ABSTRACT

Despite the increased number of cadaver donors and overall organ transplantations, we have observed a dramatic increase in the waiting list. We evaluated transplantations performed using marginal (n = 63) and “ideal” or optimal donors (n = 86). Donor and recipient functional and histopathological data were studied at 1 and 5 years after transplantation. Among the marginal donor group, we investigated whether the age or pre-existent hypertension in the donor showed a strong impact on the functional deterioration of the grafts. Twenty-three graftectomies were performed in marginal, and 39 in ideal recipients (P < .002). Evaluating graft function, at 5 years, we observed the serum creatinine level (P < .0001) and the estimated glomerular filtration rate (P = .003) are significantly different between the two groups. At this time there was a significant difference in the serum creatinine level of patients who were older than the age of 55 years compared with those who showed hypertension (P = .0003). Evaluating morphological changes in the kidneys, acute rejection episodes (P = .0004) and interstitial fibrosis/tubular atrophy (P = .002) were significantly greater among the marginal versus the ideal groups. At 1 year after kidney transplantation, despite no significant difference regarding renal function, they were significant in the histology of marginal versus ideal donor kidneys.

THE end-stage renal disease (ESRD) population is increasing worldwide; in Europe has doubled during the past decade. ESRD patients either remain on dialysis or undergo renal transplantation, which is a more beneficial treatment for various reasons. Despite the increased number of cadaver donors and overall organ transplantations, the waiting list has shown a dramatic increase. Because of the shortage of organs available for transplantation, marginal donors are now accepted to increase the donor pool. We have performed transplantations using marginal (MDK) and ideal donor kidneys (IDK). Increased donor age is a major determinant of graft outcome; the number of older cadaver donors (>50 years) as a fraction of all procedures in Hungary has increased from 12.5% in 1995 to 25.3% in 2005. Although there is no universal definition an ideal versus marginal kidneys the latter enginer believed to display one or more of the following pretransplantation factors: donor age > 55 years; non–heart-beating donor (NHBD); cold ischemia time (CIT) > 36 hours and/or donor hypertension or diabetes mellitus of > 10-year duration. Allograft outcomes with marginal kidneys turn to be inferior to those of organs considered to be ideal. Notwithstanding the diminished graft survival of marginal kidneys, renal transplantation improves the quality of life and an economic analysis suggested that transplantation with a marginal donor kidney was more cost-effective than dialysis treatment. Improved patient survival is a well-established benefit of renal transplantation, but the magnitude of increased longevity is not uniform among patient subgroups. The rapidly growing organ transplantation list and increasing mortality of waiting patients have prompted interest in the use of organs from marginal donors.

The aim of our study was to evaluate the survival of kidney grafts from marginal or ideal donors, as well as their functional and histopathological changes. We examined whether there was a significant difference in the function...
and/or morphology of grafts from the two groups at 1 or 5 years after transplantation.

PATIENTS AND METHODS

Patients who received a cadaver donor renal transplant were divided into two groups—marginal (MDK) or ideal (IDK)—recipients based on the characteristics of the organ. A recipient was defined as receiving an MDK if one or more of the following pretransplantation factors was present: donor age > 55 years, donor history of hypertension longer than 10 years duration, donor history of diabetes mellitus longer than 10 years duration, NHBD or CIT > 36 hours. We defined a cadaver kidney transplantation in which none of the listed factors was evident as an IDK. From January 1, 2005, to December 31, 2009, we performed 249 kidney transplantsations using 63 marginal and 186 ideal kidneys. The marginal group included 2 NHBDs, 3 CIT more than 36 hours, 27 hypertensive donors, and 31 who were older than 55 years.

The following data were examined in our study: gender, creatinine levels, diuresis in the last 24 hours, CIT, HLA-mismatch, cause of death, and recipient age.

Functional and histopathological changes regarding serum creatinine and estimated glomerular filtration rate (eGFR) were studied in the two patient groups at 1 and 5 years by measuring functional and histopathological changes, serum creatinine levels, and eGFR, using the Cockcroft-Gault formula. We evaluated whether the age of or hypertension in the marginal donor accelerated the functional deterioration of the graft.

