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Bilateral nephrectomy of the native kidneys reduces the incidence of arterial hypertension and erythrocytosis in kidney graft recipients treated with cyclosporin

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Abstract. Since the use of cyclosporin (CsA) the incidence of post-transplant arterial hypertension and erythrocytosis has increased sharply. In a retrospective analysis of 707 consecutive first cadaveric kidney graft recipients treated with CsA as basic immunosuppression, the effect of bilateral native nephrectomy on arterial hypertension and erythrocytosis was studied. Patient and graft survival as well as kidney function of the 264 nephrectomized patients were identical to those of the 443 non-nephrectomized patients. In the nephrectomized patients the mean number of rejections during the first year was 0.62 ± 0.88 versus 0.78 ± 1.02 in the non-nephrectomized patients ($P = 0.0285$). At 1 year after transplantation, 65.8% of the non-nephrectomized patients needed hypotensive drugs versus 45.3% of the nephrectomized patients ($P < 0.0001$). Notwithstanding the use of more antihypertensive drugs, diastolic blood pressure in the former group was significantly higher than in the latter group (87 ± 25 versus 83 ± 10 mm Hg; $P < 0.02$). During the first year 44 (9.9%) of the non-nephrectomized patients had haemoglobin levels higher than 17 g/dl versus only six (2.3%) of the nephrectomized patients ($P < 0.0001$). Comparable differences were also found up to 5 years after transplantation. These findings indicate that native nephrectomy is helpful in controlling arterial hypertension and erythrocytosis.

Key words: Renal transplantation – Arterial hypertension – Erythrocytosis – Bilateral nephrectomy – Cyclosporin

Although pretransplant bilateral nephrectomy was routine in the early years of transplantation, most transplant centres now consider that the risks of the procedure do not outweigh the benefits and therefore have abandoned routine native nephrectomy in favour of a more selective approach, such as in cases of chronically infected kidneys [4]. Since the availability of potent antihypertensive agents, even arterial hypertension refractory to haemodialysis alone is often not considered as an indication for removal of the native kidneys. Because the use of CsA has resulted in a sharp increase in the incidence of arterial hypertension, the potential benefits of pretransplant native nephrectomy should be reassessed.

Overproduction of erythropoietin by the native kidneys has been considered as one of the possible causes of post-transplant erythrocytosis, the occurrence of which is often masked by a concomitant bone marrow suppression by azathioprine [13]. As CsA is not a bone marrow suppressant, an increased incidence of erythrocytosis has been reported [7].

The present retrospective study analyses the effect of bilateral native nephrectomy on the incidence of arterial hypertension and erythrocytosis in renal graft recipients treated with CsA as basic immunosuppression.

Patients and methods

Between February 1983 and February 1991, 707 consecutive patients received a first cadaver kidney transplant with CsA as basic immunosuppression. Starting doses of CsA have decreased over the past years from 15 to 10 mg/kg per day. During the last 3 years CsA dose has been adjusted to maintain CsA whole blood levels (specific RIA method) between 200 and 250 ng/ml during the first 3 months. Corticosteroids have been started at a dose ranging between 16 and 24 mg/day tapered every month by 2 mg to 8 mg/day. First rejection crises have been treated with corticosteroids. Corticoresistant rejections have been treated with ATG (Fresenius) or OKT_3 (Ortho).

Of the 707 patients, 264 (37.3%) had received a bilateral nephrectomy. In most cases one kidney was removed before transplantation, the other at the time of transplantation. In the remaining 443 patients (66.7%), one or both native kidneys remained in place. Reasons for bilateral nephrectomy were persistent hypertension after starting haemodialysis, chronic pyelonephritis, grade 3 and 4 vesico-ureteral reflux, analgesic nephropathy, bleeding or infected polycystic kidneys and renal malignancies. Demographic data of the nephrectomized and the non-nephrectomized patients are compared in Table 1.

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Table 1. Demographic data in nephrectomized and non-nephrectomized patients

	Nephrectomized	Non-nephrectomized	Significance of difference
Age at transplant (years)	44 ± 13	43 ± 12	n.s.
Number of pretransplant blood transfusions	17 ± 21	10 ± 15	$P < 0.0001$
Number of B-DR mismatches	1.3 ± 0.8	1.33 ± 0.8	n.s.
Number of HLA-A matches	0.9 ± 0.6	0.9 ± 0.6	n.s.
Number of HLA-B matches	1.0 ± 0.5	1.0 ± 0.6	n.s.

