ORIGINAL ARTICLE

The impact of donor body mass index on outcomes after deceased kidney transplantation – a national population-cohort study

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SUMMARY

The aim of this study was to determine the effect of donor body mass index (BMI) on deceased donor kidney transplant outcomes. Data were collected from the UK Transplant Registry for all deceased donor kidney transplant recipients between January 2003 and January 2015. Univariable and multivariable analyses were undertaken to assess the impact of donor BMI on a range of outcomes. Donor BMI (kg/m^2) was stratified as <18.5 (n = 380), 18.5–25.0 (n = 6890), 25.1–30.0 (n = 6669), 30.1–35.0 (n = 2503) and >35.0 (n = 1148). The prevalence of delayed graft function increased significantly with donor BMI (P < 0.001), with an adjusted odds ratio of 1.38 (95% CI: 1.16–1.63) for the >35.0 vs. 18.5–25.0 groups. However, there was no significant association between donor BMI and 12-month creatinine (P = 0.550), or patient (P = 0.109) or graft (P = 0.590) survival. In overweight patients, increasing donor BMI was associated with a significant increase in warm ischaemia time and functional warm ischaemia time, by an average of 4.6% (P = 0.043) and 5.2% (P = 0.013) per 10.0 kg/m^2. However, rising warm ischaemic time and functional warm ischaemic time was not significantly associated with delayed graft function, 12-month creatinine levels, graft loss or patient death. In this population cohort study, we identified no significant association between donor BMI and long-term clinical outcomes in deceased donor kidney transplantation.

Transplant International 2018; 31: 1099–1109

Key words
donor body mass index, donor registries, kidney clinical, post-transplant outcomes

Received: 30 November 2017; Revision requested: 8 January 2018; Accepted: 10 April 2018;
Published online: 9 May 2018

Introduction

The continued disparity in the supply versus demand for deceased donor kidneys to facilitate transplantation is well known. Efforts have been made to bridge this gap by expanding the donor pool, using approaches such as increasing the utilization of more 'marginal' donors that may have been declined previously [1]. Data from the UK Transplant Registry highlight the trend for increasing body mass index (BMI) among deceased organ donors, with the proportion of clinically obese donors (BMI 30 or higher) increasing from 19% to 25% over the last decade [2]. Obesity continues to be a major public health issue and it is inevitable that current trends of increasing donor BMI will continue. This mirrors parallel increases in recipient BMI and

doi:10.1111/tri.13263

subsequent inferior post-transplantation outcomes noted for obese recipients with a BMI greater than 35 (although underweight recipients with BMI <18.5 also perform badly, with worse graft survival overall) [3].

Deceased donor procurement surgery is more challenging for donors with elevated BMI. There are particular concerns in the context of donors after cardiac death (DCD), whereby a delay in achieving aortic cannulation and cold perfusion would result in a more prolonged warm ischaemia time (WIT), which is known to confer impaired recipient outcomes [4–7]. In addition to these technical factors, general adiposity has been shown to cause significant kidney damage, predominantly through dysregulation of adipokines and promotion of kidney-specific inflammation [8]. It could be hypothesized that inflammatory processes after transplantation may result in greater immune-mediated damage to the kidney from obese donors, significantly impairing their outcomes. Finally, while the association between obesity and disease processes affecting renal function (e.g. diabetes and hypertension) are well established, the degree of risk conferred by elevated BMI alone is not clear [9].

There is a paucity of evidence on the impact of deceased donor BMI on post-kidney transplant outcomes. There are no national or international recommendations in relation to the limit of donor BMI extremes that is acceptable. Resultantly, there is broad variability in practice and heterogeneous acceptance criteria of deceased donor BMI by transplantation centres, with some centres adopting arbitrary donor BMI limits (e.g. 35.0 kg/m^2). However, in the absence of clear clinical evidence to suggest adverse recipient outcomes, such arbitrary restrictions may be misguided and limit the potential donor pool for people on the deceased donor national waiting list.

Therefore, the aim of our study was to determine whether increased donor BMI is an independent risk factor for poor outcomes following deceased donor kidney transplantation. In addition, we assessed a subcohort of DCD kidney transplants to determine if a raised BMI significantly increases WIT and whether this had prognostic implications. This will help inform transplant clinicians to make evidence-based decisions as to the clinical utility of deceased donor kidneys offered for transplantation.

Patients and methods

Our analysis included all adult patients (aged 18 years of age 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 paediatric donors). Data were obtained from the UK Transplant Registry, held by NHS Blood and Transplant, to which every kidney transplant centre 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 dataset, with approval sought and obtained from the Kidney Advisory Group.

