RENAL FUNCTION AND BLOOD PRESSURE
AFTER DONOR NEPHRECTOMY


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Summary

Pre- and post-nephrectomy renal function and blood pressure were compared in 75 subjects who had donated a kidney for transplantation during the past 20 years. The function of the remaining kidney was not adversely affected by prolonged compensatory hyperfiltration. However, an increased prevalence of hypertension was found in 'long-term' kidney donors.

Introduction

The advantage of living related kidney transplantation to the recipient are well recognised. Any benefits to the donor, however, are limited to the possible detection of remedial disorders during pre-nephrectomy evaluation and to the positive psychological effects of giving. Donor nephrectomy is a major procedure and is associated with significant morbidity, and a small risk of mortality [1]. For these reasons, many European centres consider living related kidney transplantation to be 'ethically unjustified' [2].

Recent experimental work also questions the long-term safety of donor nephrectomy. In animals, destruction of a critical mass of renal tissue is followed by the development of proteinuria, hypertension and progressive loss of function of the remaining nephrons, and it has been suggested that compensatory hyperfiltration of remnant nephrons is responsible for these developments [3]. As hyperfiltration occurs consistently following unilateral nephrectomy in man, kidney donors would seem to be at risk. In support of this concern is the observation by Kiprovo that patients with unilateral renal agenesis may develop focal glomerulosclerosis in their single kidney [4].

Studies of kidney donors performed during the first six years after nephrectomy have all demonstrated compensatory hyperfiltration but have not shown any progressive deterioration of function in the remaining kidney [5,6]. However, there is no information available from these studies on urinary protein
excretion or blood pressure, and until recently, long-term follow-up of kidney donors has not been reported. This paper examines glomerular filtration rate (GFR), urinary albumin excretion and blood pressure in subjects who have donated a kidney during the past 20 years in Newcastle.

Methods and materials

Seventy-five subjects (38 males, 37 females) who had undergone donor nephrectomy during the period of March 1963 to June 1982, participated in the study. Patients who had donated a kidney less than one year before the study were excluded.

All donors had been investigated before nephrectomy to exclude renal or systemic disease. Their case notes were reviewed and all subjects were interviewed and examined. Blood pressure was measured after resting on three separate occasions, each in supine, sitting and erect positions. Diastolic pressure was taken at the fifth phase of Korotkoff.

Blood was drawn for electrolytes, urea, creatinine, calcium, phosphate, magnesium, albumin and haemoglobin estimations. A 24 hour urine collection was provided for protein and creatinine measurement. On a separate occasion, a timed overnight urine collection was performed for measurement of albumin excretion. All patients gave a freshly voided mid-stream urine specimen for culture and microscopic examination.

A ‘single-shot’ Cr\textsuperscript{51}-EDTA clearance test was performed on all subjects.

Biochemical determinations were performed using routine laboratory methods. Urinary albumin was measured using a single antibody radioimmunoassay. The antibody was specific for human albumin, and separation was by polyethylene glycol precipitation (intra-assay coefficient of variance, 2.5%; inter-assay coefficient of variance, 5.2%).

Sixty-one of the 75 donors completed a week weighed dietary record for assessment of daily sodium, protein and phosphate intake.

For statistical evaluation, the Student’s ‘t’ test, the Student’s paired ‘t’ test, and the test for the Spearman correlation coefficient were used. All means are expressed as the mean ± standard error. P values of less than 0.05 are considered statistically significant.

Results

As no long-term prospective longitudinal study of renal function in donors had been undertaken, we examined the effect of prolonged hyperfiltration by comparing 38 ‘short-term’ donors, studied between 1.4 and 9.9 (mean 4.7 ± 0.3) years after nephrectomy with 37 ‘long-term’ donors who had given a kidney between 10.4 and 20.8 (mean 13.5 ± 0.4) years earlier. There were 19 males and 19 females in the ‘short-term’ group and 19 males and 18 females in the ‘long-term’ group. There was no significant difference between the current age of the ‘short-term’ donors (51.6 ± 1.6 years) and the ‘long-term’ group (53.4 ± 1.6 years). We have also analysed the relationship between renal function and blood pressure, and time since nephrectomy for the group as a whole.
Renal function

The current renal function of the 'short-term' donors is compared with predonation figures in Table I.

