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Glomerular hyperfiltration after unilateral nephrectomy in living kidney donors

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Abstract. Glomerular hyperfiltration, which is expected to occur after uninephrectomy, could potentially damage the non-transplanted donor kidney in living donor transplantation. We therefore prospectively measured renal function (inulin and PAH clearance), albumin excretion and blood pressure in the donors of 30 consecutive living donor kidney transplants before uninephrectomy ($n = 29$) and 1 week ($n = 27$) and 1 year ($n = 16$) after. Hyperfiltration was defined as: (post-nephrectomy inulin clearance)/(0.5 x pre-nephrectomy inulin clearance); hyperperfusion was defined in an analogous way for PAH clearance. Hyperfiltration averaged 128 ± 5% [SEM] and hyperperfusion 133 ± 6% 1 week after uninephrectomy. Hyperfiltration was nearly unchanged (126 ± 7%) 1 year after nephrectomy, whereas hyperperfusion had significantly decreased to 118 ± 8% ($P < 0.02$). There was no significant change in blood pressure after nephrectomy, and no new cases of hypertension were observed during the 1-year follow-up. The degree of hyperfiltration did not correlate with donor age. Microalbuminuria > 30 mg/24 h was found in two donors 1 week after nephrectomy (one of which normalized at 1 year) and in one additional donor 1 year after nephrectomy. The degree of hyperfiltration did not correlate with albumin excretion rate. In conclusion, no adverse consequences of hyperfiltration were demonstrable during the 1-year observation period, but the prognostic role of occasional microalbuminuria should be further investigated.

Key words: Glomerular hyperfiltration – Living kidney donors – Unilateral nephrectomy

An increased glomerular filtration rate, also termed 'hyperfiltration' is considered an important factor in the pathogenesis of various nephropathies and in the non-immunological progression of chronic renal failure [4]. The paradigmatic example for this is the hyperfiltration which accompanies the early phase of diabetes mellitus [10], and which is considered relevant for the later development of diabetic nephropathy. Since glomerular hyperfiltration is also expected to occur after unilateral nephrectomy for living donor renal transplantation, in 1988 we began a prospective study of hyperfiltration in living kidney donors. The aims of this study were: (1) to determine the degree of hyperfiltration after unilateral nephrectomy; and (2) to determine the incidence of potential consequences of uninephrectomy, such as progressive impairment of renal function, microalbuminuria or arterial hypertension, all of which have been reported to occur with varying frequency after uninephrectomy [2, 3, 7, 9].

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Methods

The kidney donors (13 M, 17 F) were studied the day before transplantation ($n = 29$), 1 week after nephrectomy ($n = 27$) and 1 year after nephrectomy ($n = 16$; in one of these, the pre-nephrectomy and the 1-week studies were not carried out for technical reasons). Each study consisted of a hospital admission with overnight urine collection for the determination of albumin excretion and, on the next morning, a combined inulin and PAH clearance with four collections of 40 min each. Blood pressure was measured before the clearance study in the supine position. Urine albumin excretion was measured with an immune-turbidimetric assay, and inulin and PAH using laboratory methods. The hyperfiltration index was computed for each donor as:

$$\frac{\text{Inulin clearance after nephrectomy}}{0.5 \times \text{Inulin clearance before nephrectomy}}$$

An analogous formula was used to calculate hyperperfusion from PAH clearance.

Non-parametric tests (Mann-Whitney U test, paired Wilcoxon test, Spearman's rank correlation) were used for the statistical analysis.

Results

Baseline data

Donor age was between 22 and 68 years (mean 46 ± 2 years); four of the donors were over 60-years-old.

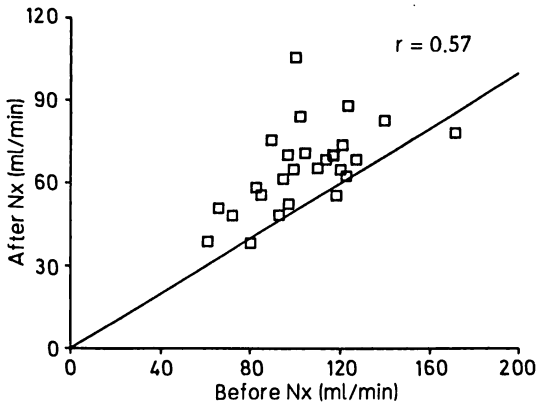

Fig. 1. Inulin clearance of 27 kidney donors before and 1 week after transplantation. The line indicates where the points would be expected if renal function was exactly cut in half by the uninephrectomy. Points above the line indicate hyperfiltration

