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Cadaveric kidney donation beyond the age of 60 years – a comparative analysis of 1180 grafts from different donor age groups

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Abstract. The impact of high donor age on transplantation outcome was analysed in 1180 consecutive cadaveric grafts transplanted in adult recipients. Grafts were divided into three groups acording to donor age (< 55 years ($n = 1073$, group 1), 55–59 years ($n = 51$, group 2), ≥ 60 years ($n = 56$, group 3)) and transplantation outcome was compared for these groups. Criteria investigated were the incidence of primary non-function (PNF), initial function (IF) (urine production first 24 h) and long-term function (LTF). The impact of donor age on LTF was analysed among other potential donor, graft and recipient risk factors by the multivariate proportional hazardous model analysis (Cox model). The incidence of PNF was 5.8% (group 1), 11.8% (group 2), and 16.1% (group 3) ($P = 0.002$). Analysis of paired kidneys of PNF grafts in group 2 and group 3 revealed good function for all paired grafts except for one in each group. IF was anuria in 19.7% of group 1, 29.4% group 2 and 21.5% of group 3, oliguria in 18.2% of group 1, 23.5% of group 2 and 32% of group 3. Normal diuresis was found in 62.1% of group, 47.1% of group 2 and 47.3% of group 3 ($P = 0.05$). Independent risk factors for graft survival were year of transplantation, recipient age, panel reactive antibodies, donor age group and number of transplantation. After the exclusion of PNF grafts from the analysis, recipient age, year of transplantation and level of panel reactive antibodies remained as independent risk factors.

Key words: Kidney transplantation – High donor age – Multivariate analysis – Risk factors

The growing gap between organs available for transplantation and patients on the waiting lists has led to the consideration of new borderline donor pools such as non-heart-beating donors and donors in extreme age groups [1] during recent years. The use of grafts retrieved from older donors has been discussed widely [3, 6–8]. The objections to the use of such organs, reported as proven signs of kidney aging [2, 4], have been confirmed as well as disproved by analysis of clinical data [3, 8, 9]. Different cut-off points for the subdivision of younger and older donors have been used in reported studies [8, 9]. In the recent past the importance of age-matching between donor and recipient has been discussed [5]. Since 1982, a growing number of recipients have been transplanted with grafts from aged donors at the Vienna Transplant Unit when parameters of donor kidney function were within the normal range. We investigated whether grafts retrieved from older donors or certain donor-recipient age combinations bear a higher risk of graft loss after transplantation. Different higher age groups were introduced to reveal any potential increase of risk over a greater span of increasing donor age.

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Patients and methods

Of 1222 consecutive renal transplantations carried out between 1982 and 1991, all cadaveric grafts transplanted to adult recipients (16-years-old and over) were included in the study ($n = 1180$). To investigate the relevance of different cut-off points for donor age, patients were divided into three groups according to donor age: under 55 years (group 1), 55–59 years (group 2), and 60 years and over (group 3).

Variables investigated were donor criteria (sex, cause of death, circulatory condition before explantation, vasopressor therapy, and donor procurement centre), and graft criteria (warm ischaemic time (WIT) and cold ischaemic time (CIT) (Table 1). Recipient criteria were sex, age, primary disease, number of transplantation, panel reactive antibodies (PRA), HLA match, blood units transfused while on dialysis, pregnancies and year of transplantation (Table 2). Potentially interacting variables analysed were age match (donor age = recipient age ± 5 years; donor age = recipient age ± 10 years; or outside these categories) and the simple interaction of donor and recipient age as continuous variables.

