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The Influence of Donor to Recipient Size Matching on Kidney Transplant Outcomes

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Background. Nephron endowment in renal transplantation is infrequently considered, but may have important implications for post kidney transplantation outcomes. In this population-cohort study, we analyzed the deceased-donor kidney transplant outcomes stratified by donor-to-recipient size ratios. **Methods.** Data for all deceased-donor adult kidney transplantation recipients between 2003 and 2015 were extracted from the UK Transplant Registry. We used weight as a surrogate marker for kidney size and defined the following mismatch categories (donor weight/recipient weight × 100): less than 75% (small donor kidney), 75% to 125% (weight matched kidney), and greater than 125% (large donor kidney). Univariable and multivariable analyses were undertaken to assess the relationship between this marker and patient outcomes. **Results.** Outcomes for 11720 transplants were analyzed with weight mismatch stratified as follows; small donor kidney (n = 1608, 13.7%), weight matched kidney (n = 7247, 61.8%) and large donor kidney (n = 2865, 24.4%). On multivariable analysis, no significant differences were detected in overall ($P = 0.876$) or death-censored ($P = 0.173$) graft survival, or in rates of delayed graft function ($P = 0.396$) between these 3 groups. However, 12-month creatinine levels were found to decline progressively across the groups ($P < 0.001$), with adjusted averages of 144.2 μmol/L for recipients of small donor kidneys, 134.7 μmol/L in weight matched kidneys, and 124.9 μmol/L in recipients of large donor kidneys. In addition, patient survival was found to be significantly shorter in recipients of larger kidneys than those with weight matched kidneys (hazard ratio, 1.21; 95% confidence interval, 1.05-1.40; $P = 0.009$), which is inconsistent with the existing literature. **Conclusions.** Our data demonstrate that 12-month creatinine is influenced by donor-to-recipient difference in body weight, but that no such difference is observed for either delayed graft function or death-censored graft survival. However, we observed increased mortality in recipients receiving larger kidneys; an observation which conflicts with the existing literature and warrants further investigation.

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The hyperfiltration hypothesis in the setting of kidney transplantation postulates that reduced renal mass from small donor kidneys results in nephron exhaustion due to size mismatch.[1] From this hypothesis, we can speculate that small donor kidneys fail to meet the metabolic demands of a larger recipient, resulting in nephron hypertrophy, exhaustion and ultimately premature graft failure, whereas the reciprocal may be true for larger donor kidneys. There is a physiological rationale why donor size could influence long-term graft survival, attributed to the greater number of transplanted nephrons from larger individuals, and this has been shown in basic science rat models.[2,3] However, selection of kidneys for allocated recipients is rarely considered in the context of physiological capacity of the donor kidney to meet recipient metabolic needs. At present, the overriding principle persists that the benefits of proceeding with kidney transplantation, regardless of donor size, outweighs the risk of remaining on the waiting list.

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Given that patients with a lower weight/body mass index (BMI) have smaller kidneys (and a reduced cortical volume), attenuating donor and recipient weight mismatching may lead to improved kidney transplant outcomes. Although the importance of donor-to-recipient size mismatch is acknowledged in the setting of pediatric kidney transplantation,[4] it is rarely considered in the setting of adult kidney transplantation. Published data from single-center studies is conflicting with regards to the outcomes associated with donor size mismatching. Population-cohort studies from the United States have suggested that transplanting deceased kidneys from small donors into larger recipients is associated with inferior graft survival. For example, Kasiske et al[5] analyzed data for deceased-donor kidney recipients from the United States Renal Data System and found increased risk for late graft failure in both large and medium-size recipients of kidneys from small donors (using body surface area as surrogate for kidney size). More recent analysis, using data from 69737 deceased donor kidney transplant recipients from the Scientific Registry of Transplant Recipients for a 1992 to 2005 cohort, also shows recipients receiving kidneys from substantially smaller donors have an increased risk of graft loss (more pronounced in recipients of extended criteria kidneys).[6]