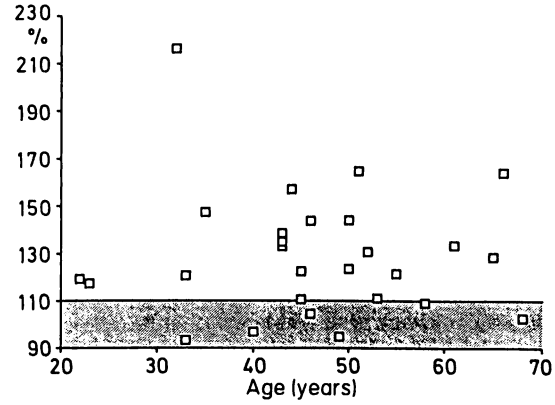

Fig. 3. Donor age versus hyperfiltration after uninephrectomy. No correlation existed

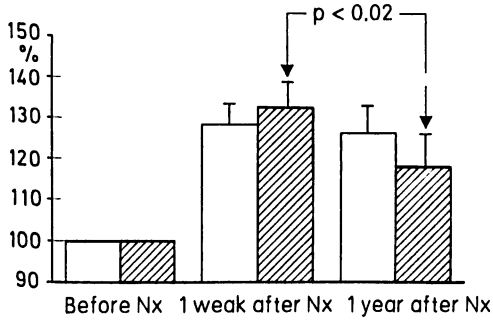

Fig. 2. Hyperfiltration and hyperperfusion after nephrectomy (mean ± SEM). The decrease in hyperperfusion was significant both when all donors were considered (Mann-Whitney U test) or only the ones where follow-up was complete (paired Wilcoxon test). □, hyperfiltration, ▨, hyperperfusion

Of the transplantations, 16 were parent-to-child, 13 were sibling-to-sibling and one was spouse-to-spouse. Weight, the clearances of inulin, PAH and creatinine as well as serum creatinine were normal at baseline (Table 1). The hypertensive maxima of baseline blood pressure (Table 1) are from a 66-year-old and a 58-year-old donor. These two donors were accepted despite known, moderate essential hypertension, because of their urgent wish to donate a kidney to their child. The remaining 28 donors were normotensive.

Course after nephrectomy

Figure 1 shows inulin clearance before nephrectomy and 1 week after nephrectomy. It is evident that most of the donors' inulin clearance after nephrectomy exceeded 50% of their pre-nephrectomy clearance, i.e. hyperfiltration was present. Mean hyperfiltration (Fig. 2) was 128 ± 5% (SEM) at 1 week after nephrectomy, mean hyperperfusion 133 ± 6%. Hyperfiltration 1 year after nephrectomy was essentially unchanged (126 ± 7%), whereas hyperperfusion had decreased significantly to 118 ± 8% ($P < 0.02$). Hyperfiltration exceeding 110% was present in 21 of 27 donors at 1 week after transplantation, and in 12 of 15 donors at 1 year after transplantation. Hyperperfusion of more than 110% was present in 21/27 donors at one week but only in 9/15 donors at one year. The degree of hyperfiltration or hyperperfusion did not correlate with sex, weight, height or donor age (Fig. 3).

Although mean inulin clearance (and, therefore, hyperfiltration) did not change between 1 week and 1 year after nephrectomy, there was a slight, non-significant increase in creatinine clearance which contributed to

Table 1. Weight, blood pressure, and renal function before and after nephrectomy (Nx). Data are given as mean ± SEM [range]

	Before Nx ($n = 29$)		One week after Nx ($n = 27$)		One year after Nx ($n = 16$)	
Weight (kg)	71 ± 2	[47–102]	71 ± 3	[44–100]	69 ± 2	[51–86]
Systolic blood pressure	126 ± 3	[105–170]	126 ± 3	[110–175]	123 ± 3	[110–140]
Diastolic blood pressure	78 ± 2	[60–105]	81 ± 2	[60–100]	82 ± 3	[60–100]
Inulin clearance (ml/')	104 ± 4	[61–171]	66 ± 3	[38–106]	66 ± 4	[43– 97]
PAH clearance (ml/')	548 ± 28	[310–941]	358 ± 20	[213–330]	317 ± 17	[205–326]
Filtration fraction	19 ± 1%	[13– 29]	19 ± 1%	[14– 30]	21 ± 1%	[17– 26]
Creatinine clearance (ml/')	150 ± 8	[88–280]	88 ± 5	[49–196]	101 ± 6	[64–166]
S-creatinine (μmol/l)	64 ± 3	[45– 90]	106 ± 3	[69–169]	90 ± 5	[63–134]

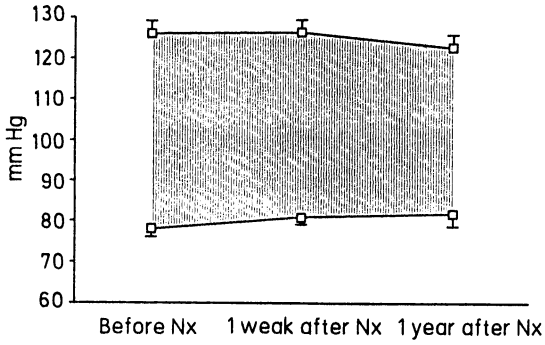

Fig. 4. Mean systolic and diastolic blood pressures (± SEM) before and after nephrectomy

the decrease in serum creatinine between 1 week and 1 year of nephrectomy (Table 1).