Criteria of transplantation outcome were incidence of primary non-function (PNF), urine production during the first 24 h (anuria, < 200 ml; oliguria, 200–1500 ml; sufficient function, > 1500 ml) and long-term function at 1, 3, and 5 years. Graft function was specified in percent ± SE. Function according to groups was estimated univariately by the Kaplan-Meier method and statistically analysed by

Table 1. Donor and graft variables investigated

Variable	Donor < 55 years	Donor 55–59 years	Donor ≥ 60 years	Significance of difference
Donor:				
Sex (male/female) (%)	68/32	49/51	55/45	$P = 0.02$
Cause of death (%)				
Brain trauma	57	39	40	
Intracereb. bleeding	32	49	53	$P = 0.002$
Other	11	12	7	
Circulatory condition (%)				
Stable	68	53	69	n.s.
Instable	25	39	25	n.s.
Critical	7	8	6	n.s.
Cardiac arrest (yes/no) (%)	8/92	7/93	8/92	n.s.
Donor centre (own/other) (%)	48/52	43/57	44/56	n.s.
Graft:				
WIT (mean) (min)	0.61	0.64	0.60	n.s.
CIT (mean) (h)	21.9	24.6	24.6	n.s.

WIT, warm ischaemic time; CIT, cold ischaemic time

Table 2. Recipient variables investigated

Variable	Donor < 55 years	Donor 55–59 years	Donor ≥ 60 years	Significance of difference
Age (years)	43.7	49.2	48.2	n.s.
Sex (male/female) (%)	61/39	59/41	60/40	n.s.
Primary disease (%)				
Diabetes	8	5	12	n.s.
Other	92	95	88	
PRA (%)				
0%	70	70	85	
1–20%	13	20	7	n.s.
21–60%	10	8	4	
> 60%	7	2	4	
Nr. of transplantation (%)				
1	83	88	89	
2	13	10	7	n.s.
> 2	4	2	4	
A + B + DR mismatch (%)				
1–2	55	57	61	
3–4	43	43	37	n.s.
5–6	2	0	2	
Fullhouse (yes/no) (%)	6/94	8/92	5/95	n.s.
Blood units (%)				
0	13	8	18	
1–5	45	42	46	
6–10	17	14	10	n.s.
> 10	25	36	26	
Pregnancies (%)				
0	74	70	71	
1–2	16	18	18	n.s.
> 2	10	12	11	

the Breslow and Mantel-Cox tests. Distribution of donor, graft and recipient variables in group 3 was compared by the chi-squared test and *t*-test where appropriate.

All donor, graft and patient criteria were entered in a multivariate proportional hazardous model analysis (Cox model). The impact of factors with an independent significant influence is given as relative risk (RR), indicating the increase or decrease in the risk of graft loss in an arbitrary small interval of time. In addition, to avoid misinterpretation of donor-related factors concerning transplantation outcome, grafts of group 2 and group 3 that showed PNF were compared with their paired kidneys retrieved from the same donor. Cox model analysis was also carried out after exclusion of PNF grafts.

Results

Group 1 contained 1073 grafts, group 2 51 grafts and group 3 56 donor organs. Distribution of the variables was equal in all three groups, except cause of death (brain trauma, 58.3% group 1, 39.2% group 2 and 40% group 3;

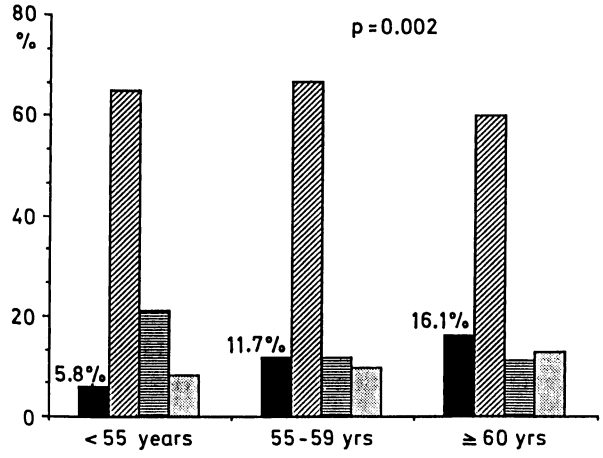

Fig. 1. Incidence of PNF (■), functioning grafts (▨), function loss (▤) and recipient death with functioning graft (▩) ($P = 0.002$)

