Nephrol Dial Transplant (2011) 0: 1–9
doi: 10.1093/ndt/gfr524

NDT
Nephrology Dialysis Transplantation

Original Article

Age is an important predictor of kidney transplantation outcome

Massimiliano Veroux[1], Giuseppe Grosso[2], Daniela Corona[1], Antonio Mistretta[2], Alessia Giaquinta[1], Giuseppe Giuffrida[1], Nunzia Sinagra[1] and Pierfrancesco Veroux[1]

[1]Department of Surgery, Transplantation and Advanced Technologies, Vascular Surgery and Organ Transplant Unit, University Hospital of Catania, Catania, Italy and [2]Department 'G.F. Ingrassia', Section of Hygiene and Public Health, University Hospital of Catania, Catania, Italy

Correspondence and offprint requests to: Massimiliano Veroux; E-mail: veroux@unict.it

Abstract

Background. Donor and recipient age may have an impact on the renal transplant outcome. Kidney transplantation from older donors may result in a worse outcome, and the survival benefit of kidney transplantation compared with dialysis may be reduced. The aim of this study was to evaluate the impact of donor and recipient age on kidney transplant outcome.

Materials and methods. Two hundred and twenty-three recipients of kidney transplants performed at our institution between 2002 and 2007 were analysed. The role of donor and recipient age matching on survival rate were investigated performing the Kaplan–Meier survival time analysis by decades, considering the donor's age of 60 and 70 years. The Cox proportional hazard uni- and multivariate regressions were also performed. Finally, Kaplan–Meier survival time analysis was performed to assess survival rates of patients transplanted stratified by donor age compared with wait-listed renal transplant candidates.

Results. Elderly recipients had a significant lower graft and patient survival as well as a significantly higher risk of graft loss and patient death. Recipients younger and older than 65 years of age were at higher risk of graft loss if they received grafts from donors >65 years [hazard ratio (HR) = 2.59, 95% confidence interval (CI): 1.12–6 and HR = 5.65, 95% CI: 2.31–13.79, respectively]. Elderly recipients displayed a worse survival compared with transplant candidates on the waiting list.

Conclusions. Age is an important predictor of kidney transplantation outcome. Kidney transplantation does not offer a significant survival benefit in the intermediate term, compared to the waiting list, to elderly recipients transplanted with grafts from older donors. However, it cannot be excluded that it is still possible that there is a long-term benefit of transplantation over dialysis in this group of patients.

Keywords: age; elderly patients; expanded criteria donor; kidney transplantation, marginal donor

Introduction

Renal transplantation represents the best replacement therapy for patients with end-stage renal disease (ESRD). Significant advances in surgical techniques and immunosuppressive strategies have led to a dramatic improvement of the short- and medium-term results of kidney transplantation, which may improve survival [1–3], the quality of life [4–7] and is more cost-effective than dialysis treatment [4, 8, 9]. With its increasing success, kidney transplantation has been offered to a growing number of elderly patients, and older recipients comprise currently the highest proportional increase of those on the waiting list; almost half of the patients awaiting renal transplants are ≥50 years [10]. However, this created a great disparity between the number of transplantable grafts and the number of patients on the waiting list. Nowadays, the shortage of donor kidneys is the main factor limiting the wider use of kidney transplantation, and, as a result, the use of kidneys from older donors has become widely accepted.

Expanded criteria donor (ECD) kidneys became a reality more than a decade ago with the term of 'kidneys nobody wanted' [11] and, despite controversies on shorter graft survival, ECD kidneys are largely utilized in the USA and more commonly in Europe especially in old-for-old allocation [12], and >50% of all currently transplanted kidneys are from donors >50 years [10].

Although most of the recent studies reported acceptable medium-term graft and patient survival in patients receiving marginal donor kidneys [13–16], kidney transplantation from ECD donors may result in a higher risk of graft failure with the increasing of donor age [17–21], and the estimated remaining lifetime is reduced when sub-optimal grafts are used [22].

While it has been shown that the benefit of kidney transplantation is linked to recipient criteria such as age, waiting time and cause of ESRD [23], graft quality may be not strictly linked to ageing processes, and even compromized repair mechanisms in older kidneys as a consequences of ischaemia/reperfusion injury may also play a crucial role [24]. More recently, it has been shown that the increasing

recipient age is associated with an improved transplant survival, lower rates of rejection and superior outcome of older donor organs [25].

We hypothesize that donor and recipient age will impact transplant outcome and may have an effect on survival benefit in wait-listed patients. To evaluate this interplay, we have studied the effect of recipient and donor age on graft and patient survival; moreover, we have studied the survival benefit of transplanted patients compared with wait-listed transplant candidates.

Materials and methods

Study population

We analysed the data of 223 recipients of first deceased donor kidney transplant performed between January 2002 and December 2007 at the Organ Transplant Unit of the University of Catania. Kidney recipients <18 years, donors under the age of 18 and living kidney transplants were excluded from our study.

Study design

The aim of this study was to evaluate the impact of both donor and recipient age on kidney transplant outcome. Firstly, we collected and compared demographic and clinical data of the study population according to donor age.

Baseline characteristics of population included recipient, donor and transplantation characteristics. Recipient characteristics regarded age, sex, body mass index (calculated using the formula codified by the World Health Organization [26]), primary cause of ESRD, duration of dialysis, history of diabetes and recent history of hypertension. Donor sex, age, history of diabetes and/or hypertension and cause of death, cold ischaemia time and Human Leukocyte Antigen mismatch were also collected.

