

defined as the number of different OPOs to which a particular OPO has given a kidney. In-degree is defined as the number of different OPOs from which a particular OPO has received a kidney. Figure 2 demonstrates the concepts underlying these network metrics.

Variables

The unit of analysis in our study was a procured kidney. The primary outcome was whether a kidney was discarded (i.e. not transplanted in any individual). We additionally looked at transplant recipient outcomes such as cold ischemia time (CIT) in hours, delayed graft function (DGF), and death-censored graft loss. DGF was defined as receipt of dialysis in the first week post-transplant. Dichotomous graft loss at 1 year from the transplant date was assigned to the procuring OPO and calculated from time to recorded graft failure or time to the start of chronic maintenance dialysis in the SRTR database, whichever was shorter. Patients who died with functioning grafts were not included in the graft loss outcome.

The primary exposures examined in this study were two measures of social network centrality, out-degree and in-degree, for the procuring OPO in the year prior to the year of kidney procurement. We lagged our out-degree and in-degree measures by 1 year in order to test the effect of pre-established relationships on our outcomes of interest and to minimize possibility of endogeneity with whether a kidney was discarded. Although it is possible to weight measures using number of kidneys shared along connections, we chose un-weighted measures of centrality because we were interested in the social network effects of the number of different OPOs to which a particular OPO was connected, as opposed to simply the volume of kidneys shared non-locally, which has been examined briefly elsewhere (14). We also included as covariates individual Kidney Donor Risk Index (KDRI) (15) and the median time spent on the waiting list among transplant recipients in an OPO in a particular year, and the percentage of kidneys that were pumped in an OPO in a particular year.

Statistical analysis

Networks were visualized using the Fruchterman-Reingold algorithm (16). We summarized network characteristics quantitatively and graphically over time. We estimated hierarchical logistic regression models with each individual kidney as an observation. Regression analysis was conducted on kidneys procured between 2001 and 2010 using lagged network metrics calculated from years 2000 to 2009. We included either out-degree or in-degree as the independent variable and whether a kidney was discarded as the dependent variable, and an OPO-year level random intercept. We additionally controlled for KDRI and median waiting time in adjusted models. We then estimated the association of out-degree and in-degree with CIT, graft loss, and DGF. All such models included KDRI, median waiting time, and whether kidneys were pumped as outlined above.

Since we hypothesized that increased connections among OPOs would lead to decreased discard rates, we limited our analysis to observations from OPOs that were in the upper half of discard rates over the study period in order to increase the event rate to improve robustness of models and increase our ability to detect an association. Because of a strong association between likelihood of kidney discard and number of kidneys procured, we stratified analyses by whether a kidney came from an OPO with a kidney procurement

volume in the top 50% of OPOs included in our analysis. As a robustness check, we repeated our analyses of DGF as our dependent variable while including CIT as a covariate to understand the independent association of social network connections with DGF. Additionally, we conducted a robustness check using fixed effects instead of random effects and the results were the same for high volume OPOs. Since this paper was exploratory and hypothesis-generating in nature, we did not adjust for multiple comparisons. All network analyses were created using Gephi (Gephi Consortium, Paris, France). For all statistical analyses, we generated point estimates and 95% confidence intervals and used a type I error of 5% (two-sided) to test for statistical significance using STATA 11.0 IC (StataCorp, College Station, TX).

Results

Transplant network

Our sample of 106,160 kidneys, including 15,588 kidneys shared across OPOs, came from 58 OPOs over 11 years resulting in a total of 638 unique OPO-year values. The OPO network and density over various years in our study period is detailed in Figure 3. The combined global network density for all 11 years was 0.653, indicating that 65.3% of the 3306 possible connections (58 OPOs times 57 possible other OPOs) in our network were present if we consider all 11 years at once. This increased to 0.806 if directionality was ignored (i.e. OPO A sending a kidney to OPO B is the same as OPO B sending a kidney to OPO A). The global network density was 0.162 in 2000, indicating that 16.2% of the 3306 possible connections in our network were present in our sample in 2000. This decreased to 0.152 in 2001 and then, aside from a decrease in 2006, increased steadily to 0.216 in 2008 before falling off precipitously to 0.165 in 2010 (Panel A).