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 creatinine levels at 12-months' post-kidney transplantation. Analysis of patient survival and overall graft survival only included those patients receiving their first graft. DGF was defined as need for dialysis within the first week after kidney transplantation. The standard definition of warm ischemia time (WIT) is the period of time from asystole until aortic cannulation and cold perfusion. However, we additionally defined functional warm ischaemia time (fWIT) as the time commencing once the donor's physiological variables drop below certain thresholds, namely a systolic blood pressure of less than 50 mm Hg or an arterial oxygen saturation less than 70%, until aortic cannulation and cold perfusion.

Statistical analysis

We first compared a range of factors across the donor BMI groups, using Kruskal–Wallis tests for continuous variables, and χ^2 tests for nominal variables. A range of outcome measures were then compared across the groups, with Kaplan–Meier curves and log-rank tests used for those relating to survival. Multivariable analyses were then performed, to assess the relationship between donor BMI and the outcomes being considered, after accounting for the potentially confounding effects of various demographic and perioperative characteristics. Analysis of the survival outcomes were performed with Cox regression models, with binary logistic regression models used for DGF. Creatinine levels were found to follow a skewed distribution, and so values were $\log_{10}$-transformed to normalize the distribution, before being analysed using general linear models. Variables were selected for inclusion in the models using a stepwise approach, to identify independent predictors of

Transplant International 2018; 31: 1099–1109

outcome. A full description of the statistical methodology used in the multivariable analysis can be found as a Supporting Information.

Associations between donor BMI and both WIT and fWIT were then assessed. Both WIT and fWIT were found to follow a skewed distribution; hence, values were $\log_{10}$-transformed, prior to the analysis, to normalize the distribution and improve model fit. Potential non-linearity was assessed by producing penalized cubic spline regression models. Where a linear relationship was indicated by these models, a linear regression approach was used, to give a more easily interpretable summary of the relationship between BMI and both WIT and fWIT. A set of multivariable analyses were then performed, to assess the relationships between WIT/fWIT and recipient outcomes, using a similar approach to that previously described.

Categorical variables are presented as numbers and rates, with continuous variables reported as medians and interquartile ranges (IQRs). All analyses were performed using SPSS® version 22 (IBM, Armonk, NY, USA). A P value <0.050 was considered statistically significant in our analysis.

Results

Study cohort

Data were available for a total of 17 590 deceased donor kidney transplants. Breakdown of the cohort, stratified by donor BMI, was as follows; <18.5 kg/m^2 (n = 380, 2.2%), 18.5–25.1 kg/m^2 (n = 6890, 39.2%), 25.1–30.0 kg/m^2 (n = 6669, 37.9%), 30.1–35.0 kg/m^2 (n = 2503, 14.2%) and >35.0 kg/m^2 (n = 1148, 6.5%). Table 1 compares a range of factors between these five groups of donor BMI. Data were relatively complete for the majority of factors, being recorded in >90% of cases. The only exception was the recipient BMI, which was only available for 66.6% of cases. In addition, the WIT and/or fWIT was only applicable to the 5521 DCD transplants and was recorded in 62.6% and 56.2% for WIT and fWIT, respectively.

Increasing donor BMI was found to be associated with increasing donor age, as well as increasing rates of donor diabetes and hypertension, but decreasing rates of smoking (all $P < 0.001$). A significant association with donor gender was also observed ($P < 0.001$), with males underrepresented in the extreme BMI categories (i.e. <18.5 and >35.0 kg/m^2). Organs from donors with increasing BMI were found to be transplanted into recipients of significantly higher age and BMI ($P < 0.001$), and to be significantly less likely to be used in recipients on dialysis at transplant ($P = 0.042$). CIT was found to decrease significantly with increasing BMI, whilst WIT showed a small increase (both $P < 0.001$). fWIT, on the other hand, appeared to have a U-shaped relationship with donor BMI, being highest in the extremes (median = 22 vs. 19 min for <18.5 vs. >35.0 kg/m^2), whilst remaining relatively consistent for the centre groups, at a median of 18 min.