To evaluate differences in post-transplantation outcomes according to donor's age, we compared graft function, rate of delayed graft function (DGF), acute rejection (AR), patient death and mean serum creatinine level 1, 2 and 3 years post-transplant data stratified by donor age.

Then, we compared graft and patient survival between donor age group, and we assessed the risk of graft failure and patient death using multivariate regression model.

We further investigated the effects of age matching on survival. To give a statistical significance to the analysis, we considered the threshold of 65 years and we stratified our transplant population into four sub-groups: (i) recipients and donors <65 years of age; (ii) recipients <65 years and donors >65 years; (iii) recipients >65 years and donors <65 years and (iv) recipients and donors >65 years.

Finally, we compared graft and patient outcome with a cohort of wait-listed patients to define the survival benefit of kidney transplantation. For this purpose, we compared survival data of 336 patients in dialysis between January 2000 and December 2006. Of these candidates, 171 received a deceased donor kidney transplantation by December 2006. Data of patients on the waiting list were collected by the Regional Organ Procurement Organization.

Statistical analysis

Donor, recipient and transplant characteristics as well as outcome results were presented as means ± SDs or frequencies, and donor age group differences were compared with the *t*-test or Chi-square test as appropriate. Survival data according to donor age were obtained analysing graft loss and mortality rate using the Kaplan–Meier method with P-values generated by the log-rank test and a univariate Cox regression model was performed to identify specific risk factors associated with graft loss and patient death. Then, those with significant impact in one of the study groups ($P < 0.1$) were implemented in three different Cox proportional hazard multivariate regressions adjusted according to (i) donor age 60–69 years, (ii) donor age >70 years and (iii) recipient and donor matched by age (65 years). The role of donor and recipient age matching on survival rate were investigated performing the Kaplan–Meier survival time analysis stratified by the four age-matched groups as described above. The Cox proportional hazard uni- and multivariate regressions were also performed. Finally, Kaplan–Meier survival time analysis was performed to assess survival rates of those transplanted stratified by donor age compared with renal transplant candidates on the waiting list.

All statistical tests were two tailed. Data were entered into Microsoft Excel for Windows (Microsoft Corporation, Redmond, WA). Statistical analysis was performed using SPSS for Windows release 17.0 (SPSS Inc., Chicago, IL).

Results

A total of 223 kidney transplant recipients were included in the study. Baseline characteristics of the study population are listed in Table 1. Older individuals were more likely to receive organs at higher risk for graft failure: older donors with diabetes and hypertension and had died from cerebrovascular accident (Table 1). Outcome results showed that recipients that received an older organ had a higher rate of DGF post-transplant ($P = 0.01$). Recipients of grafts <60 years of age maintained stable renal function at 3 years after transplantation, while recipients of older donors displayed a slight increase of serum creatinine during the follow-up, even if this did not reach a statistical significance (Table 2).

Patient survival was affected by donor's age: recipients of younger kidney grafts displayed a better 5-year graft survival (96.1%) than recipients of graft of 60–69 years (92.9%, $P = 0.33$) and of grafts >70 years (87.5, $P = 0.024$). However, when all donor age classes were inserted in the same analysis, no statistical significance was found ($P = 0.079$).

Similarly, age influenced graft survival (Figure 1): recipients of younger donors displayed a better 5-year graft survival (89%) when compared with recipients of kidney grafts aged 60–69 years (78.6%, $P < 0.062$) and >70 years (72.5%, $P = 0.005$). When death-censored and -uncensored graft survival were analysed for all donor age classes, graft survival results were significantly different between age groups ($P = 0.012$, Figure 1).

Adjusted results from the Cox regression analysis showed that recipients of donors 60–69 years had a higher relative risk of graft loss [hazard ratio (HR) = 3.13, 95% confidence interval (CI): 1.4–6.98, $P = 0.005$; Table 3] and patient death (HR = 4.66, 95% CI: 1.44–15.15, $P = 0.01$; Table 4) compared with recipients of grafts from younger donors. A similar trend has been found for death-censored graft survival and patient survival according to donor age >70 years (HR for graft loss was 3.43 with 95% CI of 1.52–7.72 and $P = 0.003$, Table 3; HR for patient death was 3.09 with 95% CI of 1.01–9.47 and $P = 0.047$, Table 4).

The second survival analysis according to recipient and donor age match is shown in Figure 2. Statistically significant differences were found in both graft and patient 5-year survival with lower rates for groups with recipients transplanted with grafts from older donors (log-rank $P = 0.001$ and $P < 0.001$, respectively). Uni- and multivariate Cox regression analysis of risk of patient death and graft loss according to recipient and donor age-matched groups are shown in Tables 3 and 4. Again, donor age is a risk factor for graft loss, independent of recipient's age: recipients younger and older than 65 years were at higher risk of graft loss if they received grafts from donors >65 years (HR = 2.59, 95% CI: 1.12–6, $P = 0.025$ and HR = 5.65, 95% CI: 2.31–13.79, $P < 0.0001$, respectively; Table 3). After adjustment for covariates, a significantly higher risk of graft

Table 1. Recipient, donor and transplant characteristics by donor age group[a]