Baseline characteristics

The median OPO discard rate for OPOs from years 2001 to 2010 was 20.1%. Thus, we limited all subsequent analysis to the 55,493 kidneys from the 29 OPOs with a discard rate greater than 20.1%. Among these 29 OPOs, the median total kidney volume summed over the 10 years between 2001 and 2010 was 1669 kidneys. We subsequently stratified our sample of 55,493 kidneys into the group of 15,025 kidneys from the 15 OPOs with a total kidney volume less than or equal to 1669 and the group of 40,468 kidneys from the 14 OPOs with a total kidney volume greater than 1669. Of note, KDRI did not differ significantly between these two strata ($p=0.198$). The baseline characteristics of OPOs and transplant recipients are detailed in Table 1.

Network centrality and discard

Our regression analysis of the association of network characteristics with discard is in Table 2. Among kidneys from high-volume OPOs, an increase in out-degree was significantly associated with a decrease in likelihood of kidney discard (OR:0.986, CI:0.974,0.998). In contrast, among kidneys from low-volume OPOs, an increase in out-degree was significantly associated with an increase in likelihood of kidney discard (OR:1.021, CI:1.006,1.037). There was no association between in-degree and likelihood of kidney discard

among kidneys from high-volume OPOs (OR:0.990, CI:0.979,1.002) or low-volume OPOs (OR:1.007, CI:0.999,1.015).

Network centrality and transplant outcomes

The associations between network metrics and CIT among high and low-volume OPOs were mixed (Tables 3a and 3b). Regardless, in both high-volume and low-volume OPOs, an increase in both out-degree and in-degree was associated with a higher incidence of DGF (out-degree – high:OR:1.018, CI:1.007,1.029; low:OR:1.023, CI:1.006,1.041; in-degree – high:OR:1.020, CI:1.010,1.030; low:OR:1.016, CI:1.006,1.025). Nevertheless, in both high-volume and low-volume OPOs, there was no association between either out-degree or in-degree and 1-year graft loss (out-degree – high:OR:0.989, CI:0.978,1.000; low:OR:0.995, CI:0.976,1.014; in-degree – high:OR:0.999, CI:0.988,1.009; low:OR:1.005, CI:0.995,1.015).

Supplementary results

Inclusion of CIT as a covariate in models with DGF as the dependent variable did not attenuate the association with out-degree (OR:1.022, CI: 1.01, 1.034; $p<0.01$) or in-degree (OR:1.018, CI:1.007, 1.029; $p<0.01$) in high-volume OPOs or the association with in-degree in low-volume OPOs (OR: 1.015, CI:1.006, 1.024; $p<0.01$), but did attenuate the association with out-degree in low-volume OPOs (OR:1.013, CI:0.996, 1.031; $p=0.138$).

Discussion

Our study describes the trends in the kidney transplant network over time and examines the association of social network centrality of OPOs with likelihood of discard and kidney transplant outcomes. This is the first comprehensive analysis of organ transplant network trends. Furthermore, we demonstrate that sharing kidneys with a greater number of different OPOs is associated with a significantly lower likelihood of kidney discard among OPOs with high discard rates and high kidney volumes, but a higher likelihood of kidney discard among OPOs with low kidney volumes. For high volume OPOs, an increase in one additional OPO to which kidneys were given in the preceding year by a procuring OPO is significantly associated with a 1.4% lower likelihood of discard for a given kidney. However, for low volume OPOs, an increase in one additional OPO to which kidneys were given in the preceding year by a procuring OPO is significantly associated with a 2.1% higher likelihood of discard for a given kidney. Based on 2010 kidney procurement volumes, if a high-discard, high-volume OPO had formed a sharing relationship with 1 additional OPO in 2009, our findings suggest an increase in 5 additional kidney transplants on average for that OPO in that year. However, if a high-discard, low-volume OPO had formed a sharing relationship with 1 additional OPO in 2009, our findings suggest an decrease in 3 additional kidney transplants on average for that OPO in that year.

