



OUTCOMES

Renal Transplantation in Patients Over 60 Years of Age: A Single-Center Experience

S. Pedroso, L. Martins, I. Fonseca, L. Dias, A.C. Henriques, A.M. Sarmento, and A. Cabrita

ABSTRACT

The prevalence of end-stage renal disease (ESRD) increases with advancing age. In most countries renal transplant recipients are getting older, too. Transplantation must be considered for ESRD patients older than 60 years; however, there are few data regarding outcomes in this population. We retrospectively reviewed the clinical course of recipients aged ≥ 60 years ($n = 43$) who underwent primary or repeated grafts from August 1988 to December 2004. We then compared recipient and donor characteristics as well as graft and patient survivals with recipients aged 18 to 59 years ($n = 1058$) who were transplanted during the same time. Donor age tended to be higher among the oldest recipient group ($P < .001$). Mean follow-up was significantly shorter in the group aged ≥ 60 years ($P < .001$), as our institution only recently has frequently accepted patients ≥ 60 years. Older recipients showed more frequent delayed graft function ($P = .007$), longer initial hospitalization ($P = .005$), and a significantly lower incidence of posttransplant acute rejection episodes ($P = .015$). Patient ($P = .057$), graft ($P = .407$), and death-censored graft ($P = .649$) survivals were not different between the two groups. Seven recipients aged ≥ 60 years died; the main cause of which was cardiovascular in origin. The loss of organs ($n = 11$) in the older patients was mainly due to death with a functioning kidney (54.5%). Our results confirm that renal transplant must be considered in selected patients older than 60 years as patient and graft survivals are similar to those of younger patients.

ELDERLY PATIENTS are the fastest growing population in dialysis programs.¹ Hemodialysis is the more commonly used modality, although it is associated with significant morbidity, mortality, and a poor quality of life. The prevalence of end-stage renal disease (ESRD) increases with advancing age. In most countries, renal transplant recipients are also getting older. In the precyclosporine era the unsatisfactory results of grafting in the elderly lead to the exclusion of patients more than 60 years of age due to higher risks for patient death and graft loss.² With widespread use of calcineurin inhibitors, the age limit for transplantation has expanded. Today, transplantation is considered the best treatment option for ESRD patients regardless of age when compared with dialysis.³⁻⁵ With the development of new immunosuppressive alternatives, transplantation is safe and successful. It should be considered an alternative to dialysis even among older patients. Older ESRD patient survival after transplantation is higher than on the waiting list.³⁻⁵ However, the organ donor shortage makes clinicians reluctant to transplant kidneys into older patients. Controversy

has emerged regarding the appropriateness of transplantation in this patient group with a shortened life expectancy. Numerous studies have reported worse patient and graft survivals in older patients compared with younger patients, while other analyses did not find any difference.⁶⁻⁹

There is also a paucity of data concerning long-term patient and graft survivals in this population, especially after undergoing uniform screening for comorbidities before being added to the waiting list. So it remains difficult for clinicians involved in these programs to know whether the possible benefits from transplantation are sufficiently relevant to advocate this option over dialysis for the elderly. The purpose of this study was to evaluate our policy for recipients 60 years or older. We reviewed the outcomes of

From the Nephrology and Transplant Departments, Hospital Geral de Santo António, Porto, Portugal.

Address reprint requests to Sofia de Lima Pedroso, Departamento de Nefrologia, Hospital Geral de Santo António, Largo Professor Abel Salazar, 4050-011 Porto, Portugal. E-mail: sofiapedroso@sapo.pt

transplantation in recipients over 60 years of age and compared that data with graft and patient survivals among recipients aged 18 to 59 years in the same time period.

PATIENTS AND METHODS

From July 1983 to December 2004, 1297 ESRD patients underwent transplantation at our center, including first recipient over 60 years in 1988. We retrospectively reviewed the clinical course of 43 consecutive recipients aged 60 years or older who underwent primary or repeated renal transplant.

The outcome of the 43 patients aged 60 years or older was compared with that of the 1058 renal allograft recipients aged 18 to 59 years whose recruitment occurred during the same period (August 1988 to December 2004). The majority of older patients (70%, $n = 30$) were transplanted after 1998. Pretransplantation screening for patients over 60 years of age included stress thallium testing or coronary angiography; femoral and iliac Doppler studies; intensified screening for neoplasia; and all other studies included in the pretransplant screening for patients younger than 60 years. Patients were then admitted to the waiting list after correction of any significant coronary or other vascular lesions. Immunosuppressive regimens were not different among older versus younger patients, with variations related to the transplant year. A calcineurin inhibitor was used in all elderly patients. Fourteen patients aged 60 or older received polyclonal or monoclonal antibodies.

