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Young deceased donor kidneys show a survival benefit over older donor kidneys in transplant recipients ages 20–50 years: a study by the ERA–EDTA Registry

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ABSTRACT

Background. Updated survival outcomes of young recipients receiving young or old deceased donor kidneys are required when considering accepting a deceased donor kidney.

Methods. We examined outcomes in 6448 European kidney allografts donated from younger (≥20–<50 years) and older (≥50–<70 years) deceased donors when transplanted into very young (≥20–<35 years) or young (≥35–<50 years) adult recipients. Outcomes of first kidney transplantations during 2000–13 and followed-up to 2015 were determined via competing risk, restricted mean survival and Cox regression methods.

Results. The 10-year cumulative incidence of graft failure was lowest in very young {22.0% [95% confidence interval (95% CI) 19.1–24.9]} and young [15.3% (95% CI 13.7–16.9)] recipients of younger donor kidneys and highest in very young [36.7% (95% CI 31.9–41.5)] and young [29.2% (95% CI 25.1–33.2)] recipients of older donor kidneys. At the 10-year follow-up, younger donor kidneys had a 1 year (very young) or 9 months (young) longer mean graft survival time compared with older donor kidneys. Graft failure risk in younger donor kidneys was 45% [very young adjusted hazard ratio (aHR) 0.55 (95% CI 0.44–0.68)] and 40% [young aHR 0.60 (95% CI 0.53–0.67)] lower compared with older donor kidneys. A 1-year increase in donor age resulted in a 2% [very young aHR 1.02 (95% CI 1.00–1.04)] or 1% [young aHR 1.01 (95% CI 1.00–1.01)] increase in the 10-year risk of death.

Conclusions. Younger donor kidneys show survival benefits over older donor kidneys in adult recipients ages 20–50 years. Updated survival outcomes from older deceased donors are necessary due to advances in transplantation medicine and the increasing role these donors play in organ transplantation.

Keywords: deceased donor, donor age, epidemiology, ERA-EDTA Registry, kidney transplantation

INTRODUCTION

The median age of deceased kidney donors is now as high as 55 years in some European countries [1, 2]. Studies conducted in the 1990s and early 2000s reported worse patient and allograft outcomes in young recipients of older deceased donor kidneys (defined as deceased donors >55 years) compared with outcomes in young recipients of young deceased donor kidneys [3–5]. Based on these studies, it was concluded that kidneys retrieved from these older deceased donors were not viable options for younger transplant recipients and that, where possible, matching donors and recipients by age should feature in organ allocation algorithms. Most countries do consider the

degree of the donor–recipient age difference in the allocation of deceased donor kidneys; however, the extent to which this influences kidney allocation varies [6].

Allograft survival from older deceased donor kidneys (with a median age of 60 years) transplanted into young and old recipients is better than previously reported [7]. The advances in the procurement of organs and in transplant medicine overall may have benefited the somewhat physiologically vulnerable older deceased donor kidney, resulting in improved outcomes. At a time when the median age of deceased donors is continually rising, it is not possible to continue providing the best quality kidneys to younger recipients, as demand for better quality and younger kidneys exceeds supply. As such, updated knowledge of survival outcomes of young recipients receiving either younger or older deceased donor kidneys will be of use to clinicians and potential younger recipients when considering whether to accept an offer of an older deceased donor organ. Furthermore, from a utilitarian view, it is important to know whether older deceased donor kidneys survive equally long in younger and older recipients [8].

Using renal registry and transplant registry data from six European countries, the aim of this study was to examine in the current transplant era the patient and allograft survival outcomes of kidney allografts donated from either younger (≥20–<50 years) or older (≥50–<70 years) deceased donors when transplanted into very young (≥20–<35 years) or young (≥35–<50 years) recipients.

MATERIALS AND METHODS

Data collection

Data from the European Renal Association–European Dialysis and Transplant Association (ERA-EDTA) Registry with additional data collection from nine individual renal and transplant registries in six countries were used, including the Austrian Dialysis and Transplant Registry, Danish Nephrology Registry (DNS), Scandiatransplant, the Finnish Registry for Kidney Diseases, Finnish Transplantation Registry, Catalonia Renal Registry (RMRC), Information unit about renal patients from the Basque Country (UNIPAR), Dutch Transplant Foundation and the Norwegian Renal Registry.

Study cohort

The study cohort consisted of all first kidney-only deceased donor transplant recipients ≥20–≤50 years of age at the time of transplantation and transplanted between 1 January 2000 and 31 December 2013. The transplant recipients formed two groups: those ≥20–<35 years (termed very young recipient) and those ≥35–≤50 years (termed young recipient). The deceased donors had to be either ≥20–<50 years (termed younger donor) or ≥50–<70 years (termed older donor) at the time of donation. From the two recipient age groups and the two donor age groups we formed four donor–recipient categories: very young recipient/younger donor, very young recipient/older donor, young recipient/younger donor and young recipient/older donor. To provide a quantitative measure of donor quality, we calculated the crude kidney donor risk index (KDRI) for each allograft [9, 10]. The crude KDRI was calculated using the formula as described by Rao *et al.* [9] (see Appendix 1). Chi-squared and Mann–Whitney *U*-tests were used to compare the group characteristics.

