Transplant International ISSN 0934-0874

ORIGINAL ARTICLE

Estimated donor glomerular filtration rate is the most important donor characteristic predicting graft function in recipients of kidneys from live donors

Carmel M. Hawley,[1] Jamie Kearsley,[2] Scott B. Campbell,[1] David W. Mudge,[1] Nicole M. Isbel,[1] David W. Johnson,[1] Kylie May,[1] John Preston,[2] Anthony Griffin,[3] Daryl Wall,[3] John Burke,[1] Steven J. McTaggart,[1] Gayle Frohloff[2] and David Nicol[2,3]

1 Department of Nephrology, Southern Clinical School, University of Queensland, Princess Alexandra Hospital, Brisbane, Qld, Australia
2 Department of Urology, Princess Alexandra Hospital, Brisbane, Qld, Australia
3 Department of Surgery, Southern Clinical School, University of Queensland, Princess Alexandra Hospital, Brisbane, Qld, Australia

Keywords
cohort study, glomerular filtration rate, living donor, renal transplantation.

Correspondence
Dr David Nicol, Department of Urology, Princess Alexandra Hospital, Ipswich Road, Woolloongabba, Brisbane, Qld 4102, Australia. Tel.: +61 7 3240 5562; fax: +61 7 3240 2560; e-mail: d.nicol@uq.edu.au

Received: 24 April 2006
Revision requested: 15 May 2006
Accepted: 12 September 2006

doi:10.1111/j.1432-2277.2006.00400.x

Abstract

We hypothesized that predictors of outcome in live donor transplants were likely to differ significantly from deceased donor transplants, in which cold ischaemia time, cause of donor death and other donor factors are the most important predictors. The primary aim was to explore the independent predictors of graft function in recipients of live donor kidneys (LDK). Our secondary aim was to determine which donor characteristics are the most useful predictors. A retrospective analysis was undertaken of all patients receiving live donor ($n = 206$) renal transplants at our institution between 31 May 1994 and 15 October 2002. Twelve patients were excluded from the analysis. Follow-up was completed on all patients until graft loss, death or 22 November 2003. We explored predictors of Nankivell glomerular filtration rate (GFR) at 6 months by multivariate linear regression. In the 194 patients studied, the mean recipient 6-month Nankivell GFR was 59 ± 15 ml/min/1.73 m^2. Independent predictors of recipient GFR in at 6 months were donor Cockcroft-Gault GFR (CrCl; β 0.16; CI 0.13 to 0.29; $P < 0.0001$), steroid resistant rejection (β–6.07; CI −12.05 to −0.09; $P = 0.006$) and delayed graft function (DGF) (β–10.0; CI −19.52 to −0.49; $P = 0.039$). Renal function in an LDK transplant recipients is predicted by donor GFR, episodes of steroid resistant rejection and DGF. Importantly, donor Cockcroft-Gault GFR is the most important characteristic for predicting the recipient renal function.

Introduction

The spotlight in renal transplantation is increasingly shifting from the end-point of early rejection and graft loss to the level of renal function and long-term graft survival. Live donors as a proportion of all donors are increasing and now provide 40% of kidneys for transplantation in Australia [1]. Thus, the factors that predict outcomes of live donor kidney (LDK) transplants are also becoming increasingly relevant. Factors which affect graft outcomes in renal allograft recipients can be categorized into donor, recipient and immunological factors. However, many of the donor factors that have been characterized as predictors of graft outcomes relate to factors such as cold ischaemia time and cause of donor death, which are not relevant to recipients of LDKs.

Predictors of graft outcomes in recipients of live donor transplants are not as well described as they have been in the recipients of deceased donor renal transplants. Matas *et al.* [2] have reported that whereas both immunologic and nonimmunologic factors are important in determining the outcome of deceased donor renal transplantation,

immunologic factors were of pre-eminent importance in live-donor transplants. However, despite the obvious ability to explore donor characteristics in detail in recipients of LDK transplants, there is a paucity of published information in this area.

There have been a number of studies reporting that renal function in the first year of transplantation is an important factor influencing long-term survival [3]. This single centre study examined predictors of renal function at 6 months (both immunological and nonimmunological) in recipients of LDK transplants and explored which donor characteristics are the most useful in predicting the post-transplant graft function.

