The living kidney donor: giving life, avoiding harm

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Introduction

During the past 12 years, the time spent on the waiting list for renal transplantation rose progressively in the Eurotransplant area and specifically in Germany, whilst during the same time period, unfortunately, the number of cadaveric kidneys available for transplantation did not increase (Table 1). In the face of a crushing organ shortage, nephrologists in Mid Europe have resorted increasingly to living-related or unrelated kidney donation in order to increase the number of grafts available. In our unit in Heidelberg, the proportion of living-related renal allografts increased from 11% in 1991 to 21% in 2001.

In contrast, in Scandinavia, there has been a long tradition of living-related renal transplantation dating back more than 30 years. Single centre reports from Sweden have summarized outcomes of no less than 177 living donor nephrectomies from 1996 to 2001.
accounting for 40% of all transplanted kidneys (I. Fehrman-Ekholm, personal communication). The same trend is now also seen in the USA where in the past 2 years more living-related allografts were transplanted, compared with cadaveric renal allografts [1].

Living-related renal transplantation: beyond expanding the donor pool

The consequences of living-related kidney transplantation go beyond expansion of the donor pool. It permits earlier, possibly even pre-emptive, transplantation. This is not a banal consequence, since the risk of acute rejection after transplantation increases progressively with the time spent on the waiting list.

Against these obvious advantages one has to balance the risk of potential harm to the donor. It is our opinion that this can be absolutely minimized by careful evaluation and optimized surgical techniques. Discussion of the potential risks and strategies to minimize them is the subject of the following communication.

What are the short-term and long-term risks of living-related kidney donation?

Serious post-operative complications, such as bleeding, wound infection and pain, have been reported in 0.5–3% of donors [2]. It is difficult to obtain reliable and honest figures on peri-operative mortality, but a total of 17 deaths (0.03%) have been reported [3].

Apart from these peri-operative risks, are there potential long-term risks with respect to renal function, proteinuria and hypertension? Ellison et al. [1] reported 53 cases in which end-stage renal disease (ESRD) developed in kidney donors. This does not presumably exceed the spontaneous risk of ESRD in the background population, granted that pre-operatively primary renal disease has carefully been excluded in the donor. This conclusion is further supported by observations in patients who had undergone uninephrectomy because of some urological indication: after more than 20 years of follow-up no substantial impairment of renal function was noted [3]. Even after 70% kidney resection because of tumour or tuberculosis, stable renal function was noted after an observation period of 5–30 years [4]. In these cases, the remnant renal parenchyma had not been obviously affected by primary renal disease. The risk of developing microalbuminuria or proteinuria is somewhat higher according to long-term follow-up studies of kidney donors [5]. The risk to develop hypertension is increased [6].

Evaluation of potential kidney donors (Table 2)

Renal function

Uninephrectomy will accelerate progression of pre-existing primary renal disease. It is therefore of paramount importance to exclude such disease before donor nephrectomy is considered. Occult primary renal disease is not uncommon: the prevalence of albuminuria in the general population is 4–10% [7]. In an autopsy study, mesangial IgA deposits were noted in 4.8% of the individuals [8]. This is of particular importance because up to 10% of first-degree relatives of patients with IgA glomerulonephritis suffer from proteinuria, microhaematuria and/or biopsy-confirmed glomerulonephritis [9] and a high frequency of familial IgA glomerulonephritis has been confirmed by recent genetic studies [10]. Repeated examination of the urinary sediment in morning urine samples is indispensable, as is measurement of albumin concentration in the morning urine and protein excretion in 24 h urine collections. Known confounders such as urinary

Table 1. Active waiting list and transplants (cadaveric donor) in Germany and Eurotransplant (Eurotransplant, Annual Report 2000)

<table>
<thead>
<tr>
<th>Year</th>
<th>Germany WL</th>
<th>Germany Tx</th>
<th>Germany LD</th>
<th>Eurotransplant WL</th>
<th>Eurotransplant Tx</th>
<th>Eurotransplant LD</th>
</tr>
</thead>
<tbody>
<tr>
<td>1990</td>
<td>5091</td>
<td>1979</td>
<td>37</td>
<td>7681</td>
<td>3171</td>
<td>105</td>
</tr>
<tr>
<td>1993</td>
<td>6735</td>
<td>2107</td>
<td>58</td>
<td>9418</td>
<td>3293</td>
<td>127</td>
</tr>
<tr>
<td>1996</td>
<td>8112</td>
<td>1887</td>
<td>130</td>
<td>10988</td>
<td>3083</td>
<td>247</td>
</tr>
<tr>
<td>1999</td>
<td>9441</td>
<td>1895</td>
<td>380</td>
<td>12273</td>
<td>3055</td>
<td>579</td>
</tr>
<tr>
<td>2000</td>
<td>9663</td>
<td>1871</td>
<td>346</td>
<td>12524</td>
<td>3145</td>
<td>569</td>
</tr>
</tbody>
</table>

WL, cadaveric waiting-list; Tx, transplants (per year); LD, living donor transplants (per year).

