Nephrol Dial Transplant (2001) 16: 824–828

Nephrology Dialysis Transplantation

Original Article

Renal transplantation in the elderly: a long-term, single-centre experience

Patrick Saudan[1], Thierry Berney[2], Michel Leski[1], Philippe Morel[2], Jean-François Bolle[1] and Pierre-Yves Martin[2]

[1]Division of Nephrology, Department of Medicine and [2]Clinic of Visceral and Transplantation Surgery, University Hospital, Geneva, Switzerland

Abstract

Background. End-stage renal failure increases with advancing age and renal transplantation should be considered in end-stage renal failure patients older than 60 years. However, there is a paucity of data on long-term patient and graft survival in this population.

Methods. From October 1983 to March 1999, 310 renal transplantations were performed at Geneva University Hospital in 283 patients, of which 49 were done in 48 patients older than 60 years (mean age 65.6 ± 4.1 years). The following data were analysed at 1, 5, and 10 years, and compared between the patients >60 years and <60 years old: actuarial patient and graft survival, serum creatinine, causes of graft loss, and patient death.

Results. Patient survival at 10 years was 81% for patients <60 years and 44% for patients >60 years. Graft survival at 10 years was 59% for patients <60 years and 32% for patients >60 years. Graft survival at 10 years censored for death with functioning graft was 65% for patients <60 years and 81% for patients >60 years. Main causes of mortality in the older patients were related to cardiovascular events (47%), neoplasia (41%), and sepsis (18%). Overall, recipient and donor age were not predictive factors for graft survival, as shown by multiple logistic regression.

Conclusions. Renal transplantation should be considered in patients older than 60 years, since graft survival is excellent in this population. Although these patients have a shorter life expectancy, they benefit from renal transplantation similarly to younger kidney transplant recipients.

Correspondence and offprint requests to: Pierre-Yves Martin MD, Nephrology Division, Department of Internal Medicine, Geneva University Hospital, 24 Rue Micheli-Du-Crest, CH-1211 Geneva 14, Switzerland.

Keywords: elderly; end-stage renal disease; haemodialysis; kidney graft failure; renal transplantation; retrospective study; survival

Introduction

End-stage renal disease increases with advancing age and nowadays patients older than 60 years account for more than 53% of the population requiring renal replacement therapies [1]. Haemodialysis is the most commonly used modality in these patients, but is associated with significant morbidity, mortality, and poor quality of life [2,3]. Before the widespread use of calcineurin inhibitors, renal transplantation was not advocated as a treatment of end-stage renal failure for patients older than 60 years because of poor graft and patient survival rates [4].

However, transplantation is the best treatment demonstrated for end-stage renal disease patients [5] and in the cyclosporin era, renal transplantation became an alternative to dialysis for these patients [6] and some centres have reported good 5-year graft and patient survivals [7–9]. Among elderly patients with end-stage renal failure, patient survival is increased in transplanted patients in comparison with haemodialysed patients awaiting transplantation. Between 1991 and 1997, in the United States, renal transplantation in patients older than 60 years was associated with a 61% decrease in long-term risk of death and with an additional 4-year life expectancy, as compared to haemodialysis [5]. However, few data on long-term follow-up in elderly transplant recipients are available. Moreover, due to scarcity of organs and shorter life expectancy in this population, allocating cadaveric kidneys to these patients is still controversial.

In this retrospective study, we report a single-centre, long-term follow-up of kidney transplantation in

patients older than 60 years. The aims of this study were to determine whether 10-year patient and graft survival could support a policy of cadaveric kidney transplantation for patients older than 60 years in our centre, and which factors played a role in long-term graft and patient survivals.

Subjects and methods

This retrospective study spans the period from October 1983, when we started to use cyclosporin routinely, to March 1999. During this period, 310 kidney transplantations were performed in 283 patients. Transplantation procedures were performed in 188 males and 122 females, with a median age of 46.7 years (range 13.3–78.1). Of these, 49 transplants were carried out in 48 patients older than 60 years (median 65 years; range 60.2–78.1).

Pre-transplantation screening included cardiac ultrasound, stress thallium testing, and cerebrovascular and inferior limb Doppler studies. Patients were then admitted to the waiting list after correction of any significant vascular and coronary lesions. The main exclusion criteria were: positive cross-match for T-cell lymphocytes, evidence of active infection, clinically significant cardiac abnormality, malignancy within the previous 5 years, and severe psychiatric disorders.