Missing data

Overall, 25% of cases had all 10 variables necessary to compute the crude KDRI, therefore the missing donor variables were imputed in SAS software (SAS Institute, Cary, NC, USA) using the multiple imputation procedure (proc mi). Where the donor ethnicity and hepatitis C status were unavailable, we assumed that, in this European setting, the donor was Caucasian and hepatitis C negative. The missing variables for cold ischaemia time (CIT), percentage of panel reactive antibodies (PRAs) and human leucocyte antigen (HLA) mismatch were imputed using the same procedure. Twenty imputed datasets were created. Log transformations were used for non-normally distributed data, which were then transformed back to their original form before the analysis [11].

Data analysis

For all survival analyses, the date of kidney transplantation was taken as the starting point. Patients were followed until either the event of interest or the end of the study period (31 December 2015) or censored for loss to follow-up, depending on which occurred first. For graft failure, the events of interest were either a return to dialysis, retransplantation or death with a functioning graft. For patient survival, the event of interest was patient death. We adjusted for transplant- and recipient-related parameters selected *a priori* that could influence the functioning of the graft, i.e. CIT, PRA (0%, >0–9%, ≥9–79% and ≥79%), HLA mismatch (less than two or two or more mismatches), country of transplantation, year of transplantation, recipient age at transplantation, recipient sex, pre-transplantation dialysis duration and primary renal disease.

Mean number of functioning graft years

The restricted mean survival is the mean survival of a treatment group measured up to a specific time point [12]. It is calculated as the total area under the covariate-adjusted graft survival curve up to the specific time point. The comparison of the mean survival of a number of groups allows one to obtain an assessment of a treatment effect over a specific time interval. We calculated the mean number of functioning graft years (i.e. the mean number of years the graft was functional before loss secondary to graft failure or death with a functioning graft) by the donor–recipient group. We restricted the curve to 2-, 5-, 7- and 10-year follow-ups and adjusted for the aforementioned variables.

Risk of graft failure and patient death

The cumulative incidence competing risk method was used to estimate the unadjusted 10-year cumulative risk and the Cox regression method was used to calculate the unadjusted and adjusted hazard ratios (aHRs) of graft failure, graft failure censored for death and patient death by donor–recipient group. We also examined the aHR with either deceased donor age or KDRI as a continuous variable. We examined for a non-linear relationship between either donor age or KDRI and the survival

Table 1. Transplant recipient characteristics by donor–recipient group for very young (≥20–<35 years) or young (≥35–<50 years) first kidney-only transplant recipients receiving younger (≥20–<50 years) or older (≥50–<70 years) deceased donor kidneys and transplanted between 2000 and 2013

Characteristic	Very young recipient			Young recipient		
	Younger donor	Older donor	P-value[a]	Younger donor	Older donor	P-value[b]
Number	1119	539	0.367	2793	1997	
Male, %	60.6	62.9		63.6	60.4	0.122
Age at Tx (years), median (IQR)	30.0 (26.0–32.6)	29.4 (26.0–32.8)	0.031	43.0 (39.0–47.0)	44.5 (40.3–47.1)	<0.001
Donor–recipient age difference (years)	+7	+16.6		−4	+11.6	
Dialysis time (years), median (IQR)[c]	2.0 (1.0–4.0)	3.0 (1.6–4.5)	<0.001	2.2 (1.1–3.9)	2.6 (1.4–4.2)	<0.001
Primary renal disease						
Diabetes mellitus type I and II	26.4	19.5	<0.001	34.0	26.0	<0.001
Hypertension/renovascular disease	9.1	9.3		12.1	14.3	
Glomerulonephritis	42.7	43.6		34.2	39.2	
Other/missing	21.7	27.6		19.7	20.4	
Initial RRT modality, %						
Dialysis	90.3	95.7	<0.001	87.8	95.4	<0.001
Kidney transplant	9.7	3.9		11.9	4.2	
Missing	0	0.4		0.3	0.2	
≤2 mismatches at HLA-A, -B or -DR, % (% missing)	18.2 (20.3)	23.8 (36.7)	<0.001	18.3 (24.0)	26.0 (31.2)	<0.001
Panel reactive antibodies, %						
0	83.7	86.0	0.653	83.9	84.2	0.756
1–9	10.1	7.3	0.780	9.4	7.5	0.127
10–79	4.7	5.0	NA	4.6	6.0	0.366
>79	0.5	0.8	NA	0.9	1.2	0.604
Cold ischaemia time (h), median (IQR)	16.3 (13.0–19.9)	17.6 (14.5–21.0)	<0.001	16.0 (13.0–19.3)	17.5 (14.6–21.0)	<0.001
Donor age (years), median (IQR)	37.0 (28.0–44.0)	56.0 (53.0–60.0)	<0.001	39.0 (31.0–45.0)	56.1 (53.0–60.5)	<0.001
KDRI, median (IQR)	0.98 (0.86–1.09)	1.32 (1.25–1.44)	<0.001	1.01 (0.89–1.12)	1.34 (1.25–1.47)	<0.001
Donation after brain death, %	90.2	83.7	<0.001	88.9	86.9	<0.001
Mean follow-up time (years), mean (SD)	7.81 (4.3)	7.33 (4.4)	0.031	7.41 (4.2)	6.83 (4.2)	<0.001
Total follow-up time (patient-years)	8758.7	3954.1		20 703.2	13 646.0	

Tx, transplant.
[a]The P-value refers to very young recipients receiving either a younger donor or an older donor kidney or [b]young recipients receiving either a younger donor or an older donor kidney.
[c]Excludes pre-emptive transplantations.

outcome in question using Cox regression with restricted cubic splines. In the adjusted analysis we adjusted for the aforementioned variables.