The aim of this study was to determine whether mismatching weight is an independent risk factor for poor outcomes following deceased donor kidney transplantation, after accounting for other potentially confounding factors. The rationale for our study was (1) data from the United States may not be translatable to the United Kingdom due to acknowledged differenced in long-term graft outcomes,[7] and; (2) a more contemporary analysis is warranted, due to the evolution of transplant-related care in the last few decades. This will allow clinicians to assess the importance of nonimmunological factors (eg, kidney size) in determining long-term allograft survival.

METHODS

Our analysis included all adult patients (aged 18 years and older) receiving a deceased donor kidney transplant between January 2003 and January 2015 in the United Kingdom (excluding recipients of multiple organs and transplants from pediatric donors). Data were obtained from the UK Transplant Registry, held by NHS Blood and Transplant, to which every kidney transplant center within the United Kingdom is mandated to submit demographic and clinical data for each transplant performed. We utilized data from the standard national organ transplant data set, with approval sought and obtained from the Kidney Advisory Group.

We used weight as our surrogate marker for kidney size. Percentage weight difference in each transplantation was calculated as (donor weight/recipient weight) × 100. We then stratified each transplantation into 1 of 3 groups: (1) <75% (small donor kidney), (2) 75%-125% (weight matched kidney), and (3) >125% (large donor kidney).

Outcome Measures

Our primary outcome measures were patient and graft survival (death-censored and overall). Secondary outcome measures of interest were rates of delayed graft function (DGF) and 12-month (or nearest time point) creatinine values postkidney transplantation. Delayed graft function was defined as need for dialysis within the first week after kidney transplantation.

Statistical Analysis

We first assessed for differences across the weight mismatch groups using χ^2 tests and Kruskal-Wallis tests, as appropriate. Patient outcomes were then compared between the groups using a similar approach, with Cox regression models used to analyze survival outcomes. We then conducted a set of multivariable analyses, to assess the associations between the weight mismatch group and the outcomes being considered, after accounting for the potentially confounding effects of various demographic and perioperative characteristics. Analyses of survival outcomes were assessed using Cox regression models, with binary logistic regression used to analyze rates of DGF and general linear models used for creatinine levels. Variables were selected for inclusion in the models using a stepwise approach, to identify independent predictors of outcome. The analyses were then repeated with the addition of an interaction term between weight mismatch and recipient BMI, to assess whether the impact of weight mismatch varied by the size of the recipient.

A full description of our statistical methods can be found as **SDC, Materials and Methods**; including a full list of variables included in the multivariable analyses (**Tables S1-S9, SDC,** http://links.lww.com/TXD/A139, http://links.lww.com/TXD/A140, http://links.lww.com/TXD/A141, http://links.lww.com/TXD/A142, http://links.lww.com/TXD/A143, http://links.lww.com/TXD/A144, http://links.lww.com/TXD/A145, http://links.lww.com/TXD/A146, http://links.lww.com/TXD/A147). Categorical variables are presented as numbers and rates. Continuous variables are reported as medians and interquartile ranges (IQRs) or as geometric means, with 95% confidence intervals (CI). The results of the multivariable analysis are presented as odds ratios, hazard ratios (HRs) or fold-differences along with 95% confidence intervals. All analyses were performed using SPSS version 22 (IBM, Armonk, New York). A P value less than 0.050 was considered statistically significant in our analysis.

RESULTS

Study Cohort

Data were available for a total of 11720 deceased donor kidney transplants with both donor and recipient weight. This cohort was stratified by percentage weight difference as follows: small donor kidney (n = 1608, 13.7% of the cohort), weight matched kidney (n = 7247, 61.8% of the cohort), large donor kidney (n = 2865, 24.4% of the cohort).