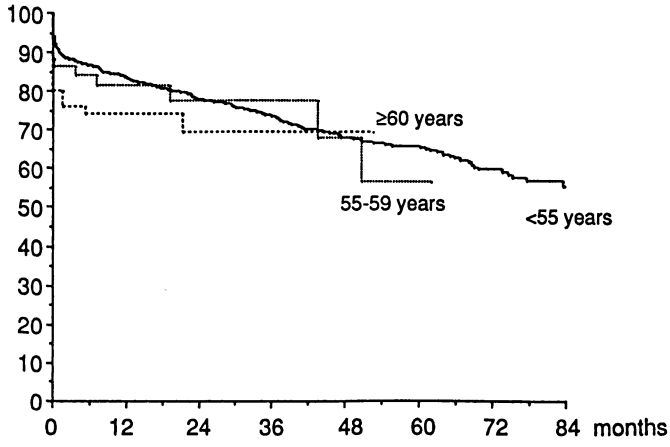

Fig. 2. Graft survival by donor age (Kaplan-Meier estimates); all patients

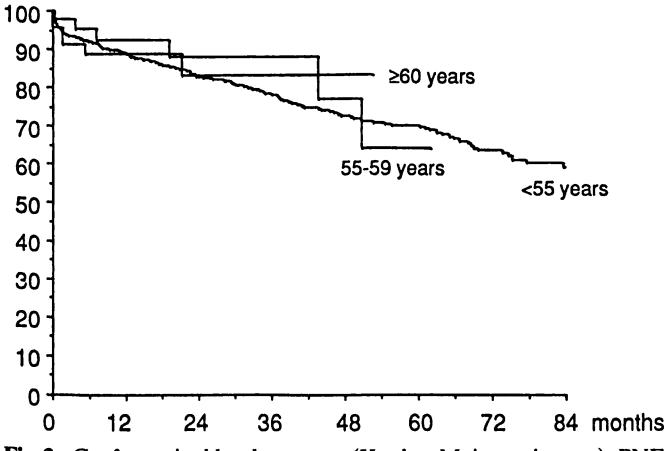

Fig. 3. Graft survival by donor age (Kaplan-Meier estimates); PNF grafts excluded

cerebral bleeding, 30.3% group 1, 49% group 2 and 52.7% group 3; other, 11.4% group 1, 11.8% group 2 and 7.3% group 3; $P = 0.001$). The proportion of grafts from aged donors differed from 1982 to 1990 from 0 to 6.5% (group 2) and 0 to 7.7% (group 3) ($P = 0.004$, 1982–1985 vs 1986–1990).

The incidence of PNF was 5.8% (group 1), 11.7% (group 2) and 16.1 (group 3) ($P = 0.002$) (Fig. 1). Initial diuresis was anuria in 19.7% of group 1, 29.4% of group 2 and 21.5% of group 3, oliguria in 18.2% of group 1, 23.5% of group 2 and 32% of group 3. Normal diuresis was found in 62.1% of group 1, 47.1% of group 2 and 47.3% of group 3 ($P = 0.05$). LTF at 1, 3 and 5 years in univariate analysis (Kaplan-Meier estimates) was 83.7 ± 1%, 73.4 ± 4% and 65.8 ± 2% for group 1, 81.5 ± 5%, 77.5 ± 6% and 56.5 ± 13% for group 2 and 74.1 ± 6% and 69.5 ± 7% for group 3 (observations of group 3 were not made for as long as 5 years) (NS) (Figs. 2 and 3).

Independent factors increasing or decreasing the risk of graft loss revealed by the multivariate proportional hazardous model analysis were: year of transplantation (RR = 0.86 for 1 year, RR = 0.32 for 1990 vs 1982, $P < 0.0001$); recipient panel-reactive antibodies (RR = 1.3 (0% vs 1–40%), RR = 1.7 (0% vs > 40%), $P < 0.0001$); recipient age (0.98 (step of 1 year), RR 0.87 (step of 10 years), $P = 0.001$); donor age group (RR = 1.5 (group 2 vs group 1), RR = 2.2 (group 3 vs group 1), $P = 0.004$); and number of transplantation (RR = 1.3 (first vs second), RR = 1.75 (first vs third and subsequent), $P = 0.017$) (Table 3). Six grafts in group 2 and nine grafts in group 3 showed PNF.

