LONG-TERM OUTCOME OF RENAL FUNCTION AND PROTEINURIA IN KIDNEY TRANSPLANT DONORS

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Summary

Ten to eighteen years after donor uninephrectomy (UN) there was no evidence for deterioration of renal function. The mean urinary albumin excretion was slightly increased. There was a positive correlation between the assessed protein intake at investigation and the glomerular filtration rate (GFR).

Introduction

Living donors are important sources of transplant kidneys in many centres. Donor uninephrectomy (UN) has been considered in both short and long-terms to carry little risk as reported by us and others [1—4]. The recent suggestion that donor UN may cause hypertension and proteinuria and eventually progressive renal failure has caused considerable concern [5]. It prompted us to re-examine the living donors in Göteborg more than ten years after donation with special reference to glomerular filtration rate (GFR), hypertension and proteinuria. These data have been correlated to the actual protein intake in these subjects as this factor has been incriminated in causing long-term deterioration of renal function.

Subjects

During the years 1965—1973 sixty-four living donor UN were performed at our transplant centre in Göteborg, Sweden. Thirty-eight donors were men with a mean age at donation of 42 (23—63) years while 26 were women with a mean age of 47 (23—69) years. Ten donors have died during the observation period. Thirty-eight donors have been investigated 10—18 years after donation. Sixteen donors have not yet been investigated but they have been interviewed and their case records have been examined.
Methods

Glomerular filtration rate (GFR) was measured as renal clearance of inulin and the plasma clearance of $^{51}$CrEDTA using the single injection technique. The results of these methods are almost identical and expressed by the equation:

$$\text{Plasma } ^{51}\text{CrEDTA clearance} = \frac{\text{renal inulin clearance}}{1.10} + 3.7$$

The reference values of Granerus and Aurell [6] for various age groups were used.

Urinary excretion of total protein, albumin, beta_2 microglobulin and nitrogen was measured in three consecutive 24hr samples in each individual. Protein intake was calculated as 6.25 x (urinary nitrogen + 2) g/24hr according to Isaksson [7]. Reference values were obtained in a group of 14 healthy 55-year-old men. Glomerular and tubular proteinuria were defined according to Petersson, Evrin and Berggard [8].

Student’s ‘t’ test, Wilcoxon rank sum test, Spearman’s rank correlation and multiple linear regression analysis have been used for statistical evaluation of the results.

Results

Renal function

GFR 10–18 years after donor UN is shown in Figure 1. Mean GFR for the whole group of donors was 75.8 per cent (50.0–103.9%) of pre-UN GFR for two kidneys. Only seven donors had reduced GFR. Their GFR was 62.5 per cent (50.0–80.0%) of their pre-UN value.

GFR was also measured one year after kidney donation in 10 donors and after five years in 11 donors. As shown in Table I there was a significant increase in GFR from one year to ten years after donation but not between five years and 10 years after donation.

Protein excretion is given in Table II. Only albumin excretion was significantly increased in the donor UN group but a total protein excretion of more than 0.5g/24hr was found in four donors.

Four donors had glomerular proteinuria and two had tubular proteinuria. Mean GFR for these six subjects was 70 (58–84) ml/min1.73m$^2$ (Figure 1).

Nitrogen excretion

The nitrogen excretion was 11.4 (7.1–18.4) g/24hr corresponding to 79.2 (54.6–113.7) g protein intake/24hr/1.73m$^2$. As seen in Figure 2 there was a positive correlation between protein intake and GFR after donor UN (p<0.02). Age accounted only partly for this significant correlation.
Figure 1. Glomerular filtration rate (GFR) at follow up 10–18 years after donor uninephrectomy (UN) in 38 subjects: • normotensive subjects without proteinuria; □ subjects with proteinuria; ▲ subjects with hypertension; ▼ subjects with both hypertension and proteinuria

TABLE I. Mean glomerular filtration rate (GFR) before, 1, 5, and 10–18 years after uninephrectomy (UN) in 32 living kidney transplant donors