Materials and methods

Study population

A retrospective analysis was undertaken of all patients who underwent live-donor kidney transplantation at a single centre, Princess Alexandra Hospital, during the 8-year period between 31st May 1994 and 15th October 2002. During this period, 206 live donor transplants were performed. There were 12 donors of pathological kidneys, mostly which had undergone removal by wedge resection of a small (<1 cm) tumour. The data on these patients are included in the tables describing the live donor transplant population, but excluded from the univariate and multivariate analyses described. Thus, the analyses of predictors of renal function at 6 months relate to the remaining 194 patients. Follow-up was completed on all patients until graft loss, death or 22nd November 2003. For each recipient and corresponding live donor, demographic data, immunological details, operative data, postoperative complications, medical complications, admission histories, medication dosages and renal function were prospectively recorded on a computerized integrated renal database. Patients were considered to be highly sensitized if their peak panel-reactive lymphocytotoxic antibody (PRA) titre exceeded 50%. Delayed graft function (DGF) was defined as the need for dialysis postrenal transplantation. Acute rejection was recorded if proven by biopsy and classified according to the Banff 1997 criteria [4]. Renal biopsies were performed if there was a significant (≥10%) rise in serum creatinine concentration.

Immunosuppressive regimens

Standard initial immunosuppression for live donor recipients consisted of cyclosporin (2.5 mg/kg body weight twice daily together with diltiazem slow release 180–240 mg daily), prednisolone (0.3 mg/kg daily) and either azathioprine (2 mg/kg daily; prior to 1997) or mycophenolate mofetil (MMF; 1 g b.i.d.; 1997 onwards). Between 1998 and 2002, 9% of patients received tacrolimus (in place of cyclosporin) and 6% received sirolimus or everolimus (in place of mycophenolate) as a result of their participation in clinical research trials and were included in the analysis. Until mid-2001, cyclosporin dosages were titrated to achieve trough blood concentrations of 180–200 ng/ml as measured by high-performance liquid chromatography (HPLC) in the early post-transplant period and reduced to achieve levels of 100–150 ng/ml after 12 months. From 2001 onwards, we utilized cyclosporin 2-h (C2) peak levels in the first month aiming for levels of 1200–1500 ng/ml (HPLC), converting to trough blood concentrations after the first month as described above. Prednisolone dosage was decreased after 1 month at a rate of 1 mg every week, until a dose of 10 mg daily was attained. Thereafter, dosages were reduced further depending on the presence or absence of previous rejection episodes and steroid side effects (such as diabetes mellitus, infection and osteopenia), usually to a maintenance dose of 5 mg daily. Dosages of azathioprine and MMF were also reduced to maintenance doses at 12 months of 1.5 mg/kg body weight and 500 mg b.i.d., respectively. Antithymocyte globulin (ATG) was administered for the first 5–10-day post-transplant to patients who were considered to be at high immunological risk, with a peak PRA of >20% ($n = 12$). Interleukin-2-receptor antagonists were used also from mid-2001 in all recipients of LDK transplants except human leucocyte antigen (HLA)-identical donor–recipient pairs.

The first-line treatment of acute rejection was usually three consecutive daily 1000-mg doses of i.v. methylprednisolone, whilst orthoclone OKT3 (muronomab-CD3; 5 mg daily for 7–10 days) was reserved for cases of steroid-refractory or severe vascular rejection (13% of patients). Patients receiving cyclosporin were converted to tacrolimus following their first rejection event.

Assessment of live donors and donor surgical approach

Potential live donors were assessed by a multi-disciplinary assessment team, independently of the nephrologist caring for the proposed recipient. The work-up consisted of a detailed history and physical examination, psychiatric review, as well as biochemical, haematological and cardiac testing. Patients over 50 years of age or with risk factors for coronary artery disease underwent cardiac stress testing. All smokers were required to have stopped for at least 4 weeks prior to surgery. An estimation of donor glomerular filtration rate (GFR) was assessed in all patients by the formula of Cockcroft and Gault ($GFR_{C\text{-}G}$) and by chromium-EDTA clearance (GFR_{CrEDTA}) where possible. Donor kidneys and blood vessels were imaged by high-resolution computed tomography angiography.