Histopathological changes in the grafts were evaluated using a protocol biopsy at 1 year after transplantation in 102 cases. Before the transplantation, a (“zero biopsy”) histological sample was obtained before implantation using a 16-G Tru-Cut needle and a biopsy gun. Morphological examinations included light microscopic staining (hematoxylin and eosin stain, periodic acid-Schiff trichrome, and methenamine silver), as well as immunofluorescence analysis of frozen sections using antibodies to HLA class II antigens, complement components 4d (C4d) and C3, immunoglobulin G (IgG), IgA, and IgM. Embedding for electron microscopy was performed in all cases with ultrastructural evaluation. Renal lesions were graded and IF/TA were analyzed using logistic regression. The level of significance was set at \( P < .05 \).

Statistical Analysis

Descriptive statistics were used to assess donor and recipient data. As the distribution of samples was mostly non-normal by the Kolmogorov-Smirnov test, we used the Mann-Whitney test to compare marginal versus ideal kidney recipients. Two group comparisons for categorical data used the chi-square or Fisher exact tests. The multivariable dependences of acute rejection episodes and IF/TA were analyzed using logistic regression. The level of significance was set at \( P < .05 \). SPSS version 15.0 (2007 SPSS Inc.) was used for statistical analysis.

RESULTS

In our study, graftectomy was performed in 23 (36.5%) of the 63 (25.3%) marginal patients and in 39 (20.9%) of 186 (74.7%) ideal recipients \( (P = .002) \). Four (6.3%) MDK patients and 20 (10.8%) IDK patients died with functioning grafts \( (P = .223; \) chi-square test).

The creatinine levels of marginal versus ideal donors were 107.60 ± 173.100 \( \mu \text{mol/L} \) versus 93.72 ± 171.45 \( \mu \text{mol/L} \) \( (P = .0001) \) and mean recipient ages, 53.94 ± 8.15 versus 40.81 ± 6.86 years \( (P = .002) \) were significantly different.
Table 3. eGFR and Serum Creatinine Levels at First and Fifth Post transplantation Year in MDK >55 Years and in the MDK Hypertension Groups

<table>
<thead>
<tr>
<th></th>
<th>MDK &gt; 55 Years</th>
<th>MDK Hypertension</th>
<th>P Value</th>
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<tbody>
<tr>
<td>1 year after Tx</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>eGFR (mL/min/1.73 m²)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SCr (µmol/L)</td>
<td>50.15 ± 19.28</td>
<td>52.64 ± 17.48</td>
<td>.436</td>
</tr>
<tr>
<td>5 year after Tx</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>eGFR (mL/min/1.73 m²)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SCr (µmol/L)</td>
<td>152.60 ± 79.01</td>
<td>137.00 ± 59.08</td>
<td>.124</td>
</tr>
<tr>
<td></td>
<td>41.20 ± 22.72</td>
<td>47.80 ± 18.20</td>
<td>.174</td>
</tr>
</tbody>
</table>

Abbreviations: MDK, marginal donor kidney; IDK, ideal donor kidney; Tx, transplantation; eGFR, estimated glomerular filtration rate; SCr, serum creatinine.

Table 4. Protocol Biopsy Results in the MDK and IDK Groups

<table>
<thead>
<tr>
<th></th>
<th>AR n (%)</th>
<th>IF/TA n (%)</th>
<th>CNI-tox n (%)</th>
<th>Other n (%)</th>
<th>Normal n (%)</th>
<th>Total n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDK</td>
<td>8 (28.5%)</td>
<td>5 (17.9)</td>
<td>5 (17.9)</td>
<td>5 (17.9)</td>
<td>5 (17.9)</td>
<td>19 (72)</td>
</tr>
<tr>
<td>IDK</td>
<td>5 (6.7)</td>
<td>7 (9.5)</td>
<td>3 (6.8)</td>
<td>12 (16.2)</td>
<td>45 (60.8)</td>
<td>74 (100)</td>
</tr>
<tr>
<td>P value</td>
<td>.0004</td>
<td>.002</td>
<td>.158</td>
<td>.248</td>
<td>.0001</td>
<td>—</td>
</tr>
</tbody>
</table>

Abbreviations: MDK, marginal donor kidney; IDK, ideal donor kidney; AR, acute rejection; IF/TA, interstitial fibrosis/tubular atrophy; CNI-tox, calcineurin inhibitor toxicity.

