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Impact of donor age on living related donor kidney transplantation

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Abstract. Two comparable groups of kidney transplant recipients were identified according to the age of their kidney donors. The first group (A) comprised 42 recipients of donors aged < 40 years, and the second group (B) comprised 48 recipients of donors aged > 50 years. The patients were followed for a mean period of 26 months (range 13–50 months). Post-transplant renal function and graft survival were assessed together with the frequency of post-transplant proteinuria and hypertension. Moreover, the functional reserve of the grafts was determined by comparing the clearance values, obtained by both isotope and chemical means, before and after a combined infusion of dopamine and an amino acids preparation. The graft function was significantly better in group A according to the serum creatinine levels (μmol/l) at 1 month (107 ± 4.5 vs. 134 ± 10.7, $P < 0.01$), 12 months (119 ± 5.3 vs. 181 ± 88, $P < 0.05$) and at last follow-up visit (118 ± 6.2 vs. 223 ± 63, $P < 0.03$) for groups A and B, respectively. The graft survival in group A was significantly higher than that in group B (100% vs. 87% at 1 year, $P < 0.05$). The graft functional reserve was significantly better in group A than in group B. Post-transplant proteinuria was significantly more frequent in group B recipients (70% vs. 40%, $P < 0.03$). The age of the donors had no impact on the incidence of post-transplant hypertension. These observations suggest that the transplantation of a kidney from an older live kidney donor is associated with an inferior post-transplant outcome.

Key words: Donor age – Kidney transplantation

In many countries, living related donors are still the main source of kidneys for transplantation in view of the poor legal definition and deficient organization of cadaveric donor work-up. The excessive demand for donor kidneys has necessitated the continued use of those available as efficiently as possible. In many cases these donors are more than 50 years old. The impact of kidney age on graft survival is contradictory; Matas et al. [1] showed no difference in graft survival of kidneys from living donors older or younger than 45 years. Similarly, Wetzels et al. [2] found that donor age did not affect the outcome of renal transplantation. On the other hand, Rao et al. [3] reported that graft survival and renal function in recipients of older donor kidneys (> 50 years) were significantly lower than in a control group who received kidneys from donors between 11 and 50 years of age.

With a view to clarifying the impact of kidney age on the outcome of kidney transplantation, we evaluated 90 consecutive patients who received kidneys from young and older living related donors. Evaluation involved estimation of the graft functional reserve and the trends of decline in graft function over time.

Materials and methods

In this analysis we studied 90 consecutive renal transplants performed in our centre between 1987 and 1989. All patients received kidneys from living related donors (24 from fathers, 26 from mothers and 40 from siblings). The recipients were stratified into two groups according to the age of the donors. The first group (A) comprised 42 recipients of donors aged < 40 years (31.2 ± 6.1 years), and the second group (B) comprised 48 recipients of donors aged > 50 years (56 ± 8.0 years).

Both groups of recipients were comparable with respect to age, sex, duration of pretransplant dialysis, frequency of blood transfusions prior to transplantation and mean time since transplantation. Table 1 summarizes the characteristics of the recipients in both groups. In addition, the HLA-A, B and DR tissue antigens were similarly distributed in both groups, with the majority having an one-haplotype HLA match. Furthermore, the surgical technique employed was similar in the two groups. Retransplantation and children below the age of 16 years were excluded.

The protocol of immunosuppression was identical for both groups of recipients and included simultaneous administration of prednisolone and azathioprine (AZA). In selected cases, cyclosporine (CsA) was used with variable doses of prednisolone. The initial dose of CsA was 12.5 mg/kg daily, and it was decreased thereafter to maintain the whole blood trough levels at 100–200 ng/ml

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Table 1. Characterestics of patients

Factors analysed	Group A ($n = 42$)	Group B ($n = 48$)
Age (years)	26.9 ± 7	30.6 ± 8
Sex (male/female)	31/11	35/13
Duration of pretransplant dialysis (months)	42.2 ± 4	41.5 ± 5
Prior transfusions (units)	3.2 ± 2	3.1 ± 2.5
Mean time since transplantation (months)	23 ± 4	25 ± 5
Tissue matching		
One haplotype	39	38
Full match	2	9
Complete mismatch	1	1
Type of primary immunosuppression		
Prednisone + azathioprine	25	19
Prednisone + cyclosporine	9	8
Triple	8	21

Table 2. Post-transplant serum creatinine level (μmol/l; mean ± SD)

Time of measurement after transplantation	Serum creatinine		*P* value
	Group A	Group B	
At 1 month	107 ± 4.5	134 ± 10.7	0.015
At 3 months	107 ± 4.5	151 ± 13.4	0.03
At 6 months	116 ± 4.5	160 ± 16	0.02
At 12 months	119 ± 5.3	181 ± 88	0.05
At the most recent follow-up visit	118 ± 6.2	223 ± 63	0.03

(Sandoz, radioimmunoassay, RIA kits). AZA in an initial dose of 2–3 mg/kg daily, was adjusted according to the white blood cell counts, and prednisolone was slowly tapered from a dose of 90 mg/day to 10 mg/day over a period of 6 months.

Acute rejection episodes were diagnosed on a clinical basis and confirmed by fine needle aspiration cytology (FNAC) [4]. Tru-cut biopsy was performed when FNAC result was inconclusive. Rejection episodes were treated by 750 mg methylprednisolone given intravenously on 5 consecutive days.