Patients were excluded from donation if they had a creatinine clearance <80 ml/min/1.73 m^2, proteinuria over 150 mg/day, impaired glucose tolerance, a strong family history of type 2 diabetes mellitus, hypertension that was not easily controlled with a single antihypertensive agent or any systemic condition that was felt to unreasonably increase the risk of either the donation operation or of long-term renal impairment.

From January 2000, patients were offered either laparoscopic or open donor nephrectomy. Prior to this, all donor procedures were undertaken as open operations. These involved an extraperitoneal approach via a flank incision. Laparoscopic donor operations were via a transperitoneal approach using three or four upper abdominal ports with CO_2 pneumoperitoneum maintained at 12 mmHg. After mobilization, the kidney was retrieved via a small Pfannenstiel incision. Diuresis was maintained in donors via vigorous i.v. hydration without administration of diuretics or mannitol. Heparin was not given to donors. After removal, kidneys were flushed with Collins preservation solution containing 10 000 U of heparin per litre. Donor and recipient procedures were performed simultaneously in adjacent-operating theatres with cold ischaemia times usually <1 h. The type of operation (open or laparoscopic) was based on patient choice following an intensive informed consent process, which included all available information from published literature, unit experience and specific risks associated or possibly associated with both (laparoscopic versus open nephrectomy).

Assessment of recipient renal allograft function: outcome factor

For this analysis, the creatinine clearance of the recipient's kidney was the main outcome variable. This was calculated by using the Nankivell method [5], yielding a creatinine clearance corrected for body surface area (BSA) (i.e. per 1.73 m^2).

Donor, recipient and immunological factors

We explored donor, recipient and immunological factors as predictors of renal function at 6-month post-transplant. Donor characteristics included age, gender, relationship to recipient, body mass index (BMI), BSA, body weight, donor height, donor creatinine clearance, change in creatinine clearance in the donor postprocedure and type of donor surgical procedure (laparoscopic versus open nephrectomy).

For the purpose of the primary analysis, donor GFR was estimated by the Cockcroft-Gault formula ($GFR_{C\text{-}G}$). However, we did not perform a correction to adjust for BSA as for this analysis we thought it more useful to look at creatinine clearance without this adjustment. Although GFR_{CrEDTA} is a better validated estimator of donor GFR, it was not used in the primary analysis as the results were only available in 147 patients. The postdonation creatinine clearance was derived by using a serum creatinine concentration 1-month postdonation from which change in creatinine clearance in the donor was calculated.

Recipient characteristics used as explanatory variables included age, gender, race, pretransplant dialysis duration, BMI, BSA, weight, era of transplantation, cause of end-stage renal disease (ESRD: glomerulonephritis, reflux nephropathy, polycystic kidney disease, diabetic nephropathy, analgesic nephropathy, renal vascular disease or 'other') and pre-emptive versus nonpre-emptive. In relation to era of transplantation, this was categorized into eras during which major changes in immunosuppressive therapy were made in the unit: 1994–1997, 1998–2001 and 2002–2003.

Transplant factors (immunological and nonimmunological) included as explanatory variables were: presence or absence of DGF, donor:recipient weight ratio, donor:recipient BMI ratio, transplant number (first versus subsequent), peak and current PRA titres (%), HLA mismatch number, immunosuppressive protocol (including tacrolimus versus cyclosporin, IL-2 receptor antibody induction, polyclonal antibody induction, sirolimus use, everolimus use, MMF or mycophenolate sodium versus azathioprine), cytomegalovirus (CMV) mismatch between donor and recipient, CMV disease, cold ischaemia time, warm ischaemia time and rejection details (rejection versus no rejection, vascular rejection versus no vascular rejection and steroid-resistant rejection versus no steroid-resistant rejection).