DISCUSSION

We followed the courses of kidneys from 25.3% marginal and 74.7% ideal donors among our recipients between 2005 and 2009. The ratio of MKDs was only 12.5% in the 1990s, but it has continuously increased due to expansion of donor criteria to address the rapid increase in the number of waiting patients. We observed that the ratio of graftectomies between the two groups was significantly different (P = .002) consistent with the literature. Ojo et al\(^2\) reported 35.9% graftectomy in an MDK versus 24.9% in the IDK group (P < .001). Gopalakrishnan et al\(^1\) published ratios of 47% versus 25%.\(^1\)\(^1\) Evaluating donor and recipient data we observed that the creatinine level of the donors (P = .003), occurrence of stroke (P = .001) or trauma (P = .001) as cause of death as well as recipient age were significantly different between the two groups. In the study of Ojo et al.\(^5\)

Recipients age was significantly different between the MDK and IDK patients (47 ± 13.2 years versus 43 ± 13.8 years; P < .001). Younger renal transplant recipients often outlive their allografts adding to the waiting list; whereas older recipients may die before their allograft fails. Introducing a new method to assess the survival of marginal cadaver kidneys, has Baskin-Bey et al\(^1\) proposed a deceased donor score (DDS). Rather than defining a donor as meeting expanded criteria the DDS seeks to be a quantitative approach providing a continuum scale from 0 to 39. The deceased donor kidney is assigned one of four grades (A, B, C, or D). They reported that a significant number of cadaver donor kidneys (10.7%) that were identified by the DDS system as likely to have decreased posttransplantation function and graft survival were missed by the ECD system, suggesting DDS to display greater predictive ability. We studied renal function similar to Eytan et al\(^7\) and Persson et al\(^8\) at 1 year after transplantation: there were no significant differences in the serum creatinine levels or eGFR between the two groups. However, at 5 years, the serum creatinine level (P = .0001) and eGFR (P = .003) were significantly different.\(^13\)\(^14\) We evaluated whether hypertension or advanced age influenced graft function among the MDK group. At 5 years after transplantation, the serum creatinine level was significantly greater among patients older than 55 years compared with hypertensive patients, as previously suggested by other authors.\(^15\)\(^16\)

Based on the histopathological changes at 1 year after the transplantation, AR and IF/TA seemed to be significantly increased risk of developing an AR episode, and in 26% increase in the risk of developing IF/TA (Table 5).
different in MDK compared with IDK patients although there was no significant difference in renal function. Analyzing 937 first and second cadaver transplants Matas et al sought to determine whether information available at the time of an offer could be used to predict long-term graft survival. The questions voiced by ideal recipients whether they should accept a marginal kidney provided the background for their study. These studies have suggested that there is no functional difference between kidneys from marginal donors and from ideal donors at 1 year after the transplantation, although they are evident at 5 years.

Regarding the lower quality of life of patients undergoing dialysis and the lower long-term survival compared with these receiving a kidney from marginal donors, we have concluded that expanded donor criteria have enabled more patients to undergo transplantation, and thus improving their quality of life and long-term survival. Further studies are needed to establish whether there is a significant difference in the 10-year graft survival between grafts from marginal versus ideal donors and to define differences in function and morphology.

REFERENCES


Table 5. Results of Logistic Regression Analysis

<table>
<thead>
<tr>
<th></th>
<th>AR</th>
<th></th>
<th>IF/TA</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>P Value</td>
<td>OR</td>
<td>P Value</td>
<td>OR</td>
</tr>
<tr>
<td>MDK</td>
<td>.005</td>
<td>1.221</td>
<td>.004</td>
<td>1.268</td>
</tr>
<tr>
<td>IDK</td>
<td>.331</td>
<td>0.621</td>
<td>.421</td>
<td>0.712</td>
</tr>
</tbody>
</table>

Abbreviations, MDK, marginal donor kidney; IDK, ideal donor kidney; AR, acute rejection; IF/TA, interstitial fibrosis/tubular atrophy; OR, odds ratio.