Variable	Donor age <60 years ($N = 144$)	60–69 years ($N = 39$)	P	≥70 years ($N = 40$)	P
Recipient characteristics					
Mean age (years)	46.1 ± 11.2	53.3 ± 10.3	**<0.001**	52.8 ± 9.5	**0.012**
Age > 60 years (%)	88.9	67.1	**<0.001**	75	0.71
Male (%)	65.3	67.1	0.78	62.5	0.61
Body mass index (kg/m^2) (%)			0.71		0.83
<28	60.4	59.5		64.1	
28–32	17.4	22.8		23.1	
>32	9.0	10.1		12.8	
Recipient diabetes	12.5	1.2	**<0.001**	**1.2**	**0.08**
Recipient hypertension	75.4	83.2	0.85	68.4	0.75
Duration of dialysis (%)			0.31		0.45
<3 years	47.9	45.6		44.7	
3–5 years	12.5	21.5		23.7	
>5 years	27.1	29.1		31.6	
Donor characteristics					
Male, *n* (%)	63.9	55.7	0.23	50	0.11
Cause of death (%)					
Vascular	11.8	15.2	0.47	2.5	0.029
Haemorrhagic	45.1	64.6	**0.006**	**80**	**<0.001**
Traumatic	36.8	12.7	**<0.001**	**17.5**	0.09
Hypertension	45.4	68.5	**<0.001**	**73.4**	0.07
Diabetes	3.5	8.5	**<0.05**	**1.8**	0.14
Transplant characteristics					
Cold ischaemia time (%)			**<0.001**		0.005
0–24 h	87.5	65.8		62.5	
25–36 h	11.1	34.2		37.5	
>36 h	1.4	0		0	

[a]Results with statistical significance are expressed as bold values.

Table 2. Transplant outcomes by donor age group

Variables	Donor age <60 years ($N = 144$)	60–69 years ($N = 39$)	P	>70 years ($N = 40$)	P
DGF (%)[a]	26.4	43	**0.01**	42.5	0.12
AR (%)					
At discharge	2	5	0.22	5	0.45
Within 6 months	11.1	17.7	0.16	17.5	0.4
Within 1 year	9.7	10.1	0.92	7.5	0.58
Serum creatinine (mg/dL)					
At discharge	1.38 ± 1.07	1.53 ± 0.99	0.34	1.58 ± 1.11	0.35
At 6 months	1.34 ± 0.9	1.52 ± 1.03	0.22	1.56 ± 1.23	0.26
At 1 year	1.35 ± 0.67	1.35 ± 0.73	0.98	1.34 ± 0.85	0.96
At 3 years	1.34 ± 1	1.46 ± 0.97	0.64	1.55 ± 0.65	0.63

[a]DGF was defined as the need for dialysis in the first week post-transplant. Results with statistical significance are expressed as bold values.

loss remained for older recipients (HR = 3.47, 95% CI: 1.92–9.34, P = 0.013). The risk of death was higher among older recipients of grafts from older donors (HR = 9.5, 95% CI: 2.69–33.99, P < 0.0001; Table 4). Among the other covariates, the most relevant risk factors for graft loss, but not for patient survival, were donor hypertension and diabetes mellitus and recipient obesity (Tables 4 and 5).

Table 5 summarizes the data of the sub-group of 171 transplant recipients compared with 165 renal transplant candidates who remained on the waiting list. Log-rank test demonstrated a statistically significant better long-term survival among transplant recipients compared with patients on waiting list (P = 0.01; Figure 3). Interestingly, recipients of younger donors had a better survival compared with other groups but those receiving grafts from older donors had worse survival rates compared with wait-listed patients (P = 0.002). Thus, kidney transplantation did not confer a significant survival benefit in older recipients receiving a graft >65 years. A risk analysis demonstrated a significantly lower risk of patient death in transplant recipients of younger donors compared with patients on the waiting list (HR = 0.21, 95% CI: 0.07–0.59; P = 0.003) but no

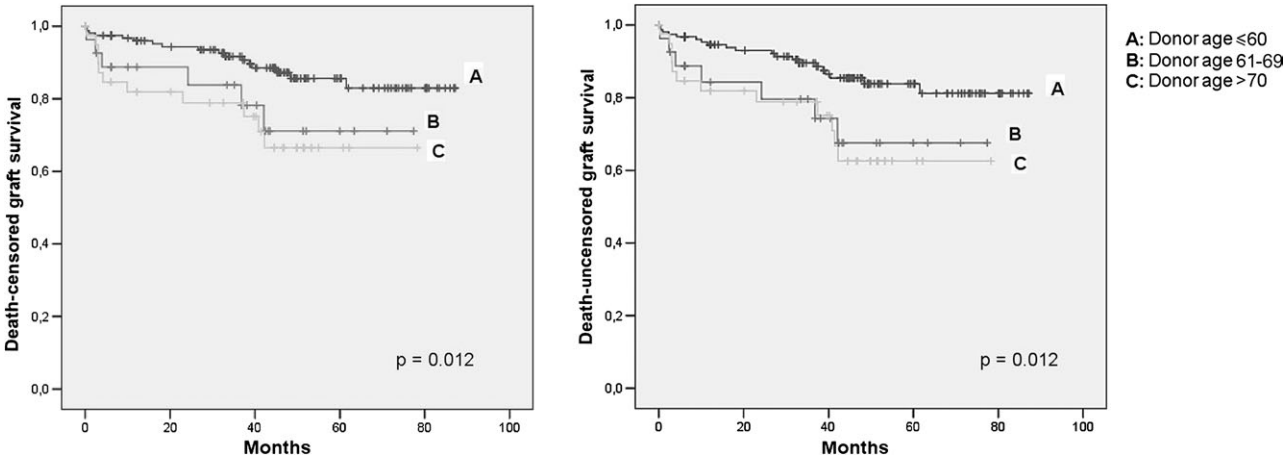

Fig. 1. Actuarial Kaplan–Meier death graft survival demonstrated that graft survival decreased with increasing donor's age. Death-censored and -uncensored graft survival among recipients of donors >70 years had the worst outcome.

statistically significant difference of risk in those from older (data not shown).