The standard immunosuppressive regimen consisted in a cyclosporin, steroids, and azathioprine triple therapy. The Neoral formulation (Novartis, Basel, Switzerland) was used as of 1994. Mycophenolate mofetil (Cell-cept, Roche, Basel, Switzerland) replaced azathioprine as of 1996. Thymoglobulins (ATG, Merieux-Pasteur, Marcy l'Etoile, France) and tacrolimus (Prograf, Fusjisawa, Killorglin, Ireland) were used as a rescue therapy.

The following data were analysed at 1, 5, and 10 years and compared between the patients >60 years and <60 years of age: actuarial patient and graft survival, serum creatinine, causes of graft loss, and patient death.

Graft survival for the overall population was also analysed according to donor age, with a cut-off value arbitrarily set at 50 years. Selected parameters were assessed as independent factors for graft outcome by multiple regression analysis.

A complete follow-up was obtained for 301 transplantation procedures (97%). Median follow-up was 6.6 years (range 0.2–16 years).

All statistics were performed using the Statistica software package (Statsoft, Tulsa, Oklahoma). Patient and graft survivals were calculated with the Kaplan–Meier method. Survival curves were compared with the Mantel-Cox log-rank test. Cox's proportional hazard method was used for multiple regression analysis. Comparison of parametric data was done with Student's *t*-test for continuous variables, and with χ^2 test with Yates' correction or Fisher's exact test, wherever appropriate, for categorical variables. Values of $P<0.05$ were considered significant.

Results

The statistically significant differences in patient characteristics between both groups were lower peak panel-reactive antibodies (PRA; $P=0.005$), and lower prevalence of diabetes ($P=0.03$) and higher prevalence of hypertension ($P=0.02$) as original nephropathies in the older group (>60 years). Male to female ratio tended to be higher in the older group, but the difference failed to reach statistical significance. The

Table 1. Patient characteristics

	>60 years ($n=48$)	<60 years ($n=235$)	*P*
Transplants (*n*)	49	261	NS
Recipient age (years)	65.6 ± 4.1	43.1 ± 10.4	
Haemodialysis/peritoneal dialysis/ no dialysis ratio	82/14/4	78/18.5/3.5	NS
Dialysis duration (weeks)	87.2 ± 73.5	104.1 ± 140.9	NS
Male/female ratio	73.5/26.5	58.2/41.8	NS
Diabetes (%)	4	16	0.03
Hypertension (%)	24	11	0.02
Chronic GN (%)	35	28	NS
PCKD (%)	14	19	NS
Others (%)	22	26	NS
Cerebro-cardiovascular disease pre-transplant prevalence (%)	12.5	12.4	NS
Cerebro-cardiovascular disease post-transplant prevalence (%)	22.9	26.7	NS
Retransplant (%)	9	18	NS
Cadaveric donor (%)	98	93	NS
Living donor (%)	2	7	NS
Donor age (years)	36.9 ± 15.9 (8–69)	34.5 ± 14.7 (4–66)	NS
Max PRA $>40\%$ (%)	2	15	0.005
HLA mismatch (1–6)	3.6 ± 1.3	3.5 ± 1.5	NS
Cold ischaemia time (h)	19.2 ± 5.2	19.2 ± 6.9	NS
Delayed graft function (%)	27	20	NS
Acute rejection episodes (%)	31	42	NS
Kidney graft $t_{½}$ (months)	99	165	

GN, glomerulonephritis; PCKD, polycystic kidney disease; PRA, panel reactive antibodies.

living donor rate was 7% in the younger group and 2% in the elderly group. No significant difference between the two groups was found for mean donor age, cold ischaemia time, delayed graft function, and acute rejection rates. Patient characteristics are summarized in Table 1.

Actuarial patient survival at 1, 5, and 10 years was respectively 98, 78, and 44% for patients >60 years and 97, 93, and 81% for patients <60 years ($P<0.0001$, Figure 1A). Actuarial graft survival at 1, 5, and 10 years was 93, 65, and 32% for patients >60 years and 87, 74, and 59% for patients <60 years ($P=0.09$, Figure 1B). When observations were censored for patient death with functioning graft, actuarial graft survival at 1, 5, and 10 years was 96, 85, and 81% for patients >60 years and 88, 78, and 65% for patients <60 years ($P=0.18$, Figure 1C). Actuarial graft survival did not differ between patients transplanted with kidneys from donors younger than 50 years (<50 years) ($n=62$, mean 29.5 ± 11.7 years) and older than 50 years (>50 years) ($n=239$, mean 55.3 ± 4.8 years) (10-year survival: 59 *vs* 48%, $P=0.12$; Figure 2). Multivariate analysis of selected variables showed only peak PRA and HLA mismatch to be significant predictive factors for graft survival in this population (Table 2).