Table 1 summarizes the demographic and transplant characteristics of the cohort, stratified by the percentage weight difference. As would be expected, the recipient weight and BMI both decreased significantly from the small donor kidney to large donor kidney groups ($P < 0.001$). In addition, those recipients that received large donor kidneys were significantly less likely to be male, of white ethnicity, diabetic or receiving their first kidney graft and to be more likely to be CMV-positive (all $P < 0.001$). Large kidney donors were significantly more likely to be male and had higher rates of diabetes and hypertension, but were less likely to be smokers than the other groups (all $P < 0.001$). Rates of donation after brain death were highest in the large donor kidney group,

TABLE 1.

Baseline demographics of the study cohort

		% Weight mismatch			
		<75%	*75%-125%*	*>125%*	
	Valid, N	**Small donor kidney (relative to recipient)**	**Donor-recipient match**	**Large donor kidney (relative to recipient)**	***P***
N (%)	11 720	1608 (13.7%)	7247 (61.8%)	2865 (24.4%)	—
Recipient					
Age, y	11 720	51 (43-59)	53 (43-62)	50 (38–60)	<0.001
Sex (male)	11 714	1302 (80.9%)	4904 (67.7%)	1193 (41.6%)	<0.001
BMI, kg/m^2	11 720	30.6 (27.6-33.5)	26.3 (23.8-29.4)	22.6 (20.5-25.1)	<0.001
Weight, kg	11 720	94.0 (84.5-104.0)	77.0 (68.8-85.7)	60.2 (53.2-67.5)	<0.001
Ethnicity	11 706				<0.001
White		1370 (85.2%)	5857 (80.8%)	2143 (74.8%)	
Asian		119 (7.4%)	900 (12.4%)	517 (18.0%)	
Black		104 (6.5%)	404 (5.6%)	157 (5.5%)	
Other		13 (0.8%)	76 (1.0%)	46 (1.6%)	
Diabetes	11 720	159 (9.9%)	627 (8.7%)	154 (5.4%)	<0.001
Graft no	11 720				<0.001
1		1415 (88.0%)	6224 (85.9%)	2369 (82.7%)	
2		162 (10.1%)	859 (11.9%)	392 (13.7%)	
> 2		31 (1.9%)	164 (2.3%)	104 (3.6%)	
CMV-positive	11 190	733 (45.6%)	3693 (51.0%)	1532 (53.5%)	<0.001
Dialysis at transplant	11 720	1457 (90.6%)	6462 (89.2%)	2562 (89.4%)	0.235
Donor					
Age, y	11 720	51 (39-61)	53 (42-62)	51 (41-60)	<0.001
Sex (male)	11 720	1132 (29.6%)	3372 (53.8%)	986 (65.6%)	<0.001
Ethnicity	11 717				0.542
White		1544 (96.0%)	6978 (96.3%)	2762 (96.4%)	
Asian		36 (2.2%)	137 (1.9%)	54 (1.9%)	
Black		9 (0.5%)	67 (0.9%)	21 (0.7%)	
Other		19 (1.2%)	62 (0.8%)	28 (1.0%)	
Diabetes	11 412	76 (4.7%)	410 (5.6%)	254 (8.9%)	<0.001
Hypertension	11 291	332 (20.6%)	1881 (26.0%)	873 (30.5%)	<0.001
Smoking	11 456	832 (51.7%)	3382 (46.7%)	1230 (42.9%)	<0.001
Transplant					
DBD (%)	11 720	1014 (63.1%)	4647 (64.1%)	1964 (68.6%)	<0.001
Waiting time, d	11 704	831 (375-1402)	922 (424-1484)	964 (439-1564)	<0.001
HLA mismatch	11 719				<0.001
1		255 (15.9%)	1015 (14.0%)	424 (14.8%)	
2		514 (31.9%)	2298 (31.7%)	986 (34.4%)	
3		721 (44.8%)	3316 (45.7%)	1296 (45.2%)	
4		118 (7.3%)	617 (8.5%)	159 (5.5%)	
Sensitization (>0%)	11 720	497 (69.0%)	2416 (66.7%)	1152 (59.8%)	<0.001
Antibody incompatibility	11 720				0.119
Compatible		1600 (99.5%)	7166 (98.8%)	2826 (98.6%)	
HLAi		8 (0.5%)	79 (1.1%)	38 (1.3%)	
ABOi		0 (0.0%)	2 (0.0%)	1 (0.0%)	
CIT, min	11 598	900 (718-1110)	893 (712-1088)	910 (732-1096)	0.056
fWIT, min	2561	18 (15-25)	18 (15-23)	18 (15-22)	0.246
sWIT, min	2836	12 (10-15)	12 (10-15)	13 (10-15)	0.314