Transplant network

Our construction of the kidney transplant network adds to the literature on applying network science to organ transplant. One study constructed a kidney transplant network using U.S. states as nodes and found a combined density of 0.87 in looking at all living and deceased-donor transplants between 1987 and 2010 while ignoring directionality (i.e. differences in

whether kidneys were received or sent) (17). Similarly, while our study found much lower densities for each year, if we combined all years and ignored directionality, we found a density of 0.81. The slightly lower density in our study likely stems from the greater number of possible connections among 58 OPOs relative to 50 states. Our study also examined trends in density by year, finding a linear increase in density over our study period until 2008, aside from decreases in 2001 and 2006. Understanding the dynamics underlying trends in kidney transplant network density remains a rich area for further inquiry, especially as changes to the kidney allocation algorithm are implemented in 2014.

Network centrality and discard

In Europe, a center-oriented rescue algorithm that encourages broader sharing after five organ refusals was found to be an effective way to achieve lower discard rates (18). In contrast, in the United States, the implementation of DonorNet in 2007 increased non-local sharing but resulted in an increase in overall discard rate (19). While DonorNet required systematic offers in concert with the national match run list to facilitate broader sharing, many centers listed overly relaxed acceptance criteria in DonorNet from which they could later reject kidneys once offered, resulting in surplus offers and network-wide inefficiency of allocating hard-to-match kidneys (19, 20). In our study, giving kidneys to a broader network was associated with a lower likelihood of kidney discard by a procuring high-volume OPO, but a higher likelihood of kidney discard by a procuring low-volume OPO in the following year. Given that much of the local variation in discard rates cannot be explained by observable kidney characteristics (21), our results suggest that an OPO or transplant center's social knowledge of and familiarity with the originating OPO through previous relationships or sharing of kidneys can influence the likelihood of kidney acceptance. Likewise, in light of how kidney acceptance may be a function of a center-level aggressiveness phenotype (22), having a broader network of transplant centers with which an OPO is familiar can allow OPOs to target more aggressive centers outside of the approved algorithm. Higher volume OPOs may be more likely to take advantage of such relationships whereas lower volume OPOs may suffer from the added administrative burden. While anecdotal evidence suggests that such sharing outside of the approved algorithm is not infrequent, understanding its magnitude in aggregate remains a rich area for further inquiry.

Network centrality and patient outcomes

Several studies have found that the implementation of DonorNet had no effect on CIT locally or regionally, but resulted in a slightly higher CIT among all kidneys shared nationally (14, 19, 23). Our study combined regionally and nationally-shared kidneys and found mixed results on the impact of broader sharing of kidneys on CIT among high and low-volume OPOs. Regardless, we found that greater OPO in-degree or out-degree centrality was associated with increased risk of DGF in kidneys for both high-volume and low-volume OPOs, irrespective of associations with CIT, suggesting that DGF may be mediated through non-CIT mechanisms (24). In fact, with the exception of the out-degree model in low-volume OPOs, inclusion of CIT in all of our models in supplementary analyses did not attenuate the association of broader kidney sharing with DGF. Thus, the increased risk of DGF in our study likely stems from unaccounted-for characteristics of

donors or recipients, as opposed to direct effects of broader kidney sharing. Nevertheless, we found no association between giving kidneys to a broader network of OPOs and likelihood of 1-year graft loss among either high or low-volume OPOs. This is consonant with outcomes of kidneys allocating using Europe's rescue algorithm, which did not result in worse outcomes among rescued kidneys (25).

Limitations

Our findings should be interpreted in light of our limitations. First, we cannot control for volume of kidneys due to multicollinearity with likelihood of kidney discard. However, we are able to stratify by volume of kidneys to understand the moderating effect of this variable. Additionally, our findings may not generalize to the entire population of procured kidneys, as we only look at kidneys from OPOs with a high discard rate. However, one can argue that methods to improve utilization of kidneys are most necessary in the high-discard-rate OPOs that our study examined. Also, we cannot take into account transplant center effects because we do not have such data available, and this may represent some residual confounding. Finally, in our models for kidney discard, we cannot differentiate between the kidneys offered strictly along the allocation algorithm versus those offered out of sequence, such as through social ties. However, the inclusion of strict algorithm-allocated kidneys would bias our results towards the null and we still find an association.