Donor BMI and outcomes

Univariable analysis

Univariable comparisons of recipient outcomes between the five donor BMI groups are reported in Table 2. Both patient survival ($P < 0.001$) and overall graft survival ($P < 0.001$) were found to differ significantly with donor BMI, with rates at 1 year for the 18.5–25.0 kg/m^2 vs. >35.0 kg/m^2 groups of 98.3% vs. 96.6% for patient survival, and 91.6% vs. 90.6% for overall graft survival. No significant difference in death-censored graft survival was detected ($P = 0.603$), with 1-year survival rates of 92.6% vs. 94.3%. Furthermore, recipient creatinine levels at 1 year were found to increase significantly with donor BMI ($P < 0.001$), from a median of 130 mmol/l in the 18.5–25.0 kg/m^2 group to 135 mmol/l in the >35.0 kg/m^2 group. Rates of DGF were also found to increase significantly with donor BMI ($P < 0.001$), with 25.6% vs. 32.2% in the 18.5–25.0 kg/m^2 vs. >35.0 kg/m^2 groups.

Multivariable analysis

To account for the effect of potentially confounding factors, comparisons between the donor BMI groups were then repeated using a multivariable approach. The resulting models are reported in full in Tables S3–S7, and summarized in Table 3. On multivariable analysis, no significant associations were detected between donor BMI and either patient survival ($P = 0.109$), death-censored graft survival ($P = 0.093$), overall graft survival ($P = 0.590$) or creatinine levels at 12 months ($P = 0.550$). Further analysis found that this was largely due to the adjustment for donor age, which was found to be significantly associated with donor BMI, and to be significantly predictive of all of the outcomes considered. As such, multivariable models containing only donor age and BMI as predictors found the latter to be non-significant for all four of these outcomes. To assess whether the short-term graft outcomes differed by donor BMI, and as a validation of the proportional

Table 1. Baseline demographics of the study cohort.

		Donor BMI (kg/m^2)					
	Valid *N*	<18.5	18.5–25.0	25.1–30.0	30.1–35.0	>35.0	*P* value
N (%)	17 590	380 (2.2%)	6890 (39.2%)	6669 (37.9%)	2503 (14.2%)	1148 (6.5%)	–
Recipient							
Age (years)	17 590	49 (41–60)	50 (40–59)	52 (42–61)	52 (42–62)	52 (42–61)	**<0.001**
Gender (male)	17 580	56.6%	62.6%	63.5%	63.0%	64.5%	0.600
BMI (kg/m^2)	11 720	25.9 (23.7–29.7)	25.6 (22.7–29.3)	26.0 (23.2–29.6)	26.3 (23.2–29.6)	26.2 (23.0–29.2)	**<0.001**
Ethnicity							
White	17 541	77.8%	78.2%	78.1%	78.1%	77.6%	0.739
Asian		11.9%	13.9%	13.6%	13.9%	13.1%	
Black		8.4%	6.5%	7.0%	6.6%	8.1%	
Other		1.8%	1.4%	1.3%	1.4%	1.2%	
Diabetes	17 590	7.4%	7.5%	8.7%	8.7%	7.1%	**0.041**
Graft no							
1	17 590	86.6%	84.6%	85.7%	86.3%	85.9%	0.328
2		9.5%	12.6%	12.1%	11.7%	11.8%	
>2		3.9%	2.7%	2.1%	2.4%	2.5%	
CMV positive	16 047	51.0%	51.4%	53.4%	53.2%	52.0%	0.203
Dialysis at transplant	17 567	91.5%	91.6%	89.9%	88.9%	88.3%	**0.042**
Donor							
Age (years)	17 590	43 (30–55)	49 (36–59)	54 (44–62)	54 (45–63)	53 (45–61)	**<0.001**
Gender (male)	17 590	42.1%	51.3%	58.2%	52.5%	37.3%	**<0.001**
Ethnicity							
White	17 582	95.8%	95.8%	96.2%	96.4%	95.6%	0.701
Asian		2.6%	2.0%	2.0%	1.7%	1.9%	
Black		0.8%	1.1%	1.0%	1.3%	1.4%	
Other		0.8%	1.0%	0.8%	0.7%	1.1%	
Diabetes	16 112	3.6%	3.1%	5.6%	10.6%	15.9%	**<0.001**
Hypertension	16 967	11.1%	18.4%	28.9%	38.4%	42.3%	**<0.001**
Smoking	17 176	65.1%	53.4%	46.5%	41.3%	37.7%	**<0.001**
Transplant							
Waiting time (days)	17 571	810 (355.5–1420)	870 (374.5–1498.5)	887 (388–1476)	856 (381–1461)	876 (425–1429)	0.670
HLA mismatch							

Table 1. Continued.