Data are reported as median (IQR), with *P* values from Kruskal-Wallis tests, or as column percentages, with *P* values from χ^2 tests, as applicable. *P* values in bold emphasis are significant at $P < 0.05$. Sensitization is greater than calculated reaction frequency 0%. HLAi is the presence of preformed donor specific anti-HLA antibodies.

DBD, donation after brain death; HLAi, HLA-incompatible; ABOi, ABO-incompatible; CIT, cold ischemia time; fWIT, functional warm ischemia time; sWIT, standard warm ischemia time.

which also had longer waiting times, but lower rates of sensitization (all $P < 0.001$).

Weight Mismatch and Outcomes

A total of 11 696 patients had data recorded for graft survival, with a median follow up of 37 months (IQR, 13-72). During this period, there were a total of 1524 graft losses, after censoring for patient deaths. Patient survival was only assessed for those patients receiving their first graft. As such, data were available for 9992 cases, with a median follow up of 43 months (IQR, 18-73), during which time there were 1177 deaths and 2132 total graft losses (ie, including deaths

TABLE 2.

Univariable analysis of patient outcomes by weight difference

		Weight difference (donor weight/recipient weight)			
		<75%	75%-125%	>125%	
	N	Small donor kidney (relative to recipient)	Donor-recipient match	Large donor kidney (relative to recipient)	*P*
Mortality[a]	9992	0.87 (0.73-1.04)	Reference (1.0)	1.05 (0.92-1.20)	0.189
Overall graft loss[a]	9987	0.94 (0.83-1.07)	Reference (1.0)	0.98 (0.89-1.09)	0.660
DCGL[a]	11696	1.06 (0.92-1.23)	Reference (1.0)	0.93 (0.83-1.05)	0.308
12-mo Creatinine[b]	9690	147 (120-183)	133 (108-168)	117 (95-148)	<0.001
DGF[c]	11720	29.5%	29.0%	27.0%	0.093

[a] Survival outcomes were analyzed using Cox regression models, and the reported statistics are HRs and 95% CIs, relative to the 75%-125% group.

[b] Creatinine levels are reported as median (IQR), with a *P* value from a Kruskal-Wallis test.

[c] DGF was analyzed using a χ^2 test.

P values in bold emphasis are significant at $P < 0.05$.

DCGL, death-censored graft loss; DGF, delayed graft function.

with working grafts). Delayed graft function occurred in 3350 (28.6%) of cases, and 12-month creatinine levels were recorded in 9690 cases, with a median of 131 μmol/L (IQR, 106-166).

On univariable analysis (Table 2), the weight difference was not found to be significantly associated with patient survival ($P = 0.189$), or with overall ($P = 0.660$) or death-censored ($P = 0.308$) graft survival. Rates of DGF were also similar in the 3 groups ($P = 0.093$). However, a significant difference in creatinine at 12 months was detected ($P < 0.001$), with median levels declining from 147 μmol/L in recipients of small donor kidneys to 117 μmol/L in recipients of large donor kidneys.

