Deceased donor renal transplantation—does side matter?

David W. Johnson, David W. Mudge, Mohammed O. Kaisar, Scott B. Campbell, Carmel M. Hawley, Nicole M. Isbel, Daryl Wall, Anthony Griffin, John Preston and David L. Nicol

Queensland Renal Transplant Service, University of Queensland, Princess Alexandra Hospital, Brisbane, QLD, Australia

Abstract

Background. The aim of the present study was to determine whether the deceased donor kidney side (left or right kidney) was predictive of subsequent kidney transplant outcomes.

Methods. A retrospective analysis was undertaken of the left–right deceased donor kidney pairs transplanted into recipients with end-stage renal failure in Queensland between 1 April 1994 and 31 March 2004.

Results. A total of 201 left–right deceased donor kidney pairs were transplanted into 402 patients. The baseline characteristics of the recipients in the two groups were comparable, except that the patients receiving right kidneys had lower body mass indices and shorter cold ischaemic times. No differences were seen between the left and right kidney recipient groups with respect to operative duration (3.02 ± 0.67 vs 3.12 ± 0.72 h, P = 0.16), warm ischaemic time (0.62 ± 0.18 vs 0.65 ± 0.21, P = 0.09), delayed graft function (4 vs 6%, respectively, P = 0.26) or a composite vascular, haemorrhagic, ureteric and infective post-operative complication end-point (22 vs 22%, P = 0.90). Estimated glomerular filtration rates were almost identical at 1 month (52.7 ± 39.6 vs 51.0 ± 24.0 ml/min/1.73 m², P = 0.34) and remained comparable thereafter. Respective death-censored graft survival rates for left and right kidney recipients were 100 and 100% at 1 year, 99.4 and 96.4% at 3 years and 96.3 and 95.5% at 5 years, respectively (P = 0.67).

Conclusions. Although left and right deceased donor kidneys present different operative challenges, the present results suggest that the probability of early post-operative complications, delayed graft function, impaired early and medium-term renal allograft function or death-censored graft failure is comparable between left and right kidney recipients.

Keywords: delayed graft function; graft survival; kidney transplantation; left kidney; post-operative complications; right kidney

Introduction

A number of donor factors have been reported to significantly influence renal transplant outcomes, including age, sex, race, body size, cause of death, terminal renal function, comorbidities and beating heart vs non-beating heart [1–4]. Other donor factors may also be relevant to renal allograft outcomes, but have been poorly studied.

There is limited evidence suggesting that donor kidney side (left or right kidney) may significantly have an impact on subsequent kidney transplant results [5,6], possibly related to technical complications stemming from the disparity in the lengths of the left and right renal veins [7,8]. Analysis of 35 625 renal transplants reported to the United Network for Organ Sharing (UNOS) Registry between 1988 and 1991 demonstrated that 3 month graft survival rates were superior in recipients of left kidneys compared with those transplanted with right kidneys (90.4 vs 85%, respectively, P = 0.0005), although 1 and 2 year graft survivals were comparable [5]. A subsequent analysis of 48 541 deceased donor kidneys transplanted throughout the US between October 1987 and November 1994 again demonstrated a small benefit of left kidney transplantation on 1 year graft survival rates (83 vs 81%, respectively, P = 0.028), but not at 2, 3 or 4 years after transplantation [6]. However, it is uncertain whether left kidney transplantation continues to be a contemporary, independent predictor of early post-transplant graft survival in light of the substantial improvements in renal transplant outcomes achieved over the last decade [9]. Nevertheless, the Australian National Organ Matching Scheme (NOMS) recommends the allocation of right kidneys rather than left kidneys to patients with the highest allocation algorithm score (including interstate exchanges).
The aim of the present study was to determine whether deceased donor kidney side (left/right kidney) was predictive of early post-transplant complications, delayed graft function, renal allograft function or death-censored graft survival.

