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Transplantation of both kidneys from 408 donors; comparison of results

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Abstract The outcome of 816 paired kidney transplantations from 408 cadaveric donors was evaluated. The transplantations were divided according to order of transplant surgery into group 1 [mean cold ischemia time (CIT) 22 h] and group 2 (mean CIT 28 h). In group 1 the frequency of delayed onset of graft function (DGF) was 22% versus 35% in group 2 ($P < 0.005$). The 1-year patient survival and graft survival (GS) in group 1 was 98% and 93% versus 94% ($P < 0.005$) and 90% in group 2. Hemodialysis patients in group 2 had significantly greater DGF (43%) and poorer GS (88%) than peritoneal dialysis patients and the success of transplantation was particularly poor in recipients over 50 years of age.

Key words Kidney transplantation · Delayed onset of graft function · Graft survival · Patient survival · Type of dialysis

Introduction

Our earlier yet unpublished data has demonstrated the detrimental effect of delayed onset of graft function (DGF) on allograft survival in cadaveric renal transplantation. Our data showed further that the onset of graft function depends on many donor and recipient factors which alone were not significant factors in determining graft survival (GS). Many studies have demonstrated that long preservation time is a major factor leading to DGF in cadaveric renal transplantation [13, 14, 19] and, therefore, transplantations from living donors ensure the recipient a minimal length of cold ischaemia time (CIT) and usually immediate onset of diuresis [15]. Early inflammatory events caused by long preservation time and reperfusion injury contribute to poor initial graft function and inferior long-term survival [7]. There are, however, factors other than CIT, which, depending on the clinical setting and organ allocation policy, can be more or less involved. To study the impact of these other factors, we examined the outcome of renal transplantations where both kidneys of the donor were transplanted at our centre. Our aim was to minimise the effect of donor and organ procurement factors as well as the impact of CIT in this study. We analysed the results of 816 cadaveric renal transplantations performed during 1991–1997 using 408 pairs of kidneys, all retrieved and transplanted within our own transplant programme.

Materials and methods

From 1991 to 1997, 1047 adult cadaveric kidney transplantations were performed at our centre. For the purposes of this study, only transplantations where both kidneys of the donors were retrieved and transplanted within our own transplant programme were analysed. Thus, 816 transplantations with kidneys from 408 organ donors were included. The transplantations of the kidneys from one donor are usually performed consecutively by one team, and the two recipients usually have surgery in the order in which they arrive at the transplant unit. The 816 transplantations were grouped for the analyses of this study as follows: group 1, transplantations of a donor's first kidney and group 2, transplantations of a donor's second kidney.

The mean age of the donors was 39.2 years (range 1–66 years), 63.2% of them were male, and the cause of death was intracranial bleeding in 60.8% and trauma in 31.1%. Multiorgan donors comprised 54.2% the total.

All recipients were on maintenance dialysis before transplantation and had undergone a blood transfusion programme before ac-

ceptance to the waiting list, unless having been pregnant or transfused earlier. Our kidney allocation policy included obligatory sharing of at least two class I and one class II antigens with the donor, a negative T-cell cross match test against donor spleen cells and avoidance of repeated mismatched class I antigens. Age match between donor and recipient has been used as a secondary selection criterion with minor weight. Hemodialysis patients usually had dialysis performed within 24 h before transplant operation.

The routine immunosuppression was a combination of cyclosporine, azathioprine and methylprednisolone. The administration of oral cyclosporine was started prior to the transplant operation and continued postoperatively whether the graft started to function immediately or not.

We used the criteria described by Halloran [5] for definition of DGF: DGF is defined as a situation where plasma creatinine concentration remains above 500 µmol/l throughout the first post-transplant week, or more than one dialysis session is needed during the first week, or where oliguria < 1 l/24 h lasts longer than 2 days. In DGF, the day of onset of graft function was defined as the day of first spontaneous decrease of serum creatinine concentration.

In acute rejection, the first line therapy was oral methylprednisolone 5 mg/kg for 5 days. In rejections not responding to steroids, mono- or polyclonal T-cell antibody preparations were used. Suspected acute rejections were verified with Doppler ultrasound, fine needle aspiration biopsies and core biopsies.

Acute rejection episodes during the first 100 days after transplantation were recorded.

The graft was defined as failed when the patient returned to maintenance dialysis, transplant nephrectomy was performed or when the patient died with a functioning graft.

