Kidney transplantation from related and unrelated living donors in a single German centre

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Abstract

Background. Organ transplantation began in 1954 with living related donation (LRD). Because of organ shortage from cadavers, unrelated kidney donation (LURD) has been proposed and shown to have good results despite complete HLA mismatching. This study aims to look at differences and similarities comparing LRD and LURD performed in our centre since the implementation of the German transplant law in 1997.

Methods. Between January 1997 and July 2001, 62 out of 112 potential living donors and their recipients were accepted. Immunosuppression consisted of triple therapy (steroids, cyclosporin, mycophenolate) in patients with three or fewer mismatches, or quadruple therapy including mono- or polyclonal antibody treatment in patients with four or more mismatches or cytotoxic antibodies. LRD and LURD groups were compared for number and type of rejections, complications and kidney function at the end of observation (median 15.5 months, range 1–50 months).

Results. Out of 112 pairs presenting, transplantation was performed in only 62 cases (55.4%). Reasons to deny transplantation were medical problems of the potential donors in 19, psychological problems in 13, recipient problems in seven and other reasons in 11 pairs. In 38 cases LRD transplantation and in 24 cases LURD transplantation was carried out. Recipient age was significantly lower in the LRD group (37.7 ± 12.1 years) compared with the LURD group (53.6 ± 7.8 years). Mean donor age was 49.7 ± 9.2 years in the LRD group and 50.3 ± 9.1 years in the LURD group (ns). The number of mismatches was lower in LRD (2.1 ± 1) than in LURD (4.4 ± 0.9) (P = 0.001) transplantation. The acute rejection rate was similar in both groups (52.2% vs 54.2%). OKT3 and tacrolimus rescue therapy for more severe rejections was more often applied in the LRD group but the difference did not reach the level of significance. There were more infectious complications in LURD transplantation (66.7% vs 36.4%, P = 0.036) and a trend towards more surgical complications in LRD transplantation (28.9% vs 8.3%, P = 0.062). One graft was lost due to transplant artery thrombosis and one recipient died 4 months after transplantation subsequent to cerebral ischaemia. Both patients belonged to the LRD group. Creatinine values at the end of observation time were 1.76 ± 0.6 mg/dl in the LRD group and 1.62 ± 0.5 mg/dl in the LURD group (ns).

Conclusion. Although kidney transplantation from unrelated donors was performed with a lower HLA match and although the recipients were older, the results are equivalent to living related transplantation. Therefore, kidney transplantation from emotionally related living donors represents a valuable option for patients with end-stage renal disease. Careful selection of donors and recipients is a prerequisite of success.

Keywords: kidney transplantation; living kidney donation; related donors; unrelated donors

Introduction

Organ shortage and a steadily increasing waiting time for a cadaver kidney transplant have made it necessary to search for alternatives. Kidney transplantation with organs from living related donation (LRD) has been performed for many years with good results [1]. Kidney transplantation from living unrelated donors (LURD), i.e. between persons, who have close emotional bonds only, have therefore been proposed as another possibility. In the US in particular, but also in other countries, kidney transplantation from LURD was described as early as the mid-1980s with good short-term [2,3] and long-term results [4–7] and low short-term and long-term risks for the donors [8,9].
Until 1996 LRD transplantation in Germany was performed in 2.7–6.7% of all kidney transplantations [10]. For many years there was almost no LURD transplantation. Since the implementation of the German transplant law in 1997, which allowed living kidney transplantation not only between related but also between genetically unrelated but emotionally closely related persons, LRD and LURD transplantations have been performed increasingly and now represent about 16% of all kidney transplantations [10].

In our centre living kidney transplantation has been performed since 1975. From 1975 until the end of 1996 a total of 32 living donor kidney transplantations (LRD) have been performed. As a new era has started since the implementation of the German transplant law, we evaluated the results of 62 living kidney donor transplantations by comparing LRD with LURD from 1997 to July 2001. We intended to provide more detailed information about the donor selection procedure and patient outcome in a German centre and aimed to look at differences and similarities among living related and unrelated transplantation.