A two-tailed P-value <0.05 was considered statistically significant. Analyses were performed using SAS software version 9.4 (SAS Institute) and R version 3.3.1 (R Project for Statistical Computing, Vienna, Austria).

RESULTS

Between 2000 and 2013, 6448 recipients >20–≤50 years of age received a kidney transplant from a deceased donor >20–≤70 years of age (Table 1). The very young recipients had a median age of 30.0 years [interquartile range (IQR) 26.0–32.6; $n = 1119$] when receiving a younger deceased donor kidney transplant [donor 37.0 years (IQR 28.0–44.0)] and a median age of 29.4 years (IQR 26.0–32.8; $n = 539$) when receiving an older deceased donor kidney transplant [donor 56.0 years (IQR 53.0–60.0)]. The young recipients had a median age of 43.0 years (IQR 39.0–47.0; $n = 2793$) when receiving a younger deceased donor kidney transplant [donor 39.0 years (IQR 31.0–45.0)] and a median age of 44.5 years (IQR 40.3–47.1; $n = 1997$) when receiving an older deceased donor kidney transplant [donor 56.1 years (IQR 53.0–60.5)]. Recipients of younger donor kidneys regardless of whether they were very young or young were more likely to have experienced a shorter period of pre-transplantation dialysis, were more likely to receive a pre-emptive transplant, had a shorter CIT and were more likely to receive an allograft with a lower KDRI; however, they were more likely to have two or more HLA mismatches (Table 1).

Graft failure

The 10-year cumulative incidence of graft failure was lowest in the recipients of younger donor kidneys regardless of whether they were very young recipients {22.0% [95% confidence interval (CI) 19.1–24.9]} or young recipients [15.3% (95% CI 13.7–16.9); Figure 1A and C]. The 10-year cumulative incidence of graft failure was 29.2% (95% CI 25.1–33.2; Figure 1D) in young recipients of older donor kidneys and was highest in the very young recipients of older donor kidneys [36.7% (95% CI 31.9–41.5), Figure 1B].

The restricted mean survival is the average number of years a graft is functional within a certain time period before loss to graft failure or death with a functioning graft. The restricted mean survival at the 10-year follow-up was 1 year longer in the very young and 9 months longer in the young recipients of younger donor kidneys [8.57 versus 7.54 years (Figure 2A) and 8.52 versus 7.76 years (Figure 2B)] compared with the recipients of older donor kidneys. For those transplanted within <2 years