On account of the previously identified baseline differences between the 3 groups in recipient, donor and transplant related factors, multivariable analyses were performed in order to account for potentially confounding factors. The resulting models are reported in full in **Tables S1-S5, (SDC,** http://links.lww.com/TXD/A139, http://links.lww.com/TXD/A140, http://links.lww.com/TXD/A141, http://links.lww.com/TXD/A142, http://links.lww.com/TXD/A143) and summarized in Tables 3 and 4. As in the univariable analyses, no significant association were detected between donor/recipient weight differences and DGF ($P = 0.396$) and either overall ($P = 0.876$) or death-censored ($P = 0.173$) graft survival. The previously noted difference in 12-month creatinine levels remained significant on multivariable analysis ($P < 0.001$). After adjustment for confounding factors, the estimated average creatinine levels were found to decline from 144.2 μmol/L in recipients of small donor kidneys to 134.7 μmol/L in recipients of weight matched kidneys, and 124.9 μmol/L in recipients of large donor kidneys.

The multivariable analysis of patient survival found that, after accounting for confounding factors, a significant difference existed between the groups ($P = 0.021$). Whilst survival was similar in the matched weight and small donor kidney groups (HR, 0.95; 95% CI, 0.79-1.15; $P = 0.601$), recipients of large donor kidneys were found to have significantly shorter survival than those that received matched weight kidneys (HR, 1.21; 95% CI, 1.05-1.40; $P = 0.009$). No difference was identified in underlying cause of death when compared across the BMI groups (based on death certificate registrations) ($P = 0.146$).

In addition to the main multivariable analyses, a secondary set of analyses were performed to assess the potential for an

TABLE 3.

Adjusted relationship between weight difference and posttransplant outcomes by multivariable analysis

			Weight difference (donor weight/recipient weight)				
			<75%		75%-125%	>125%	
			Small donor kidney (relative to recipient)		Donor-recipient match	Large donor kidney (relative to recipient)	
	N	Overall, *P*	Statistics	*P*	Statistics	Statistics	*P*
Mortality[a]	9611	0.021	0.95 (0.79-1.15)	0.601	Reference (1.00)	1.21 (1.05-1.40)	0.009
Overall graft loss[a]	9526	0.876	1.00 (0.97-1.15)	0.989	Reference (1.00)	0.97 (0.86-1.09)	0.608
DCGL[a]	11016	0.173	1.05 (0.90-1.24)	0.530	Reference (1.00)	0.88 (0.77-1.02)	0.086
12-mo Creatinine[b]	9127	<0.001	1.07 (1.05-1.09)	<0.001	Reference (1.00)	0.93 (0.91-0.94)	<0.001
DGF[c]	11137	0.396	0.97 (0.84-1.11)	0.618	Reference (1.00)	1.08 (0.96-1.21)	0.214

All statistics are relative to the donor-recipient match group (75%-125%). A full list of factors considered for inclusion is available in the SDC (Tables S1-S5, SDC, http://links.lww.com/TXD/A139, http://links.lww.com/TXD/A140, http://links.lww.com/TXD/A141, http://links.lww.com/TXD/A142, http://links.lww.com/TXD/A143), Materials and Methods, as well as further information about the methodology used, as well as the full multivariable models.

[a] Survival outcomes were analyzed using Cox regression models, and the reported statistics are HRs.

[b] Creatinine was found to follow a skewed distribution, and so was $\log_{10}$-transformed, then analyzed using a general linear model. The resulting coefficients were then antilogged, and are reported as fold-differences in creatinine levels between groups.

[c] DGF was analyzed using a binary logistic regression model, and the reported statistics are odds ratios.

Values in brackets are 95% percent confidence intervals. The "N" column reports the number of patients included in each analysis, after excluding those with missing data on 1 of the factors in the final model. *P* values in bold emphasis are significant at $P < 0.05$.

TABLE 4.

