Deceased-donor kidney transplantation: improvement in long-term survival

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Abstract

Background. Despite marked improvement in short-term renal allograft survival rates (GSR) in recent years, improvement in long-term GSR remained elusive.

Methods. We analysed the kidney transplant experience at our centre accrued over four decades to evaluate how short-term and long-term GSR had changed and to identify risk factors affecting graft survival. The study included 1476 adult recipients of a deceased-donor kidney transplant who were transplanted between 1963 and 2006 and who had received one of five distinct immunosuppressive protocols.

Results. Five-year actual GSR steadily improved over the years as immunosuppressive therapy evolved (22–86%, P < 0.001) in spite of an increasing trend in the transplantation of higher-risk donor–recipient pairings. For those whose grafts functioned for the first year, subsequent 4-year GSR (5-year conditional GSR) also improved significantly (63–92%, P < 0.001). Acute rejection and delayed graft function (DGF) were the most significant risk factors for actual graft survival, while acute rejection was the only significant risk factor for conditional GSR. Use of kidneys from expanded-criteria donors (ECD) was not a risk factor, compared to the use of standard-criteria donor kidneys for either 5-year actual or conditional GSR. There was an impressive decline in the incidence of acute rejection events (77.4–5.8%, P < 0.001). While the DGF rate had decreased, it still remained high (68.7–38.5%, P < 0.001).

Conclusions. We found a significant improvement in both short-term and long-term GSR of deceased-donor kidney transplants over the last four decades. These improvements are most likely related to the decreased incidence of acute rejection episodes. Minimizing acute rejection events and preventing DGF could result in further improvement in the GSR. Our experience in the judicious use of ECD kidneys suggests that this source of kidneys could be expanded further.

Keywords: acute rejection; deceased donors; delayed graft function; immunosuppressive therapy; kidney (renal) transplantation

Introduction

The management of kidney transplantation has evolved over more than half a century. Published literature has documented the remarkable progress made in surgical techniques, types and use of immunosuppression, diagnosis and management of complications and patient and graft outcomes [1]. Despite these advances, improvement in long-term graft survival after the first year of successful transplant has not been consistently found.

Harihan et al. [2] reported a substantial increase in both short-term and long-term graft survival between 1988 and 1996 in the United States and attributed this improvement to a significant decrease in the incidence of acute rejection. On the other hand, Meier-Kriesche et al. [3] reported a lack of improvement in long-term renal allograft survival despite a marked decrease in the acute rejection rate between 1988 and 1995. Recent analyses of large databases revealed no substantive evidence for finding improved long-term renal allograft survival in the last decade [4,5]. It is also unclear why there has been no improvement in long-term graft survival given the availability of more effective immunosuppressive medications, better control of acute transplant rejection and improved antimicrobial prophylaxis.

The kidney transplant programme at our centre began in 1963 and five distinct immunosuppressive protocols were sequentially introduced from that time to the present. We
reviewed our kidney transplant experience over the past four decades to study what effect evolving immunosuppressive therapies had on short-term and long-term kidney transplant outcomes. In addition, we attempted to identify risk factors that had a significant adverse impact on short-term and long-term graft survival.

Materials and methods

We used a single-centre, nonrandomized, retrospective study designed to evaluate outcomes in kidney transplant recipients treated with one of five different immunosuppressive protocols under the coordinated effort of a multidisciplinary team over four decades.

Patients

The study included 1476 adult kidney transplant patients who had received a kidney from deceased donors between 1963 and 2006 at The New York-Presbyterian Hospital/Weill Cornell Medical Center, New York, NY. It excluded paediatric patients, recipients of a living-donor kidney and those who had received dual kidneys or a simultaneous kidney–pancreas transplant. Demographic and other pertinent information are shown in Table 1.