Methods

Study population

A retrospective analysis was undertaken of the left–right deceased donor kidney pairs transplanted into recipients with end-stage renal failure in Queensland during the 10 year period between 1 April 1994 and 31 March 2004. In order to ensure that all other donor factors were equally represented in the left/right kidney groups, recipients were not included if one or both renal allografts were shipped to another centre for kidney transplantation. The preservation fluid used was University of Wisconsin solution. The recipients were treated with a calcineurin inhibitor (cyclosporin or tacrolimus), prednisolone and either azathioprine or mycophenolate mofetil (MMF). For each patient, demographic data, operative data, post-operative complications, medical complications, admission histories, medications and renal allograft function were prospectively recorded on a computerized integrated renal database. Patients were considered to be highly sensitized if their panel-reactive lymphocytotoxic antibody (PRA) titre exceeded 50%. Delayed graft function was defined as the need for dialysis post-retransplantation. Deep and superficial surgical site infections were defined according to standard criteria. Estimation of post-transplant glomerular filtration rate (eGFR) was performed using the abbreviated modification of diet in renal disease (MDRD) formula. All transplant recipients were followed until death or otherwise to the end of the study (1 October 2004), at which point data were censored. The causes of graft failures and patients’ deaths were classified according to the Australian and New Zealand Dialysis and Transplant Registry codes. No patient was lost to follow-up.

Operative procedure

The transplant procedures were performed by six transplant surgeons over the 10 year period. Prior to the period of the study, all surgeons had performed in excess of 100 renal transplants as the principal surgeon. Transplants were performed on an evenly rostered basis and hence numbers per surgeon were equivalent. A standard operative procedure was employed by all the surgeons. In the absence of other factors (e.g. previous transplants, abdominal scarring, ipsilateral peritoneal dialysis catheters), kidneys were implanted on the contralateral side (i.e. right kidneys to the left and left kidneys to the right) to allow medial positioning of the collecting system. In some cases, the right renal vein was extended using attached donor inferior vena cava. The use of this strategy was variable and depended on the availability of a suitable attached segment of the inferior vena cava as well as the body habitus of the recipient. Within our programme, surgeon choice was used to determine which kidney would be used in a particular case. Left kidneys were used where possible for the recipient who was felt to be more technically challenging (e.g. obese or previous pelvic surgery) because of the greater flexibility afforded by the longer vein.

Immunosuppressive regimens

Standard initial immunosuppression for cadaveric renal transplant recipients consisted of (i) either ciclosporin (4 mg/kg body weight twice daily together with slow-release diltiazem 180–240 mg daily) or tacrolimus (0.1 mg/kg twice daily with slow-release diltiazem 180–240 mg daily); (ii) prednisolone (0.3 mg/kg mane) and (iii) either azathioprine (2 mg/kg daily; prior to 1997) or mycophenolate mofetil (1 g twice daily; 1997 onwards). From 2001 onwards, patients also routinely received intravenous basiliximab (20 mg statim on days 0 and 4). Ciclosporin was administered in the microemulsion formulation (Neoral, Novartis, Basel, Switzerland). Dosages were titrated to achieve trough blood concentrations of 350–400 ng/ml high performance liquid chromatography (HPLC) in the early post-transplant period and slowly reduced to achieve levels of 100–150 ng/ml after 12 months. Tacrolimus dosages were titrated to achieve trough blood concentrations of 10–15 ng/ml in the early post-transplant period and slowly reduced to achieve levels of 5–8 ng/ml after 12 months. Prednisolone dosage was decreased after 1 month at a rate of 1 mg mane every week until a dose of 10 mg mane was attained. Thereafter, dosages were more slowly reduced by 1 mg mane every 2–4 weeks, depending on the presence or absence of previous rejection episodes and steroid side effects (such as diabetes mellitus, infection and osteopenia). Dosages of azathioprine and MMF were also gradually reduced to maintenance levels at 12 months of 1–1.5 mg/kg body weight and 500 mg b.d., respectively.

Statistical analysis

Normality of data was evaluated by the Kolmogorov–Smirnov test with Lilliefors’s correction. Results are expressed as mean ± SD for continuous parametric data, median (interquartile range) for continuous non-parametric data, and frequencies and percentages for categorical data. Comparisons between the recipients of left and right donor kidneys were performed using Student’s t-test or the Mann–Whitney U-test, depending on the data distribution. Differences in proportions were evaluated by the chi-square test or Fisher’s exact test, as appropriate. Multivariate analysis of categorical outcome variables was performed using logistic regression. Death-censored graft survival curves, survival probabilities and estimated mean survival times were generated according to the Kaplan–Meier method. Differences in the survival curves between the two groups were evaluated using the log rank test. The characteristics of the recipients of left and right donor kidneys were compared at baseline, and any variables on which differences were found (at P < 0.2), or could otherwise be considered as potential confounders, were adjusted for in a subsequent multivariate Cox regression analysis. A backward elimination procedure was also carried out with removal testing based on the probability of the likelihood ratio until the most parsimonious model was identified. The proportional hazards assumption was verified by the Schoenfeld’s method; a P-value for overall fit of the model > 0.05 was considered acceptable. Data were analysed using the software package, SPSS for Windows release 13.0.
**Results**