Renal function, as assessed by serum creatinine in patients with functioning grafts, was not different between the two groups at 1 and 5 years follow-up (Table 3).

Graft loss due to patient death was 29% among the recipients >60 years, as compared to 6% in the <60 years group ($P<0.0001$). In contrast, kidney transplants were lost to acute or chronic rejection in 22% of patients in the <60 years group, as compared

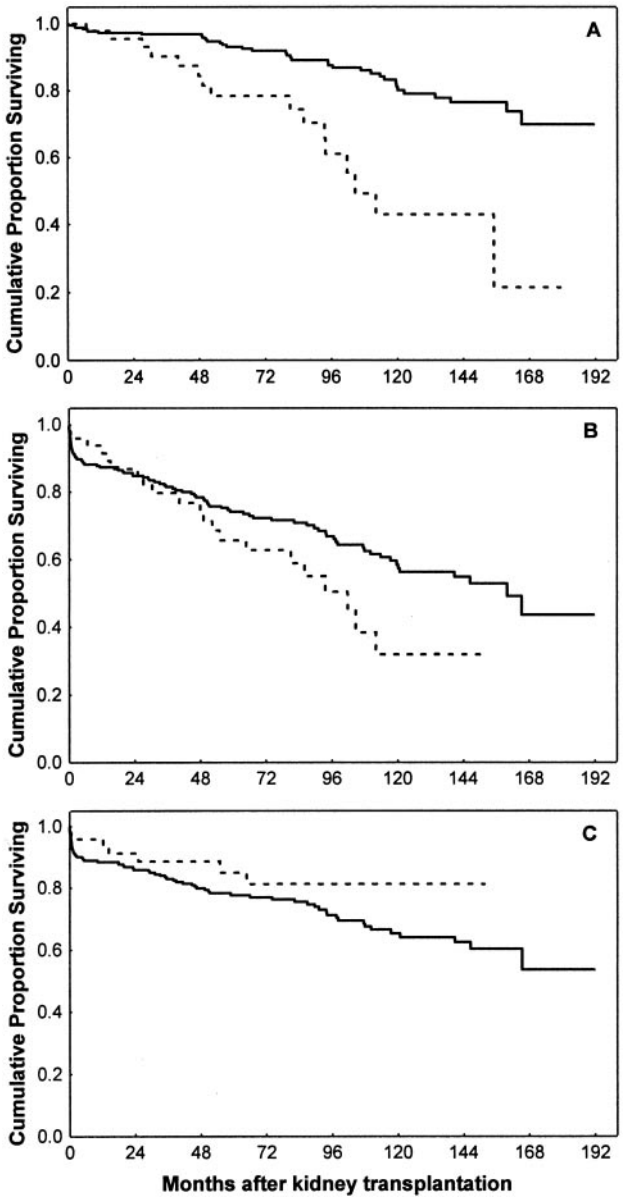

Fig. 1. Kaplan–Meier analysis of patient and graft survival after kidney transplantation according to age of recipient. (**A**) Patient survival of recipients <60 years (continuous line, $n=261$) and >60 years (dashed line, $n=49$) at the time of transplant; $P=0.00001$ (Mantel–Cox log-rank test). (**B**) Graft survival in recipients <60 years (continuous line, $n=261$) and >60 years (dashed line, $n=49$) at the time of transplant; $P=0.09$, NS. (**C**) Graft survival censored for patient death with functioning graft in recipients <60 years (continuous line, $n=261$) and >60 years (dashed line, $n=49$) at the time of transplant; $P=0.18$, NS.

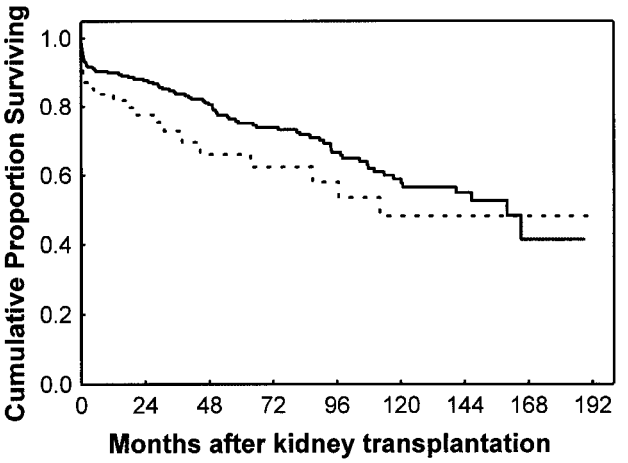

Fig. 2. Kaplan–Meier analysis of graft survival after kidney transplantation according to age of donor. Graft survival from donors <50 years (continuous line, $n=239$) and >50 years (dashed line, $n=62$); $P=0.12$ (Mantel–Cox log-rank test), NS.