**TABLE I. Renal function before and up to 10 years after nephrectomy ('short-term' donors)**

<table>
<thead>
<tr>
<th></th>
<th>Pre-Nx</th>
<th>Post-Nx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urea (mmol/L)</td>
<td>4.8 ± 0.2</td>
<td>5.4 ± 0.2</td>
</tr>
<tr>
<td>Serum creatinine (µmol/L)</td>
<td>88.4 ± 2.7</td>
<td>104.0 ± 2.8</td>
</tr>
<tr>
<td>Creatinine clearance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(mls/min)</td>
<td>105.1 ± 3.9</td>
<td>78.3 ± 3.0</td>
</tr>
<tr>
<td>(mls/min/1.73m²)</td>
<td>-</td>
<td>74.9 ± 2.8</td>
</tr>
<tr>
<td>Cr⁵¹-EDTA clearance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(mls/min/1.73m²)</td>
<td>-</td>
<td>66.9 ± 2.6</td>
</tr>
</tbody>
</table>

Nx = Nephrectomy

Only one of the 38 'short-term’ donors had pathological proteinuria (700mg/24hrs). The mean albumin excretion rate of this group was 7.6 ± 3.2µg/min (reference range for age-sex matched non-nephrectomised controls: 0–10.4µg/min).

The pre- and post-nephrectomy renal function of the ‘long-term’ donors is compared in Table II.

**TABLE II. Renal function before and between 10 and 20 years after nephrectomy ('long-term' donors)**

<table>
<thead>
<tr>
<th></th>
<th>Pre-Nx</th>
<th>Post-Nx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urea (mmol/L)</td>
<td>4.6 ± 0.2</td>
<td>5.3 ± 0.2</td>
</tr>
<tr>
<td>Serum creatinine (µmol/L)</td>
<td>87.2 ± 3.6</td>
<td>98.6 ± 2.1</td>
</tr>
<tr>
<td>Creatinine clearance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(mls/min)</td>
<td>101.4 ± 5.3</td>
<td>83.3 ± 3.7</td>
</tr>
<tr>
<td>(mls/min/1.73m²)</td>
<td>-</td>
<td>81.5 ± 2.7</td>
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<tr>
<td>Cr⁵¹-EDTA clearance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(mls/min/1.73m²)</td>
<td>-</td>
<td>76.9 ± 2.3</td>
</tr>
</tbody>
</table>

Nx = Nephrectomy
No patient in the ‘long-term’ donor group had pathological proteinuria and the mean albumin excretion rate was 8.6 ± 2.6μg/min.

None of the 75 donors had an abnormal urine sediment on microscopy to suggest parenchymal renal disease. Three women in each group had asymptomatic urinary tract infections.

No significant difference was found between the pre- and post-nephrectomy values of calcium, magnesium, phosphate, albumin and haemoglobin in either group of donors.

When the two groups of donors were combined, there was a positive correlation between time since nephrectomy and current creatinine clearance (r = +0.26) and current Cr\textsuperscript{51}-EDTA clearance (r = +0.25), neither of which reached significance.

**Blood pressure**

The mean systolic blood pressure of the ‘short-term’ donors rose from 128.4 ± 2.1 pre-nephrectomy to 132.8 ± 2.6 post-nephrectomy (p<0.05), and the mean diastolics from 78.0 ±1.2 to 83.8 ± 1.4 (p<0.01). No patient in this group was hypertensive prior to nephrectomy, but at follow-up, four had systolic hypertension (>160mmHg) and five had diastolic hypertension (>95mmHg).

In the long-term group, systolic blood pressure rose from 129.9 ± 3.9 pre-nephrectomy to 144.1 ± 4.8 post-nephrectomy (p<0.01) and the diastolics from 80.1 ± 1.3 to 89.7 ± 2.1 (p<0.01). Eleven donors in this group had developed de novo systolic hypertension and 14 diastolic hypertension.