In group 2 one pair of grafts showed PNF in both recipients, but four of the paired grafts had good function at 6, 14, 15 and 31 months (CIT 23 h (PNF) vs 19 h (paired grafts)). In group 3 also one pair of transplants never showed function, and of the remaining seven paired grafts, six functioned at 6, 8, 13, 14, 21 and 45 months, one recipient died with a functioning graft after 1 month and one graft lost function after 4 months (CIT 28 h (PNF) vs 22 h (paired grafts)).

After exclusion of PNF grafts the Cox model analysis for the remaining transplants revealed an independent influence on graft survival of the following factors: recipient age (RR = 0.97 (1 year step), RR = 0.81 (10 year step), $P < 0.0001$); year of transplantation (RR = 0.89 (1 year step), RR = 0.40 (1990 vs 1982), $P = 0.001$); and level of panel reactive antibodies (RR = 1.2 (0% vs 1–40%), RR = 1.57 (0% vs > 40%), $P = 0.021$).

Age-matching by donor age ± 5 years of recipient age and ± 10 years of recipient age, and the interaction of donor and recipient age entered as continuous variables in the Cox model analysis did not show any effect on transplantation outcome.

Discussion

Grafting of organs retrieved from older donors has increased steadily at the Vienna Transplant Unit during the past 8 years according to the loosening of donor age criteria. In a general comparison with grafts harvested from younger donors the higher incidence of immediate graft loss and early function disorders in aged transplants is noticed.

Donor age above both defined cut-off points ranked among the strongest factors affecting long-term graft function. Yet when grafts suffering PNF were compared

Table 3. Results of Cox model analysis. All grafts vs PNF grafts excluded

Variable	Relative risk (all grafts)	Relative risk (PNF grafts excluded)
Year of transplant		
Single step	0.86 ($P = 0.0001$)	0.89 ($P = 0.001$)
1982–1990	0.32 ($P = 0.0001$)	0.40 ($P = 0.001$)
Number of transplant (first, second, third +)		
Single step	1.30 ($P = 0.017$)	not in the model
First vs third +	1.75 ($P = 0.017$)	
Recipient age (increasing)		
Single year	0.98 ($P = 0.007$)	0.98 ($P = 0.001$)
Ten years	0.87 ($P = 0.007$)	0.81 ($P = 0.001$)
Panel reactive antibodies (0–20%, 21–60%, > 60%)		
Single step	1.30 ($P = 0.001$)	1.20 ($P = 0.021$)
0% vs > 60%	1.70 ($P = 0.001$)	1.57 ($P = 0.021$)
Donor age (< 55, 55–59, ≥ 60)		
–55 vs 55–59	1.50 ($P = 0.004$)	not in the model
–55 vs ≥ 60	2.20 ($P = 0.004$)	

with their paired kidneys it appeared that the occurrence of PNF could not solely be accounted for by poor donor quality but had to be interpreted as mainly recipient- and maybe CIT-dependent and might be attributable to immunologically-related failure [10]. A second finding that supports this suspicion is the fact that repeated transplantation, known as a strong risk factor for recipient sensitization and thus poor transplantation outcome, did not show as a significant influence on transplantation outcome in the Cox model when PNF grafts were excluded from the analysis. General factors influencing graft survival were recipient sensitization and recipient age. The positive influence of increasing recipient age on graft survival may be caused by a decrease in immunological response [11]. The improvement in transplantation outcome during recent years, as documented by the decreasing risk of graft loss, can be interpreted as a result of growing technical and immunological management experience of transplantation.

There was no evidence of a favourable effect of age-matching in our data as has been reported recently [5]. Neither could interactions between recipient age and donor age be demonstrated in this cohort of patients as has been shown by the Eurotransplant Group [5]. Nevertheless a possible effect may have been masked by the strong influence of other factors.

High donor age in itself is no obstacle to succesful transplantation. The acceptance of aged donors can increase the number of organs procured substantially. Hence, greater consideration should be given to this reservoir of potential donors.

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