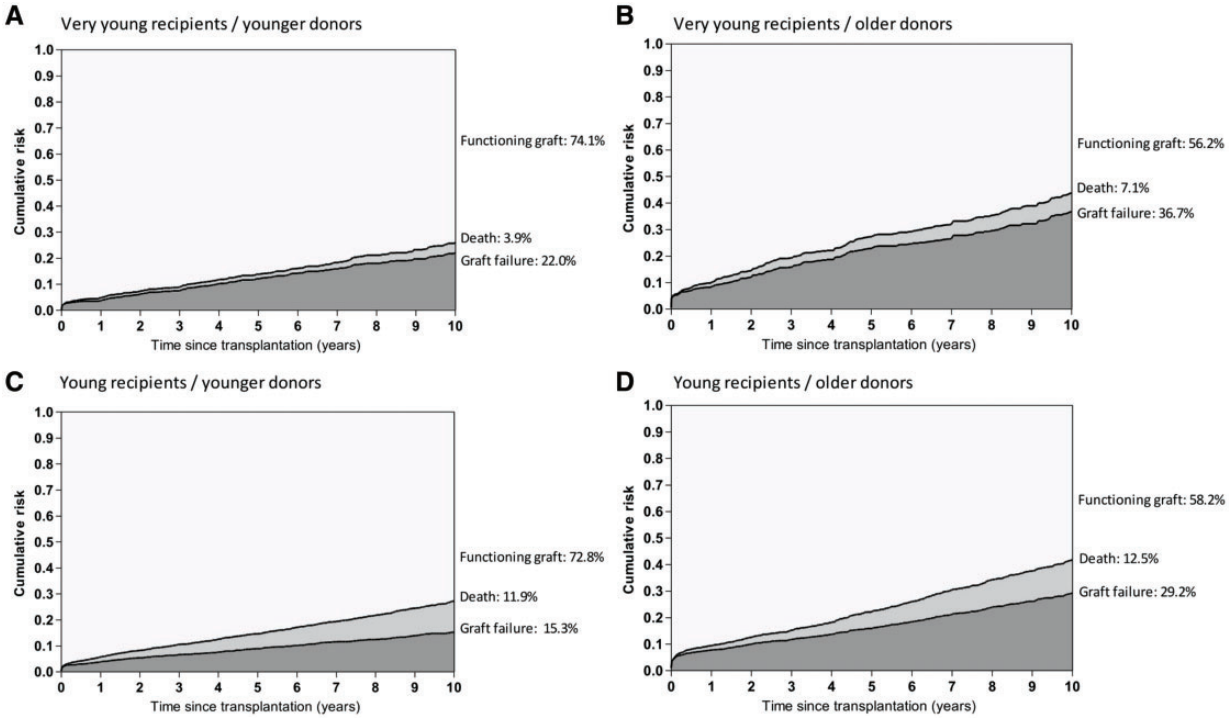


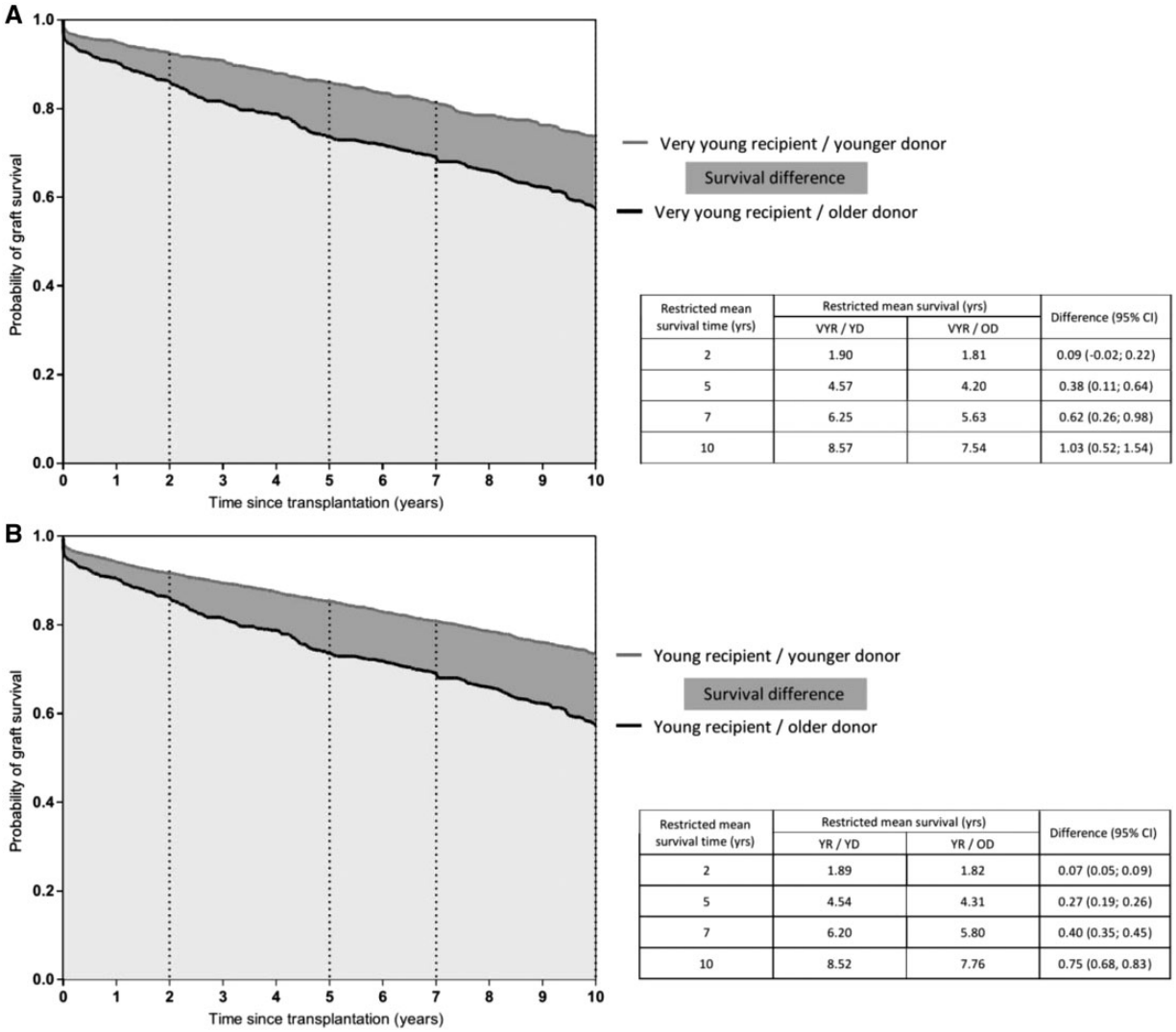
FIGURE 1: Ten-year cumulative risk of graft loss from graft failure or death with a functioning graft for (**A**) very young recipients of younger donor kidneys, (**B**) very young recipients of older donor kidneys, (**C**) young recipients of younger donor kidneys and (**D**) young recipients of older donor kidneys.

of commencing dialysis (including pre-emptive transplantations), the restricted mean survival at the 10-year follow-up was 11 months longer in recipients of younger donor kidneys regardless of whether they were young or very young (Supplementary data, Table S1). For those transplanted ≥2 years after commencing dialysis, the restricted mean survival at the 10-year follow-up was 13 months longer in the very young recipients of younger donor kidneys and just 8 months in the young recipients of younger donor kidneys (Supplementary data, Table S1).