All donors found to be hypertensive were subsequently reviewed by their general practitioner and in all cases hypertension was confirmed and appropriate therapy commenced.

When the ‘short-term’ and ‘long-term’ groups were combined, there was a positive correlation between time since nephrectomy and systolic (r = +0.21; p = NS), diastolic (r = +0.26; p<0.05) and mean arterial (r = 0.25; p <0.05) blood pressure.

**Effect of diet on renal function and blood pressure**

No correlation was found between current renal function (or the percentage change in renal function after nephrectomy) and protein or phosphate intake. Similarly, there was no significant correlation between salt intake and current blood pressure.

**Discussion**

This study demonstrates a remarkable preservation of GFR in ‘long-term’ kidney donors. We found no significant difference between the post-nephrectomy creatinine clearances of our ‘long-term’ donors compared to the ‘short-term’ group. Cr\textsuperscript{51}-EDTA clearance was significantly greater in the ‘long-term’ donors (p<0.01). Both of these findings, considered with the positive correlations bound between both current creatinine clearance and Cr\textsuperscript{51}-EDTA clearance.
and time since nephrectomy for the group as a whole, suggest that over this
time course at least hyperfiltration had not resulted in glomerular damage. We
did not assess renal function in the early post-operative period, but our late
measurements are similar to those reported by others at one week after nephe-
tomy [5], again suggesting stable function. It seems unlikely that the greater
GFR in the long-term donors could be accounted for by their slightly younger
age at donation, since although compensatory hypertrophy of the remaining
kidney is greater when nephrectomy is performed in childhood than in later
life, the mean difference in age at donation in our patients was only seven
years (39.9 ± 1.1 years vs 46.9 ± 1.5 years).

The second marker of hyperfiltration-induced renal damage is proteinuria.
Only one of our 75 donors had pathological proteinuria. There was also no
significant difference between the urinary albumin excretion rates of our ‘short-
term’ and ‘long-term’ donors. Both figures were within the normal range for
non-nephrectomy controls in our laboratory. These findings are in agreement
with the study of long-term kidney donors reported by Vincent et al [7] and
again argue against any progressive glomerular damage in this group of patients.

Both mean systolic (p<0.05) and diastolic (p<0.05) blood pressure were
greater in the ‘long-term’ donors compared with the ‘short-term’ group. Our
data suggest that there is an increased prevalence of hypertension in ‘long-
term’ kidney donors. Thirty-eight per cent of our ‘long-term’ group had de
novo diastolic hypertension, a figure far in excess of that observed in
the otherwise similar group of ‘short-term’ donors (13%), and more than would
be expected in the general population of this age (15%) [8]. In fact, a figure
less than that for the general population would be expected as all donors were
selected in being normotensive at the time of nephrectomy. The younger age
of the ‘long-term’ donors at nephrectomy gives a possible explanation of their
greater proneness to hypertension in that essential hypertension was less likely
to have manifest itself at the time of pre-nephrectomy assessment than in the
older ‘short-term’ donors and may have subsequently emerged. However, the
age difference between the groups at the time of nephrectomy (7 years)
does not seem sufficient to explain the observed difference in prevalence of hyper-
tension.

After partial renal ablation in animals, the perfusion of remnant nephrons
is augmented by a high protein diet and it is suggested that this contributes to
the eventual destruction of these nephrons [9]. In addition, preservation of
renal function by phosphate restriction has been demonstrated in the renal
ablation model [10]. Using an assessment of current dietary intake as an index
of eating habits since nephrectomy, we found no correlation between protein
or phosphate intake, and either present renal function or the percentage change
in creatinine clearance since surgery. However, the range of dietary intake of
protein and phosphate and of change of renal function in our patients was
small so that any effect of diet may have been missed.

We would conclude from our observations that unilateral nephrectomy
does not result in progressive deterioration in renal function, nor in the de-
velopment of albuminuria. However, nephrectomised patients do appear to be at
increased risk of developing systemic hypertension, the mechanism of which is
not clear.
Open Discussion

ALBERTAZZI (Chairman) Dr Tapon can you tell us some detailed information concerning the number of patients in your series having serum creatinine values of more than 1.5mg/dl and also having a glomerular filtration rate of less than 60ml/min.