Discussion

Given the increasing demand for kidneys and evidence supporting good results of transplantation in elderly patients, the indication for this treatment in patients with ESRD has been expanded to include more of the elderly population [27–29]. Moreover, given the greater susceptibility that may lead to brain death and to organ donation, in recent years, the offer of kidneys from donors >60 years old has increased, although donor age is known to be a risk factor for long-term survival. Thus, such older kidneys have been considered the solution for elderly recipients, whose lower life expectancy would compensate for the lower survival rate of the aged kidney [30–32]. Additionally, several studies showed a substantial reduction in mortality and improvement in life expectancy in transplanted patients when compared with transplant candidates who remain on dialysis treatment, even considering kidneys from elderly donors [33, 34].

We performed an analysis of our deceased donor kidney transplant cohort. Relevant covariate donor and recipient risk factors predicting patient and graft survival were identified, and risk ratios for graft survival were analysed both in a combination of patient and graft survival. The combination of donor and recipient age cohorts allowed for an independent analysis of age effects on graft and patient survival. Our analysis demonstrated the critical role of recipient and donor age on transplant outcome and showed (i) a worse graft and patient survival as well as a significantly higher risk of graft loss and patient death among recipients of an aged kidney, (ii) that the rate of AR is not significantly different between the two groups but is lower in older recipients, (iii) that donor age has a significant impact on transplant outcome irrespective of recipient age and (iv) probably the most interesting finding of this study, that kidney transplantation from older donors, in the medium-term, does not confer a significant survival benefit when compared with wait-listed transplant candidates.

Elderly patients represent the fastest growing group of patients awaiting transplantation [10], and recent high-volume registry studies have shown reduced mortality rates for elderly patients receiving renal transplants compared with wait-listed patients [35]. When considering kidney transplantation from ECDs, donor age is most strongly associated with transplant outcomes [17, 25, 36, 37]. Our multivariate analysis demonstrated that age is a critical factor affecting transplant outcome: kidney transplantation from older donors had a significantly worse outcome compared with recipients of younger donors.

Age matching of donors and recipients is currently clinical practice, but recipient age may be a crucial point in determining the graft outcome since it has been linked in previous clinical studies with the development of chronic rejection and graft failure [38]. A recent analysis of both OPTN/UNOS database showed a worse outcome in younger recipients of grafts from ECDs [31], suggesting the positive role of age matching of donor and recipient in long-term outcome of kidney transplantation [39–42].

An important finding of our study is the combination effect of donor and recipient age on transplant outcome, suggesting that transplant outcome is closely related to donor characteristics and organ quality. Our multivariate analysis showed that older recipients and those receiving an aged kidney had the higher risk of graft loss and death. When a multivariate risk-adjusted analysis was performed to determine the influence of recipient age on transplant outcome, there appeared to be a strong effect of donor and recipient age on graft loss: younger recipients, even though transplanted with the aged kidney, had better survival and a lower risk of graft loss and death compared to older recipients transplanted with a kidney from an older donor. Interestingly, a similar risk appeared when an older recipient received a kidney from a younger donor.

These results are in contrast with the study of Tullius *et al.* [25], who performed an analysis among 108 188 recipients of a kidney from a deceased donor, testing the relevance and consequences of donor and recipient age on transplant outcome. Their multivariate analysis demonstrated that increasing age was associated with an improved transplant outcome. However, when analysing the patient

Table 3. Unadjusted and adjusted risk of graft loss[a]

	Graft loss							
	Non-adjusted		Adjusted for donor age 60–69 years		Adjusted for donor age >70 years		Adjusted for age-matched patients	
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
Recipient								
Male	1.12 (0.55–2.3)	0.751						
Body mass index (kg/m^2)								
<28	1	reference	1	reference	1	reference	1	reference
28–32	1 (0.36–2.73)	0.996	0.91 (0.33–2.51)	0.857	0.96 (0.35–2.69)	0.947	0.86 (0.36–2.75)	0.987
>32	3.41 (1.33–8.73)	**0.011**	3.5 (1.35–9.19)	**0.01**	3.95 (1.5–10.55)	**0.006**	3.85 (1.23–9.1)	0.02
Cause of ESRD								
Glomerulonephritis	1.94 (0.75–3.52)	0.245						
Tubulopathy	0.89 (0.36–1.84)	0.758						
Cystic disease	0.95 (0.43–2.35)	0.457						
Diabetes	21.8 (0.26–180)	0.369						
Hypertension	3.25 (0.07–1.36)	0.125						
Duration of dialysis								
<3 years	1	reference						
3–5 years	0.71 (0.23–2.12)	0.544						
>5 years	0.95 (0.44–2)	0.895						
Donor								
Age > 65 years	3.44 (1.72–6.9)	**<0.001**	3.13 (1.4–6.98)	**0.005**	Excluded from analysis		Excluded from analysis	
Age > 70 years	2.4 (1.17–4.95)	**0.017**	Excluded from analysis		3.43 (1.52–7.72)	**0.003**	Excluded from analysis	
Male	1.2 (0.6–2.37)	0.605						
Cause of death								
Vascular	0.28 (0.14–0.61)	**0.001**	0.41 (0.14–1.25)	0.119	0.39 (0.12–1.23)	0.109	0.43 (0.12–1.25)	0.112
Haemorrhagic	0.75 (0.38–1.48)	0.414						
Traumatic	4.69 (1.43–15.4)	**0.011**	2.39 (0.7–8.18)	0.166	2.84 (0.83–9.75)	0.095	2.75 (0.95–8.95)	0.084
Diabetes	3.51 (1.21–8.45)	**0.005**	3.21 (1.12–7.85)	**0.007**	3.32 (1.22–7.45)	**0.007**	3.23 (1.06–7.43)	**0.009**
Hypertension	2.25 (1.03–5.95)	**0.042**	2.35 (1.12–5.35)	**0.032**	2.51 (1.24–5.49)	**0.03**	2.42 (1.21–5.2)	**0.039**
Age matching (years)			Excluded from analysis		Excluded from analysis			
Recipient <65 to donor <65	1	reference					1	reference
Recipient <65 to donor >65	2.59 (1.12–6)	**0.025**					2.31 (0.87–6.13)	0.092
Recipient >65 to donor <65	1.99 (0.55–7.14)	0.292					1.28 (0.25–6.44)	0.761
Recipient >65 to donor >65	5.65 (2.31–13.8)	**<0.0001**					3.47 (1.92–9.34)	**0.013**