In all cases, the aHR of graft failure or death-censored graft failure was lower in the recipients of younger donor kidneys compared with the recipients of older donor kidneys (Table 2 and Supplementary data, Table S2). The 10-year adjusted risk of graft failure of younger donor kidneys compared with older donor kidneys was 45% [aHR 0.55 (95% CI 0.44–0.68)] and 40% [aHR 0.60 (95% CI 0.53–0.67)] lower in very young and young recipients, respectively. Deceased donor age was linearly associated with the risk of graft failure (check for non-linearity; $P = 0.358$ and $P = 0.183$ for very young and young recipients, respectively), whereby every 1-year increase in the deceased donor age was associated with a 3% [aHR 1.03 (95% CI 1.02–1.04)] or 2% [aHR 1.02 (95% CI 1.018–1.03)] increase in the 10-year risk of graft failure in very young or young recipients, respectively (Figure 3A and B). Similarly, every 10-year increase in the deceased donor age was associated with a 57% [very young aHR 1.57 (95% CI 1.16–2.13)] or 59% [young aHR 1.58 (95% CI 1.36–1.86)] increase in the 10-year risk of graft failure. Deceased donor age was also linearly associated with the risk of graft failure censored for death (check for non-linearity; $P = 0.568$ and $P = 0.314$ for very young and young recipients, respectively; Figure 3C and D). The KDRI was linearly associated with the risk of graft failure (check for non-linearity; $P = 0.179$ and $P = 0.210$ for very young and young recipients, respectively), whereby every 0.10 increase in KDRI was associated with a 9% [aHR 1.09 (95% CI 1.06–1.12)] or 7% [aHR 1.07 (95% CI 1.06–1.09)] increase in the 10-year risk of graft failure in very young or young recipients, respectively (Figure 4A and B).

Patient death

The 10-year adjusted risk of patient death was lower in the recipients of younger donor kidneys compared with the recipients of older donor kidneys by 40% [aHR 0.60 (95% CI 0.39–0.92)] and 20% [aHR 0.80 (95% CI 0.68–0.94)] in very young and young recipients, respectively (Table 2). This was also observed in recipients of younger donor kidneys transplanted within 2 years of commencing dialysis but not in those transplanted beyond 2 years (Supplementary data, Table S2), although this is likely to reflect the small number of events in this subgroup analysis. Deceased donor age was linearly associated with the adjusted risk of patient death (check for non-linearity; $P = 0.527$ and $P = 0.224$ for very young and young recipients, respectively), whereby every 1-year increase in deceased donor age was associated with a 2% [aHR 1.02 (95% CI 1.00–1.04)] or 1% [aHR 1.01 (95% CI 1.00–1.01)] increase in the 10-year risk of death in very young or young recipients, respectively (Figure 5A and B). Similarly, every 10-year increase in the deceased donor age was associated with a 52% [very young aHR 1.52 (95% CI 0.76–3.02)] or 42% [young aHR 1.42 (95% CI 1.13–1.80)] increase in the 10-year risk of death. The KDRI was linearly associated with the adjusted risk of patient death (check



Restricted mean survival time (yrs)	Restricted mean survival (yrs)		Difference (95% CI)
	VYR / YD	VYR / OD	
2	1.90	1.81	0.09 (-0.02; 0.22)
5	4.57	4.20	0.38 (0.11; 0.64)
7	6.25	5.63	0.62 (0.26; 0.98)
10	8.57	7.54	1.03 (0.52; 1.54)

Restricted mean survival time (yrs)	Restricted mean survival (yrs)		Difference (95% CI)
	YR / YD	YR / OD	
2	1.89	1.82	0.07 (0.05; 0.09)
5	4.54	4.31	0.27 (0.19; 0.26)
7	6.20	5.80	0.40 (0.35; 0.45)
10	8.52	7.76	0.75 (0.68, 0.83)

FIGURE 2: Adjusted graft survival curves for (**A**) very young recipients (VYRs) of younger (YD) or older donor (OD) kidneys and for (**B**) young recipients (YR) of younger or older donor kidneys. The difference in the adjusted graft survival curves is shaded in dark grey. Adjustments were made for CIT, PRA, HLA mismatch (<2 or ≥2 mismatches), country of transplantation, year of transplantation, recipient age at transplantation, recipient sex, dialysis duration and primary renal disease.

for non-linearity; P = 0.181 and P = 0.399 for the very young and young recipients, respectively), whereby every 0.10 increase in KDRI was associated with a 7% [aHR 1.07 (95% CI 1.00–1.13)] or 3% [aHR 1.03 (95% CI 1.00–1.06)] increase in the 10-year risk of death in very young or young recipients, respectively (Figure 6A and B).