Statistical analysis

Results are expressed as mean ± SD for continuous parametric data, median (interquartile range) for continuous nonparametric data, and frequencies and percentages for categorical data. Comparisons between continuous variables were performed by using Student's *t*-test or the Wilcoxon's rank sum test, depending on data distribution. Differences in proportions were evaluated by the chi-squared test or Fisher's exact test where appropriate. Pearson's coefficient of correlation was determined where appropriate. Multivariate analysis was performed by using linear regression to determine independent predictors of renal function at 6 months. Covariates included in the model were donor, recipient and immunological factors, as described in detail in the methods above. For the analyses presented, $GFR_{C\text{-}G}$ was used as the covariate to represent donor GFR as this data were available in all

patients. However, similar analyses done utilizing GFR_{CrEDTA} (limited to 147 patients) were also performed. Covariates included in the analyses were those with *P*-value of <0.2 in the univariate analyses and those variables shown to be significant in previous published analyses. A backward elimination procedure was carried out utilizing likelihood ratio until the most parsimonious model was identified. A number of explanatory continuous variables were not normally distributed and were converted to a categorical variable or log-converted as indicated. Regression diagnostics, including plots of residuals against the explanatory variables and against the fitted values, were carried out and tests for normal distribution of the residuals were performed. Variance inflation factor was checked as an index of collinearity. *A priori* *P*-values <0.05 were considered significant. STATA version 9 (Stata Corporation, College Station, TX, USA) was used for the analysis.

Results

Table 1 outlines donor, patient and transplant characteristics of the cohort of 206 living donor transplants included in this analysis.

Donor characteristics

Of the 206 donors in this cohort, the average age of the donor at the time of donation was 48 ± 11 years, with less than half (45%) being male donors. Their relationship to the recipient included siblings in 61 (30%), parent in 56 (27%), spouse in 49 (24%), other genetic relation in 16 (8%), and emotionally related in 11 (5%). The mean (±SD) $GFR_{C\text{-}G}$ of donors was 109 (±23) ml/min and the mean (±SD) change in GFR postnephrectomy was −27 (±16) ml/min. The majority (81%) of donor procedures were laparoscopic, and usually involved the left kidney.

Recipient characteristics

Recipients were predominantly Caucasian, and had a relatively short (0.4 years) duration of dialysis. This was due to a significant proportion (34%) being pre-emptive transplants. For the 66% nonpre-emptive patients, the duration of dialysis was 2.2 (0.4–2.5) years. In terms of the cause of ESRD, almost half had glomerulonephritis, with only a minority having diabetes (4%) as the cause. This was probably a reflection of the relatively younger age of patients receiving LDK transplants as opposed to deceased donor transplants in our unit. There was no difference between the Nankivell GFR at 1- and 6-month post-transplant (60 ± 17 compared with 59 ± 15 ml/min).

Table 1. Characteristics of donor and recipients and other key transplant parameters. Results are expressed as mean ± SD for continuous parametric data, median (interquartile range) for continuous nonparametric data, and frequencies and percentages for categorical data.

Donor characteristics	
Donor age (years)	48 ± 11
Male gender (%)	45
Relationship to recipient (%)	
Sibling	30
Parent	27
Spouse	24
Other genetic relation	8
Emotionally related	5
Pathological	6
Body mass index (BMI)	26.1 ± 4.0
Body surface area (BSA) (m^2)	1.9 ± 0.2
Weight (kg)	75 ± 15
Donor glomerular filtration rate (GFR) (ml/min, Cockcroft- Gault)	109 ± 23
Donor serum creatinine (μmol/l)	81 ± 17
Change in GFR (ml/min, GFR preprocedure – postprocedure)	27 ± 16
Donor procedure (open versus laparoscopic)	81%
Side of nephrectomy (left kidney)	77%
Recipient characteristics	
Age (years)	43 ± 14
Male Gender (%)	57
Caucasian (%)	89
Pretransplant dialysis duration (years)	0.4 (0–1.9)
Pretransplant dialysis duration (years): transplant not pre-emptive	2.2 (0.4–2.5)
BMI	24.9 ± 4.5
BSA (m^2)	1.8 ± 0.2
Weight (kg)	72 ± 13
Number living donor kidney transplants by era of transplantation	
1994–1997	41
1998–2001	118
2002–2003	46
Cause of end-stage renal disease (%)	
Glomerulonephritis	48
Reflux nephropathy	12
Polycystic kidney disease	12
Diabetic nephropathy	4
Other (hypertension, analgesic nephropathy, etc.)	24
Pre-emptive (%)	34
Dialysis type pretransplant (%)	
Haemodialysis	45
Peritoneal dialysis	21
GFR at 1-month post-transplant (Nankivell) ml/min/1.73 m^2	60 ± 17
GFR at 6-month post-transplant (Nankivell) ml/min/1.73 m^2	59 ± 15
Transplant specifics	
Donor recipient weight ratio	1.09 ± 0.29
Donor recipient BMI ratio	1.07 ± 0.22
Donor recipient BSA ratio	1.03 ± 0.16
Retransplant (%)	4

Table 1. (contd).