Subjects and methods

Selection procedure

Potential donors and recipients were first informed by the medical team, without any pressure or obligation, about risks and advantages of the procedure for living donor transplantation. Prerequisites for further evaluation were blood group compatibility and a negative cross-match. Subsequently, potential donors underwent an extensive medical and psychological examination. Kidney function was measured by means of serum creatinine, 24 h urine collection for creatinine clearance and proteinuria, urine specimen and renal scintigraphy. In the event of proteinuria and/or microerythrocyturia a kidney biopsy was performed. Blood pressure was measured with 24-h ambulatory blood pressure (ABP) monitoring. Angiography was performed as one of the last examinations.

As required by law since October 1999, an external commission consisting of a psychologist, a person qualified for the position of a judge and a physician independent of the transplant community evaluated the donor for voluntainers and the absence of ‘organ commerce’. Before the existence of this external commission, we had established an ethics committee at our centre consisting of the nephrologist, the transplant surgeon, a psychologist and a physician independent of our transplant centre for the final acceptance of a donor and recipient.

Donor characteristics and reasons for refusal during the selection procedure were documented.

Transplantation procedure

Donors in whom the renal angiogram did not show any left- or right-sided vessel abnormalities, and/or kidney function was about the same on both sides, underwent removal of the left kidney by lumbotomy. In case of anatomical abnormalities or significant differences comparing the two kidneys by renal scintigraphy we preferred to choose the organ with the ‘lower quality’ for donation.

At our centre living kidney donation and transplantation is performed exclusively by the most experienced surgeon (W.S.). Donor and recipient were prepared in parallel localized operating theatres. Usually the incision for transplantation was not started until the kidney was dissected and ready to be removed. Warm and cold ischaemia times were recorded as for cadaveric kidney transplantation.

Post-nephrectomy donor follow-up

All donors were examined closely after transplantation. To date, 32 of the 62 donors have received subsequent extensive examinations during follow-up by measuring serum creatinine, creatinine clearance and proteinuria from 24-h urine collection. As before surgery, blood pressure was again monitored thereafter with 24-h ABP monitoring. Donor data as described above were compared before and after donation. Further short-term and long-term complications were recorded.

Recipients management and outcome

Immunosuppression consisted of triple therapy in patients with three or fewer mismatches (steroids, cyclosporin, mycophenolate mofetil) and quadruple therapy including mono- or polyclonal antibody treatment (ATG-Fresenius S®, Fresenius HemoCare, Graefling, Germany; ALG, Lymphoglobulin Méérieux®, Institut Méérieux, Leimen, Germany; Basiliximab®, Simulect, Novartis Pharma, Nürnberg, Germany; OKT3, Orthoclone®, Jansen-Cilag, Neuss, Germany) in patients with four or more mismatches or patients with cytotoxic antibodies (panel reactive activity, PRA > 50%). Immunosuppression with mycophenolate mofetil (Cell Cept®, Roche, Herfordshire, UK) (2 × 1 g/day) was started 5 days before and cyclosporin 3 days before the scheduled transplantation. Target trough levels for cyclosporin (Sandimmun oral forte®, Nuessa, Nürnberg, Germany) were ~150–180 ng/ml.

Patients receiving antibody treatment were given Pneumocystis carinii prophylaxis with pentamidine inhalation once a week for the first 6 months after transplantation. We did not perform CMV prophylaxis but patients were regularly screened for pp65-antigen. In the event of conversion, early therapy for CMV infection was started.

At the occurrence of clinical signs of rejection, renal biopsy was performed. Rejections were treated with steroid bolus of 250 mg methylprednisolone (Urbason solubile forte®, Hoechst Marion Roussel, Bad Soden, Germany) i.v. over 5 days. OKT3 treatment was used for 7–10 days in the event of histological signs of vascular rejection. Cyclosporin was substituted by tacrolimus (Prograf®, Fujisawa, München, Germany) in cases of steroid-resistant interstitial rejection, signs of cyclosporin toxicity in kidney biopsies or other cyclosporin related side effects. Target trough levels for tacrolimus were 8–12 ng/ml.

Delayed graft function (DGF) was defined as a post-operative requirement of dialysis, even in cases, in which only one dialysis was necessary.