Adjusted outcomes from multivariable analyses

	Weight difference (donor weight/recipient weight)		
	<75%	75%-125%	>125%
	Small donor kidney (relative to recipient)	Donor-Recipient match	Large donor kidney (relative to recipient)
Patient survival, y			
1	97.4%	97.3%	96.7%
3	94.6%	94.3%	93.1%
5	91.0%	90.6%	88.7%
Overall graft survival, y			
1	91.7%	91.8%	91.9%
3	85.4%	85.7%	85.8%
5	78.9%	79.3%	79.5%
Death-censored graft survival, y			
1	93.6%	93.9%	94.6%
3	89.6%	90.2%	91.2%
5	86.0%	86.7%	88.1%
Delayed graft function	37.7%	37.8%	40.2%
Average creatinine at 12 mo, μmol/L	144.2	134.7	124.9

Values were produced by evaluating the multivariable models reported in the supplementary material at the midpoint of all of the included factors. This was achieved by calculating the proportion of patients in each category of the factors in the final models and multiplying these by the associated regression coefficients. The sum of the resulting values, along with the intercept term, were then calculated, with the result added separately to the coefficients of the 3 categories of weight difference. These values were then converted into rates of survival/DGF or average creatinine levels, which represent the estimated values of these outcomes for the "average" patient, ie, after accounting for differences in the donor, recipient and transplant factors between the 3 groups.

interaction between recipient BMI and the weight mismatch. Of the 5 outcomes considered, this interaction term was only significant in the analysis of patient survival (P = 0.047). Further investigation of this finding (Table 5 and **Tables S6-S9, SDC,** http://links.lww.com/TXD/A144, http://links.lww.com/TXD/A145, http://links.lww.com/TXD/A146, http://links.lww.com/TXD/A147) found that, after accounting for other factors, the effect of receiving a large donor kidney increased with the recipient BMI. For recipients of normal BMI (18.5-25.0), the HR for large donor kidneys, relative to weight matched kidneys was 1.09 (95% CI, 1.02-1.18; P = 0.012), which increased to 1.38 (95% CI, 0.63-3.02; P = 0.417) in obese (BMI > 35) recipients. In addition, there was a tendency for recipients of normal BMI to have worse outcomes when receiving a small donor kidney, relative to a weight matched kidney (HR, 1.27; 95% CI, 1.05-1.54; P = 0.014).

Sensitivity Analysis

We undertook some sensitivity analyses replacing the weight mismatch with BSA mismatch to check the translatability of our findings between the 2 surrogate markers of nephron mass. We observed a correlation coefficient of 0.975 between weight and BSA mismatches, with 77% of cases being in the equivalent category. As such, reanalyzing the data using BSA mismatch gave similar findings (see **SDC, Materials and Methods; Tables S10-S11, SDC,** http://links.lww.com/TXD/A148, http://links.lww.com/TXD/A149).

DISCUSSION

In this contemporary analysis of deceased-donor kidney transplant recipients using a UK cohort of 11720 recipients receiving a deceased donor kidney between 2003 and 2015, we sought to investigate whether size mismatching based on weight was associated with any difference in graft and patient-related outcomes. Our analysis demonstrated that 12-month creatinine levels decline significantly as the weight of the donor, relative to the recipient, increases, although this does not appear to impact on risk for either delayed graft function or death-censored graft survival. However, multivariable analysis did identify an increased risk for death among recipients receiving larger kidneys.