Methods

Between 1963 and 2006, we utilized five distinct immunosuppressive protocols: prednisone and azathioprine (Imuran®, Prometheus Lab., San Diego, CA) between 1963 and 1983 (Protocol 1); prednisone, azathioprine and cyclosporine (Neoral®, Novartis, East Hanover, NJ) between 1983 and 1994 (Protocol 2); prednisone, cyclosporine and mycophenolate mofetil (CellCept®, Roche, Nutley, NJ) between 1995 and 1997 (Protocol 3); prednisone, mycophenolate mofetil and tacrolimus (Prograf®, Astellas, Deerfield, IL) between 1997 and 2006 (Protocol 4); antibody induction with rabbit anti-thymocyte globulin (Thymoglobulin®, Genzyme, Cambridge, MA), tacrolimus, mycophenolate mofetil and a steroid-sparing protocol (intravenous methylprednisone for Post-operative Days 0–4) between 2001 and 2006 (Protocol 5). In addition to these basic protocols, various other adjunctive medications and procedures were utilized at different times to prevent and/or treat acute rejection. For example, local irradiation, anti-lymphocyte globulin, human gamma globulin and donor-specific blood transfusion were also utilized along with Protocol 1. Similarly, Orthoclone OKT3, basiliximab, daclizumab, anti-thymocyte globulin, human gamma globulin, plasmapheresis and donor-specific blood transfusions with Protocols 2–4 and sirolimus, rituximab and alemtuzumab with Protocol 5. The presence of overlapping time periods for protocols was usually caused by a need to use the prior protocol due to ‘medical necessity’, such as the need for corticosteroid therapy or by the presence of hypersensitivity to a drug used in the current protocol. In addition, there had been considerable advancement in surgical and organ preservation techniques, use of antimicrobial prophylaxis, as well as overall patient care over the study period. In this study, assignment of patients to the treatment protocol was based on intention to treat at the beginning of transplantation. Patients who expired with a functioning kidney were counted as graft failures. The definition of expanded-criteria donor (ECD) was that established by Port et al. [6]. The last day of the follow-up period was 23 December 2009.

Statistical methods

Data analyses included graft survival rates (GSR) and identification of risk factors for graft survival. Demographic and clinical characteristics were compared across protocols by the ANOVA test or Kruskal–Wallis test for continuous variables and the chi-square test for categorical variables. The Kaplan–Meier method was used to calculate survival probabilities and survival function, and the log-rank test was used to compare survival rates between immunosuppressive therapy protocols. Cox proportional regression models were used to estimate the hazard ratios (HR),

Table 1. Demographic and other pertinent information of transplant patients

<table>
<thead>
<tr>
<th>Immunosuppressive therapy protocols</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>Total</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients, n (%)</td>
<td>623 (42)</td>
<td>372 (25)</td>
<td>157 (11)</td>
<td>136 (9)</td>
<td>188 (13)</td>
<td>1476</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age (years), mean ± SD</td>
<td>38.2 ± 11.5</td>
<td>43.5 ± 12.3</td>
<td>48.5 ± 13.1</td>
<td>48.8 ± 10.8</td>
<td>54.1 ± 12.2</td>
<td>43.7 ± 13.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Gender</td>
<td>Male (%)</td>
<td>70.8</td>
<td>59.1</td>
<td>54.1</td>
<td>56.6</td>
<td>63.3</td>
<td>63.8</td>
</tr>
<tr>
<td>Gender</td>
<td>Female (%)</td>
<td>29.2</td>
<td>(40.9)</td>
<td>(45.9)</td>
<td>34.3</td>
<td>36.7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Race</td>
<td>White (%)</td>
<td>72.6</td>
<td>69.8</td>
<td>58.6</td>
<td>50.0</td>
<td>47.9</td>
<td>65.2</td>
</tr>
<tr>
<td>Race</td>
<td>Black (%)</td>
<td>24.5</td>
<td>17.3</td>
<td>22.9</td>
<td>36.8</td>
<td>34.6</td>
<td>24.9</td>
</tr>
<tr>
<td>Race</td>
<td>Others (%)</td>
<td>2.9</td>
<td>12.9</td>
<td>18.5</td>
<td>13.2</td>
<td>17.6</td>
<td>9.9</td>
</tr>
<tr>
<td>Time on dialysis (months), mean ± SD</td>
<td>26.6 ± 23.4</td>
<td>44.5 ± 40.5</td>
<td>53.8 ± 42.7</td>
<td>77.7 ± 59.4</td>
<td>60.2 ± 39.1</td>
<td>44.0 ± 41.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Panel reactive Ab, mean ± SD (%)</td>
<td>6.1 ± 14.9</td>
<td>12.7 ± 19.2</td>
<td>15.5 ± 23.7</td>
<td>9.7 ± 17.0</td>
<td>3.3 ± 6.9</td>
<td>8.8 ± 17.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Pre-Txpl diabetes, yes (%)</td>
<td>6.6</td>
<td>12.4</td>
<td>15.9</td>
<td>17.7</td>
<td>27.7</td>
<td>12.7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Transplant number</td>
<td>1</td>
<td>499</td>
<td>324</td>
<td>143</td>
<td>101</td>
<td>178</td>
<td>1245</td>
</tr>
<tr>
<td>Transplant number</td>
<td>2–4</td>
<td>124</td>
<td>48</td>
<td>14</td>
<td>35</td>
<td>10</td>
<td>231</td>
</tr>
<tr>
<td>Donor type</td>
<td>ECD (%)</td>
<td>0</td>
<td>3.0</td>
<td>14.0</td>
<td>17.2</td>
<td>41.9</td>
<td>9.1</td>
</tr>
<tr>
<td>Donor type</td>
<td>SCD (%)</td>
<td>100</td>
<td>97.0</td>
<td>86.0</td>
<td>82.8</td>
<td>58.2</td>
<td>90.9</td>
</tr>
<tr>
<td>Donor type</td>
<td>DGF, yes (%)</td>
<td>68.7</td>
<td>57.7</td>
<td>50.6</td>
<td>35.2</td>
<td>58.5</td>
<td>55.0</td>
</tr>
<tr>
<td>Acute rejection, yes (%)</td>
<td>77.4</td>
<td>52.8</td>
<td>35.0</td>
<td>33.1</td>
<td>5.8</td>
<td>49.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>5-year survival</td>
<td>Patients (%)</td>
<td>75</td>
<td>86</td>
<td>85</td>
<td>82</td>
<td>92</td>
<td>82</td>
</tr>
<tr>
<td>5-year survival</td>
<td>Actual GSR (%)</td>
<td>22</td>
<td>56</td>
<td>64</td>
<td>74</td>
<td>86</td>
<td>48</td>
</tr>
<tr>
<td>5-year survival</td>
<td>Conditional GSR (%)</td>
<td>63</td>
<td>76</td>
<td>77</td>
<td>85</td>
<td>92</td>
<td>77</td>
</tr>
</tbody>
</table>