[a]Results with statistical significance are expressed as bold values.

Table 4. Unadjusted and adjusted risk of patient death[a]

	Patient death	
	HR (95% CI)	P
Recipient		
Male	1.73 (0.47–6.31)	0.4
Body mass index (kg/m^2)		
<28	1	reference
28–32	1 (0.2–5.1)	0.971
>32	3.05 (0.61–15.19)	0.456
Cause of ESRD		
Glomerulonephritis	2.65 (0.89–4.84)	0.189
Tubulopathy	0.94 (0.35–2.72)	0.856
Cystic disease	1.15 (0.55–3.91)	0.356
Diabetes	0.67 (0.08–4.91)	0.639
Hypertension	20.82 (0–40.08)	0.725
Duration of dialysis		
<3 years	1	reference
3–5 years	1.26 (0.24–6.5)	0.781
>5 years	1.53 (0.44–5.31)	0.499
Donor		
Age > 60 years	4.66 (1.44–15.15)	**0.01**
Age > 70 years	3.09 (1.01–9.47)	**0.047**
Male	1.19 (0.64–5.71)	0.243
Cause of death		
Vascular	0.44 (0.12–1.61)	0.218
Haemorrhagic	0.64 (0.2–1.94)	0.428
Traumatic	5.25 (0.68–40.43)	0.111
Diabetes	1.35 (0.31–5.5)	0.611
Hypertension	1.65 (0.56–6.01)	0.344
Age matching		
Recipient <65 to donor <65	1	reference
Recipient <65 to donor >65	1.9 (0.42–8.52)	0.398
Recipient >65 to donor <65	0	0.984
Recipient >65 to donor >65	9.5 (2.69–33.99)	**<0.0001**

[a]Results with statistical significance are expressed as bold values.

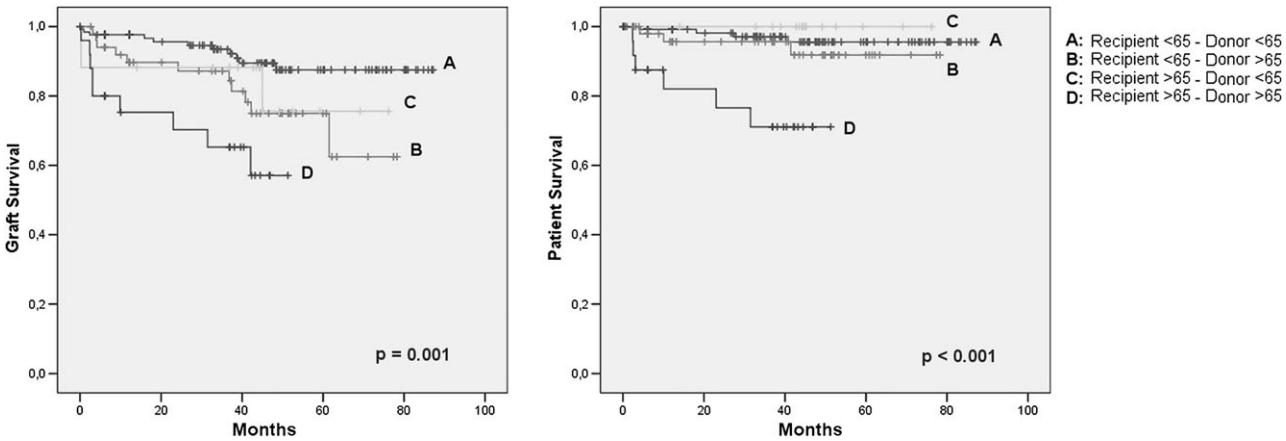

Fig. 2. Actuarial Kaplan–Meier death-censored graft and patient survival curves according to age-matched patient groups demonstrated significant worse results in older recipients of kidney graft >65 years.

survival and uncensored graft survival, the transplant outcome among the recipients >60 years was the worst among the entire study population; moreover, the risk of graft loss in recipients >60 years was the highest when they received a graft from a donor >60 years.

While it clearly appears that the shortage of kidneys is the most important limit to a wider use of transplantation for patients in ESRD, there are no definitive conclusions on the survival benefit of kidneys from older donors compared to those remaining on dialysis. Kidneys from less than suboptimal donors are more and more frequently used to meet the increasing demand, and optimal allocation of these kidneys is related to many factors: although these kidneys have a relative risk of graft loss >1.7 compared with optimal kidney transplants, clinical studies confirmed that the use of these grafts may be associated with reduced

mortality rates compared with staying on dialysis [33]. However, a more recent analysis have shown that only sub-groups of recipients >40 years, unsensitized patients and those with a history of diabetes and arterial hypertension benefited from ECDs kidneys in areas with shorter waiting times [23].