DISCUSSION

The question of whether one should transplant older deceased donor kidneys into younger recipients was more or less laid to rest in the early 2000s when the evidence was overwhelmingly in favour of avoiding such practices [13]. As such, there are limited data, particularly from Europe, showing the survival outcomes of younger recipients in receipt of older deceased donor kidneys in the current transplant era. However, over time the field of transplant medicine has progressed and the median age of deceased kidney donors [1] and the use of marginal kidney donors has substantially increased. As such, knowledge of the survival outcomes of these older donor kidneys in the current transplant era is required for decision-making processes.

In this study, using renal registry and transplant registry data from six European countries, we examined in the current transplant era the survival outcomes of 6448 kidney allografts donated from either younger (median age 39 years) or older (56 years) deceased donors when transplanted into very young (30 years) or young (44 years) recipients. Despite improvements in transplantation medicine over the past decades, we have shown that graft and patient outcomes in recipients of older donor kidneys are inferior to those seen in recipients of younger donor kidneys. In fact, by the 10-year follow-up, very young recipients of younger donor kidneys had on average 1 year extra graft function and young recipients had on average 9 months extra graft function compared with the respective recipients of older donor kidneys.

It should be kept in mind that even though we refer to 'older donors' in this study, these donors had a median age of 56 years, which now reflects the median age of deceased kidney donors

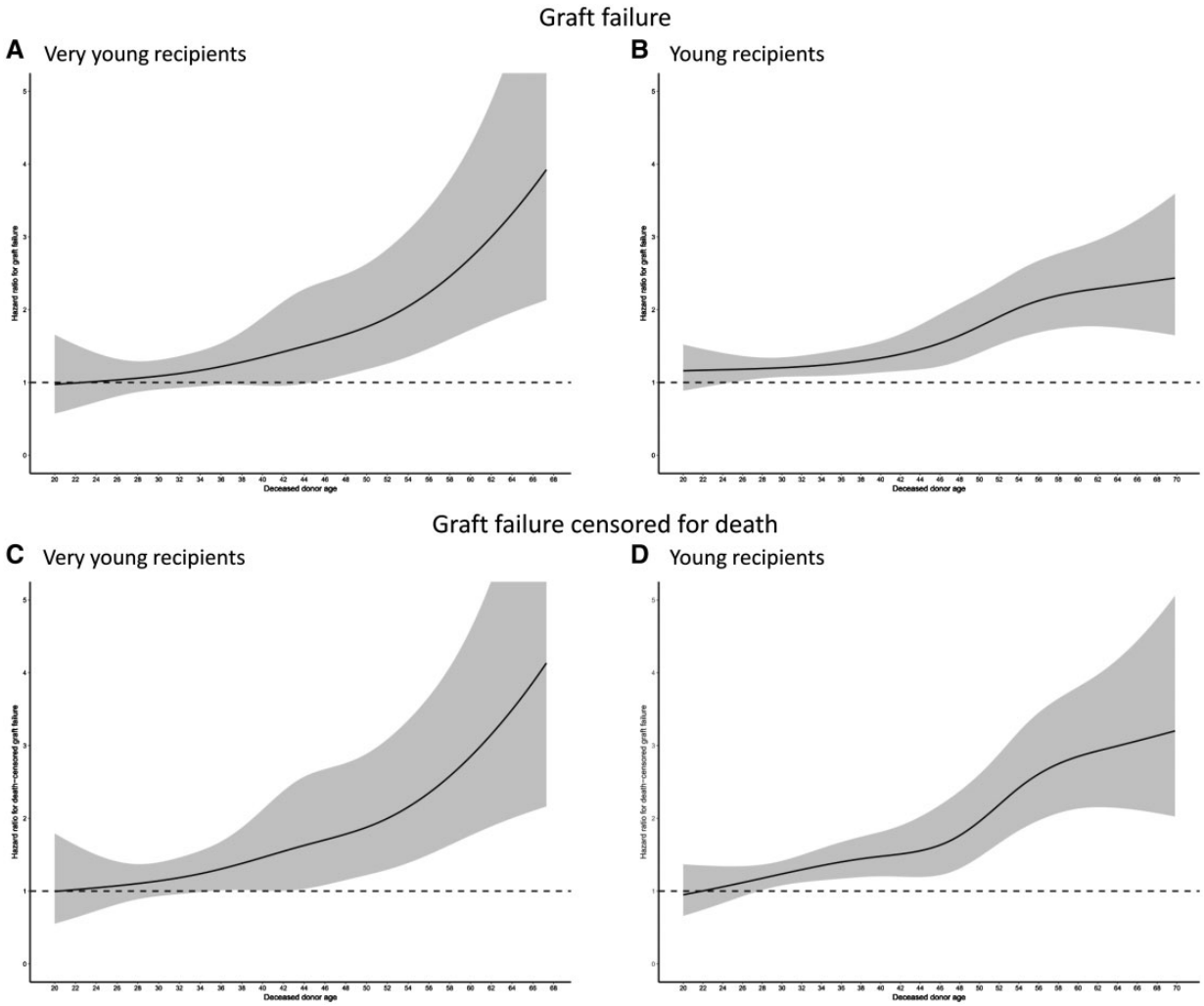


FIGURE 3: Effect of deceased donor age on the hazard of graft failure (all causes) for (**A**) very young recipients and (**B**) young recipients and for graft failure censored for death for (**C**) very young recipients and (**D**) young recipients with 95% confidence bands. Adjusted for CIT, PRAs, HLA mismatch (<2 or ≥2 mismatches), country of transplantation, year of transplantation, recipient age at transplantation, recipient sex, dialysis duration and primary renal disease.