Recipients were compared for DGF, number and type of histologically proven rejections, rejection treatment, infectious, surgical or medical complications, kidney function measured by serum creatinine and graft and patient survival during the time of observation (median 15.5 months, range 1–50 months).
Values are expressed as mean values ± standard deviation. In order to examine differences between groups, Fisher’s exact test and the Mann–Whitney test were employed for categorical and quantitative data, respectively. Statistical significance was accepted for \( P < 0.05 \).

**Results**

**Selection procedure**

Out of 112 pairs presenting for living donor transplantation (54.6%) were not accepted, the main reason being medical problems of the donor \( (n = 19) \). Diagnosis of early stage malignoma \( (n = 8) \), kidney disease \( (n = 6) \), HBs AG or HCV antibody positivity \( (n = 2) \), coronary artery disease \( (n = 1) \), chronic obstructive pulmonary disease \( (n = 1) \) and alcoholism \( (n = 1) \) were reasons to be excluded from donation. Out of the six potential donors with renal disease one had polycystic degeneration and one suffered from asymptomatic nephrolithiasis. The other four patients were discovered to have microhaematuria and mild proteinuria. A renal biopsy was therefore performed, revealing thin basement membrane. Because of the relatively young age of these potential donors and additional fibrosis of glomerula and interstitium we did not consider nephrectomy for donation in these cases.

Other reasons for denial were doubts and anxiety after information about risks or other psychological factors \( (n = 13) \), medical or immunological reasons of the recipients \( (n = 7) \), migration to another transplant centre \( (n = 6) \), cadaveric kidney transplantation which was offered before the living donation could be accomplished \( (n = 3) \) and blood group incompatibility \( (n = 2) \) in potential donors tested as having blood group O in other laboratories, while A2 was detected in negative recipient \( (n = 1) \).

Immunological reasons for denial were a positive X-match \( (n = 2) \) and specific antibodies against HLA antigens of the potential donor \( (n = 2) \). The two patients with positive X-match were actually on the waiting list. One patient with specific antibodies received a cadaveric kidney transplant and the other presented in another transplant centre where she received living kidney transplantation from the donor, which had not been accepted in our centre.

Medical reasons for denial of recipients were multimorbidity of one and prostate cancer of another. One female patient was considered not transplantable because of anorexia nervosa. After psychiatric treatment she has been accepted for transplantation and living kidney transplantation was performed in November 2001.

Among the 62 (55.4%) accepted pairs, donors and recipients were genetically related (LRD group) in 38 cases and unrelated (LURD group) in 24 cases.

Mean donor age was 49.7 ± 9.2 (range 30–65) years in the LRD and 50.3 ± 9.1 (range 28–66) years in the LURD group \( (n s) \). In both groups more women donated a kidney and more men received a living kidney donation. Donor characteristics are presented in Table 1. As expected, the mismatch number was lower in the related group \( (2.1 ± 1) \) than in the unrelated group \( (4.4 ± 0.9) \) \( (P < 0.001) \).

In two accepted donors with microhaematuria kidney biopsy revealed in one case a thin basement membrane and in the other mild tubulo-interstitial changes. Because of higher donor age, lack of hypertension and lack of fibrosis or glomerulosclerosis in kidney biopsy and in the presence of normal renal function we accepted donation. This is in contrast to the four potential donors with kidney biopsy who were denied because they were younger and in whom interstitial fibrosis was present. Both donors belong to the LRD group.

Mild hypertension, which was controlled by only one antihypertensive drug was present in six \( (15.7\%) \) of the living related donors and in two \( (8.4\%) \) of the living unrelated donors.

In most cases the left kidney was removed \( (26 \text{ in the LRD group and } 18 \text{ in the LURD group}) \) representing 71% of the donated kidneys. Although the kidneys with normal anatomy were preferred for donation, in several cases vascular and ureteral norm variants and anomalies had to be dealt with. In the LRD group eight \( (23.5\%) \) patients had multiple (two to three) arteries and/or veins or fibromuscular dysplasia \( (n = 2) \). In the LURD group, five \( (20.8\%) \) patients had two arteries and/or veins, of which two had also a split
ureter (ureter fissus). Some examples are presented in Figures 1 and 2.

Recipient age was significantly lower in the LRD group with 37.7 ± 12.1 years (range 18–64) compared with 53.6 ± 7.8 years (range 31–65) in the LURD group (Table 1). Only four of all recipients were receiving a second kidney transplant (three in LRD and one in LURD group). Pre-emptive transplantation was performed in three recipients of the LRD group and in four recipients of the LURD group. Other recipient characteristics are presented in Table 1.