TAPSON Yes, well the numbers were very small but I can’t remember the actual numbers for you.

HABERAL (Ankara) How do you explain why some patients develop hypertension?

TAPSON I have no idea why some patients should become hypertensive and others should not become hypertensive. I think from our study, being of relatively small numbers, it is difficult to come to firm conclusions. Other workers have also found this increased incidence of hypertension in kidney donors. Brenner [1] found that in 25 long-term donors 10 became hypertensive, Friedman in New York [2] found that 60 per cent of their donors had become hypertensive and in a study by Miller [3] that was reported as an abstract at the American Society of Nephrology meeting in 1982 it was found that 33 per cent of their donors had also become hypertensive. I have no explanation as to why some should and some should not become hypertensive.

HABERAL Did you biopsy these patients?

TAPSON No, they only have one kidney and so it would be wrong to biopsy.

SOBH (Mansoura, Egypt) You have one donor who developed end-stage renal failure needing haemodialysis and some other patients who died for other reasons. What is the fate of the kidney donated from people who have subsequently died?

TAPSON As far as the patient whose function deteriorated after he donated a kidney to his brother so that he required haemodialysis, the donated kidney
is still functioning extremely well. This patient developed three years after donor nephrectomy severe malignant hypertension associated with nephrotic range proteinuria and there was subsequently a period of poor blood pressure control and gradual deterioration of his function.

SOBH Do you know what was the cause of death in the donor who died?

TAPSON In one of the four subjects who died I have no information. In the other three all died of malignancies, one died of carcinoma of the bladder, one died of carcinoma of the lung and one died of skin lymphoma. Incidentally since reporting this work one of the donors that we studied has also died, an unfortunate young 39 year old man, who as a matter of interest had the best function of all 75 donors, dropped dead with a myocardial infarction.

BANKS (Bristol) I take your point that the 30 per cent or more in your long-term follow-up of hypertensive patients is more than you would expect in the normal population although it depends on what age your patients ended up at. The trend towards an increased blood pressure surely is an age related phenomenon.

TAPSON I think a lot depends on whether you feel that blood pressure increases with age in the individual. If you do feel that way then perhaps long-term donors who were on average seven years younger than the short-term donors at the time of nephrectomy may not yet have had time for their essential hypertension to become manifest. Cross sectional studies of normal populations have certainly shown that systolic blood pressure increases with age but diastolic blood pressure increases to a much lesser extent with time. This is one of the reasons why I reported the diastolic trends. Probably what is more relevant to our study is the longitudinal studies, one in 1967 of Welsh miners [4] and another in 1973 of a group of American fighter pilots [5], where these healthy men were studied longitudinally for 30 years. The conclusions were that the rate of rise of the blood pressure had no correlation whatsoever with the original age of the patient at the time of entry into the study. It was correlated with the level of blood pressure entry into the study, i.e. those patients with a higher blood pressure at entry developed a greater rate of rise, so I think for these reasons our point is valid.

AVIRAM (Tel Aviv) Your data seems to disprove Brenner’s theory [6]. Do you support de Wardener’s theory [7] about the natriuretic factor being the agent for hypertension?

TAPSON I think there is little in our work to support Brenner’s theory but one presumes that reduction of the nephron mass by 50 per cent isn’t enough. The other point of course being Brenner’s work was done on rats and rats tend to get proteinuria with advancing age and so I don’t think there is very much in our work that supports Brenner’s theory. As far as de Wardener’s natriuretic hormone is concerned I can’t answer that, although we are studying our hypertensive kidney donors.
MAGGIORE (Reggio Calabria) Is the hypertension and proteinuria of some of your donors due to them being the relatives of patients with inherited renal diseases?

ONUZO (Lagos) I wonder what observations you have made on the family history of hypertension in the relatives of the patients to whom the kidneys were donated?

TAPSON We did not study the family history further than the patients to whom the kidney was donated so I'm afraid I can't answer that.

References

2. Delano BG, Lazar IL, Friedman EA. Kidney Int 1983; 23: A168