Table 2. Predictive factors of graft survival

Factor	*P*	
Recipient age*	0.46	NS
Donor age*	0.28	NS
Peak % PRA*	0.05	
Cold ischaemia time*	0.56	NS
HLA mismatches*	0.02	
Gender†	0.67	NS
Nephropathy†	0.53	NS
Living donor†	0.63	NS

NS, non-significant. *Cox's proportional hazard method; †Mantel–Cox log-rank test.

Table 3. Serum creatinine level by age in kidney recipients

Follow-up	>60 years (*n*)	s-creat. (μmol/l)	<60 years (*n*)	s-creat. (μmol/l)	*P*
1 year	39	131 ± 54	216	135 ± 43	NS
5 years	23	131 ± 62	125	137 ± 43	NS

Table 4. Causes of graft loss in kidney recipients

Aetiology	>60 years (*n* = 49)		<60 years (*n* = 261)		*P*
	n	%	*n*	%	
Death with functioning graft	14	29	15	6	<0.0001
Acute rejections	1	2	22	8	NS
Chronic rejections	4	8	36	14	NS
Rejection (acute + chronic)	5	10	58	22	0.04
Technical complications	2	4	7	3	NS
Recurrence	1	2	2	1	NS
Others	0	0	2	1	NS

to 10% in the >60 years group ($P = 0.04$). Other causes of graft loss were similar in both groups (Table 4).

Discussion

Despite their limited life expectancy, patients older than 60 years seem to benefit from renal transplantation, as witnessed by the excellent graft survival rate reported herein.

Patient and graft survivals after a 5-year follow-up in this transplanted elderly population (78 and 65% respectively) compare favourably with what was previously reported in the literature. American centres reported 5-year patient and graft survivals in recipients over 60 ranging from 64 to 68% and from 55 to 62% respectively [7,8]. These studies included 18–30% of patients transplanted with living donors kidneys. In Europe, an 80% patient and graft survival at 5 years was reported for elderly recipients of cadaveric kidneys by Cantarovich *et al.* [9]. Recently published data from The UK National Data Base showed slightly more than 50% cadaveric kidney graft survival at 5 years for patients older than 60 years [10]. The difference in graft survival between these two studies may be partially related to the pre-transplant cardiovascular co-morbidities of the recipients.

Studies with long-term analysis of patient and graft survival are lacking. With a median follow-up of 6.6 years, we report 44% patient survival, and 81% graft survival censored for death with function in actuarial terms. Measured serum creatinine at 5 years in patients with functioning grafts indicates good renal function. This result is probably explained by a lower rejection rate in this population, as previously reported [8]. Accordingly in our study, there is less immune-induced graft loss in the older group.

Many centres, including ours, still hesitate to accept older patients for renal transplantation list on account of their shorter life expectancy. However, our results as well as those from other studies [7–10] might convince more centres that age *per se* is not a contraindication to renal transplantation. Prior to analysing our results, less than 20% of the dialysed patients over 60 years were considered potential transplant candidates. We should be able to increase this percentage by considering every patient over 60 years as a potential recipient. Their survival can be improved by a careful selection and thoroughly assessing cardiac and infectious risk as well as a tailored immunosuppression [11].

A controversial point in kidney transplantation in the elderly is donor age. It is well known that kidney graft failure increases with donor age [10,12,13]. The use of older kidneys is nonetheless considered as acceptable, because of the scarcity of cadaveric kidney donors. Moreover, some authors have also shown a good graft survival when kidneys from older donors are transplanted into older recipients, and advocated a donor–recipient age matching [14]. In contrast, a recent publication reported a 14% decrease in 5-year graft survival for patients over 60 years who are transplanted with kidneys from donors over 60 years of age compared to kidneys from donors under the age of 60 years [15].