	Valid *N*	Donor BMI (kg/m^2)					*P* value
		<18.5	18.5–25.0	25.1–30.0	30.1–35.0	>35.0	
1	17 589	12.9%	15.6%	14.2%	13.1%	11.4%	**<0.001**
2		31.8%	34.7%	34.5%	33.1%	34.3%	
3		49.2%	42.3%	44.5%	46.7%	48.2%	
4		6.1%	7.5%	6.8%	7.1%	6.1%	
Sensitization (>0)	17 590	33.4%	33.9%	33.6%	33.8%	33.8%	0.990
Antibody incompatibility							
Compatible	17 590	98.4%	98.9%	99.0%	99.2%	99.0%	0.451
HLAi		1.6%	1.1%	0.9%	0.8%	1.0%	
ABOi		0.0%	0.0%	0.0%	0.0%	0.1%	
CIT (minutes)	17 384	958 (739.5–1178)	941 (763–1161)	937 (750–1144)	921.5 (727–1123)	908.5 (725.5–1087)	**<0.001**
WIT (minutes)	3457	12 (10–23)	12 (10–15)	12 (10–15)	13 (10–16)	13 (11–15.5)	**<0.001**
fWIT (minutes)	3104	22 (17–30)	18 (15–23)	18 (15–23)	18 (15–24)	19 (16–23)	**<0.001**

HLAi, HLA-incompatible; ABOi, ABO-incompatible; CIT, cold ischaemia time; fWIT, functional warm ischaemia time; WIT, warm ischaemia time.

Data are reported as median (IQR), with p values from Kruskal–Wallis tests, or as column percentages, with p values from Chi-square tests, as applicable. Bold *P* values are significant at $P < 0.05$.

hazards assumption in the primary survival outcomes, we also performed a multivariable analysis of 90-day overall-graft survival. This found no significant difference across the BMI groups ($P = 0.794$, Table S9).

The association between donor BMI and DGF remained significant on multivariable analysis ($P < 0.001$). The rates of DGF were found to increase progressively as donors became increasingly overweight, with odds ratios of 1.12 ($P = 0.022$), 1.23 ($P < 0.001$) and 1.38 ($P < 0.001$) for donor BMIs of 25.1–30.0, 30.1–35.0 and >35.0 kg/m^2, respectively, relative to those of a normal weight (BMI: 18.5–25.0 kg/m^2).

Donor BMI and warm ischemic time

A set of analyses were then performed on the subgroup of DCD kidney transplant procedures, to assess whether increasing donor BMI was associated with a longer WIT or fWIT. There were a total of 5521 DCD transplants, making up 31.4% of the total cohort. Of these, 3593 had either WIT and/or fWIT recorded. Median WIT and fWIT for the entire cohort was 13 min (IQR: 10–25) and 18 min (IQR: 15–23), respectively, and both were found to differ significantly with donor BMI ($P < 0.001$, Table 1), as previously described.

As this relationship appeared to be non-linear, penalized cubic spline regression models were initially produced for the two outcomes (Fig. 1). These found that both WIT and fWIT demonstrated a near-linear increase with donor BMI in overweight (>25 kg/m^2) donors, with a weaker or inverse relationship for normal or underweight donors. As a result, linear regression models were produced for donors with BMI >25 kg/m^2, to quantify the relationship between donor BMI and both WIT and fWIT in this cohort. The resulting models found a small but significant association between BMI and both WIT and fWIT, with WIT increasing by 4.6% (0.1–9.2%, $P = 0.043$) and fWIT by 5.2% (95% CI: 1.1–9.5%, $P = 0.013$) per 10.0 kg/m^2. Although significant, these increases are equivalent to differences between donors with BMIs of 50.0 vs. 25.0 kg/m^2 of only 1.5 min (14.0 vs. 12.5 min) in WIT and 2.5 min (21.2 vs. 18.7 min) in fWIT.

A set of multivariable analyses were then performed, to assess whether increasing WIT could adversely affect patient outcomes. These analyses found no evidence that either WIT (Table 4) or fWIT (Table 5) had a significant association with patient, graft, or death-censored graft survival, or with either DGF or 12-month creatinine.

Table 2. Relationship between donor BMI and post-transplant outcomes by univariable analysis.