Transplantation procedure

During the operative procedure the first warm ischaemia time was 2.5 ± 1.7 min in LRD and 3.0 ± 2.5 min in LURD, the second warm ischaemia time was 22.5 ± 7.1 min in LRD and 22.8 ± 6.7 min in LURD and cold ischaemia was 34.5 ± 25.1 min and 33.1 ± 21.3 min, respectively, thus significant differences by comparison of the ischaemia times could not be detected.

Post-nephrectomy follow-up

There was no early or late surgical mortality. Early complications after donor nephrectomy are shown in Table 2. In two donors we observed life-threatening complications (one resuscitation due to hypovolaemic shock from bleeding and one attempt of suicide). Mean hospitalization time was 10.2 ± 4.7 days in the related donors and 10.8 ± 8.8 in the unrelated donors.

Thirty-two out of 62 donors were examined more extensively in our centre at 3–24 months follow-up after donation. This group included the two donors, who had renal biopsy before donation. Data on the 32 donors are shown in Table 3. A significant increase in creatinine (0.88 ± 0.12 mg/dl before and

Fig. 1. Angiography of a 62-year-old donor without hypertension showing fibromuscular dysplasia of the right renal artery. The right kidney was chosen for living related transplantation for her sister.

Fig. 2. Intravenous urography of a 49-year-old donor revealing ureter fissus on the right side. The right kidney was removed for living unrelated transplantation for her husband. Additionally this kidney was supplied by two arteries and one vein.
Recipient management and outcome

Antibody induction therapy (antithymocyte globulin, ATG) was given to two patients in the LRD group because of high antibody panel reactive activity (PRA). All other recipients of this group received triple immunosuppression according to the above-mentioned HLA matching. In the LURD group 20 out of 24 recipients received quadruple immunosuppression (ATG n = 16, ALG n = 1, OKT3 n = 1, Basiliximab n = 2). Four patients received triple immunosuppression because of allergic reaction to ATG during intracutaneous testing (n = 2) or unexpectedly good HLA matching (two or three mismatches n = 2).

DGF was seen more often in LRD transplantation (15.8%) than in LURD transplantation (4.2%) without reaching statistical significance (P = 0.2). In three of the six patients with the DGF in the LRD group vascular problems were encountered. Two patients with severe atherosclerosis of the iliac arteries had stenosis, which hampered normal perfusion of the organ and one patient with APC resistance due to factor V Leiden mutation developed transplant artery thrombosis. In the latter case additional mild renal artery stenosis was left behind within the donor artery at the time of transplantation. All three patients underwent immediate reoperation 2–7 days after transplantation. After reconstruction of the iliac arteries renal function recovered immediately in the first two patients and in the third patient the graft was definitely lost and had to be explanted within the first week after transplantation.

All rejections in both groups were confirmed by biopsy (Table 4). The incidence of acute rejection was 52.2% in the LRD group and 54.2% in the LURD group. The number of patients suffering from more than one acute rejection and from more severe rejections was somewhat higher in the LRD group. OKT3 treatment or switch to tacrolimus was performed more often in the LRD group but did not reach statistical significance (P = 0.3) (Table 4).

Table 2. Early and late complications after nephrectomy in 62 living donors

<table>
<thead>
<tr>
<th>Complications</th>
<th>Cases (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resuscitation due to hypovolaemic shock + acute renal failure</td>
<td>1</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>1</td>
</tr>
<tr>
<td>Attempt of suicide/depression</td>
<td>1</td>
</tr>
<tr>
<td>Major bleeding needing surgical revision or blood transfusion</td>
<td>2</td>
</tr>
<tr>
<td>Seroma/lymph fistula</td>
<td>2</td>
</tr>
<tr>
<td>Wound haematoma</td>
<td>2</td>
</tr>
<tr>
<td>Incisional hernia/relaxatio</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>13</td>
</tr>
</tbody>
</table>

Table 3. Renal function, proteinuria and blood pressure measured with 24-h ABDM in our centre at 3–24 months after nephrectomy in 32 donors—including two donors with renal biopsy before donation