Conclusion

This study introduces the utilization of network analysis to understand transplant outcomes and discard rates. We found that, greater social network centrality was associated with lower likelihood of kidney discard in high-volume OPOs and a higher likelihood of kidney discard in low-volume OPOs, with unclear effect on patient outcomes. These findings suggest that broader connections and utilization of the social knowledge created as a result could be encouraged through policy to potentially improve organ utilization for some OPOs, but may come at a cost for others. Some have called for an improved allocation system to share locally-rejected organs in a more timely manner (14), highlighting that the current tiered allocation system creates room for inefficiencies (26). The changes in allocation policy slated for implementation in 2014 make progress in many respects, such as sharing of kidneys with higher Kidney Donor Profile Index on a wider basis more rapidly and eliminating variance within local allocation (3). Future policy could potentially encourage OPOs to seek out and take advantage of social knowledge to utilize their difficult-to-place kidneys, perhaps through education programs targeted to high-volume OPOs with fewer connections, support for low-volume OPOs to manage broader sharing, public reporting of OPO and center acceptance rates, measuring of OPO connectivity to promote utilization, or even implementation of a rescue algorithm similar to Europe. Future research should examine the application of other network science concepts, such as modularity, hierarchy, or diffusion, to kidney transplant and investigate social network effects in other organ transplant networks.

Acknowledgments

Funding Sources: Dr. Parikh was supported by the K24-DK090203 grant from NIH.

We would like to thank Dr. Nicholas Christakis, Sol Goldman Family Professor of Social and Natural Science and Co-Director, Yale Institute for Network Science, for his insights with regards to methodology.

The SRTR data system includes data on all donor, wait-listed candidates, and transplant recipients in the US, submitted by the members of the Organ Procurement and Transplantation Network (OPTN), and has been described elsewhere.⁽¹³⁾ The Health Resources and Services Administration, U.S. Department of Health and Human Services provides oversight to the activities of the OPTN and SRTR contractors. The data reported here have been supplied by the Minneapolis Medical Research Foundation as the contractor for the SRTR. The interpretation and reporting of these data are the responsibility of the author(s) and in no way should be seen as an official policy of or interpretation by the SRTR or the U.S. Government.

Abbreviations

CIT	cold ischemia time
DGF	delayed graft function
KDRI	Kidney Donor Risk Index
OPO	organ procurement organization
SRTR	Scientific Registry of Transplant Recipients
UNOS	United Network of Organ Sharing

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Figure 1.
Construction of Sample

Figure 2. Concepts underlying network metrics

Panel A shows a network with 3 nodes and 3 kidneys shared among those nodes along with network metrics for each node.

Panel B shows the same network with 4 additional kidneys given from X to Y. There is no change in in-degree or out-degree, but weighted in-degree increases for node Y and weighted out-degree increases for node X.

Panel C shows how network density is calculated. The 3 solid arrows represent connections in the original network. The 3 dashed arrows describe other possible connections. The density of this network is calculated as the number of connections present (3 solid) divided by the total possible connections (3 solid+3 dashed), and is thus 0.5, or 50%.

Panel B

Panel C

Panel D

Figure 3. OPO network and density from 2000 to 2010

Panel A. Transplant network density by year

Density = number of distinct connections between nodes/number of possible connections between nodes

Panel B. Transplant network in 2000

Panel C. Transplant network in 2008

Panel D. Transplant network in 2010

Panels B–D.

Node position is based on 2000 network connections.

Node color:

Blue = (discard rate lower than median discard rate) OR (discard rate greater than median discard rate and kidney volume less than or equal to 1657)

Red = discard rate greater than median discard rate AND kidney volume greater than 1657

Edge thickness is proportional to number of kidneys shared. Edge color is same as node color. If connecting nodes are different colors, edge color is gray.

Table 1

Characteristics of OPOs and kidneys procured

OPO-year characteristics	Low kidney volume OPOs ^A				High kidney volume (>1669) OPOs ^B			
	n	Mean	SD	Range	n	Mean	SD	Range
<i>Network measures</i>								
Out-degree (lagged)	150	8.9	5.02	1–25	140	14.83	5.71	2–36
In-degree (lagged)	150	10.24	8.4	1–40	140	13.71	5.94	4–33
<i>Operational measures</i>								
Mean of median days on waiting list	150	697	293	198–1809	140	765	307	220–2004
Mean percentage of kidneys pumped	150	0.15	0.2	0–0.81	140	0.22	0.2	0–0.69
<i>Individual kidney/recipient characteristics^C</i>								
Mean KDRI	15009	1.07	0.40	0.43–3.12	40381	1.07	0.40	0.40–3.60
Probability of discard	15025	0.25			40468	0.24		
CIT (hours)	10492	18.22	9.32	0.02–99	28492	18.53	8.88	0.08–99
Probability of DGF	11224	0.24			30615	0.27		
Probability of 1-year graft loss	10750	0.07			29293	0.07		