			Donor BMI (kg/m^2)									
			<18.5 (underweight)		18.5–25.0 (normal weight)		25.1–30.0 (overweight)		30.1–35.0 (obese)		>35.0 (morbidly obese)	
	N	Overall *P* value	Statistic	*P*-value	Statistic	*P* value	Statistic	*P* value	Statistic	*P* value	Statistic	*P* value
Patient survival*	15 000	**<0.001**	0.71 (0.49–1.10)	0.059	1.00 (reference)	–	1.17 (1.06–1.29)	**0.002**	1.18 (1.03–1.36)	**0.014**	1.33 (1.11–1.59)	**0.002**
Overall graft survival*	14 992	**<0.001**	0.91 (0.72–1.15)	0.429	1.00 (reference)	–	1.14 (1.06–1.23)	**<0.001**	1.10 (0.99–1.22)	**0.068**	1.28 (1.12–1.47)	**<0.001**
DCGS*	17 561	0.603	0.95 (0.72–1.25)	0.723	1.00 (reference)	–	1.05 (0.96–1.14)	0.278	1.05 (0.93–1.19)	0.418	1.11 (0.95–1.31)	0.198
12-Month creatinine†	14 750	**<0.001**	0.95 (0.90–1.01)	0.080	1.00 (reference)	–	1.03 (1.02–1.05)	**<0.001**	1.05 (1.02–1.07)	**<0.001**	1.03 (1.00–1.07)	**0.042**
DGF‡	17 590	**<0.001**	0.97 (0.76–1.23)	0.798	1.00 (reference)	–	1.23 (1.14–1.32)	**<0.001**	1.36 (1.23–1.50)	**<0.001**	1.38 (1.21–1.58)	**<0.001**

DCGS, death-censored graft survival; DGF, delayed graft function.

All statistics are relative to the normal BMI group of 18.5–25.0 kg/m^2.

*Survival outcomes were analysed using Cox regression models, and the reported statistics are hazard ratios.

†Creatinine was found to follow a skewed distribution, and so was $\log_{10}$-transformed, then analysed using a general linear model. The resulting coefficients were then anti-logged, and are reported as fold-differences in creatinine levels between groups. Values in Brackets are 95% per cent confidence intervals. Bold *P* values are significant at $P < 0.05$.

‡DGF was analysed using a binary logistic regression model, and the reported statistics are odds ratios.

Table 3. Adjusted relationship between donor BMI and post-transplant outcomes by multivariable analysis.

			Donor BMI (kg/m^2)									
			<18.5 (underweight)		18.5–25.0 (normal weight)		25.1–30.0 (overweight)		30.1–35.0 (obese)		>35.0 (morbidly obese)	
	N	Overall *P* value	Statistic	*P* value	Statistic	*P* value	Statistic	*P* value	Statistic	*P* value	Statistic	*P* value
Patient survival*	9865	0.109	0.61 (0.34–1.08)	0.089	1.00 (reference)	–	0.98 (0.86–1.12)	0.745	1.04 (0.88–1.24)	0.649	1.25 (0.98–1.59)	0.062
Overall graft survival*	9792	0.590	1.04 (0.75–1.46)	0.810	1.00 (reference)	–	0.97 (0.88–1.07)	0.550	0.96 (0.84–1.10)	0.520	1.11 (0.93–1.33)	0.240
DCGS*	11 237	0.093	1.17 (0.81–1.70)	0.401	1.00 (reference)	–	0.88 (0.78–0.99)	0.033	0.84 (0.72–0.99)	0.040	0.91 (0.73–1.14)	0.415
12-Month creatinine†	9314	0.550	0.98 (0.95–1.01)	0.470	1.00 (reference)	–	0.99 (0.97–1.01)	0.580	1.00 (0.98–1.01)	0.440	0.98 (0.94–1.03)	0.110
DGF‡	11 564	**<0.001**	1.06 (0.78–1.44)	0.720	1.00 (reference)	–	1.12 (1.00–1.23)	**0.022**	1.23 (1.08–1.39)	**<0.001**	1.38 (1.16–1.63)	**<0.001**

DCGS, death-censored graft survival; DGF, delayed graft function.

All statistics are relative to the normal BMI group of 18.5–25.0 kg/m^2. A full list of factors considered for inclusion is available in the statistical methodology section of the Supporting Information. Further information about the methodology used is reported in the Supporting Information.

*Survival outcomes were analysed using Cox regression models, and the reported statistics are hazard ratios.

†Creatinine was found to follow a skewed distribution, and so was $\log_{10}$-transformed, then analysed using a general linear model. The resulting coefficients were then anti-logged, and are reported as fold-differences in creatinine levels between groups. Values in Brackets are 95% per cent confidence intervals. Bold *P* values are significant at $P < 0.05$.

‡DGF was analysed using a binary logistic regression model, and the reported statistics are odds ratios.