<table>
<thead>
<tr>
<th></th>
<th>Before donation</th>
<th>After donation</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum-creatinine (mg/dl)</td>
<td>0.88 ± 0.12</td>
<td>1.24 ± 0.19</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Creatinine clearance (ml/min)</td>
<td>107 ± 23.4</td>
<td>75.7 ± 20.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Proteinuria in 24 h (mg)</td>
<td>125.9 ± 196</td>
<td>173.4 ± 320.2</td>
<td>ns</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>122 ± 10</td>
<td>122 ± 12</td>
<td>ns</td>
</tr>
<tr>
<td>(24-h measurement)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>78 ± 7</td>
<td>80 ± 10</td>
<td>ns</td>
</tr>
<tr>
<td>(24-h measurement)</td>
<td></td>
<td></td>
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</tbody>
</table>

1.24 ± 0.19 mg/dl after donation, P < 0.001) and a significant decrease in creatinine clearance (107 ± 23.4 ml/min before and 75.7 ± 20.4 ml/min after, P < 0.001) was observed. There was a slight increase in proteinuria without reaching the level of significance. Arterial blood pressure was comparable before and after donation (Table 3).

Table 4. Outcome after kidney transplantation from LRD and LURD between January 1997 and July 2001, Düsseldorf

<table>
<thead>
<tr>
<th></th>
<th>LRD (n = 38)</th>
<th>LURD (n = 24)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>DGF</td>
<td>6 (15.8%)</td>
<td>1 (4.2%)</td>
<td>ns</td>
</tr>
<tr>
<td>Number of patients with rejection</td>
<td>20 (52.5%)</td>
<td>13 (54.2%)</td>
<td>ns</td>
</tr>
<tr>
<td>Patients with more than one rejection</td>
<td>9 (23.7%)</td>
<td>2 (8.3%)</td>
<td>ns</td>
</tr>
<tr>
<td>OKT3 therapy</td>
<td>5 (13.2%)</td>
<td>1 (4.2%)</td>
<td>ns</td>
</tr>
<tr>
<td>Tacrolimus therapy</td>
<td>16 (42.1%)</td>
<td>8 (33.3%)</td>
<td>ns</td>
</tr>
<tr>
<td>Immunological reasons</td>
<td>12</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Non-immunological reasons</td>
<td>4</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Patients with infectious complications</td>
<td>14 (36.8%)</td>
<td>16 (66.7%)</td>
<td>0.036</td>
</tr>
<tr>
<td>(Urine tract/pneumonia/CMV/other)</td>
<td>(8/2/3)</td>
<td>(11/1/0)</td>
<td></td>
</tr>
<tr>
<td>Patients with surgical complications</td>
<td>11 (28.9%)</td>
<td>2 (8.3%)</td>
<td>ns</td>
</tr>
<tr>
<td>(Lymph fistula/urinoma/vascular/other)</td>
<td>(2/2/4)</td>
<td>(0/1/0)</td>
<td></td>
</tr>
<tr>
<td>Patients with medical complications</td>
<td>9 (23.7%)</td>
<td>7 (29.2%)</td>
<td>ns</td>
</tr>
<tr>
<td>(Cerebral/cardiac/diabetes/other)</td>
<td>(2/2/1/4)</td>
<td>(1/2/1/3)</td>
<td></td>
</tr>
<tr>
<td>Serum creatinine at end of observation (mg/dl) (at 19.6 ± 15.4 months)</td>
<td>1.76 ± 0.6</td>
<td>1.62 ± 0.5</td>
<td>ns</td>
</tr>
<tr>
<td>Graft survival at the end of observation time</td>
<td>94.8%</td>
<td>100%</td>
<td>ns</td>
</tr>
<tr>
<td>not censored for death with functioning graft</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient survival at the end of observation time</td>
<td>97.4%</td>
<td>100%</td>
<td>ns</td>
</tr>
</tbody>
</table>
Interestingly, we found thin basement membrane in two recipients and benign nephrosclerosis in another during graft biopsy, which was probably already present in the donor. The corresponding donors presented with mild hypertension in two cases and one had had a creatinine clearance that was at the lower limit of the normal range but no abnormalities were found in the urine analysis, therefore these donors did not undergo kidney biopsy before donation.