The patients were followed for a mean period of 26 months (range 13–50 months). Patient and graft survival were assessed together with the frequency of post-transplant proteinuria and hypertension. Chronic rejection was diagnosed on a clinical basis and confirmed in all cases by the examination of a core biopsy. The serum creatinine level was measured at 1, 3, 6 and 12 months and at the most recent follow-up visit. The graft glomerular filtration rate (GFR) was measured by technetium-99m diethylene triamine peuta-acetic acid (^{99m}Tc-DTPA) scans [5] and by the determination of the endogenous creatinine clearance. Moreover, the functional reserve of the graft was assessed by the simultaneous infusion of dopamine (2.5 μg/kg·min) and a 10% solution of an amino acid preparation, Vamin N (80 ml/h) for 12 h. During the procedure, a diuresis of at least 100 ml/h was maintained by orally administered fluids. At 6 h after combined dopamine and amino acids infusion, when the GFR reaches its maximum level, the isotope clearance was measured using ^{99m}Tc-DTPA scans. Furthermore, an urine sample was collected, and the endogenous creatinine clearance was measured at the end of the 12 h. The functional reserve of the graft was determined by comparing the clearance values obtained by both isotope and chemical means with the corresponding values obtained before the infusion of dopamine and amino acids.

For statistical analysis we used Student's *t*-tests for paired and unpaired comparisons, χ^2 test of proportions and Fisher's exact test.

Results

Patient and graft survival

At 1 year, the patient survival rate was not significantly different among the 2 groups (100% vs. 96% for groups A and B, respectively). However, the 1-year graft survival in recipients of group A was significantly higher than that of group B (100% vs. 87%, $P = 0.05$). Six patients from group B lost their grafts; 2 of them had died of uraemia by 1 year post-transplant.

Graft function, functional reserve and post-transplant complications

The serum creatinine values at 1, 3, 6 and 12 months and at the last follow-up visit were significantly lower in group A recipients compared with those of group B (Table 2). The response of the graft to the infusion of dopamine and the amino acids preparation is depicted in Table 3. The graft functional reserve, measured by both chemical and isotope means, was significantly higher in the recipients of group A than in those of group B. Acute rejection episodes were documented equally in both groups (in 35 out of 42 patients in group A, and in 40 out of 48 patients in group B). Although the incidence of post-transplant hypertension was higher in group B recipients, the difference was not statistically significant (36% in group A vs. 49% in group B, $P = 0.5$). Furthermore, post-transplant proteinuria was significantly more frequent in group B (70%) than in group A (40%) recipients ($P = 0.03$).

Discussion

The results of our analysis showed that the recipients of kidneys from living related donors older than 50 years have a lower graft survival and reduced post-transplant renal function compared with recipients whose donors were younger than 40 years of age. These observations are in agreement with the clinical data reported by other in-

Table 3. Effect of infusion of dopamine (D) and amino acids preparation (A) on the glomerular filtration rate (GFR; ml/min)

	GFR estimated by creatinine clearance			Isotope GFR		
	Value before D&A	Value after D&A	Graft reserve	Value before D&A	Value after D&A	Graft reserve
Group A	72.05 ± 13.43	89.54 ± 10.79	15.9 ± 9.43*	63.7 ± 8.07	75 ± 10.09	11.24 ± 7.5**
Group B	51.18 ± 18.5	66.5 ± 16.5	7.7 ± 5.06*	64.75 ± 7.8	70 ± 11.29	5.2 ± 6.15**

Mean ± SD

* $P = 0.0001$, ** $P = 0.0002$

vestigators [3, 6, 7]. Moreover, our study draws attention to the fact that kidneys from older donors have less functional reserve capacity as reflected by a smaller increase in GFR after the infusion of a dopamine and amino acids preparation. The decline in graft function observed in kidneys obtained from older age donors could be explained by the anatomical and functional changes known to occur in human kidneys with aging. The aged kidney is a seat of progressive glomerular sclerosis, atherosclerotic occlusion of renal vessels and hyalinization, causing a reduction in the number of functioning nephrons [3, 8]. Rao and associates [3] summarized the factors that may shorten the survival of aged kidneys when transplanted into a uraemic patient as the combined effects of compensatory renal haemodynamic injury (pre-existing aging effect) and the post-transplant exposure to noxious events such as acute tubular necrosis, graft rejection, sepsis and nephrotoxic drugs.

This study showed that the development of hypertension in allograft recipients is not dependent on the age of donation. This result is supported by Torres et al. [9], who concluded that neither the age of the donors nor their predisposition to developing hypertension significantly influences the blood pressure status of the recipients. Darmady [6], however, reported a higher risk of post-transplant hypertension in recipients of older grafts compared with younger ones. Differences among authors may reflect the multiplicity of risk factors associatied with the development of hypertension in renal transplant patients.

A significant association between post-transplant proteinuria and the age of the kidney donors is evident in our study. Indeed, post-transplant proteinuria may be attributed to several causes, including recurrence of the original kidney disease, the appearance of de novo nephropathy, chronic rejection or ligation of one of the long veins draining the graft [10]. Since the age of a kidney graft is unlikely to affect all the causes of proteinuria equally, the demonstrated association may reflect variation in the relative frequency of each of these causes among different populations of kidney recipients. Indeed, an earlier report by Talseth and associates [11] stated that donor age is not related to an increase in blood pressure or protein excretion at follow-up.

In conclusion, the levels of renal function and the renal functional reserve of kidneys obtained from older live donors are significantly inferior to those of younger live donors when measured at corresponding time points following renal transplantation. The clinical significance of these findings, however, should await longer follow-up studies, particularly in view of the continuous shortage of organs for renal transplantation.

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