Several studies assessing the impact of a donor-to-recipient size mismatch in the setting of adult kidney transplantation have reported conflicting outcomes. However, it is best to discuss the population-cohort studies, which have tended to show inferior long-term graft survival associated with smaller donor kidneys. First, Kasiske et al analyzed 32083 deceased donor kidney recipients from the USRDS data set for recipients between 1994 and 1999.[5] Their analysis found large recipients receiving kidneys from small donors (calculated from body surface area) had a 43% (95% CI, 17-75%; P = 0.0004) increased risk of late graft failure compared with medium-size recipients who received kidneys from medium-size donors. Medium-size recipients who received kidneys from small donors made up 12.0% of the population and had a 16% (95% CI, 6-26%; P = 0.0012) increased risk of late graft failure. In contrast to our surprise finding of increased mortality associated with receiving larger donated kidneys, Kasiske et al showed a nonsignificant trend toward better survival beyond 4-months for small recipients receiving large kidneys (although there was a trend toward poorer survival within the first 4-months). Goldberg et al,[6] analyzing SRTR data on 69737 deceased donor kidney recipients between 1992 and 2005, identified recipients of kidneys from substantially smaller donors (calculated by body surface area) had a similar 15% higher rate of graft loss (95% CI, 1.08-1.21, P < 0.0001), that was more pronounced in expanded criteria donors kidneys. Again, in contrast to our patient survival findings, Goldberg and colleagues identified a trend toward increased mortality in those with the largest BSA ratio (ie, larger recipient receiving smaller donor kidney), with an HR of 1.08 (95% CI, 0.99-1.08, P = 0.08). No significant

TABLE 5.

Summary of the significant interaction between weight difference and recipient BMI observed in the analysis of patient survival

	Univariable analysis						Multivariable analysis					
			Weight difference (donor weight/recipient weight)						Weight difference (donor weight/recipient weight)			
			<75%		>125%				<75%		>125%	
Recipient BMI, kg/m^2	N	Overall, *P*	Small donor kidney (relative to recipient)		Large donor kidney (relative to recipient)		N	Overall, *P*	Small donor kidney (relative to recipient)		Large donor kidney (relative to recipient)	
18.5-25.0	3789	0.025	1.10 (0.91-1.31)		1.10 (1.03-1.18)		3547	0.005	1.27 (1.05-1.54)		1.10 (1.02-1.18)	
25.1-30.0	3652	0.020	0.94 (0.85-1.05)		1.13 (1.02-1.25)		3428	0.155	0.97 (0.87-1.09)		1.10 (0.99-1.22)	
30.1-35.0	1889	0.100	0.94 (0.85-1.04)		1.31 (1.06-1.63)		1785	0.144	1.01 (0.91-1.13)		1.24 (1.00-1.55)	
>35.0	424	0.089	0.80 (0.65-0.99)		1.12 (0.55-2.28)		398	0.565	0.94 (0.76-1.17)		1.38 (0.63-3.02)	

Both univariable and multivariable Cox regression models were produced for each subgroup of recipient BMI, with the exception of <18.5, due to insufficient sample size. A full list of factors considered for inclusion in the multivariable analyses, as well as the methodology used and the full multivariable models (Tables S6-S9, SDC, http://links.lww.com/TXD/A144, http://links.lww.com/TXD/A145, http://links.lww.com/TXD/A146, http://links.lww.com/TXD/A147) are reported in the supplementary material. Quoted statistics are HRs and 95% CIs, and are relative to the no mismatch group (75%-125%). The "N" column reports the number of patients included in each analysis, after excluding those with missing data on 1 of the factors in the final model. The overall *P* value is a comparison between the 3 groups of weight difference, and *P* values in bold emphasis are significant at $P < 0.05$.

difference in mortality was observed in the opposite end of the spectrum (ie, smaller recipients receiving larger donor kidney), unlike our analysis. Finally, in an analysis of 115 214 kidney transplant recipients, Miller et al demonstrated that the highest risk of graft failure was seen in female recipients of male kidney donors, as well as male recipients of female donors when the recipients were 30 kg greater in weight than the donor. Again, this differs from our analysis, which demonstrated no significant difference in graft survival (overall and death-censored) between the weight mismatch groups.[7]