More infectious complications occurred in the unrelated group (66.7%) than in the related group (36.8%, \( P = 0.036 \)), most being urinary tract infections. A trend towards a higher rate of surgical complications was seen in the LRD group (28.9% compared with 8.3%, \( P = 0.062 \)). Most striking was the difference in vascular problems, which occurred in four cases in the LRD group and not at all in the LURD group. These four complications concerned iliac artery stenosis in two patients and renal artery stenosis in another two patients who received kidneys with multiple arteries. Medical complications were comparable in both groups (Table 4). Mean follow-up within the group of recipients was 19.6 ± 5.4 months (median 15.5 months, range 1–50 months). Kidney function at the end of the observation period was acceptable with creatinine values of 1.76 ± 0.6 mg/dl in the LRD group and 1.62 ± 0.5 mg/dl in the LURD group.

By July 2001 one patient of the LRD group had died with a functioning graft following infectious complications after a major stroke and consecutive long-term ventilation, and one graft from this group had been lost because of thrombosis of the renal artery. At the end of the observation period (July 2001) 97.4% of the patients were alive and 94.8% of the grafts were functioning. At this time, all grafts in the LURD group were functioning and all patients were alive.

**Discussion**

Kidney transplantation began with living kidney donation and has the advantage of excellent graft and patient survival [4–6,11–13]. Careful planning and pre-operative initiation of immunosuppression are of utmost importance [4,11,12]. Living kidney donation also offers the advantage of avoiding dialysis completely by performing pre-empptive transplantation [11,12,14]. Until 1996, transplantation from living donors in Germany represented only 2–6% of the transplantations, mainly because of ethical concerns. During the last few years there has been a change in general attitude towards more transplantations from living donors and since the implementation of the German transplant law an increasing number of related and unrelated persons presented at our service and expressed their wish to donate a kidney. However, living unrelated donation is not without ethical problems. The motivation can be based only on emotional relations and must be offered convincingly and voluntarily, i.e. without any external pressure. The emotionally related kidney donation excludes by definition all living unrelated donations with kidneys purchased from strangers [15]. In our centre we have always considered transplantation either between related or unrelated persons only under circumstances, where emotional relation and high motivation were evident and other purposes could be excluded. A further key point during workup was to exclude even small additional risks for the donor. Therefore, the evaluation procedure consists of multiple discussions between donors and recipients and the medical and surgical team as well as with the psychologist.

In regard to the tremendous increase in living kidney donation transplantations in the Eurotransplant area each centre should consider evaluation of their own results as a basis for selection criteria, risk of donation and therapeutic strategies of the recipients.

One important observation of our study is the relatively high number of drop outs of potential donors during our selection period, mainly because of diseases accidentally discovered, which surprised the potential donors, because they believed themselves absolutely healthy. Interestingly, disappointment about the refusal as a donor was sometimes greater than the concern about the newly discovered disease, which was serious in several cases (malignoma, coronary artery or infectious disease). Renal disease also represented an exclusion criterion in 12% of the refused donors. In cases of symptoms and clinical signs of renal disease we considered renal biopsy justified because of the relatively small magnitude of this procedure in comparison with the donation procedure itself. The high incidence of thin basement membrane in kidney biopsies was remarkable. In some but not all cases with thin basement membrane, we could not accept kidney donation due to additional fibrotic changes, which presented a risk of deterioration of renal function in the donor. The high number of refusals in our series produced a large amount of work and costs without leading to transplantation. Similar experiences have been described in the literature by others who have reported a percentage of refusals as high as 66–87% [16,17]. Reimbursement of this workload and costs is still a matter of discussion. It seems further, that both malignant and renal disease were much more prevalent in persons, who did not consult a doctor for any form of symptoms but who just underwent screening for donation. One can imagine, that a work up of the adult population would probably allow detection of many, at that time asymptomatic diseases and help to start appropriate management, but who will pay for it?

We think that the donation procedure was safe from the donor point of view, albeit not without risks. Most impressive was the case of a patient with major bleeding leading to hypovolaemic shock and resuscitation. The reason for bleeding was a vascular clip, which had slipped off the renal artery. Fortunately, immediate re-operation saved the patient and since then we have not used clips for the stump of the renal artery. Instead, the aorta is closed by
conventional vascular suture techniques after removal of the renal artery [18]. In comparison, our number and types of complications in donors were in about the same range with data reported by others [12,16,19].