We compared patient survival of transplant recipients with age-matched wait-listed transplant candidates. Surprisingly, survival in transplant recipients receiving a kidney >65 years of age was worse than patients on the waiting list, and kidney transplantation did not reach a significant survival benefit in the medium term after transplantation. After this period, survival seems to remain stable among those patients who survived, and transplanted patients displayed a better survival rate.

It is well known that the mortality risk during the early post-transplantation period is higher than patients on dialysis. Our results are in contrast with those reported in the literature: Ojo *et al.* [33] suggested that this period ranged between 100 and 200 days for ECD transplant recipients; these results have been confirmed in a more recent study by Rao *et al.* [35], who compared the survival of kidney transplant recipients >70 years of age with age-matched wait-listed transplant candidates and found that the time to reach the equal risk with waiting list was 125 days. However, in this study, only 33% of patients received an ECD transplantation suggesting that a better graft quality may overestimate the survival benefit of kidney transplantation.

Many clinical studies tried to address the survival benefit of kidney transplantation in an elderly population. In the study of Rao *et al.* [35], kidney transplantation was associated with a 41% lower risk of death compared with the survival of comparable candidates on the waiting list. Similar results have been reported by Johnson *et al.* [43], who reported a 76% decreased mortality risk for transplant patients: however, the larger survival benefit may be attributed to the relatively younger age of the patients (mean age of recipients = 65.8 years) as well as the exclusion of patients >75 years from the waiting list.

There is not a clear explanation for our results: in the USA, the adjusted mortality rates among wait-listed transplant candidates in 2008 were ~7%, averaging 9.4 in the upper quintile and for first-time transplant candidates, the probabilities of dying within 1 or 5 years of listing reached 0.03 and 0.27%, respectively [44]; in Italy, in 2010, waiting list mortality rates were 1.5% [45]. Probably, our patients on the waiting list are more likely to be 'healthier' than those in the USA. On the other hand, graft quality has a strong impact on transplant outcome, and a wider use of expanded criteria kidney donors among European transplant centres may probably affect the transplant outcome, and this may explain the significant differences among the studies.

Kidney transplantation in elderly population has conflicting results: many clinical studies reported a 53–65% decrease in the probability of death among patients >60 years of age compared with wait-listed patients [3, 46–48]. In contrast, Bonal *et al.* [49] reported equivalent survival for dialysis and transplantation in patients aged 65–70 years and data from Finland suggested worse survival outcomes for patients >60 years compared with those remaining on dialysis [50].

Table 5. Characteristics of transplanted and waiting list patients

	Transplanted patients ($N = 171$)	Wait list patients ($N = 165$)	P
Mean age (years)	47	46.9	0.98
Male (%)	32.2	41.2	0.09
Primary cause of ERSD (%)			
Diabetes	18.7	12.4	0.85
Glomerulonephritis	54.4	49.6	0.75
Tubulopathy	7	9.9	0.90
Hypertension	4.7	5	0.93
Cystic disease	15.2	23.1	0.65

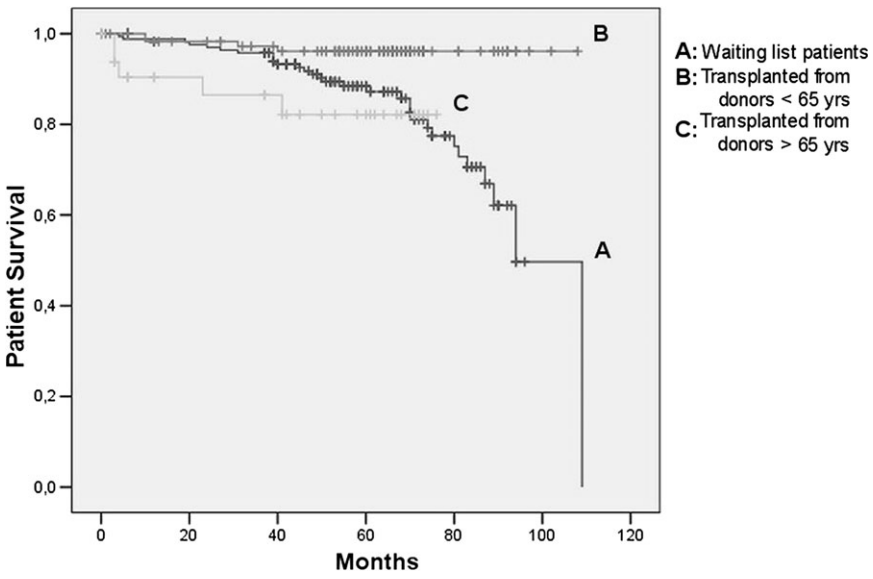

Fig. 3. Actuarial Kaplan–Meier patient survival curves analysis of patients in waiting list and recipients according to donor age. Kidney transplantation does not confer a survival benefit among elderly recipients of grafts from donors >65 years.

Our results seem to confirm this assumption and could provide an answer as to whether there should be an age limit for deceased donor kidney transplantation and, moreover, if allocating of the already scarce donor resources to the elderly might be justifiable.