Table 2. Evaluation of potential donors

<table>
<thead>
<tr>
<th>Laboratory</th>
<th>Renal</th>
<th>S-creatinine, s-urea, electrolytes, urinary sediment, albuminuria, 24 h proteinuria, creatinine clearance, glycosuria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolism</td>
<td>Fasting plasma glucose, oral glucose tolerance test, serum cholesterol and triglycerides</td>
<td></td>
</tr>
<tr>
<td>Virology</td>
<td>HBV, HCV, HIV, CMV and EBV</td>
<td></td>
</tr>
<tr>
<td>Immunology</td>
<td>Blood group, HLA-typing, cross-match of T and B lymphocytes</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>Transaminases, blood cell count, usual coagulation tests</td>
<td></td>
</tr>
</tbody>
</table>

Investigations

Renal | Renal ultrasonography, renovascular angiography, MRT-angiography, renal scintigraphy |

Blood pressure | 24 h ambulatory blood pressure measurement |

If hypertensive | Echocardiography, funduscopy, duplexsonography of carotids (intima-media thickness) |

Others | Electrocardiogram, chest X-ray, abdominal sonography, abdominal X-ray (calcifications) |

Older donors | Tumour check (gastrointestinal, gynecology, urology) |

tract infection, uncontrolled hypertension and latent diabetes mellitus must obviously be excluded.

**Hereditary renal diseases**

The risk of ESRD is greater if there is a history of renal disease in first- or second-degree relatives [11,12]. The risk is progressively higher, the greater the proportion of affected first-degree relatives. Since this risk is particularly high in IgA glomerulonephritis [9] and since pathological urinary findings may come and go, some authors consider renal biopsy even if urinary findings are normal.

The most common hereditary renal diseases are autosomal dominant polycystic kidney disease (ADPKD) and Alport disease. The diagnostic criteria to recognize ADPKD has been standardized, e.g. more than four renal cysts by ultrasonography at age 30 years makes the diagnosis of ADPKD likely [13]. Alport disease should be suspected if in a family member of an Alport patient haematuria and/or proteinuria are detected [14]. The exclusion of the diagnosis requires renal biopsy including electron microscopy.

**Diabetes mellitus**

The prevalence of latent or manifest diabetes mellitus type 2 increases progressively in the general population: the prevalence is ~6% at age 50 years and up to 20% at age 70 years. In parallel, latent, i.e. sub-clinical, diabetes mellitus is found with increasing frequency in potential kidney donors. Latent diabetes excludes an individual as a potential donor, since rapid progression of renal failure has been shown if pre-diabetic patients had undergone nephrectomy and subsequently developed diabetes [15]. In our living-related kidney donor programme we systematically perform oral glucose tolerance tests. We exclude individuals with impaired glucose tolerance from kidney donation.

**Hypertension**

At the age of 50 years the prevalence of hypertension is ~15–25% in the German population [16]. We therefore recommend ambulatory blood pressure measurement and if results are equivocal further studies (echocardiography, measurement of intima media thickness of the carotid arteries, fundoscopy and measurement of urinary albumin concentration) in order to exclude hypertension-induced target organ damage. An interesting consequence of hypertension in the donor is transmission of hypertension (but also conversely transmission of normotension) from the donor to the recipient [17].

**Anatomical and functional evaluation of donor kidneys**

Prior to nephrectomy, investigations to exclude anatomical abnormalities are necessary to minimize the peri-operative risk. Apart from conventional angio-

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**Viral infection**

The potential donor must be tested for cytomegaly (CMV), hepatitis B (HBV), hepatitis C (HCV) and human immunodeficiency virus (HIV). Documentation of the CMV status is important to permit adequate selection of protocols for post-operative prophylaxis [18]. It is not absolutely necessary to exclude HBV- or HCV-positive donors (or recipients), since in principle, treatment with interferon and/or antiviral drugs is possible prior to transplantation. For obvious reasons, treatment is prohibited after transplantation, because interferon dramatically increases the risk of rejection. There is consensus that HIV-positive donors should be excluded.

**Malignancy**

Latent malignancy is not uncommon in the general population, particularly above age 50 years and tragic single case observations of transmission of malignancies have been reported in the literature [19]. The most common sites of primaries are lung and colon in both genders, breast and cervix in female and prostate gland in male donors. The conclusions for the check-up of potential donors are obvious.

**The marginal donor**

In the past, transplant centres insisted on age limits for donors. It is true that kidneys of elderly donors, particularly above age 70 years, are more susceptible to ischaemic damage. Nevertheless, in the absence of primary renal disease or confounding cardiovascular
disease, the glomerular filtration rate (GFR) of the elderly is only slightly lower than in young individuals [20]. It is therefore not surprising that recent reports document excellent results of kidney donation from grandparents to grandchildren.

Psychological evaluation

It is indispensable that donors offer a kidney voluntarily, without being subjected to any coercion. The majority of donors interviewed after uninephrectomy have been satisfied with their decision. Only between 4 and 10% of the donors regret organ donation [21] and this may be particularly frequent if the result of transplantation has been disappointing or if difficulties in intrafamilial relationships have arisen. In the Heidelberg Transplantation Unit, a standardized programme of psychological information and consultation has been established for more than 5 years. This comprises meetings including the potential donor and the recipient, exploration of the familial situation, information about the implications of donation and potential medical complications. We put great emphasis on subsequent psychological care after transplantation. This is particularly important if depression, anxiety attacks or suicidal tendencies arise after transplantation, as has been reported in ~5% of the patients.

Social and legal aspects

Organ donation is a voluntary act and the kidney donors have to be aware that donation may lead to some social disadvantages: each individual donor has to explore potential repercussions on health insurance, life insurance costs, difficulties in obtaining new life insurance contracts, etc. It is also useful to inform the employer in time.

Summary

Living-related kidney donation is a way out of the current dilemma of insufficient supply of renal allografts. The risk to the donor is minimal, but not zero, and potential risks must be excluded by careful work-up of the donor. Nevertheless, the current results justify that living-related kidney donation is encouraged and practised on a larger scale. Follow-up, including psychological follow-up, must not only be provided to the recipient, but also to the donor.

References