Delayed graft function (%)	4
Sensitized (Peak PRA > 50%) (%)	2.4
PRA > 0% (%)	27
0 or 1 human leucocyte antigen (HLA) mismatch (%)	17
2, 3 or 4 HLA mismatch (%)	62
5 or 6 HLA mismatch (%)	21
IL-2 Antibody use (%)	30
Polyclonal antibody induction (%)	6
Cyclosporin (%)	86
Tacrolimus (%)	9
Mycophenolate mofetil or mycophenolate sodium (%)	74
Sirolimus/everolimus (%)	6
Cytomegalovirus (CMV) mismatch (%) (donor positive, recipient negative)	18
CMV prophylaxis (%)	21
CMV disease (%)	8
Follow-up time post-transplant (years)	3.7 ± 2.3
Rejection (at least 1 rejection event)	38
Steroid resistant rejection (%)	13
Cold ischaemia time (minutes)	34 (22–51)
Warm ischaemia time (minutes)	40 ± 16

Transplant factors

Most patients were recipients of a first graft, with only 4% being retransplanted. Only four percent of patients had DGF (defined as requirement for dialysis postoperatively). The majority of patients were of low immunological risk, although nearly 2/3 had 2–4 HLA mismatches. Only 6% of patients received polyclonal antibody at induction, and 30% received IL-2 receptor antibody. The majority of patients received cyclosporin and mycophenolate as their primary immunosuppressive agents. Thirty-eight per cent of patients suffered an acute rejection episode (Banff 97: IA 15%, IB 7%, IIA 13%, IIB 3%, III < 1%). Steroid resistant rejection occurred in 13% of all patients. The mean warm ischaemia time was 34 min, with an interquartile range of 22–51 min.

Predictors of recipient creatinine clearance at 6-month post-transplant

Predictors of recipient renal function on univariate and multivariate analyses for the 194 transplants studied are outlined in Table 2. For the final multivariate model, the R^2-value (coefficient of multiple determination) was 0.48. The variance inflation factor for the final model was 1.0.

On univariate analysis, *donor factors* associated with recipient Cr-Cl included GFR, age, BSA, weight, laparoscopic procedure, and nonspouse as relation to the recipient (Table 2). Pearson's coefficient of correlation for the association between donor Cr-Cl and recipient renal function was 0.32, $P < 0.0001$ (see Fig. 1). On multivariate analysis, donor GFR was the only independent predictor (β 0.16, 95% CI 0.09–0.23, $P < 0.0001$).

For *recipient factors*, there were no factors found to be significant on either univariate or multivariate analysis, including age, gender, race, era of transplantation, or cause of ESRD.

With regard to *transplant factors*, on univariate analysis, DGF, current PRA ≥ 1%, polyclonal antibody (ATG) induction, everolimus use, rejection (versus no rejection) and steroid resistant rejection were all found to predictors of recipient GFR. However, on multivariate analysis, only DGF (β–10.00, 95% CI −19.52 to −0.49, $P = 0.039$) and steroid resistant rejection (β-8.17, 95% CI −13.98 to −2.35, $P = 0.006$) were found to be independent predictors.

Additional analyses

Additional analyses were done by utilizing donor GFR by EDTA clearance in the models. This limited the analysis to 147 patients. Results were not significantly different compared with using $GFR_{C\text{-}G}$ as the index of renal function in the donor. Donor GFR, DGF and steroid resistant rejection were independent predictor variables. The point estimate and 95% CI for the coefficient of association of GFR_{EDTA} was 0.15 (95% CI 0.04–0.25) $P = 0.004$ compared with the primary analysis using $GFR_{C\text{-}G}$, 0.19 (95% CI 0.13–0.2), $P < 0.0001$.