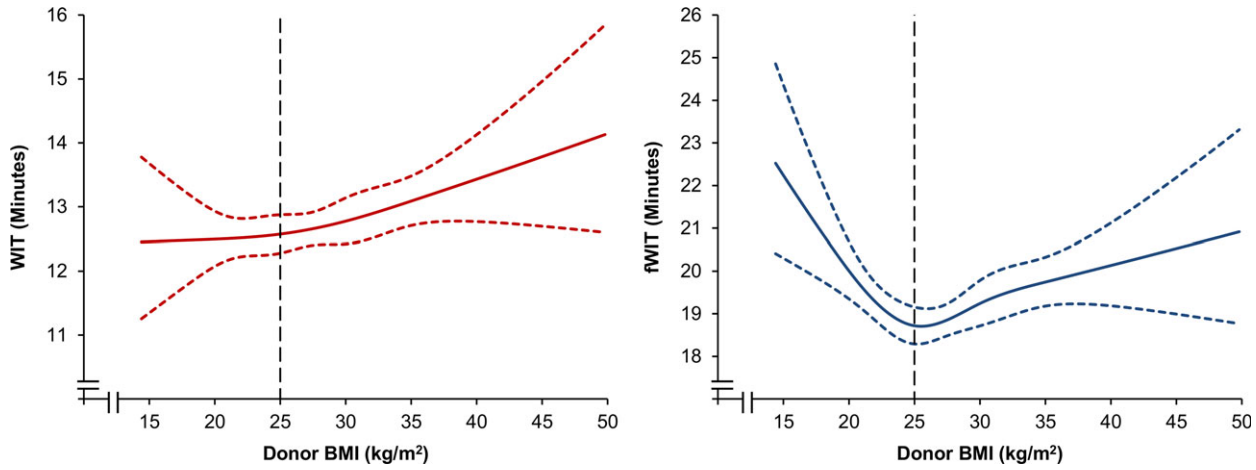

Figure 1 Results of a penalized cubic spline regression model, estimating the relationships between donor body mass index and both functional warm ischaemic time and warm ischaemic time.

Discussion

In this national population cohort study, donor BMI was found to be an independent risk factor for DGF in recipients of kidneys from overweight (OR: 1.12, 95% CI: 1.00–1.23, $P = 0.022$), obese (OR: 1.23, 95% CI: 1.08–1.39, $P < 0.001$) and morbidly obese (OR: 1.38, 95% CI: 1.16–1.63, $P < 0.001$) donors, when compared to the normal donor BMI group. However, donor BMI did not appear to influence long-term graft survival or patient survival. Furthermore, donor BMI does not appear to be associated with a deleterious increase in either the WIT or fWIT.

The finding that donor BMI is an independent risk factor for DGF, but not graft failure, are corroborated in a number of studies. In a separate multivariable analysis of 6932 recipients of DCD kidneys in the United States, Ortiz *et al.* [10] reported donors with a BMI between 30.0 and 34.9 kg/m^2 incurred a 1.77-fold increased odds of developing DGF. Furthermore, similar odds of DGF were seen for donors with a BMI between 35.0 and 39.9 kg/m^2 (OR: 1.78, $P < 0.001$). However, although BMI impacted on DGF rates, only DCD kidneys from donors with a BMI >45.0 kg/m^2 were associated with an increased risk of death-censored graft failure (adjusted HR: 1.84, 95% CI 1.23–2.74, $P < 0.001$) relative to the normal donor BMI category. Furthermore, a separate multivariable analysis of 6507 kidney transplant recipients assessed the outcomes for DCD kidneys by donor weight. Overall, it appeared that an increased donor weight was an independent predictor of DGF, but not graft failure in the first 90 days after transplantation [11].

From a causative perspective, the minimal influence of donor BMI on graft outcomes could relate to the nephron mass of the donated kidney. For example, several studies report obese individuals to have larger kidneys, which means greater cortical volume and thus higher filtration rates [12,13]. Therefore, it could be speculated that the increased nephron mass of obese donor kidneys protects the recipient from graft failure [14,15]. However, on multivariable analysis, we did not demonstrate any significant difference in the 12-month creatinine for recipients of underweight or obese donor kidneys relative to the normal BMI donor group. Therefore, the impact of nephron mass on post-transplant outcomes, especially in the context of obese donor kidneys, remains unclear.

The finding that donor BMI appears to increase the probability of DGF is of interest and requires further study. DGF is important, and has been recognized as a predictive factor for kidney transplant outcomes. In a recent meta-analysis by Yarlagadda *et al.* [16], kidneys with DGF were shown to have a 14% increased risk of failure, 8% increased risk of acute rejection and worse graft function at 3.2 years after transplantation. However, despite their higher rate of DGF, our analysis did not find obese donor kidneys to have poorer long-term outcomes. We speculate that this may relate to different pathophysiology of DGF, and therefore disparate outcomes in the context of obese donor kidneys, and feel that this hypothesis is worthy of further investigation.