The chi-square test or Student's t test were used for statistical analysis of group comparisons as appropriate. The survival functions of the patient, graft, and death-censored survival were studied by the Kaplan-Meier analysis and by the evaluation of the between-group differences using the log-rank test. $P < .05$ was considered significant. Patient and graft survival analysis was compared between the group of recipients aged over 60 years and the group between 18 to 59 years by the Kaplan-Meier method with statistical significance evaluated by the log-rank test. Primary outcomes analysis focused on patient and graft survivals. In a first analysis, graft loss was defined as the loss of graft function, resulting in the need to restart dialysis, need for retransplantation, or death (graft survival without censoring data for patients who died with functioning grafts). An additional analysis was performed after censoring data on patients who died with a functioning allograft (graft survival censored for patient death).

Statistical inferences were obtained using the SPSS software package, version 12.0 (SPSS Chicago, Ill).

RESULTS

From August 1988 to December 2004, 1101 transplantations were performed in 984 patients in our center. During this period, 43 (4%) were done in recipients 60 years of age or older (mean age 63.2 ± 2.5 years; range 60–69), and 1058 in recipients between 18 and 59 years (mean age 39.4 ± 10.9 years). Table 1 summarizes the demographic data for the two groups, the donor characteristics, the follow-up information and the P values for differences between the groups.

The causes of ESRD in the over 60 group were unknown in 27.9%; glomerular diseases in 20.9%; tubulointerstitial disease in 16.3%; autosomal dominant polycystic disease in 16.3%; systemic and vascular diseases in 13.9%, and other causes in 4.7%. Only one patient of the group aged over 60 had diabetes as the cause of renal failure versus 44 in the

Table 1. Demographic Characteristics of Recipients Over 60 Years and Recipients 18 to 59 Years

	≥ 60 Years ($n = 43$)	18–59 Years ($n = 1058$)	P
Age (y)	63.2 ± 2.5	39.4 ± 10.9	—
Male gender (%)	58.1	60.6	.407
Renal transplants (1/ ≥ 2)	40/3	944/114	.589
Diabetic nephropathy	1	44	.840
Duration of dialysis (y)	5.5 ± 4.8	4.1 ± 3.7	.078
Donor age (y)	44.1 ± 17.2	32.5 ± 15.2	$<.001$
Donor gender, male (%)	68.3	71.0	.103
Donor cadaver/living	43/0	1024/24	.636
Cold ischemia (h)	24.0 ± 6.2	23.8 ± 4.6	.826
Acute rejection (%)	7.0	24.2	.015
Delayed graft function	24	366	.007
Initial hospitalization (days)	29.7 ± 16.3	22.3 ± 14.9	.005
HLA DR mismatch	0.59 ± 0.63	0.56 ± 0.62	.806
Total HLA mismatch	3.10 ± 1.22	2.83 ± 1.31	.183
Renal follow-up (y)	4.1 ± 3.8	6.7 ± 4.8	$<.001$

P values for differences between the two groups.

group aged 18 to 59 years, but this difference was not statistically significant ($P = .840$).

Donor age tended to be higher in the oldest recipient group (44.1 ± 17.2 vs 32.5 ± 15.2 years, $P < .001$). In the older group, 37.2% ($n = 16$) of donors were 55 years old or older. The mean follow-up was significantly shorter in the group aged over 60 years (4.1 ± 3.8 vs 6.7 ± 4.8 years, $P < .001$). Renal follow-up was longer in patients aged 18 to 59 years because our institution has increasingly accepted patients older than 60 years for transplantation in more recent years. Older recipients more frequently experienced delayed graft function (24 vs 366 cases, $P = .007$) and longer initial hospitalization (29.7 ± 16.3 vs 22.3 ± 14.9 hospital days, $P = .005$). The incidence of acute rejection episodes was lower in the group of patients over 60 (7.0% vs 24.2%, $P = .015$).

No significant difference was found between the two groups for patient or donor gender, number of retransplants, cold ischemia time, HLA-mismatch, and time on dialysis. All donors for the older group were cadaveric; three patients received a second transplant.

Patient survival rates were 94.6% at 1 year, 87.5% at 5 years, and 64.0%, at 10 years for patients over 60 years and 96.4, 92.7, and 85.9%, respectively, for patients aged 18 to 59 years. Overall graft survival was 89.2% at 1 year, 73.6% at 5 years, and 48.8% at 10 years for patients over 60 years versus 88.2, 80.8, and 68.7%, for patients aged 18 to 59 years, respectively. When observations were censored for patient death with a functioning kidney, actuarial censored graft survival at 1, 5, and 10 years was 91.8, 82.4, and 82.4% for patients over 60 years and 90.4, 85.3, and 78.1% for patients aged 18 to 59 years, respectively. Figures 1, 2, and 3 show patient, graft, and censored graft survival curves for those over 60 years of age and those aged between 18 to 59 years. Patient survival tended to be lower in the older group, but the difference failed to reach statistical signifi-