Discussion

The present study demonstrates that in our cohort of 206 LDK transplant recipients, the most important predictors of recipient GFR at 6 months are donor GFR, the presence of DGF and the occurrence of steroid-resistant rejection. This is an important finding because all three are potentially modifiable, or in the case of donor GFR, measurable before embarking on the transplant procedure. DGF can potentially be minimized by optimizing perioperative care, and steroid-resistant rejection can be minimized by appropriate immunosuppressive regimens.

There is little published data in the area of prediction of recipient GFR in an LDK transplantation, particularly with regard to the usefulness or otherwise of donor GFR (estimated or measured). Although it would seem intuitive that donor GFR might be an important predictor of recipient GFR post-transplant, one series of 54 patients found it not to be the case [6]. That study did, however, find the ratio of kidney volume (assessed by magnetic resonance imaging [MRI]) to donor weight, to be predictive of recipient GFR, as measured by the Modification of

Table 2. Donor and recipient factors impacting on recipient glomerular filtration rate (GFR) by univariate and multivariate regression. The only significant factors on multivariate analysis were donor GFR, delayed graft function (DGF) and steroid resistant rejection.

	Univariate			Multivariate		
	Coefficient	95% CI	*P*-value	Coefficient	95% CI	*P*-value
Donor factors						
Donor GFR ml/min	0.16	0.09, 0.23	<0.0001	0.19	0.13, 0.29	<0.0001
Donor – male gender	0.365	−0.40, 7.71	0.077			
Donor age	−0.34	−0.51, −0.17	0.0001			
Donor body surface area (BSA)	12.2	2.83, 21.51	0.011			
Donor weight	0.16	0.25, 0.29	0.021			
Donor procedure (laparoscopic versus open)	6.07	0.83, 11.3	0.023			
Relationship to recipient (versus sibling)						
Parent	−7.87	−13.16, −2.58	0.004			
Spouse	−1.19	−6.65, 4.27	0.668			
Other relation	−6.02	−11.9, −0.18	0.04			
Recipient factors						
Recipient age	−0.55	−0.20, 0.09	0.445			
Recipient gender (male versus female)	3.31	−0.79, 7.39	0.111			
Recipient race (Caucasian versus non-Caucasian)	0.97	−3.78, 5.73	0.69			
Pretransplant dialysis duration (log converted)	−1.08	−3.14,0.97	0.300			
Pre-emptive	−3.53	−7.8, 0.74	0.105			
Era of transplant (compared to 1st era 1994–1997)						
Era 2: 1998–2001	2.05	−3.25, 7.35	0.466			
Era 3: 2002–2003	3.96	−2.38, 10.30	0.220			
Cause of end-stage renal disease (versus glomerulonephritis)						
Reflux nephropathy	0.73	5.90, 7.36	0.828			
Polycystic kidney disease	2.56	−4.32, 9.43	0.465			
Diabetes and vascular disease	8.71	−1.82, 19.23	0.105			
Other	−1.59	−6.62, 3.45	0.535			
Transplant factors						
Donor recipient weight ratio	2.77	−4.28, 9.83	0.439			
Donor recipient body mass index ratio	6.35	−2.93, 15.64	0.179			
Donor recipient BSA ratio	1.51	−10.87, 13.91	0.809			
Retransplant (compared with 1st grafts)	3.54	−7.43, 7.82	0.105			
DGF	−12.59	−22.22, −2.95	0.011	−10.00	−19.52, −.49	0.039
Human leucocyte antigen mismatch number (compared with 0 or 1 mismatch)						
2–4 mismatches	3.18	−2.38, 8.73	0.261			
5–6 mismatches	1.5	−5.18, 8.18	0.658			
Current cytotoxic antibodies (antibodies ≥1% vs. 0%)	5.39	0.804, 9.786	0.02			
Interleukin-2 antibody induction	2.75	−1.65, 7.15	0.22			
Antithymocyte globulin induction	−9.15	−17.3, −1.01	0.028			
Mycophenolate use (mofetil or sodium)	2.27	−2.52, 7.05	0.351			
Tacrolimus use (versus cyclosporin)	1.93	−5.15, 9.02	0.591			
Sirolimus use	−18.65	3.34, 0.17	0.172			
Everolimus use	13.00	0.21, 25.96	0.046			
Cytomegalovirus (CMV) mismatch	1.84	−3.44, 7.12	0.492			
CMV disease	−5.54	−12.78, 1.70	0.133			
Cold ischaemia time (≥2 h vs. <2 h)	−5.68	−11.48, 0.12	0.055			
Warm ischaemia time	−0.08	−8.59, 8.42	0.985			
Rejection (versus no rejection)	−5.50	−9.61, −1.39	0.009			
Vascular rejection (versus no vascular rejection)	−3.54	−9.77, 2.69	0.263			
Steroid resistant rejection	−6.07	−12.05, −0.09	0.047	−8.17	−13.98, −2.35	0.006