<table>
<thead>
<tr>
<th>GFR (ml/min/1.73m²)</th>
<th>pre-UN</th>
<th>1 year</th>
<th>5 years</th>
<th>10–18 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>n = 10</td>
<td>90.6</td>
<td>62.6</td>
<td>–</td>
<td>69.5*</td>
</tr>
<tr>
<td>n = 11</td>
<td>101.2</td>
<td>–</td>
<td>77.0</td>
<td>78.6</td>
</tr>
<tr>
<td>n = 32</td>
<td>99.2</td>
<td>–</td>
<td>–</td>
<td>75.8</td>
</tr>
</tbody>
</table>

*p<0.05 vs 1 year value

**Morbidity**

Ten donors have died since nephrectomy. The causes of death were malignant tumours (3), myocardial infarction (3), alcoholism (2), cerebrovascular lesion (1), and trauma (1). UN may have had some importance in only one of these cases, a 58-year-old woman who developed hypertension three years after the nephrectomy. The hypertension was well controlled but she died five years after nephrectomy from a cerebrovascular lesion.
TABLE II. Mean urinary excretion of total protein, albumin, and $\beta_2$ microglobulin 10–18 years after donor uninephrectomy (UN) and in control subjects. Three consecutive 24 hour urinary samples were collected in each individual

<table>
<thead>
<tr>
<th></th>
<th>Donor UN (n = 31)</th>
<th>Control (n = 14)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total protein (mg/24hr)</td>
<td>306 (92–1217)</td>
<td>210 (65–326)</td>
<td>NS</td>
</tr>
<tr>
<td>Albumin (mg/24hr)</td>
<td>69.5 (5–620)</td>
<td>11.4 (8–23)</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>$\beta_2$ microglobulin (µg/24hr)</td>
<td>1039 (49–28400)</td>
<td>157 (61–420)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Figure 2. Correlation between food protein and total GFR in per cent of pre-UN GFR in 29 donors 10–18 years after donor UN

No donor was treated for hypertension at the time of UN. At follow-up nine donors (seven men and two women) were treated with one to three drugs. No one had malignant or treatment resistant hypertension. For the remaining subjects the mean systolic blood pressure increased from 138 to 149 mmHg corresponding to 0.72 mm/year and mean diastolic pressure from 85 to 87 mm corresponding to 0.10 mm/year.
Urinary sediments were normal in all subjects. Four subjects developed diabetes mellitus after UN. GFR in these patients was not reduced compared to the other donors and they did not have albuminuria. Nine women had one or more urinary tract infections after the UN but their GFR was not reduced;

Discussion

Renal function 10–18 years after donor UN is well maintained and only seven donors were found to have a slightly decreased GFR compared to normal values for healthy subjects with two kidneys. Repeated determinations during the observation time did not indicate progressive decrease of renal function in any subject.

Some donors, however, developed hypertension and/or proteinuria. Twenty-four per cent of the donors were treated for hypertension. This is a high prevalence but hypertension only developed in the upper age groups (54–78 years) as shown in Figure 1. The spontaneous development of blood pressure in the remaining donors did not differ from that in population studies. Hypertension was not severe in any subject.

The determinations of nitrogen excretion showed that the donors had a normal protein intake but interestingly, a positive correlation of protein intake to the GFR after UN was observed. In short-term studies it is well known that increased protein intake stimulates GFR [9] but it was surprising to trace a similar correlation in a long-term study. This stimulated GFR has been incriminated in the hypothesis of decreased renal function after donor UN as a kind of ‘wear and tear’ phenomenon [5]. The exposure over decades to this mechanism apparently does not induce progressive renal failure in living donors.

In conclusion, in this study and many others, donor UN has not been shown to carry a risk of progressive renal failure [10]. However, some degree of proteinuria and hypertension may develop in a subgroup of donors after UN. Further studies on long-term outcome two to three decades after donor UN may provide additional insight in how donor UN affects the mechanisms of development of hypertension and proteinuria. Finally it is important to state that at present we see no reason to reconsider our positive attitude to accept living related kidney donors in our transplant programme.

References

Open Discussion

MAGGIORE (Reggio Cal.) If you look at the relatives of an unselected population with kidney disease you would expect a greater incidence of hypertension and proteinuria in the relatives of patients with polycystic kidney disease, nephrosclerosis, and hereditary nephropathies. Would it not be more reasonable to choose your control population from among the relatives of uraemic patients rather than the general population?

MATHILLAS I think that will be the idea in a future donor study following the relatives of the donor.