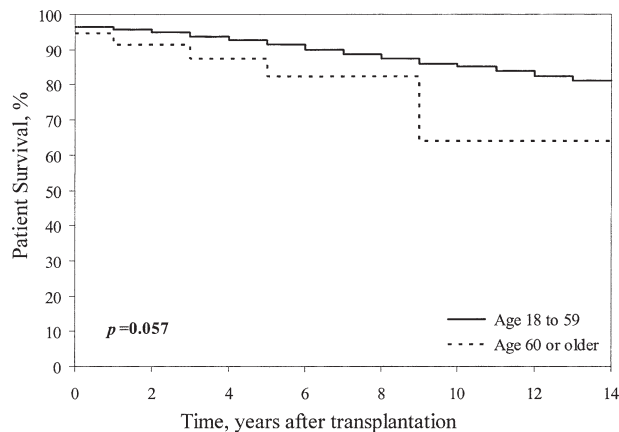


Fig 1. Kaplan-Meier estimate of the cumulative probability of patient survival according to recipient age.

icance. Patient ($P = .057$) and graft survival ($P = .407$) for those over 60 years of age versus those 18 to 59 years of age were statistically similar. The graft survival censored for patient death with a functioning kidney (death-censored graft survival) was identical in the two groups ($P = .649$).

Sixteen recipients of 60 or older were transplanted with an aged kidney (≥ 55 years). There was no statistical difference in patient ($P = .515$), graft ($P = .756$), and graft-censored ($P = .512$) survival for grafts from a donor under 55 (mean: 32.2 ± 10.4 years) versus an older donor (≥ 55 years, mean: 62.6 ± 4.4 years).

Seven (16.3%) recipients aged over 60 years died versus 129 (12.2%) in the younger group. Death in the older patients was the result of cardiovascular complications ($n = 4$), malignancy ($n = 1$), and other reasons ($n = 2$). Eleven recipients over 60 old lost their kidney after a mean follow-up of 4.1 ± 3.8 years (four lost their grafts in the first year after transplantation). Among the younger group, 289 transplants were lost. The loss of organs in the older

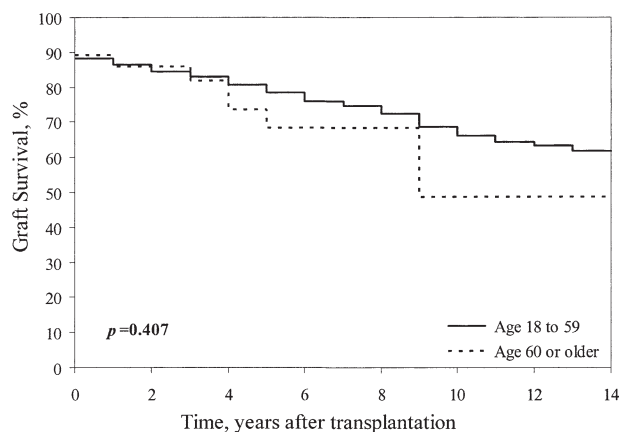


Fig 2. Kaplan-Meier estimate of the cumulative probability of graft survival according to recipient age.

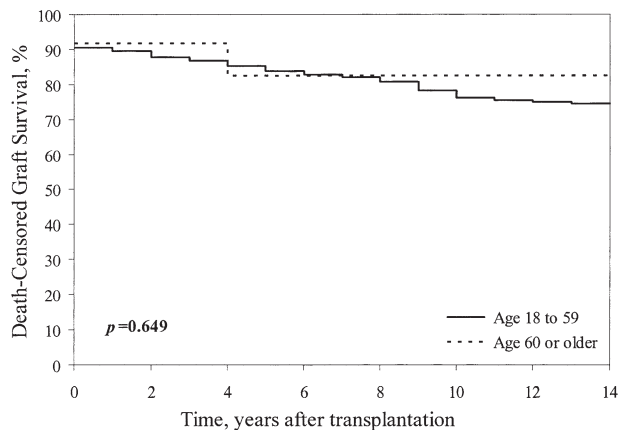


Fig 3. Kaplan-Meier estimate of the cumulative probability of death-censored graft survival according to recipient age.

patients was mainly due to death with a functioning kidney. In the elderly, 54.5% ($n = 6$) of graft losses were due to death compared with 32.5% ($n = 94$) in the younger group. In the older group the remaining kidneys were lost because of vascular thrombosis in two, chronic rejection in another two, and nephrectomy of a functional kidney (due to urinary fistula) in one.