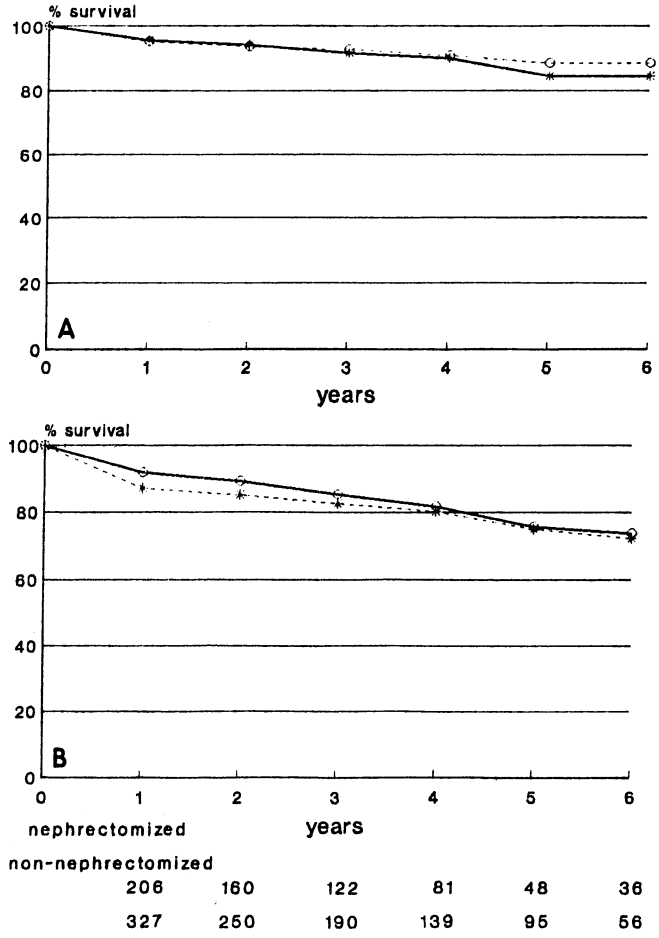

Fig. 1 A, B. Actuarial patient survival (**A**) and graft survival (**B**) in nephrectomized and non-nephrectomized patients. (*Solid line*, nephrectomized patients; *dotted line*, non-nephrectomized patients). At the bottom of the figure the number of patients at risk is given

Patient and graft survival was analysed by the actuarial method. Student's *t*-test and chi-squared or Fischer's exact probability tests were used where appropriate. Data are presented as mean ± SD.

Results

Although patient and graft survival of the nephrectomized and non-nephrectomized patients were comparable (Fig. 1), acute rejections were more frequently seen in the non-nephrectomized patients. The mean number of rejections per patient during the first post-transplant year was 0.78 ± 1.02 in the non-nephrectomized patients versus 0.62 ± 0.88 in the nephrectomized group ($P = 0.0285$). Serum creatinine and creatinine clearance were, however, not different (Table 2).

Up to 5 years after transplantation a significantly higher percentage of non-nephrectomized patients needed antihypertensive drugs to control arterial hypertension. Notwithstanding the use of more hypotensive agents, diastolic blood pressure was higher in the non-nephrectomized patients (Table 3). Mean haemoglobin and haematocrit levels were significantly lower in the nephrectomized patients (Table 4). During the first year after transplantation 44 (9.9%) of the non-nephrectomized patients had haemoglobin levels higher than 17 g/dl versus only six (2.3%) in the nephrectomized group. Up to 5 years after transplantation, all patients with erythrocytosis necessitating phlebotomy were from the non-nephrectomized group.

Discussion

The potential benefits of bilateral nephrectomy of the native kidneys in renal transplant recipients have mostly been studied in patients treated with conventional immunosuppression. Several authors have found an improved graft survival in the patients with bilateral native nephrectomy [1, 8], while others have not confirmed this finding [2]. In a large study of the SEOPF a lower incidence of renal graft rejection was found in nephrectomized patients [11]. More recently native nephrectomy after transplantation was also shown to improve renal plasma flow in hypertensive transplant recipients, a finding that was also confirmed in animals [3]. In our study no effect on patient and graft survival nor on renal function could be found. In

Table 2. Kidney function in nephrectomized and non-nephrectomized patients

	Nephrectomized	Non-nephrectomized
Serum creatinine (mg/dl)		
at 1 year	1.70 ± 0.67	1.81 ± 0.85
at 2 years	1.78 ± 0.82	1.90 ± 1.33
at 3 years	1.77 ± 1.81	1.81 ± 0.86
at 4 years	1.78 ± 0.89	1.78 ± 0.82
at 5 years	1.67 ± 0.86	1.79 ± 0.87
Creatinine clearance (ml/min)		
at 1 year	56 ± 23	55 ± 23
at 2 years	57 ± 26	54 ± 22
at 3 years	57 ± 29	54 ± 24
at 4 years	58 ± 28	57 ± 29
at 5 years	60 ± 28	56 ± 22