**Patient characteristics**

A total of 201 left–right deceased donor kidney pairs were transplanted into 402 patients. The baseline characteristics of the recipients in the two groups were comparable, except that the patients receiving right kidneys weighed less (66.9 ± 18.3 vs 71.8 ± 19.3 kg, \( P = 0.01 \)), had lower body mass indices (BMI; 23.6 ± 4.5 vs 25.2 ± 5.1 kg/m\(^2\), \( P = 0.002 \)) and had shorter cold ischaemic times (13.0 ± 4.9 vs 14.1 ± 5.0 h, \( P < 0.05 \)) (Table 1). These potentially confounding factors were therefore adjusted for by including them as covariates in the multivariate analyses. No patient was lost to follow-up.

The donor characteristics (age 37.2 ± 16.0 years, 62% male, BMI 24.3 ± 5.3 kg/m\(^2\), terminal serum creatinine concentration 80 ± 34 μmol/l) were identical in both groups due to the inclusion only of kidney transplant recipient pairs in our study. The causes of donor death included trauma (40%), anoxia (3.5%), cerebrovascular accident (56%) and unknown (0.5%).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Left kidney recipients (n = 201)</th>
<th>Right kidney recipients (n = 201)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>43.6 ± 14.0</td>
<td>45.9 ± 14.4</td>
</tr>
<tr>
<td>Male</td>
<td>127 (63%)</td>
<td>114 (57%)</td>
</tr>
<tr>
<td>Caucasian</td>
<td>173 (86%)</td>
<td>182 (91%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>7%</td>
<td>11%</td>
</tr>
<tr>
<td>BMI (kg/m(^2))</td>
<td>25.2 ± 5.1*</td>
<td>23.6 ± 4.5*</td>
</tr>
<tr>
<td>Never smoked</td>
<td>119 (59%)</td>
<td>113 (56%)</td>
</tr>
<tr>
<td>Previous blood transfusion</td>
<td>93 (46%)</td>
<td>93 (46%)</td>
</tr>
<tr>
<td>Transplant</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retransplant</td>
<td>23 (11%)</td>
<td>22 (11%)</td>
</tr>
<tr>
<td>Peak lymphocytotoxic antibodies (%)</td>
<td>8 (7–56)</td>
<td>8 (7–44)</td>
</tr>
<tr>
<td>HLA mismatch</td>
<td>3 (2–5)</td>
<td>3 (2–4)</td>
</tr>
<tr>
<td>Cold ischaemic time (h)</td>
<td>14.1 ± 5*</td>
<td>13.0 ± 4.9*</td>
</tr>
<tr>
<td>Warm ischaemic time (h)</td>
<td>0.62 ± 0.18</td>
<td>0.65 ± 0.21</td>
</tr>
<tr>
<td>Operative time (h)</td>
<td>3.02 ± 0.67</td>
<td>3.12 ± 0.72</td>
</tr>
<tr>
<td>Ciclosporin</td>
<td>178 (89%)</td>
<td>175 (87%)</td>
</tr>
<tr>
<td>Tacrolimus</td>
<td>23 (11%)</td>
<td>26 (13%)</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>128 (64%)</td>
<td>122 (61%)</td>
</tr>
<tr>
<td>Mycophenolate</td>
<td>73 (36%)</td>
<td>79 (39%)</td>
</tr>
<tr>
<td>ESRF cause</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glomerulonephritis</td>
<td>85 (42%)</td>
<td>84 (42%)</td>
</tr>
<tr>
<td>Reflux nephropathy</td>
<td>26 (13%)</td>
<td>29 (14%)</td>
</tr>
<tr>
<td>Polycystic kidney disease</td>
<td>19 (9%)</td>
<td>29 (14%)</td>
</tr>
<tr>
<td>Diabetic nephropathy</td>
<td>7 (3%)</td>
<td>12 (6%)</td>
</tr>
<tr>
<td>Analgesic nephropathy</td>
<td>5 (2%)</td>
<td>4 (2%)</td>
</tr>
<tr>
<td>Renovascular nephrosclerosis</td>
<td>6 (3%)</td>
<td>4 (2%)</td>
</tr>
<tr>
<td>Other</td>
<td>53 (26%)</td>
<td>39 (19%)</td>
</tr>
</tbody>
</table>

\( *P < 0.05 \) left vs right kidney recipients.