in many European countries [1, 2]. Furthermore, it should be noted that the recipients of older donor kidneys in this study were less likely to receive a pre-emptive transplant and spent longer on dialysis prior to transplantation. It is likely that these recipients were less healthy than the recipients of younger donor kidneys. This could have contributed to the acceptance of an older donor kidney for these recipients in the first place. In addition to these recipients being less healthy and receiving poorer quality kidneys, they were less likely to have favourable transplantation conditions, such as longer CIT. As such, the outcomes of older donor kidneys presented in this study cannot be solely attributable to the quality of the transplanted organ.

The cumulative risk of graft failure is highest in very young recipients of older donor kidneys

Very young recipients of older donor kidneys continue to have the highest cumulative risk of graft failure, most probably due to a higher incidence of acute rejection. Recipient age modifies the effect of donor age on acute rejection, and the combination of donor and recipient age is critical for determining transplant outcomes [14]. The older donor kidney is more susceptible to rejection than the younger donor kidney [5, 14, 15]. Once an episode of rejection has occurred, the older donor kidney is less able to mount a tissue repair process [16]. Therefore episodes of rejection have significantly worse impact on the long-term functioning and survival of older than younger donor kidneys [15, 17]. With increasing age there is a natural, functional deterioration of the immune system [18]. As such, the increased susceptibility to rejection of the older donor kidney in combination with the more reactive immune system of the younger recipient may be responsible for the higher cumulative risk of graft failure seen in very young recipients of older donor kidneys.

The risk of recipient death increases with increasing donor age

The finding that the risk of patient death increases as deceased donor age increases remains unchanged from earlier studies [3, 5, 19, 20]. The recipients of older donor kidneys in this study lost their graft earlier than the recipients of younger

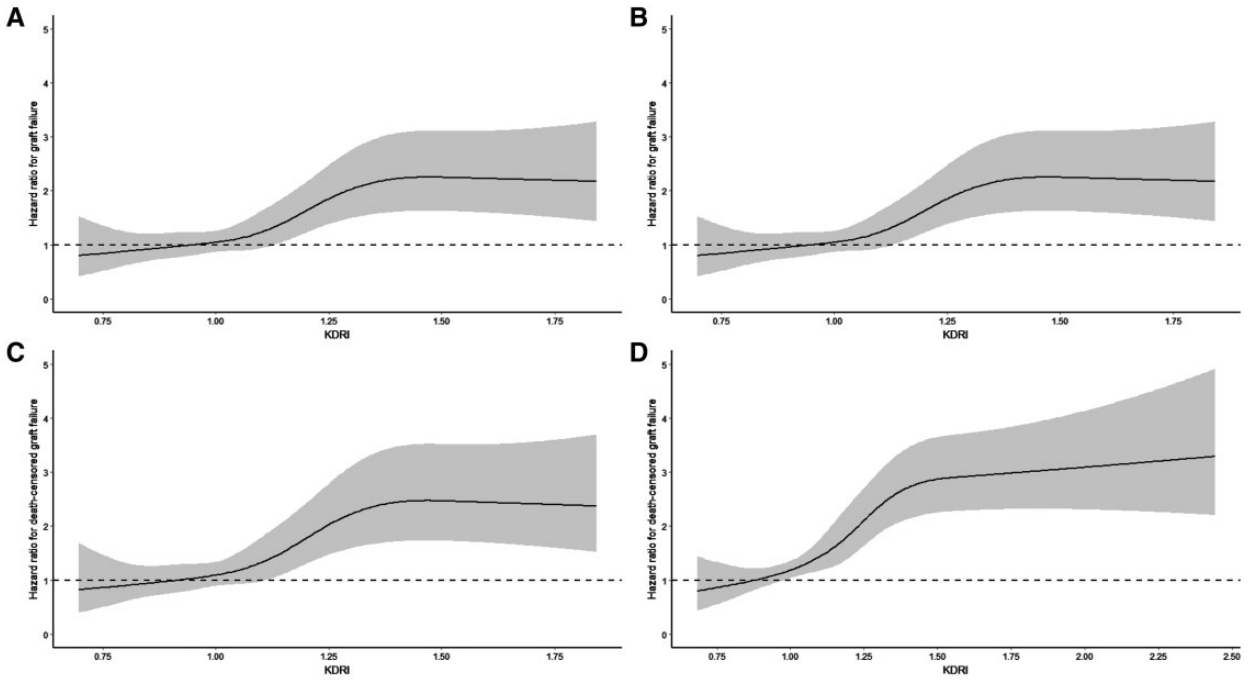


FIGURE 4: Effect of KDRI on the hazard of graft failure (all causes) for (**A**) very young recipients and (**B**) young recipients and for graft failure censored for death for (**C**) very young recipients and (**D**) young recipients with 95% confidence bands. Adjusted for CIT, PRAs, HLA mismatch (<2 or ≥2 mismatches), country of transplantation, year of transplantation, recipient age at transplantation, recipient sex, dialysis duration and primary renal disease. Note the longer *x*-axis for D.