None of the differences between nephrectomized and non-nephrectomized patients are significant

Table 3. Blood pressure in nephrectomized and non-nephrectomized patients

	Nephrectomized	Non-nephrectomized	Significance of difference
Patients treated with hypotensive drugs			
at 1 year	66%	45%	$P < 0.0001$
at 2 years	65%	52%	$P = 0.01$
at 3 years	72%	55%	$P = 0.002$
at 4 years	70%	50%	$P = 0.003$
at 5 years	65%	44%	$P = 0.01$
Systolic blood pressure			
at 1 year	142 ± 20	147 ± 20	n.s.
at 2 years	144 ± 20	145 ± 21	n.s.
at 3 years	143 ± 18	145 ± 19	n.s.
at 4 years	140 ± 18	145 ± 18	$P = 0.05$
at 5 years	138 ± 17	143 ± 17	n.s.
Diastolic blood pressure			
at 1 year	83 ± 10	87 ± 25	$P = 0.02$
at 2 years	84 ± 11	86 ± 11	n.s.
at 3 years	84 ± 10	86 ± 10	n.s.
at 4 years	84 ± 10	86 ± 10	n.s.
at 5 years	81 ± 9	85 ± 9	$P = 0.03$

Table 4. Haemoglobin and haematocrit levels in nephrectomized and non-nephrectomized patients

	Nephrectomized	Non-nephrectomized	Significance of difference
Haemoglobin (g/dl)			
at 1 year	12.3 ± 1.4	13.3 ± 2.1	$P = 0.0001$
at 2 years	12.5 ± 1.3	13.3 ± 1.3	$P = 0.0001$
at 3 years	12.4 ± 1.6	13.1 ± 2.0	$P = 0.001$
at 4 years	12.5 ± 1.5	13.0 ± 2.0	$P = 0.04$
at 5 years	12.5 ± 1.6	13.1 ± 2.1	$P = 0.06$
Haematocrit (%)			
at 1 year	37.6 ± 4.3	40.4 ± 7.0	$P = 0.0001$
at 2 years	38.5 ± 4.4	40.9 ± 6.5	$P = 0.0001$
at 3 years	38.0 ± 4.8	40.4 ± 6.3	$P = 0.0004$
at 4 years	38.7 ± 4.6	40.4 ± 6.6	$P = 0.038$
at 5 years	38.4 ± 4.1	40.2 ± 6.3	$P = 0.06$

agreement with the data of the SEOPF study, the incidence of acute rejection crises was also lower in the nephrectomized group. It may be that the lower incidence of rejections in nephrectomized patients is due to the higher number of pretransplant blood transfusions in these patients.

Several studies have shown that the incidence of hypertension is significantly higher in patients with their native kidneys in place, and that post-transplant hypertension can be controlled by post-transplant nephrectomy [9, 10]. This beneficial effect on blood pressure could, however, not be confirmed by others [2]. Our study indicates that in patients treated with CsA, in which the incidence of hypertension is significantly higher than in patients treated with conventional immunosuppression, native nephrectomy also allows significantly better control of post-transplant hypertension.

Since the use of CsA as basic immunosuppression, a higher incidence of erythrocytosis has been reported [7]. This may be due to the fact that CsA is not a bone-marrow suppressant in contrast to azathioprine, which can mask the true incidence of post-transplant erythrocytosis. Others have suggested a direct stimulating effect of CsA on bone marrow stem cells [12]. Post-transplant erythrocytosis is probably of multifactorial origin. Inappropriate production of erythropoietin by the native kidneys has been suggested as one of the possible factors [13]. In our study haemoglobin and haematocrit levels were significantly lower in the nephrectomized patients. All patients with erythrocytosis necessitating phlebotomy were from the non-nephrectomized group. The lower haemoglobin cannot be explained by a worse kidney function as serum creatinine and creatinine clearance were identical in both groups.

In the past, bilateral native nephrectomy was considered a risky procedure with a substantial morbidity and mortality. Native nephrectomy can now be performed through bilateral vertical lumbotomy incisions with minimal morbidity and no mortality, even in patients under immunosuppression after transplantation [6]. Anaemia in anephric patients, either when waiting for a renal graft or after failure of the graft, can now easily be treated by recombinant erythropoietin. The benefits of the procedure outweigh the risks.

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