Patient survival (PS) and GS over 1 year was calculated using the Kaplan-Maier product-limit method. The chi-square test was used for contingency tables.

Table 1 Data on transplantations in group 1 and group 2. Group 1 = 408 transplantations with the donor's first kidney, Group 2 = 408 transplantations with the donors second kidney. *PD* peritoneal dialysis, *HD* hemodialysis, *PRA* panel reactive antibodies, *CIT* cold ischaemia time

		Group 1	Group 2
Recipient age, mean, range		44.9, 15–71	45.0, 15–72
Male/female		233/175	252/156
Diabetic/non-diabetic		102/306	95/313
Mean time on dialysis, months		18.0	18.4
PD/HD (PD %)		212/190 (53.4 %)	153/249 (38.9 %)
Transplant number	First TX	341	343
	Re TX	67	65
PRA	< 30 %	384	362
	30–80 %	21	38
	> 80 %	3	8
Mean CIT		22.0	28.1

Table 2 Results of renal transplantations in group 1 and group 2. Group 1 = 408 transplantations with the donor's first kidney, group 2 = 408 transplantations with the donor's second kidney. *DGF* delayed graft function, *NF* never functioning graft, *PD* peritoneal dialysis, *HD* hemodialysis

	Group 1	Group 2
DGF (%)	22.1	34.6 $p < 0.005$
NF	1 % (4PD, 1HD)	1 % (4HD)
1-year PS (%)	97.8	93.6 $p < 0.005$
1-year GS (%)	93.1	90.2 NS

Results

The 816 transplantations were divided into groups 1 and 2 according to the order of surgery with respect to the other kidney transplant operation from the same donor. The recipient characteristics and data on transplantations in these two groups are given in Table 1. The two groups were otherwise very similar, but the number of patients on peritoneal dialysis (PD) was significantly ($P < 0.001$) higher in group 1, and the CIT, according to study design, was on average 6 h shorter in group 1 than in group 2.

In studying the short- and long-term success of transplantation in these two groups we found significantly more grafts with DGF in group 2 (Table 2). At 3 weeks after transplantation the mean cyclosporine concentrations in group 1 and 2 were 297 and 294 µg/l and the mean creatinine clearances were 52.4 and 49.5 ml/min per 1.72 m^2. Serum creatinine concentrations at 1 year in groups 1 and 2 were 126 and 128 µmol/l and the respective 1-year GS were 93.1 % and 90.2 % (NS). However, the 1-year PS in group 2 was significantly worse than the PS in group 1 (93.6 % versus 97.8 %, $P < 0.005$).

After observing the higher frequency of DGF and poorer PS in group 2, we analysed further the differences in the two groups by subdividing group 1 and group 2 according to the type of pretransplant dialysis. The results of the subgroups PD 1, hemodialysis (HD) 1 and PD 2, HD 2 are shown in Table 3. In CIT, there were no significant differences between the PD and HD patients in either group. Further, the time on dialysis before transplantation was similar in both groups, i.e. patients on PD had around 4 months shorter time on dialysis than patients on HD. Significantly higher frequency of DGF was observed in the HD 1 and HD 2 subgroups than in the respective PD groups ($P < 0.001$). The frequency of rejection was significantly higher ($P < 0.001$) in the HD 1 subgroup than in the other three groups. The 1-year GS in the HD2 group was significantly lower (88.1 %, $P < 0.025$) than in the other three groups. It was also evident that the decreased PS in group 2 was specific for the patients on HD, who had a significantly ($P < 0.005$) lower 1-year PS rate compared to the other three groups.

The 1-year PS was further analysed in patients over and under 50 years of age (Table 4) and we found a significantly poorer overall PS in the older patients

Table 3 Characteristics of 816 paired renal transplantations grouped according to pretransplant type of dialysis and order of transplantation

	PD 1	HD 1	PD 2	HD 2
n	214	194	155	253
Mean CIT	20.8	23.3	28.2	28.1
Recipient mean age	44.1	45.8	44.9	45.1
Mean time on dialysis (months)	16.1	20.2	16.0	20.0
DGF%	17.3	30.4	25.2	42.7
Rejection frequency (%)	22.0	31.4	18.7	19.0
1-year PS (%)	98.6	96.9	95.5	92.5
1-year GS (%)	92.1	94.3	93.6	88.1

Table 4 One-year patient survival (%) in 816 paired cadaveric renal transplantations grouped by dialysis type, order of transplantation and recipient age. *PD* peritoneal dialysis, *HD* hemodialysis