Diet in Renal Disease GFR (MDRD-GFR) method. However, it was limited by utilizing creatinine clearance as measured only by 24-h urinary collection (rather than by formulae based on serum creatinine), retrospective design and small sample size. Another recent study in an LDK transplantation attempted to correlate donor single-kidney GFR (measured by 99 mTc-DTPA scan) with recipient function (as measured by 24-h creatinine clearance),

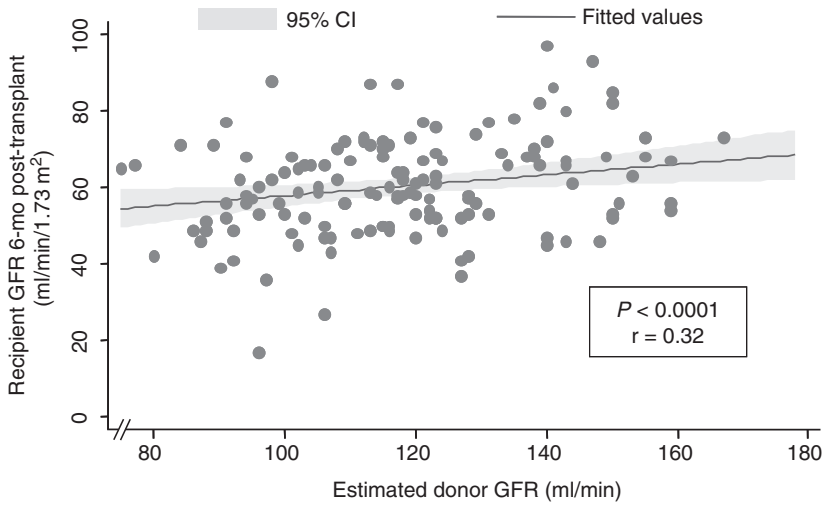

Figure 1 Recipient glomerular filtration rate (GFR) (Nankivell) in ml/min/1.73 m^2 versus Donor GFR (Cockcroft-Gault) in ml/min.

and found no significant difference between patients with GFR < 50 ml/min when compared with GFR > 50 ml/min [7]. However patients in that study were highly selected, of smaller number ($n = 70$), and were excluded if they had had either DGF or acute rejection. In addition, donor estimated GFR was not analysed as a continuous variable as performed in our analysis. These factors may explain the apparent differences in results between the studies. One study, which looked at graft survival in 344 recipients of LDKs [8], demonstrated that an absolute GFR below 80 ml/min in the living donor more than doubles the risk of graft loss.

This study did show a strong correlation between donor GFR and age, but unlike our study did not explore other donor predictors of GFR. A study of 52 LDK transplants [9] explored donor age as a predictor of patient and graft outcomes. Although patient and graft outcomes were not statistically inferior with donor ≥50 years (possibly a type 2 error), the authors demonstrated a strong correlation between donor age and recipient renal function. Although correlation studies looking at donor age and recipient GFR were outlined in the study, similar studies looking at donor GFR and recipient GFR were not outlined and the value of using donor GFR versus donor age as a predictor of outcome was not addressed.

In contrast, two studies have looked at recipient outcomes in terms of GFR in relation to donor kidney function in *deceased donor* transplants. A retrospective study from Europe of over 7000 such patients [10] found elevated donor serum creatinine to be independently predictive of poor outcome. A prospective study of 200 patients also found donor creatinine-based estimates of kidney function to be moderately correlated with recipient outcome, but not as useful as donor age alone [11]. However, creatinine-based measurement of donor kidney function in deceased donors may be unreliable because frequently such donors have a degree of cardiovascular instability and other factors affecting the serum creatinine rather than kidney function alone.