95% confidence intervals (95% CI) and P-values of the independent risk factors, which included recipients’ age, gender, ethnicity, pre-transplant panel reactive antibody (PRA), presence of acute rejection in the first postoperative year, prior dialysis time (months), delayed graft function (DGF) and diagnosis of diabetes prior to transplantation. Recipient’s gender, ethnicity and pre-transplant PRA were categorical variables, as recipients’ age, pre-transplant PRA and prior dialysis time were continuous variables. Due to skewness of pre-transplant PRA and prior dialysis time, log transformation was used to normalize data. HR for these variables were calculated by \((PRA/dialysis\ \text{time} + 1)^{\beta}\) where \(\beta\) is the coefficient of PRA/dialysis time. Backward selection method was used to eliminate covariates when events were too few in the multivariate analyses. Immunosuppressive therapy protocols were considered as predictor variables along with other predictors using Protocol 1 (pre-cyclosporine era) as the reference. For comparative analysis of GSR, Protocol 2 (cyclosporine era) was also used as the reference.

All statistical tests were two-sided and \(P < 0.05\) was considered statistically significant. Analyses were performed in SAS Version 9.1 (SAS Institute, Inc., Cary, NC).

Results

There were a total of 1476 adult patients who received a kidney transplant from a deceased donor. Among these, 623, 372, 157, 136 and 188 patients were treated with immunosuppressive therapy Protocols 1–5, respectively (Table 1). Over the four decades, there had been a steady and significant increase in deceased-donor transplants among older patients (mean age ± SD, 38.2 ± 11.5–54.1 ± 12.2; \(P < 0.001\)), African-Americans (24.5–34.6%, \(P < 0.001\)) and diabetics (6.6–27.7%, \(P < 0.001\)). In addition, increasing numbers of transplants were performed using kidneys from the ECD pool (0, 3, 14, 17.2 and 41.9% in Protocols 1–5, respectively, \(P < 0.001\)). These figures indicate that both the donor and recipient populations were older and that more higher-risk recipients were being transplanted in recent years.

Five-year actual patient survival rates were 75, 86, 85, 82 and 92% for Protocols 1–5, respectively. There was a significant improvement in patient survival rates from Protocol 1 to Protocols 2–5 (\(P < 0.001\)). However, patient survival in Protocols 2–5 did not differ significantly. Older age (HR, 1.58; 95% CI, 1.37–1.84; \(P < 0.001\)), duration of dialysis prior to transplantation (doubling interval: HR, 1.33; 95% CI, 1.15–1.54; \(P < 0.001\)) and diabetes mellitus diagnosed prior to transplantation (HR, 2.0; 95% CI, 1.31–3.05; \(P = 0.001\)) had a significant adverse impact on patient survival.