Donor blood groups were O (45%), A (39%), B (13%) and AB (3%).

**Early post-operative complications**

The complications observed within the first 6 weeks of renal transplantation are presented in Table 2. No significant differences were observed between recipients of left and right kidneys, even when a composite vascular, haemorrhagic, infective and ureteric complication end-point was analysed. The conclusions were not altered by multivariate adjustment for differences in recipient BMI or cold ischaemic time (data not shown).

**Death-censored graft survival**

During the period of the study, 15 patients in the left kidney group lost their renal allografts compared with 16 patients in the right kidney group (\( P = 0.85 \)). This translated into graft loss rates of 1.3 and 1.4 per 100 patient-years, respectively. The causes of graft failure in the left kidney group included chronic allograft nephropathy (5, 33%), chronic calcineurin inhibitor nephropathy (1, 7%), donor malignancy (1, 7%), haemolytic–uraemic syndrome (3, 20%), IgA nephropathy (2, 13%) and sepsis (1, 7%). The causes of graft loss in the right kidney group consisted of acute rejection (1, 7%), chronic allograft nephropathy (8, 50%), chronic calcineurin inhibitor nephropathy (1, 7%), donor malignancy (1, 7%), primary haemorrhage (1, 7%), secondary haemorrhage (1, 7%), haemolytic–uraemic syndrome (1, 7%), IgA nephropathy (1, 7%) and transplant renal artery stenosis (1, 7%). Actuarial graft survival was comparable.
between the two groups (log rank 0.2, \(P = 0.67\)) (Figure 1). Respective death-censored graft survivals for left and right kidney recipients were 100 and 100% at 1 year, 99.4 and 96.4% at 3 years and 96.3 and 95.5% at 5 years, respectively. Using multivariate Cox proportional hazards analysis in which recipient BMI and cold ischaemic time were included as covariates, left donor kidney transplantation was associated with a hazard ratio of 0.84 [95% confidence interval (CI) 0.40–1.80, \(P = 0.66\)], which was not statistically significant.

Renal allograft function

Mean serum creatinine concentrations were similar in the left and right kidney recipient groups at 1 month (148 ± 63 vs 146 ± 80 \(\mu\)mol/l, respectively, \(P = 0.93\)), 3 months (141 ± 50 vs 135 ± 47 \(\mu\)mol/l, \(P = 0.69\)), 6 months (144 ± 64 vs 140 ± 69 \(\mu\)mol/l, \(P = 0.87\)) and 1 year (144 ± 6 vs 136 ± 4 \(\mu\)mol/l, \(P = 0.61\)). When eGFR was calculated using the abbreviated MDRD formula, there were again no significant differences observed between the two groups at 1 month (52.7 ± 39.6 vs 51.0 ± 24.0 ml/min/1.73 m², \(P = 0.34\)), 3 months (54.1 ± 38.6 vs 53.4 ± 23.4 ml/min/1.73 m², \(P = 0.33\)), 6 months (52.0 ± 23.8 vs 52.6 ± 21.2 ml/min/1.73 m², \(P = 0.68\)) and 1 year (52.4 ± 21.8 vs 53.6 ± 22.6 ml/min/1.73 m², \(P = 0.33\)).

Discussion

The present study demonstrated that the deceased donor kidney side (left/right kidney) did not have an appreciable impact on early post-operative outcomes, including vascular complications, ureteric complications, blood transfusion requirements, lymphocele formation, surgical site infections or delayed graft function. Moreover, recipients of left donor kidneys exhibited comparable renal allograft function and death-censored graft survival rates to those patients transplanted with right donor kidneys.

These results contrast with those of the two previous UNOS Registry studies, which demonstrated a graft survival benefit associated with transplanting left kidneys [5,6]. One possible explanation for the apparent disparity in results is that kidney transplant outcomes reported in the UNOS Registry studies pertained to the late 1980s/early 1990s and were considerably poorer than those observed in our study of transplant outcomes over the last decade. It is therefore conceivable that recent improvements in transplant outcomes may have abrogated any benefit associated with donor kidney side. It is also possible that our results may represent a single-centre effect, even though Gjertson et al. [5] observed that donor kidney side accounted for only 1.24% of the assignable variation of graft outcomes between transplanting centres. Furthermore, our findings are supported by those of Roodnat and associates [13], who similarly did not observe any difference in graft outcomes between 513 left kidney recipients and 611 right kidney recipients at their centre between January 1981 and July 2000. Although it is possible that any differences in outcomes between left and right kidney recipients in the Roodnat’s article may have been potentially masked by a preferential use of right kidneys (thereby raising the possibility of selection bias), this factor did not apply to our study in which donor factors were perfectly matched between the left and right kidney recipient groups.