The answer is extremely complicated: first of all, elderly patients have the potential for additional quality years of life, and transplantation may provide a significant improvement to perceived health, vitality, social activities and mental health [7]. However, if it can be predicted for a specific patient that the potential for survival is severely limited by extrarenal causes, transplantation may not be justified [35]. Moreover, while equivalent 1- and 5-year survival rates among recipients >60 years compared with younger recipients have been reported [3], such results may suggest a greater selectivity of elderly patients for kidney transplantation. More recent studies demonstrated that survival is lower among older recipients [51], suggesting that increased placement on the waiting list and more transplants due to less selectivity may result in a smaller benefit from transplantation [35].

The relatively small number of patients is the main limit of this study: however, it should be noted that this analysis regarded homogeneous groups of both transplant recipients and wait-listed transplant candidates. This allowed the elimination of many confounding variables, such as race, different immunosuppressive protocols, different surgical techniques and different selection criteria for waiting list admission for patients with ESRD, which may finally affect the analysis of the data.

In conclusion, kidney transplantation does not fit for all. Age is an important predictor of post-transplant outcome, and elderly recipients of older kidney donors do not have a survival benefit, in the medium term, after kidney transplantation when compared with wait-listed transplant candidates, although a long-term benefit of transplantation over dialysis cannot be excluded.

The muted effect of older donor age on transplant outcome in elderly recipients are of importance to an optimized utilization of organs available for transplantation that should be offered to those patients who can really benefit from it.

References

1. Schnuelle P, Lorenz D, Trede M *et al.* Impact of renal cadaveric transplantation on survival in end-stage renal failure: evidence for reduced mortality risk compared with hemodialysis during long-term follow-up. *J Am Soc Nephrol* 1998; 9: 2135–2141
2. Port FK, Wolfe RA, Mauger EA *et al.* Comparison of survival probabilities for dialysis patients vs cadaveric renal transplant recipients. *JAMA* 1993; 270: 1339–1343
3. 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
4. Whiting JF, Zavala EY, Alexander JW *et al.* The cost-effectiveness of transplantation with expanded donor kidneys. *Transplant Proc* 1999; 31: 1320–1321
5. Simmons RG, Anderson CR, Abress LK. Quality of life and rehabilitation differences among four end-stage renal disease therapy groups. *Scand J Urol Nephrol Suppl* 1990; 131: 7–22
6. Gokal R. Quality of life in patients undergoing renal replacement therapy. *Kidney Int Suppl* 1993; 40: S23–S27
7. Veroux M, Corona D, Patel VB *et al.* Quality of life in kidney transplantation. In: *Handbook of Disease Burdens and Quality of Life Measures. New York, NY: Springer*, 2009, pp. 2227–2238
8. Kontodimopoulos N, Niakas D. An estimate of lifelong costs and QALYs in renal replacement therapy based on patients' life expectancy. *Health Policy* 2008; 86: 85–96
9. Laupacis A, Keown P, Pus N *et al.* A study of the quality of life and cost-utility of renal transplantation. *Kidney Int* 1996; 50: 235–242
10. Wolfe RA, Roys EC, Merion RM. Trends in organ donation and transplantation in the United States, 1999–2008. *Am J Transplant* 2010; 10: 961–972
11. Lee CM, Scandling JD, Shen GK *et al.* The kidneys that nobody wanted: support for the utilization of expanded criteria donors. *Transplantation* 1996; 62: 1832–1841
12. Moers C, Kornmann NS, Leuvenink HG *et al.* The influence of deceased donor age and old-for-old allocation on kidney transplant outcome. *Transplantation* 2009; 88: 542–552
13. Snanoudj R, Rabant M, Timsit MO *et al.* Donor-estimated GFR as an appropriate criterion for allocation of ECD kidneys into single or dual kidney transplantation. *Am J Transplant* 2009; 9: 2542–2551
14. Remuzzi G, Cravedi P, Perna A *et al.* Long-term outcome of renal transplantation from older donors. *N Engl J Med* 2006; 354: 343–352
15. Rigotti P, Ekser B, Furian L *et al.* Outcome of renal transplantation from very old donors. *N Engl J Med* 2009; 360: 1464–1465
16. Ekser B, Furian L, Broggiato A *et al.* Technical aspects of unilateral dual kidney transplantation from expanded criteria donors: experience of 100 patients. *Am J Transplant* 2010; 10: 2000–2007
17. Terasaki PI, Gjertson DW, Cecka JM *et al.* Significance of the donor age effect on kidney transplants. *Clin Transplant* 1997; 11: 366–372
18. Rao KV, Kasiske BL, Odlund MD *et al.* Influence of cadaver donor age on posttransplant renal function and graft outcome. *Transplantation* 1990; 49: 91–95
19. Hariharan S, McBride MA, Bennett LE *et al.* Risk factors for renal allograft survival from older cadaver donors. *Transplantation* 1997; 64: 1748–1754
20. Cho YW, Cecka JM, Gjertson DW *et al.* Prolonged hypertension (> 10 years) is a significant risk factor in older cadaver donor renal transplants. *Transplant Proc* 1999; 31: 1283
21. Vivas CA, O'Donovan RM, Jordan ML *et al.* Cadaveric renal transplantation using kidneys from donors greater than 60 years old. *Clin Transplant* 2011; 6: 77–80
22. Meier-Kriesche HU, Ojo AO, Port FK *et al.* Survival improvement among patients with end-stage renal disease: trends over time for transplant recipients and wait-listed patients. *J Am Soc Nephrol* 2001; 12: 1293–1296
23. Merion RM, Ashby VB, Wolfe RA *et al.* Deceased-donor characteristics and the survival benefit of kidney transplantation. *JAMA* 2005; 294: 2726–2733
24. Tullius SG, Reutzel-Selke A, Egermann F *et al.* Contribution of prolonged ischemia and donor age to chronic renal allograft dysfunction. *J Am Soc Nephrol* 2000; 11: 1317–1324
25. Tullius SG, Tran H, Guleria I *et al.* The combination of donor and recipient age is critical in determining host immunoresponsiveness and renal transplant outcome. *Ann Surg* 2010; 252: 662–674
26. Physical status: the use and interpretation of anthropometry. Report of a WHO Expert Committee. *World Health Organ Tech Rep Ser* 1995; 854: 1–452
27. Heldal K, Hartmann A, Leivestad T *et al.* Clinical outcomes in elderly kidney transplant recipients are related to acute rejection episodes rather than pretransplant comorbidity. *Transplantation* 2009; 87: 1045–1051
28. El-Agroudy AE, Al-Arrayed SM, Al-Arrayed AS *et al.* A single-center experience of renal transplantation in elderly patients. *Ann Transplant* 2009; 14: 26–32
29. Sener A, Schweitzer EJ, Munivenkatappa R *et al.* Deceased-donor renal transplantation in the geriatric population demonstrates equal graft survival compared with younger recipients. *Transplantation* 2009; 87: 1549–1554
30. Foss A, Heldal K, Scott H *et al.* Kidneys from deceased donors more than 75 years perform acceptably after transplantation. *Transplantation* 2009; 87: 1437–1441