Allograft survival rates (GSR) observed with the five different immunosuppressive therapy protocols are depicted in Figure 1. Five-year actual graft survival improved progressively and significantly over the decades (22, 56, 64, 74 and 86% from Protocols 1–5, respectively, \(P < 0.001\)). When Protocol 2 (cyclosporine era) was used as the reference rather than Protocol 1 (pre-cyclosporine era), we again found a significant improvement in GSR with each subsequent Protocols 3–5. Survival rates were then recalculated excluding first year failures. In this instance, the subsequent 4-year GSR (5-year conditional graft survival) was found to have improved over the same period (63, 76, 77, 85 and 92% from Protocols 1–5, respectively, \(P < 0.001\)) (Figure 2).

These findings indicated that both short-term and long-term graft survival had significantly improved in recent years.

Risk factors for 5-year actual graft survival included older age (\(P = 0.02\)), black race (\(P = 0.01\)), diabetes prior to transplantation (\(P < 0.001\)), acute rejection in the first

**ACTUAL GRAFT SURVIVALS BY TREATMENT PROTOCOLS**

![Fig. 1. Actual graft survivals of deceased-donor kidney transplant recipients treated with five different immunosuppressive therapy protocols. AZA, azathioprine; MMF, mycophenolate mofetil.](image-url)
year (P < 0.001) and presence of DGF (P < 0.001) (Table 2). Acute rejection was a risk factor (P = 0.02) for conditional survival, but DGF, recipient's age, race and diabetes were not (Table 2). In this study, we found that a kidney transplant from an ECD was not a risk factor for either the 5-year actual (adjusted HR, 0.99; 95% CI, 0.65–1.50; P = 0.96) or 5-year conditional survival (adjusted HR, 1.06; 95% CI, 0.59–1.90; P = 0.84) (Table 2).

The effect of the level of kidney function measured by serum creatinine at 1 year on 4-year survival (5-year conditional graft survival) was determined for the recipients in Protocols 3–5 combined (n = 481). Five-year conditional survival rates were 93.3, 80.7 and 56.7% for those with a serum creatinine ≤1.0, 1.1–2.0 and ≥2.1 mg/dL, respectively (Figure 3). The differences in GSR at 5 years were significant between the first two groups of recipients.

### Table 2. Adjusted HR and P-values for the various risk factors

<table>
<thead>
<tr>
<th>Variables</th>
<th>Actual allograft survival with 5-year follow-up (n = 1476)</th>
<th>Conditional allograft survival with 5-year follow-up (n = 907)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adjusted HR</td>
<td>95% CI</td>
</tr>
<tr>
<td>Recipient age (10-year interval)</td>
<td>1.10</td>
<td>1.02–1.20</td>
</tr>
<tr>
<td>Recipient gender (Ref; female)</td>
<td>1.10</td>
<td>0.90–1.35</td>
</tr>
<tr>
<td>Recipient race (Ref; white)</td>
<td>1.34</td>
<td>1.09–1.66</td>
</tr>
<tr>
<td>Black</td>
<td>0.77</td>
<td>0.53–1.10</td>
</tr>
<tr>
<td>Others</td>
<td>1.84</td>
<td>1.48–2.29</td>
</tr>
<tr>
<td>PRA (in doubling interval)</td>
<td>0.97</td>
<td>0.97–1.12</td>
</tr>
<tr>
<td>Acute rejection (Ref; no)</td>
<td>1.30</td>
<td>1.38–2.11</td>
</tr>
<tr>
<td>Dialysis time (doubling Interval)</td>
<td>1.64</td>
<td>1.24–2.16</td>
</tr>
<tr>
<td>DGF (Ref; no)</td>
<td>0.99</td>
<td>0.65–1.50</td>
</tr>
<tr>
<td>Pre-Txpl diabetes (Ref; no)</td>
<td>1.07</td>
<td>0.88–1.31</td>
</tr>
</tbody>
</table>

PRA, panel reactive antibody; Dialysis time, duration of dialysis treatment prior to transplantation; DGF, delayed graft function; Pre-Txpl diabetes, diabetes mellitus diagnosed prior to transplantation; ECD, expanded-criteria donor; SCD, standard-criteria donor; Txpl time, number of kidney transplants a patient received; Ref, reference. Medical protocol has been included as a covariate, but results were not shown here.
whose creatinine was ≤ 2.0 mg/dL and the third group who had a creatinine ≥ 2.1 mg/dL (P < 0.02). The level of graft function achieved at 1 year was significantly associated with long-term conditional survival.