To our knowledge, the present study is the first to have comprehensively examined the effect of donor kidney side on early post-operative complications and subsequent allograft function. This knowledge is important because embryological and anatomical differences between the left and right renal veins present different operative challenges in renal transplantation, which could have conceivably had an impact on subsequent clinical outcomes. In utero, the inferior vena cava evolves from the paired cardinal system of veins [14,15]. Degeneration of left-sided components results in the inferior vena cava being a right-sided structure. The left renal vein actually comprises the left renal vein proper together with remnants of the subcardinal venous system, which also includes the gonadal and adrenal veins. A further portion of the left renal vein is the remnant of the interconnecting veins which join the right and left cardinal venous systems in utero. On the right, the gonadal and adrenal veins run directly into the inferior vena cava and the right renal vein is substantially shorter than the left renal vein. It has been suggested that the shorter length of the right renal vein may make it more difficult to perform the venous anastomosis in right kidney deceased donor transplantation, especially in obese subjects in whom the iliac vessels are deep, thereby leading to an increased risk of surgical
complications [7]. One option that is available to the surgeons is to extend the right renal vein using attached inferior vena cava, depending on personal preference and the availability of vena cava. This provides a longer and more robust vein to perform the anastomosis. Consequently, most surgeons would tend to use the right kidney first or reserve it for thinner patients. In our study, a surgical preference to utilize right kidneys first and/or in smaller subjects was confirmed by the slightly lower BMIs and shorter cold ischaemic times of the right kidney recipients. However, even after adjustment for body size, there was no evidence that operative times or warm ischaemic times were any longer or that vascular anastomotic complications or post-operative complications were more common in right kidney recipients. Similar findings have been reported for laparoscopic live donor renal transplant operations [16]. It has been suggested that the technical challenges presented by the relatively short length of the right renal vein may be at least partially counterbalanced by difficulties presented by the more frequent anatomical variations in the left renal vein, particularly the greater frequency of additional renal veins and circumaortic left renal veins [17].

Our group also found that both early and late post-transplant renal allograft function, as determined by serum creatinine concentration and eGFR, were virtually identical between left and right kidney recipients. A previous study has suggested that the measured GFR of the left kidney was significantly lower than that of the right kidney in 50 consecutive kidney donors (56.6 ± 9.0 vs 61.0 ± 9.0 ml/min, \( P = 0.16 \)) [18], although other studies have found generally equivalent GFRs between left and right kidneys [19,20]. Our observations suggest that GFR is comparable between left and right kidneys and is not appreciably affected by the different operative approaches to left and right deceased donor kidney transplantation.

The strengths of our study are that all the data were prospectively collected and that left–right kidney recipient pairs were analysed to ensure that all the donor factors were equally balanced between the groups. However, these strengths must be balanced against the potential limitations, which include those of a single-centre study and the possibility of type 2 statistical errors in relation to relatively uncommon complications (such as vascular thromboses). Moreover, there was evidence from our study that the surgical decision to use a left or right kidney in a particular recipient was non-random, as evidenced by the smaller BMIs and shorter cold ischaemic times in right kidney recipients. Although statistical adjustments were made for these factors, the possibility of residual confounding cannot be entirely excluded. For example, the proportion of left vs right kidney transplant procedures performed by trainee registrars under supervision rather than directly by transplant surgeons was not captured by our database and could have conceivably differed according to transplant kidney side.

In conclusion, the results of the present study demonstrate that although left and right deceased donor kidneys present different operative challenges in renal transplantation, the probability of early post-operative complications, delayed graft function, impaired early and medium-term renal allograft function or death-censored graft failure is comparable between left and right kidney recipients.

Acknowledgements. The invaluable assistance of Kylie Reiger, Dale Bergman and the Renal Transplant Unit nursing staff is gratefully acknowledged.

Conflict of interest statement. None declared.

References

Received for publication: 22.12.05
Accepted in revised form: 18.4.06