Overall, damage to the kidney tubules caused by ischaemia and/or anoxia (either during donor nephrectomy, kidney preservation or after anastomotic integration of the kidney) is thought to be the primary

Table 4. Adjusted relationship between warm ischaemic time and post-transplant outcomes.

			Warm ischaemia time (WIT)									
			<10 min		10–12 min		13–14 min		14–16 min		>17 min	
	N	Overall *P* value	Statistic	*P* value	Statistic	*P* value	Statistic	*P* value	Statistic	*P* value	Statistic	*P* value
Patient survival*	2410	0.582	1.00 (reference)	–	0.76 (0.51–1.13)	0.170	0.86 (0.58–1.27)	0.436	0.78 (0.47–1.29)	0.324	0.73 (0.46–1.16)	0.187
Overall graft survival*	2394	0.736	1.00 (reference)	–	0.92 (0.69–1.22)	0.567	0.81 (0.60–1.09)	0.163	0.93 (0.65–1.33)	0.684	0.95 (0.69–1.31)	0.738
DCGS*	2645	0.888	1.00 (reference)	–	1.09 (0.76–1.56)	0.650	0.98 (0.67–1.42)	0.894	1.21 (0.78–1.86)	0.393	1.33 (1.02–1.72)	0.689
DGF†	2649	0.697	1.00 (reference)	–	0.96 (0.76–1.21)	0.749	0.85 (0.67–1.07)	0.163	0.90 (0.68–1.19)	0.462	0.94 (0.72–1.13)	0.644
12-Month creatinine‡	2094	0.178	1.00 (reference)	–	1.02 (0.98–1.06)	0.262	1.04 (1.00–1.09)	**0.038**	1.00 (0.95–1.05)	0.953	1.04 (0.99–1.09)	0.108

DCGS, death-censored graft survival; DGF, delayed graft function.

All statistics are relative to the shortest WIT group of <10 min. A full list of factors considered for inclusion is available in the statistical methodology section of the Supporting Information. Further information about the methodology used is reported in the Supporting Information.

*Survival outcomes were analysed using Cox regression models, and the reported statistics are hazard ratios.

†DGF was analysed using a binary logistic regression model, and the reported statistics are odds ratios.

‡Creatinine was found to follow a skewed distribution, and so was $\log_{10}$-transformed, then analysed using a general linear model. The resulting coefficients were then anti-logged, and are reported as fold-differences in creatinine levels between groups. Values in Brackets are 95% per cent confidence intervals. Bold *P* values are significant at $P < 0.05$.

Table 5. Adjusted relationship between functional warm ischemic time and post-transplant outcomes.

			Functional warm ischaemia time (minutes)							
			<15 min		16–20 min		21–25 min		>26 min	
	N	Overall *P* value	Statistic	*P* value	Statistic	*P* value	Statistic	*P* value	Statistic	*P* value
Patient survival*	2184	0.513	1.00 (reference)	–	1.02 (0.69–1.50)	0.934	1.34 (0.88–2.03)	0.178	1.09 (0.71–1.69)	0.685
Overall graft survival*	2173	0.693	1.00 (reference)	–	1.10 (0.83–1.44)	0.518	1.08 (0.78–1.49)	0.640	1.21 (0.89–1.64)	0.230
DCGS*	2393	0.486	1.00 (reference)	–	1.04 (0.74–1.44)	0.830	0.79 (0.52–1.20)	0.269	1.10 (0.76–1.60)	0.614
DGF†	2394	0.489	1.00 (reference)	–	0.85 (0.68–1.05)	0.128	0.95 (0.73–1.22)	0.677	0.93 (0.72–1.19)	0.559
12-Month creatinine‡	1895	0.148	1.00 (reference)	–	1.04 (1.00–1.08)	0.072	1.04 (0.99–1.09)	0.188	1.05 (1.00–1.10)	**0.043**

DCGS, death-censored graft survival; DGF, delayed graft function.

All statistics are relative to the shortest fWIT group of <15 min. A full list of factors considered for inclusion is available in the statistical methodology section of the Supporting Information. Further information about the methodology used is reported in the Supporting Information.

*Survival outcomes were analysed using Cox regression models, and the reported statistics are hazard ratios.

†DGF was analysed using a binary logistic regression model, and the reported statistics are odds ratios.