^A Less than or equal to 1669 kidneys procured over 10 years^B Greater than 1669 kidneys procured over 10 years^C Characteristics are summarized here for only the kidneys included in our sample as specified in Figure 1 and do not reflect estimates for all kidneys nationally.

OPO = organ procurement organization, SD = standard deviation, KDRI = kidney donor risk index, CIT = cold ischemia time, DGF = delayed graft function

Table 2

Association of OPO network centrality characteristics with kidney discard likelihood

	Kidney discard (binary)			
	<i>High kidney volume^A</i>		<i>Low Kidney volume^B</i>	
	<i>Unadjusted</i>	<i>Adjusted^C</i>	<i>Unadjusted</i>	<i>Adjusted^C</i>
Network Characteristic	OR (95%CI)	OR (95%CI)	OR (95%CI)	OR (95%CI)
Out-degree	0.994 (0.983, 1.005)	0.986* (0.974, 0.998)	1.014* (1.001, 1.026)	1.021** (1.006, 1.037)
In-degree	1.005 (0.994, 1.016)	0.99 (0.979, 1.002)	1.011** (1.004, 1.018)	1.007 (0.999, 1.015)
n	40468	40381	15025	15009

* Indicates significant at 5% level,

** Indicates significant at 1% level

^A Less than or equal to 1657 kidneys procured over 11 years

^B Greater than 1657 kidneys procured over 11 years

^C Adjusted for kidney donor risk index, median time spent on waiting list prior to transplant in a particular organ procurement organization in a particular year, and percentage of kidneys pumped in a particular organ procurement organization in a particular year.

Associations of out-degree and in-degree with discard were estimated in separate regression models.

OR = odds ratio, KDRI = kidney donor risk index, OPO = organ procurement organization

Table 3a

Association of OPO network centrality characteristics with transplant recipient outcomes from higher volume OPOs

	CIT	DGF	1-year graft loss
Network Characteristic	B (95% CI)	OR (95% CI)	OR (95% CI)
Outdegree	-0.045 (-0.142, 0.051)	1.018 ^{**} (1.007, 1.029)	0.989 (0.978, 1)
Indegree	0.116 ^{**} (0.03, 0.202)	1.02 ^{**} (1.01, 1.03)	0.999 (0.988, 1.009)
n	28434	30551	29232

* Indicates significant at 5% level,

** Indicates significant at 1% level

Associations of out-degree and in-degree with outcomes were estimated in separate regression models.

All models control for kidney donor risk index, median time spent on waiting list prior to transplant in a particular organ procurement organization in a particular year, and percentage of kidneys pumped in a particular organ procurement organization in a particular year.

CIT = cold ischemia time in hours, DGF = delayed graft function, OLS = ordinary least squares, OR = odds ratio, B = beta (regression coefficient)

Table 3b

Association of OPO network centrality characteristics with transplant recipient outcomes from lower volume OPOs

	CIT	DGF	1-year graft loss
Network Characteristic	B (95% CI)	OR (95% CI)	OR (95% CI)
Outdegree	0.317 ** (0.217, 0.417)	1.023 ** (1.006, 1.041)	0.995 (0.976, 1.014)
Indegree	0.041 (−0.022, 0.104)	1.016 ** (1.006, 1.025)	1.005 (0.995, 1.015)
n	10481	11213	10739

* Indicates significant at 5% level,

** Indicates significant at 1% level

Associations of out-degree and in-degree with outcomes were estimated in separate regression models.

All models control for kidney donor risk index, median time spent on waiting list prior to transplant in a particular organ procurement organization in a particular year, and percentage of kidneys pumped in a particular organ procurement organization in a particular year.

CIT = cold ischemia time in hours, DGF = delayed graft function, OLS = ordinary least squares, OR = odds ratio, B = beta (regression coefficient)