Our results require some explanations in the context of these comparisons to earlier population cohort studies. First, our observation of increased mortality in smaller recipients receiving larger donor kidneys must be interpreted with caution in the absence of any corroborative data to support this effect. Our data cannot ascertain a causal relationship between the 2, and it is speculative to attempt to identify any pathophysiology to link the 2. No difference in underlying cause of death was identified after review of death certificate registrations, and this association has not been observed in other data. We can speculate that recipients of larger kidneys perhaps have dynamic hemodynamic effects on their recipients, increasing cardiovascular risks, or that surgical complications associated with the size mismatch may lead to increased infective or traumatic complications, but these speculations lack any validation. Recent work from Reboldi and colleagues[8] sheds some possible insight into this, with work suggesting glomerular hyperfiltration is associated with a risk for adverse cardiovascular events. In their analysis of 8794 patients, during mean follow-up of 6.2 years, both high (HR, 1.5; 95% CI, 1.2-2.1) and low (HR, 2.0; 95% CI, 1.5-2.6) estimated glomerular filtration rate (eGFR) were independently associated with increased risk for adverse cardiovascular events in a multivariable Cox regression model, with no difference to HR magnitudes with the addition of BMI. However, although glomerular filtration rates are likely higher with a bigger kidney and hyperfiltration will occur in the context of a solitary kidney, there is no evidence to suggest a similar dynamic hyperfiltration circulation effect occurs. We suggest a corroborative data set from another contemporary population-cohort sample requires analysis to investigate whether our results are likely to be genuine.

However, we are reassured that the effects of size mismatch (although leading to a predictable difference in 1-year graft function, as determined by creatinine levels) do not impact on either the rate of DGF or longer-term graft survival in our analysis. This contrasts with findings from the aforementioned population-cohort studies, but we must distinguish the important differences between these analyses. Both cohorts were from a different era of transplantation, with Kasiske et al[5] and Goldberg et al.[6] analyzing data from cohorts from 1994 to 1999 and from 1992 to 2005, respectively. Our contemporary analysis, while lacking specific data in relation to immunosuppression, will represent a more contemporary cohort of patients on tacrolimus-based immunosuppression. Our analysis is also based on weight, in comparison to body surface area, which may limit direct comparisons between these different analyses. Our choice of weight reflected its more popular use and immediate accessibility when decisions are made regarding the acceptance of deceased donor kidneys. Therefore, from a real-world perspective, it makes more sense to analyze data using weight

rather than BSA. We acknowledge data from Tan and colleagues that suggested BSA is better than weight/BMI as a marker of renal cortical volume,[9] although there are also methodological limitations with the choice of BSA, including the arbitrary figure of 1.73 m^2 as the ideal BSA for a normal adult, which is inapplicable for a contemporary population.[10] However, our data are reassuring to show no difference in our outcome analysis regardless of whether weight difference or BSA was used for the donor.

There are several limitations in our analysis which should be acknowledged in the interpretation our results. Both weight and BSA may be poor surrogates for calculating nephron mass,[11] but they represent the only real-world data that is available that can influence the decision making process to accept a deceased donor kidney for transplantation. As per any retrospective analysis, there will be methodological limitations inherent to this type of analysis. For example, there are likely to be unmeasured and/or incompletely measured covariates that are not accounted for in the analysis that could affect graft function, survival or risk for mortality. It is unlikely that statistics can ever fully adjust for all confounding factors in a cohort study, and this is a limitation inherent to the very nature of observational analyses.

To conclude, our population-cohort analysis of a large contemporary group of deceased donor kidney transplant recipients suggests BMI mismatch affects 1-year creatinine, but has no impact on either delayed graft function or long-term graft survival. This should reassure transplant clinicians when accepting kidneys from smaller donors for larger recipients, as previous data has suggested inferior outcomes in this setting. Although our data have also raised the suggestion of increased mortality risk for smaller recipients receiving larger kidneys, this would require validation in a different cohort for confirmation. However, no causal association can be determined from our analysis, and we caution any direct conclusions to be drawn from the mortality data in the absence of any plausible biological explanation.

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