Over the four decades covered in this study, there was a progressive and significant decrease in the incidence of acute rejection events in the first year (Table 1). It was found to be as high as 77.4% in Protocol 1 patients, decreasing progressively to 5.8% for those in Protocol 5 (P < 0.001). The incidence of DGF was 68.7% with Protocol 1 and 38.5% with Protocol 5 (P < 0.001). Clearly, there was a steady decrease in acute rejection as immunosuppressive therapy evolved. The incidence of DGF also did decrease significantly, but its collective incidence remains still too high.

Five-year GSR with patients in Protocols 3–5, with and without DGF, are depicted in Figure 4. The patients with DGF had both a higher incidence of acute rejection (34.7 vs 24.5%, P = 0.001), higher levels of serum creatinine at 1 year (1.93 ± 0.80 vs 1.63 ± 0.74 mg/dL, P = 0.001) and lower 5-year actual graft survival (52.0 vs 73.2%, P < 0.001). The 5-year conditional survival was, however, not significantly different between patients with and without DGF (70.4 vs 76.4%, P = 0.24).

**Discussion**

The critical outcomes in kidney transplantation are patient and allograft survival. Improvement in these outcomes results from a combined effect of good patient care, enhanced organ preservation and surgical techniques, effective antimicrobial prophylaxis and availability of potent immunosuppressive regimens. Among these, efficacy and safety of immunosuppressive regimens play pivotal roles in the survival of grafts and patients.

Improvement in short-term renal allograft survival has been well documented in recent years [1]. Progress in long-term graft survival, however, has been debated [2–5]. We reviewed our experience with deceased-donor kidney transplantation over four decades to evaluate short-term and long-term graft survival, to identify risk factors for graft survival and to propose ways, suggested by our findings here, for improving future renal allograft survival.

This study documents progressive improvement in 5-year graft survival of deceased-donor kidney transplants coincident with the evolution of immunosuppressive therapies over the study period. This improvement was achieved despite the increased use of kidneys from ECD in older and higher-risk patients without compromising patient survival. This favourable outcome was most likely secondary to a dramatic reduction of acute rejection. The acute rejection rate in the first year with the latest protocol (Protocol 5) utilizing a combination of antibody induction, tacrolimus, mycophenolate mofetil and a 5-day steroid therapy was only 5.8%. Since this figure includes subclinical rejection diagnosed by protocol biopsy as well, the incidence of clinically apparent acute rejection was even lower. It should be noted that this low rate of acute rejection was associated with 5-year patient survival rates and GSR of 92 and 86%, respectively, despite the fact that 41.9% of transplants were performed with ECD kidneys and a higher-risk donor–recipient population. A similar favourable outcome
has been reported with combined regimens of antibody induction and a steroid-sparing protocol [7,8]. Although earlier studies reported a significant reduction in acute rejection and marked improvement in short-term outcomes, little improvement in long-term graft survival was found [3–5]. Meier-Kriesche et al. [4] suggested that part of this discordance in recent years might be related to a failure of completely reversing the sequelae of acute rejection. Contrary to these reports, we found that 5-year conditional survival had progressively improved over the years. As used here, the conditional survival rate is a surrogate indicator of long-term graft survival. Therefore, this study indicates that there had been a significant and progressive improvement in both short-term and long-term graft survivals over the last four decades. Furthermore, the improvement was significant even after the introduction of cyclosporine.

Adjusted risk analysis identified acute rejection as the only significant risk factor for both 5-year actual and conditional GSR. This finding is consistent with previous studies that reported that the occurrence, timing and number of acute rejection are all associated with increased risk of graft loss [9,12]. Older age, black population, DGF and diabetes mellitus prior to transplantation were also identified as risk factors, but only for 5-year actual graft survival, not for conditional graft survival. Treating death of a patient with a functioning graft as a graft failure might have contributed to identifying older age and diabetes mellitus as risk factors. Although DGF was not identified as a risk for long-term survival in multivariate analysis, DGF was significantly associated with a higher incidence of acute rejection, lesser graft function and a lower 5-year actual graft survival. DGF clearly has a significant adverse impact on short-term graft outcomes and possibly for conditional graft survival as well. These findings are consistent with reports of previous studies [12–14].