	PD 1	HD 1	PD 2	HD 2	All
Age < 50, *n* = 514	98.6	100.0	98.0	96.8	98.2
Age > 50, *n* = 302	98.6	92.5	90.9	85.4	91.4

Table 5 One-year graft survival (%) in 816 paired cadaveric renal transplantations grouped by dialysis type, order of transplantation and recipient age. *PD* peritoneal dialysis, *HD* hemodialysis

	PD 1	HD 1	PD 2	HD 2	All
Age < 50, *n* = 514	90.9	97.4	95.0	91.7	93.4
Age > 50, *n* = 302	94.4	90.0	90.9	82.3	88.7

(91.4% versus 98.2%, $P < 0.001$). The older patients had significantly poorer PS in groups HD 1 ($P < 0.005$), PD 2 ($P < 0.05$) and HD 2 ($P < 0.001$) compared to the younger patients in their groups.

When 1-year GS was similarly analysed (Table 5), the same trend continued in the older patient group in favour of PD and short CIT. In the older patients, the GS was significantly worse in groups HD 1 ($P < 0.05$) and HD 2 ($P < 0.025$). The HD 2 patients over 50 years of age had a GS of only 82.3%. Of the 176 patients in HD 1 and HD 2 groups, 13 died during the first post-transplant year with a functioning graft.

When the effect of donor age (over and under 50 years) was analysed we could not show any significant differences in PS or GS.

Discussion

During the 1990s, almost half of our recipients of cadaveric renal allograft have had PD as the mode of pretransplant dialysis. We [10] among others [3, 16] have earlier reported a similar GS after renal transplantation in patients on PD and in patients on HD. In our recent, yet unpublished, study we have, however, found that the mode of pretransplant dialysis is an important determinant of the onset of renal graft function. As DGF again strongly affected long-term survival of the grafts, we found it important to analyse the many factors involved. The aim of this study was to investigate whether the difference in the onset of graft function was really dependent on the mode of dialysis itself or rather on some other recipient dependent factors. To minimise the impact of donor factors, we examined the outcome of transplantation of paired kidneys. Taking into account that the CIT was substantially different between group 1 and group 2, we wanted to focus on potential factors other than CIT.

The association of high frequency of DGF with longer CIT in group 2 was consistent with earlier findings. Surprisingly, in the group with longer preservation time and high frequency of DGF, the 1-year PS was much worse than expected, whereas the GS was only marginally decreased. This difference in PS was not explained by long waiting time on dialysis, as suggested by Cosio [3]. Neither was it explained by excess co-morbidity such as diabetes nor a higher proportion of retransplantations.

As we found a large difference in PS and DGF between group 1 and group 2, but a smaller difference in GS than expected, a further division of the two groups according to the type of dialysis seemed reasonable.

After dividing group 1 and group 2 according to type of dialysis, DGF followed the expected pattern with respect to the length of preservation time, but, interestingly, the proportion of DGF was significantly higher in HD patients than in PD patients in both groups. This is in agreement with earlier reports [2, 17] and the recent report from the United Network of Organ Sharing [1], which demonstrate the association of HD to DGF. It has been suggested that hemodialysis just before the transplant operation enhances the risk of early graft dysfunction by mechanisms such as renal hypoperfusion and release of free-radical species [12]. Although earlier studies have shown a similar GS after renal transplantation in PD and HD patients, the results of our study show that patients on HD with a long CIT have more DGF and significantly poorer 1-year GS than patients on PD.

Many authors [7, 4, 18] have demonstrated an acceptable survival of elderly recipients after kidney transplantations, usually in the over-60 age group. In this study, the age limit was set to 50 years as excess mortality became evident at this age. Both PS and GS were substantially worse in patients over 50 years. Death with functioning graft explained a large part of the differences in GS. The fact that recipients over 50 years of age had significantly poorer GS after transplantation, mainly due to poor PS, could be explained by undiagnosed increased co-morbidity of this, by calendar age, still relatively young recipient group.

Old donor age has been demonstrated in many studies to be a risk factor for renal allograft survival [11, 19]. On the other hand, age matched kidneys have been recommended for transplantation in elderly patients [6, 8], mainly due to acceptable results of transplantation in the elderly in general and due to the relative scarcity of organs from young donors. The results of this study demonstrate a suboptimal success of transplantation in elderly patients, especially with a graft with long preservation time.

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