Publications in this area have recently focused on attempts to estimate nephron mass by methods including direct measurement of donor body weight at time of transplant or by radiological assessment of renal volume with methods such as magnetic resonance imaging. There have also been a number of publications exploring ratios of some index of donor nephron mass to an index of recipient size. In particular in such publications, donor nephron mass/functional donor GFR has been estimated by using donor kidney weight, donor kidney volume or other surrogate related to donor size. Indices of recipient size have included body weight, BMI, BSA and lean body weight as surrogate markers of 'metabolic needs'. Results have been variable with most studies showing one or other of these ratios to be useful [6,12,13], although not invariably [14]. However, the outcomes analysed to assess the usefulness of these ratios also varied between studies from indices of proteinuria [12,13] to hyperfiltration [13] to recipient renal function by some estimation of GFR [6,12].

Although our study did not examine the usefulness of specific assessment of donor kidney size, such as donor kidney weight or renal volume measure, we did explore the effect of donor to recipient weight ratio, BMI ratio and BSA ratio. In our analyses, these ratios were not predictive of recipient GFR, in contrast to the relationship seen by other studies. This may be explained at least in part by relatively good matching of donor and recipient size in our patients. The donor to recipient weight, BMI and BSA ratios in our study were within a very narrow range (1.09 ± 0.29, 1.07 ± 0.22 and 1.03 ± 0.16, respect-

ively) consistent with our cohort being relatively well matched for body size. This would imply that to see a substantial difference related to these ratios, larger numbers of patients would be required. Importantly then, despite a relatively well matched population in relation to body size, our data show an extremely strong relationship between donor GFR and subsequent GFR in the recipient at 6 months despite including patients with events such as DGF and rejection.

Delayed graft function remains an important issue, although uncommon in our cohort. A recent analysis of the UNOS database identified laparoscopic surgical retrieval as a risk factor for DGF in paediatric LDK transplants [15]. By optimizing surgical techniques to minimize the chance of DGF, outcomes of an LDK transplantation could be improved.

To date, our data do not show laparoscopic kidney retrieval to be a disadvantage for the recipient. Steroid-resistant rejection was also an important predictor of renal function in our study, with rejection rates being 38% and 8%, for any rejection and steroid-resistant rejection, respectively. However, rejection rates have markedly reduced with changes in immunosuppression protocols in the more recently transplanted recipients. Of note, <1/3 of our patients received IL-2 receptor antibody in the era of the study, although the use of such antibody is now almost universal in our unit.

The limitations of our study include its retrospective design, the relatively small numbers of transplants and the utilization of a creatinine-based measure of GFR for both recipient and donor rather than a gold standard measurement of GFR [16]. In addition, we were unable to explore the effect of calcineurin inhibitor drug levels on recipient GFR. Importantly, we cannot exclude residual confounding. Although we included the well-established predictor variables as covariates in our models, not every possible confounding factor can be explored in a cohort analysis of this size. We had intended developing a linear regression equation from the data of this cohort study but the R^2-value of our model (coefficient of multiple determination) was 0.48. Although this R^2-value is a reasonable one to explain the data, for a model to be useful as a predictor of outcome in future patients (in this case to predict the eGFR at 6-month post-transplant) would require the R^2 to be in the order of 0.6–0.7. It is our intention to explore this further with a larger cohort in order to define a more adequate regression equation to apply to future patients.

The strengths of our study include the prospective data collection, complete follow-up on all patients and exploration of multiple donor factors in our analysis.

In conclusion, our study found that of the live kidney donor characteristics examined, donor GFR pretransplant was the most significant and powerful predictor of recipient kidney function at 6-month post-transplant. DGF and steroid resistant rejection were also independent predictors. In contrast to some published studies, we did not find that donor recipient weight, BMI or BSA ratios were predictive of recipient renal function. Our data support the need for careful measurement of donor GFR when screening prospective live kidney donors not just to exclude inappropriate donors but to consider carefully the impact on recipient GFR. Ideally, the derivation of a robust formula to enable the pretransplant calculation of a predicted recipient GFR, utilizing donor, recipient and transplant factors, is an attractive goal, especially for live donor transplants, but would require a large, prospective, multicentre trial.

Acknowledgements

The authors gratefully acknowledge the assistance of the patients and staff of the Renal Transplant Unit at Princess Alexandra Hospital.

Funding source

No external funding sought.

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