With regard to kidney function, proteinuria and blood pressure we observed a significant decline in creatinine clearance, a non-significant increase in proteinuria and unchanged blood pressure measured over 24-h in the donors, who underwent re-evaluation at our centre. The data correspond to those published previously [7,9,11].

We observed a high rate of surgical problems in the LRD recipients. One third was due to vascular complications caused by severe atherosclerosis of the recipients, despite their young age. The other complications were observed in patients, who received kidneys with vascular abnormalities such as fibromuscular dysplasia or multiple arteries. Fortunately, in two out of three recipients graft function could be saved after an early diagnosis of perfusion problems. As the overall number of patients and complications in our material is still small, the difference between LRD and LURD groups must be regarded as random. However, we conclude from our experiences, that in preparation of the donor careful and even selective renal arteriography may be indicated and the recipient with risk factors or clinical sings of atherosclerosis should have CT scanning and sometimes also arteriography of the pelvic arteries even in the presence of good pulses. The same holds true for postoperative screening, if perfusion of the graft is in doubt. Vascular abnormalities do not necessarily represent a contraindication for donation, but donor and recipient must obtain sufficient information about the increased probability of complication and the graft must be followed by Duplex-sonography, magnet-resonance-arteriography and even digital subtraction angiography.

Excellent patient and graft survival was observed in all our living kidney transplantations. During the observation period we did not see a difference in graft function between related and unrelated kidney donation transplantations despite a younger recipient age and better HLA matching in the genetically related group. Up to July 2001 graft survival was 94.2% in the LRD group and 100% in the LURD group, making us optimistic about the long-term results. Graft survival in unrelated kidney donation reported by others is 85% at 1 year in Norway [12] and 85% after 3 years in the USA [4]. When comparing results, differences in immunosuppressive therapies must be taken into consideration. One-year graft survival of groups using similar immunosuppressive protocols to ours is as high as 92–100% [6,11]. We therefore conclude that quadruple immunosuppression in genetically unrelated living kidney transplantation results in excellent short-term graft survival. When using this immunosuppressive regime the higher risk of infectious complications should be borne in mind.

There are several arguments indicating that lower rejection rates are to be expected in living kidney donor transplantation. Brain death, long cold ischaemia times and DGF have been shown to be risk factors for acute rejection in cadaveric kidney transplantation [20–22]. Generally reported rejection rates in cadaveric kidney transplantation range from 30–50% [18,23]. Interestingly, we did not find a lower incidence of acute rejection in living kidney donation transplantation (52.5% in LRD and 54.2% in LURD) in comparison with rejection rates in cadaveric kidney transplantation in our centre (52–60%) [24,25]. Further, we did not see a higher incidence of acute rejections in LURD transplantation despite a higher HLA-mismatch number. Higher rejection rates in living kidney transplantation have been reported (70% in LRD and 84% in LURD) by two groups, where one group applied a triple immunosuppression in all living kidney donations independent if related or unrelated and the other group performed donor specific transfusion in some cases of living unrelated donation [11,12]. These procedural differences might account for the higher rejection rates when compared with our data. These groups reported higher rejection rates in LURD. On the other hand, in a large series of patients, rejection rates were reported to be 33% in LRD and 34% in LURD [7]. The data are probably more representative when compared with our results in view of the large number of patients studied.

We conclude that even though theoretical and experimental data would lead us to expect lower rejection rates in living donation, our data and data reported by others do not support this thesis. Further, with the immunosuppressive regime chosen by us, we could achieve similar rejection rates in LURD in comparison with LRD despite more differences in HLA typing in the former. In view of the trend towards more immunological problems in LRD an intensified immunosuppresion may be considered in LRD also.

In conclusion, because of excellent graft and patient outcome and acceptable risks for donors, we advocate the use of living kidney donors. It represents an excellent way of improving the shortage of donors in kidney transplantation. Although living unrelated kidney transplantation was performed with a lower HLA match and despite the older age of the recipients, kidney function was similar to that of living related transplantation. Kidney transplantation from emotionally related living donors therefore represents a valuable option for patients with end-stage renal disease. Careful selection of donors and recipients is advisable.

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