‡Creatinine was found to follow a skewed distribution, and so was $\log_{10}$-transformed, then analysed using a general linear model. The resulting coefficients were then anti-logged, and are reported as fold-differences in creatinine levels between groups. Values in Brackets are 95% per cent confidence intervals. Bold *P* values are significant at $P < 0.05$.

determinant of DGF. It has been speculated that increased technical challenges associated with organ retrieval in obese individuals may delay aortic cannulation and thus harmfully lengthen the WIT, with a subsequent negative impact on DGF and graft failure for the recipient. However, only a modest increase in both WIT and fWIT in morbidly obese donors was identified in the current analysis. Furthermore, this did not translate to inferior graft outcomes. Therefore, our results should provide cautious reassurance about the WIT/fWIT risks associated with procurement of obese deceased donor kidneys. However, our data do not assess actual recovery and extraction times, which may be prolonged in more obese donors, and this limitation should be considered in the interpretation of our data.

The results of our study should be interpreted after acknowledgement of its limitations. Firstly, while we have utilized the standard accepted definition of DGF (need for dialysis within the first year post-kidney transplantation), this definition has been criticized for its subjective nature. The lack of raw-level data relating to daily creatinine levels post-kidney transplantation limits the calculation of functional DGF, defined as a failure of serum creatinine to decrease by at least 10% daily on three successive days during the first week post-kidney transplantation. Functional DGF has been shown to be superior to the traditional definition of DGF as a predictor of long-term graft failure [17]. Although we have adjusted for several covariates in the multivariable model, it is possible that other confounding variables have not been considered (e.g. centre-specific variables). Whilst WIT/fWIT are the most pertinent variables for organ retrieval operations, it would be interesting to compare the total operative time between obese and non-obese donors. This would allow us to validate the assumption that procuring organs from obese donors is technically more challenging. Moreover, a small number of studies have reported that, for obese donor kidneys, there is a deleterious increase in the time taken to fashion the renal artery anastomosis [18]. This is important to note, as prolonged anastomosis time has been shown to lead to worse graft-related outcomes for kidney transplant recipients in a single-centre study, although donor BMI was not included in the statistical analysis as a risk factor [18]. Furthermore, once this anastomosis has been created, it has been speculated that obese donor kidneys take longer to re-perfuse. Both of these factors are thought to be caused by certain obesity-related co-morbidities (e.g. renal artery atherosclerosis and arteriosclerosis), and are shown to negatively impact graft survival. However, due to the limitations of registry data, we are unable to assess how both of these variables change with rising donor BMI although this would be of significant interest to explore further. In addition, BMI may be an inferior assessment of obesity compared to other markers assessing abdominal girth (e.g. waist–hip ratio), but this data is not collected at present for registry submissions. We also did not have the necessary data to estimate GFR values, which may have provided a more accurate assessment of kidney function after adjustment for body size and/or weight. Finally, our study is likely to be under-powered for accurate interpretation of sub-analyses for more extreme obese donors.

To conclude, this study has shown higher odds of delayed graft function in recipients of deceased kidneys with a donor BMI in the 'overweight', 'obese' and 'morbidly obese' ranges. However, this increased need for dialysis within the first week post-kidney transplantation did not result in significantly impaired patient survival, graft survival or renal function in the long-term for these recipients of organs from high BMI donors. Thus, the associated deleterious relationship between DGF and long-term outcomes may not apply to recipients of high BMI donor kidneys. Our data suggest perceptions relating to the use of obese deceased donor kidneys are misguided and, in the context of increasing BMI in the deceased donor kidney pool, support the utilization of these kidneys for transplantation.

Authorship

AA, JN and AS: designed study. AA and IC: data extraction. AA, JH, JN and AS: data analysis. AA, JH, JN, NI, AR and AS: data interpretation. AA, JH, JN and AS: wrote original draft. All authors reviewed manuscript.

Funding

The authors have declared no funding.

Conflicts of Interest

The authors have declared no conflicts of interest.

Acknowledgements

We are grateful to the UK Transplant Registry for the accessibility of the data.

SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article:

Appendix S1. Statistical methodology.

Table S1. Patient demographics.

Table S2. Matching/transplant factors.

Table S3. Multivariable analysis of factors predictive of patient survival.

Table S4. Multivariable analysis of factors predictive of graft failure.

Table S5. Multivariable analysis of factors predictive of death censored graft survival.

Table S6. Multivariable analysis of factors predictive of 12-month creatinine level.

Table S7. Multivariable analysis of factors predictive of delayed graft function.

Table S8. Adjusted relationship between donor BMI and post-transplant outcomes by multivariable analysis.

Table S9. Adjusted relationship between donor BMI and 90-day overall graft survival.

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