Mean systolic and diastolic blood pressure did not change significantly (Fig. 4, Table 1). The two donors with known hypertension remained hypertensive after nephrectomy, but there was no evidence of an increased severity of their hypertension (as judged from blood pressure and antihypertensive therapy). Besides this, a hypertensive blood pressure was only recorded in one 68-year-old donor 1 week after nephrectomy. At that time, this donor was still experiencing considerable pain from his nephrectomy. Although this donor had not yet undergone the 1-year study, he since had several normal outpatient pressure measurements.

Albumin excretion was normal in all donors prior to nephrectomy. After nephrectomy, microalbuminuria of more than 30 mg/24 h was found in a total of three donors, one of which normalized at 1 year after nephrectomy. No risk factors could be identified in these three donors (Table 2). Also, in the entire set of donors, no correlation of albumin excretion with the degree of hyperfiltration or hyperperfusion could be demonstrated.

Discussion

These data confirm that in most living kidney donors, the non-transplanted kidney hyperfilters as soon as 1 week after nephrectomy (Fig. 1). However, in almost one quarter of the donors studied, hyperfiltration was either minimal (< 110 %) or absent. The same 6 out of 27 donors also failed to show hyperperfusion. Thus the entire – presumably endocrine – response to a 50 % reduction in renal mass appeared blunted in these donors. Simple demographic data such as gender, weight, height and age (Fig. 3) were not useful in predicting the hyperfiltration/hyperperfusion response. Mean hyperfiltration in this study (+ 128 % and 126 %) was within the range reported by others [1, 6]. Its extent corresponds to the hyperfiltration found in early diabetes mellitus [10], after oral protein loading [5] and after dopamine/amino-acid infusion [8].

Hyperperfusion of approximately the same magnitude accompanied hyperfiltration early after nephrectomy. At 1 year, however, hyperperfusion had significantly decreased despite stable hyperfiltration (Fig. 2). Although PAH extraction was not measured in this study, there is no reason to suspect a decrease in PAH exctraction (which would yield a 'false low' PAH clearance) between 1 week and 1 year after nephrectomy. Rathet, the increase in creatinine clearance from 1 week to 1 year (despite constant inulin clearance, Table 1) suggests that tubular secretory processes are *increased* at 1 year after nephrectomy, perhaps as a consequence of tubular hypertrophy.

The mechanisms mediating this decrease in hyperperfusion are unknown. One may, however, speculate that this increase in renal vascular resistance represents an autoregulatory adaptation of the renal vascular bed. The maintenance of glomerular filtration during the same time (i. e. the trend for filtration fraction to increase, Table 1) could suggest that this resistance increase is predominantly post-glomerular. However, glomerular hypertrophy, such as might occur after uninephrectomy, could also mimic this pattern by increasing the glomerular ultrafiltration coefficient and, therefore, filtration fraction.

No trend to develop arterial hypertension was found in this study (Fig. 4), and there were no *de novo* cases of arterial hypertension. Microalbuminuria > 30 mg/24 h was, however, found in two donors at 1 week after nephrectomy (one of which normalized at 1 year) and in one additional donor at 1 year after nephrectomy. These three donors did not present any obvious risk factors (Table 2). The most likely explanation for this finding is a slight damage to the glomerular filtration barrier, particularly the charge-selective component, perhaps as a consequence of intraglomerular hypertension. Further follow-up of these and future donors is indicated to identify the prognostic significance of this alteration and to determine the specific conditions under which it occurs.

In summary, glomerular hyperfiltration and hyperperfusion after unilateral nephrectomy for living donor renal transplantation occurs early, but only in three-quarters of donors. Although the extent of hyperfiltration is similar to diabetic or protein-induced hyperfiltration, there is stable glomerular filtration during the first year after nephrectomy and no *de novo* hypertension appears to occur during this time. The occasional occurrence of microalbuminuria, albeit unrelated to the degree of hyperfiltration, warrants further study.

Table 2. Data of the three donors who developed microalbuminuria. One-year followup was not yet available (N/A) in the third donor

Age	Sex	Blood press at 1 week	Blood press at 1 year	Hyperfilt. at 1 week	Hyperfilt. at 1 year	Albumin 1 week (mg/24 h)	Albumin 1 year (mg/24 h)
43	f	130/80	110/70	136 %	101 %	94	11
46	m	125/85	140/95	144 %	122 %	10	94
46	m	120/80	N/A	104 %	N/A	38	N/A

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