DISCUSSION

Elderly patients are the fastest growing population in dialysis programs.¹ The prevalence of ESRD increases with advancing age. In most countries recipients are getting older, too. The elderly represent an increasing patient group on the waiting list for transplantation. However, there is a paucity of data on long-term patient and graft survivals in this population. At present, the organ donor shortage makes some clinicians reluctant to transplant kidneys into older patients, as these patients have more comorbid conditions and limited life expectancy. Controversy has emerged regarding the appropriateness of transplantation in this patient population with an inherently higher mortality risk. Before the widespread use of calcineurin inhibitors, the poor results in graft and patient survivals in the elderly and the scarce numbers of organs for transplantation led to the exclusion of patients over 60 of age. They were considered to be at high risk for transplantation.² With cyclosporine, the age limits have expanded. Nowadays, transplantation is the best renal replacement therapy for ESRD patients. With the development of new immunosuppressive alternatives, it must be considered a viable alternative to dialysis in older patients. Considering older patients with ESRD, patient survival after transplantation was higher compared with older patients on the waiting list.³⁻⁵ Comparisons between dialysis and transplantation outcomes may be affected by selection bias, as healthier patients may be referred for transplantation more frequently and rapidly. Despite these limitations, transplan-

tation in elderly ESRD patients appears to improve patient survival and quality of life over dialysis.³⁻⁵

Several studies have reported that graft and patient survivals were lower among patients 60 years or older, when compared with recipients aged 18 to 59.^{6,7} On the other hand, similar results between older and younger groups were observed for death censored graft survival and in both graft and patient survivals among the elderly with low-risk profiles.⁶ In a study comparing the survival rates of recipients older than 65 years to those aged between 60 to 64 or 50 to 59 years, after adjusting for confounders, the authors did not find significant differences for 5-year graft survival by age group.⁸ Other investigators found similar 5-year graft survivals between the oldest patients (>60 years) and the youngest group (20–29 years).⁹ Another group found that 5-year graft survivals were even superior in older recipients when compared with the younger group (90% vs. 82%).¹⁰

In our study, the survival results in the elderly group were satisfactory, not differing from those in our younger patients. The absence of significant differences in patient and graft survivals between the two groups may be partially related to the strict pretransplantation screening of our older patients, particularly for a good cardiovascular status. Less rigorous screening procedures in younger patients on dialysis for a long time, especially cardiovascular screening, may explain these discrepancies.

We did not search for risk factors in all patients of the two groups in our study. Identifying risk factors for patient and graft loss would lead to a more precise selection of older candidates and suggest interventions prior to transplantation to improve outcome. In a recent study, active smoking at the time of transplantation, obesity, and a longer time on dialysis prior to transplant were associated with a poor patient survival, while the only modifiable factor associated with poor graft survival was active smoking at transplantation.¹¹ A pretransplant history of non-skin malignancy, of cardiovascular disease, or a current smoking history were associated with decreased graft and patient survivals in the older population. In a recent study the older patients without these risk factors had patient and graft survival equivalent to younger recipients.^{6,8} Careful selection of older candidates along with a complete assessment of cardiac and infectious risk as well as tailored immunosuppression may improve survival in elderly patients.¹²

Some authors have argued that the better results reported in some series of older recipients may be due to less acute rejection in elderly recipients.^{7,13} Consistent with these observations, we also found a significantly lower rejection rate among the older group, which may also contribute to the survival results.

In a recent study, Prommool et al¹⁴ suggested that the strongest factor affecting long-term outcome after 5 years was donor age of 55 years or older. However, there is controversy regarding the outcomes with older kidneys.^{7,15,16} Donor age was significantly higher in our older recipients. We analyzed the outcome of our elderly patients

according to donor's age and failed to observe a significant difference in actuarial patient and graft survivals when comparing older recipients of kidneys from an aging donor. The use of kidneys from older donors provided acceptable results. With the current gross mismatch between demand and supply of organs, these organs might be particularly used in older recipients in whom longer graft survival is not as important as in younger patients. Although our recipient and donor populations were small, these findings suggested that allocation of older kidneys to older recipients may be a good strategy due to the paucity of donor organs.

According to the literature, graft loss in elderly recipients is mainly due to patient death that is primarily because of cardiovascular disease, infections, and malignancy.^{7,10} Our results are in accordance with these reports; more than 50% of graft losses in older individuals were due to death with a functioning kidney, and 71.4% from cardiovascular or malignant diseases.

In summary, our findings showed that transplantation must be considered in selected patients older than 60 years, as patient and graft survivals were similar to younger patients. Our study and others suggested that in spite of the limited life expectancy of the elderly in general, selected patients in this population benefit from transplantation. Referral of elderly patients for evaluation should be initiated as early as possible, and pretransplant screening must be rigorous. Age per se must not be considered a contraindication for transplantation.

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