31. Chavalitdhamrong D, Gill J, Takemoto S *et al.* Patient and graft outcomes from deceased kidney donors age 70 years and older: an analysis of the Organ Procurement Transplant Network/United Network of Organ Sharing database. *Transplantation* 2008; 85: 1573–1579
32. Giessing M, Fuller TF, Friedersdorff F *et al.* Outcomes of transplanting deceased-donor kidneys between elderly donors and recipients. *J Am Soc Nephrol* 2009; 20: 37–40
33. Ojo AO, Hanson JA, Meier-Kriesche H *et al.* Survival in recipients of marginal cadaveric donor kidneys compared with other recipients and wait-listed transplant candidates. *J Am Soc Nephrol* 2001; 12: 589–597
34. Martin NJ, Ortega M, Gutierrez MJ *et al.* Survival of patients older than 60 years with kidneys transplanted from Spanish expanded criteria donors versus patients continued on hemodialysis. *Transplant Proc* 2009; 41: 2376–2378
35. Rao PS, Merion RM, Ashby VB *et al.* Renal transplantation in elderly patients older than 70 years of age: results from the Scientific Registry of Transplant Recipients. *Transplantation* 2007; 83: 1069–1074
36. Schold JD, Kaplan B, Baliga RS *et al.* The broad spectrum of quality in deceased donor kidneys. *Am J Transplant* 2005; 5: 757–765
37. Cuende N, Cuende JI, Fajardo J *et al.* Effect of population aging on the international organ donation rates and the effectiveness of the donation process. *Am J Transplant* 2007; 7: 1526–1535
38. Meier-Kriesche HU, Cibrik DM, Ojo AO *et al.* Interaction between donor and recipient age in determining the risk of chronic renal allograft failure. *J Am Geriatr Soc* 2002; 50: 14–17
39. Lankarani MM, Assari S, Nourbala MH. Improvement of renal transplantation outcome through matching donors and recipients. *Ann Transplant* 2009; 14: 20–25
40. Kwon OJ, Kwak JY, Kang CM. The impact of gender and age matching for long-term graft survival in living donor renal transplantation. *Transplant Proc* 2005; 37: 726–728
41. Kwon OJ, Kwak JY. The impact of sex and age matching for long-term graft survival in living donor renal transplantation. *Transplant Proc* 2004; 36: 2040–2042
42. Fritsche L, Horstrup J, Budde K *et al.* Old-for-old kidney allocation allows successful expansion of the donor and recipient pool. *Am J Transplant* 2003; 3: 1434–1439
43. Johnson DW, Herzig K, Purdie D *et al.* A comparison of the effects of dialysis and renal transplantation on the survival of older uremic patients. *Transplantation* 2000; 69: 794–799
44. USRDS. *2010 Annual Data Report*, 2010. http://www.usrds.org/2010/pdf/v2_07.pdf (1 December 2010, date last accessed)
45. Centro. Nazionale Trapianti. *Attività donazione e trapianto*. 2010. http://www.trapianti.salute.gov.it/imgs/C_17_pubblicazioni_1511_allegato.pdf (1 December 2010, date last accessed)
46. Albrechtsen D, Leivestad T, Sodal G *et al.* Kidney transplantation in patients older than 70 years of age. *Transplant Proc* 1995; 27: 986–988
47. Schaubel D, Desmeules M, Mao Y *et al.* Survival experience among elderly end-stage renal disease patients. A controlled comparison of transplantation and dialysis. *Transplantation* 1995; 60: 1389–1394
48. Oniscu GC, Brown H, Forsythe JL. How great is the survival advantage of transplantation over dialysis in elderly patients? *Nephrol Dial Transplant* 2004; 19: 945–951
49. Bonal J, Cleries M, Vela E. Transplantation versus haemodialysis in elderly patients. Renal Registry Committee. *Nephrol Dial Transplant* 1997; 12: 261–264
50. Kyllonen L, Ahonen J. Kidney transplantation in the elderly in Finland. *Transplant Proc* 1990; 22: 163–164
51. Doyle SE, Matas AJ, Gillingham K *et al.* Predicting clinical outcome in the elderly renal transplant recipient. *Kidney Int* 2000; 57: 2144–2150

Received for publication: 25.2.11; Accepted in revised form: 5.8.11