Our recipient and donor populations are too small to allow us to match the age of donors and recipients. However, donor age was not a predictive factor of graft survival in a multiple regression analysis. Additionally, no significant difference in actuarial graft survival was found when comparing recipients of kidneys from donors over and under 50 years of age. This might be explained by the fact that a majority of older donors were under 60 (mean 55.3 ± 4.8 years).

Our results are in conflict with what has been previously published in the literature where graft failure increases progressively with advancing donor age [12,13]. However, recently published Japanese data on living donor kidney transplantation report that graft survival at 10 years remains at around 70% with donors from 50 to 59 years of age, but declined dramatically to 45% with donors over 60 [16].

Therefore we consider that allocating kidneys from donors between 50 and 60 years of age to elderly end-stage renal failure patients does not harm their long-term renal function. There is a consensus in the literature that cadaveric kidneys from donors up to 60 years of age should be transplanted. Kidneys from donors older than 60 years can also be transplanted, provided biopsy-proven sufficient renal integrity has been demonstrated preoperatively [17].

In summary, regarding the poor survival and quality of life of elderly patients on haemodialysis, we believe that renal transplantation should be offered to patients older than 60, after proper screening for cardiovascular and infectious disease. However, on account

of the shorter life expectancy of older recipients, and the good survival of kidney grafts from donors over 50 at 5 and 10 years, it seems logical and ethically fair to preferentially allocate kidneys from donors over 50 to these patients.

References

1. Cecka JM, Terasaki PL. The UNOS Scientific Renal Transplant Registry. In: Terasaki PL, Cecka JM (eds). *Clinical Transplantation*. UCLA Press, 1993
2. Ismail N, Hakim RM, Oreopoulos DG, Patrikarea A. Renal replacement therapies in the elderly: part I. Hemodialysis and chronic peritoneal dialysis. *Am J Kidney Dis* 1993; 22: 759–782
3. Fauchald P, Albertchtsen D, Leivestad T *et al.* Renal replacement therapy in elderly patients. *Transplant Int* 1988; 1: 131–134
4. Ismail N, Hakim RM, Helderman JH. Renal replacement therapies in the elderly: part II. Renal Transplantation. *Am J Kidney Dis* 1994; 23: 1–15
5. Wolfe RA, Ashby VB, Milford EL *et al.* Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation and recipients of a first cadaveric transplant. *N Engl J Med* 1999; 341: 1725–1730
6. Pirsch JD, Statta RJ, Armbrust MJ *et al.* Cadaveric renal transplantation with cyclosporine in patients more than 60 years of age. *Transplantation* 1989; 47: 259–261
7. Benedetti E, Matas AJ, Hakim N *et al.* Renal transplantation for patients 60 years of age or older: A single institution experience. *Ann Surg* 1994; 220: 445–460
8. Tesi RJ, Elkhamamas EA, Davies EA *et al.* Renal transplantation in older people. *Lancet* 1994; 343: 461–464
9. Cantarovich D, Baatrad R, Baranger T *et al.* Cadaveric renal transplantation after 60 years of age: a single center experience. *Transplant Int* 1994; 7: 33–38
10. Morris PJ, Johnson RJ, Fuggle SV *et al.* Analysis of factors that affect outcome of primary cadaveric renal transplantation in the UK. *Lancet* 1999; 354: 1147–1152
11. Ponticelli C. Should renal transplantation be offered to older patients? *Nephrol Dial Transplant* 2000; 15: 315–317
12. Alexander JW, Bennett LE, Breen TJ. Effect of donor age on outcome of kidney transplantation. *Transplantation* 1994; 57: 871–876
13. Terasaki PL, Gjertson DW, Cecka JM *et al.* Significance of the donor age effect on kidney transplants. *Clin Transplant* 1997; 11: 366–372
14. Cecka JM, Terasaki PL. Optimal use for older donors kidneys: older recipients. *Transplant Proc* 1995; 27: 801–802
15. Basar H, Soran A, Shapiro R *et al.* Renal transplantation in recipients over the age of 60: the impact of donor age. *Transplantation* 1999; 67: 1191–1193
16. Shimmura H, Tanabe K, Ishikawa N *et al.* Influence of donor renal reserve on the long-term results of living kidney transplantation from elderly donors. *Transplant Proc* 1999; 31: 2874–2876
17. Kumar MS, Panigrahi D, Dezii CM *et al.* Long-term function and survival of elderly donor kidneys transplanted into young adults. *Transplantation* 1998; 65: 282–285

Received for publication: 16.5.00
Accepted in revised form: 24.10.00