It is important to note that transplantation from an ECD kidney, compared to a standard-criteria donor, was not a risk factor for either actual or conditional graft survival in adjusted risk analysis. Since the use of kidneys from an ECD has been increasing rapidly in recent years, it bodes well for continued expansion of the deceased-donor pool. This finding is, however, contrary to many single-centre and registry reports [15–17] save for the experience at a few single centres [18,19]. It is not clear, however, why our result is different from many others, except that we did choose kidneys among potential ECD based on a donor’s medical history, serum creatinine, pulsatile perfusion pro-

**Fig. 4.** Actual graft survivals of deceased-donor kidney transplant recipients with or without DGF.
files, kidney biopsy findings, matching for body mass between donor–recipient pairs, as well as modifying the dose and timing of initiating tacrolimus [20].

Our study has several important limitations. Firstly, the study analysed clinical experience of kidney transplantation performed over four decades. Inherent in such an analysis, there are many uncontrollable factors and variables. Clearly, there have been many other advances besides immunosuppressive therapy, such as overall patient care, enhanced organ preservation and surgical techniques, effective antimicrobial prophylaxis, etc. Therefore, the improvement of graft survival could not be attributed solely to the evolution of immunosuppressive therapy. Secondly, we defined a patient’s death with a functioning kidney as a graft failure. If death was censored from the survival calculation, GSR would be higher than those reported here. Death-censored GSR would help establish the relationship between evolution of immunosuppressive therapy and the improvement of GSR. Unfortunately, death-censored GSR was not possible to estimate since causes of death were not available for all patients transplanted in the early transplant era. Thirdly, we did not critically analyse the relative importance of data concerning ECD kidneys, such as biopsy findings, perfusion profiles or modification of dose and timing of calcineurin inhibitor use. Analysis of such data surrounding the use of an ECD kidney might lead us to a better understanding of how improved ECD transplant outcomes come about, as well as provide us with the type of protocol needed for a large-scale, randomized prospective study.

Conclusion

In summary, we analysed our clinical experience with 1476 adult kidney transplant recipients from deceased donors performed between 1963 and 2006 utilizing five distinct immunosuppressive protocols. We found that there was a significant improvement in both short-term and long-term allograft survival in recent years, in spite of a steady increase in the use of kidneys from ECD and in a higher-risk donor–recipient population. These improvements appear to be related to a dramatic reduction of acute rejection along with the evolution of more effective immunosuppressive regimens. Adjusted risk analysis revealed that acute rejection and DGF were the most significant risk factors for short-term graft survival. While acute rejection was the sole risk factor for long-term graft survival, a lower serum creatinine at the end of the first year was significantly associated with a better long-term outcome. Compared to the dramatic reduction in acute rejection, the incidence of DGF remains unacceptably high. The use of kidneys from ECD has been rapidly rising in recent years. We did not find transplantation of a kidney from an ECD to be a risk factor for either short-term or long-term graft survival. Therefore, to improve graft survival, a continued effort to minimize acute rejection and DGF must be vigorously pursued. In addition, the further judicious use of ECD kidneys may expand the size of the donor pool without impacting on its functional status.

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Conflict of interest statement. None declared.


References

SDMA is an early marker of change in GFR after living-related kidney donation

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S.M.B.-B. and VK. contributed equally to the manuscript and are both considered last authors.

Abstract

Background. Early detection of changes in the glomerular filtration rate (GFR) is crucial in detecting acute kidney injury. There is burgeoning evidence from preclinical and clinical studies that symmetrical dimethylarginine (SDMA) correlates well with different parameters of renal function. In some studies, SDMA even outperformed creatinine as a marker of GFR. It is however unknown how fast SDMA is increasing after reduction in GFR. The aim of our study was therefore to determine the temporal change of SDMA in comparison with cystatin C after a defined reduction in GFR.

Methods. Blood samples from 24 healthy living-related kidney donors (19 F/5 M), mean age 55.2 ± 8.3 years, were collected prior to donation of the kidney as well as 1, 6, 12, 24, 72 and 168 h after unilateral nephrectomy. SDMA levels were measured using a liquid chromatography–mass spectrometry-based method.

Results. Within 6 h after unilateral nephrectomy, i.e. reduction of GFR by 50%, SDMA rose from 0.571 ± 0.120 to 0.659 ± 0.135 μmol/L (P < 0.001). Baseline cystatin C levels increased from 0.87 ± 0.16 to 1.07 ± 0.15 mg/L (P < 0.001). Also, serum creatinine rose significantly within 6 h after removal of one kidney from 65.4 ± 8.4 to 88.8 ± 10.2 μmol/L (P < 0.001).

Discussion. SDMA might be a valuable and early marker of change in GFR in the clinical and experimental setting. Future studies will have to clarify whether sensitiv-