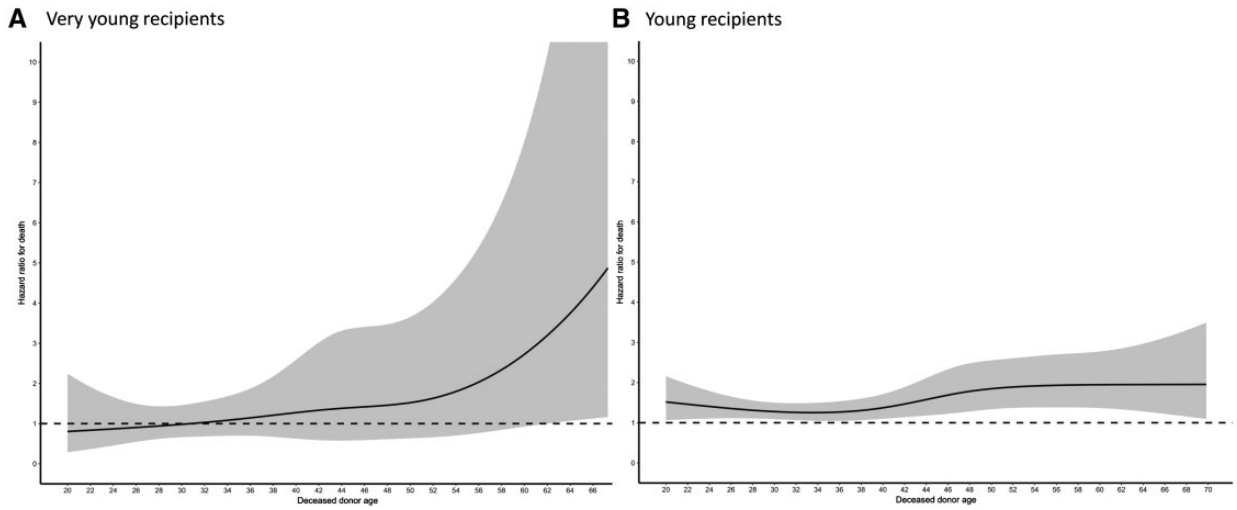


FIGURE 5: Effect of deceased donor age on the hazard of patient death for (**A**) very young recipients and (**B**) young recipients with 95% confidence bands. Adjusted for CIT, PRAs, HLA mismatch (<2 or ≥2 mismatches), country of transplantation, year of transplantation, recipient age at transplantation, recipient sex, dialysis duration and primary renal disease.

donor kidneys. Following kidney allograft failure, patients who return to dialysis have a reduced survival and lower quality of life compared with waitlisted dialysis patients who have never been transplanted [21]. The risk of earlier allograft loss may explain the increased mortality in recipients of older donor kidneys compared with recipients of younger donor kidneys. However, they may simply have a higher risk of death by virtue of the fact that they are less healthy than the recipients of younger donor kidneys.

Is it better to remain on dialysis or to accept an older kidney?

In 1999, Wolfe *et al.* [22] clearly showed that survival after kidney transplantation is superior to remaining on dialysis. However, both transplantation and dialysis practices and outcomes have improved over the last 20 years. Reese *et al.* [23] demonstrated that even in patients with the poorest functional status, by 9 months post-transplantation, survival was greater than their counterparts remaining on dialysis, although the

Table 2. Number of events, event rate per 1000 patient-years and the 10-year crude HRs and aHRs for the risk of graft failure, graft failure censored for death and patient death by donor–recipient groups

Outcome	Very young recipient		Young recipient	
	Younger donor	Older donor	Younger donor	Older donor
Number of patients	1119	539	2793	1997
Graft failure				
Number of events	244	203	657	683
Event rate per 1000 patient-years	30.01	58.10	33.61	55.11
Unadjusted HR (95% CI)	0.51 (0.42–0.62)	Reference	0.60 (0.54–0.68)	Reference
Adjusted HR (95% CI)	0.55 (0.44–0.68)	Reference	0.60 (0.53–0.67)	Reference
Graft failure censored for death				
Number of events	204	171	385	482
Event rate per 1000 patient-years	25.09	48.94	19.70	38.89
Unadjusted HR (95% CI)	0.52 (0.42–0.65)	Reference	0.54 (0.45–0.64)	Reference
Adjusted HR (95% CI)	0.56 (0.44–0.70)	Reference	0.48 (0.41–0.56)	Reference
Patient death				
Number of events	65	50	373	328
Event rate per 1000 patient-years	7.42	12.65	18.02	24.04
Unadjusted HR (95% CI)	0.51 (0.34–0.78)	Reference	0.77 (0.65–0.90)	Reference
Adjusted HR (95% CI)	0.60 (0.39–0.92)	Reference	0.80 (0.68–0.94)	Reference

Average age: very young recipient, 30 years; young recipient, 44 years; younger deceased donor, 39 years; older deceased donor, 56 years. Adjustments were made for CIT, PRAs (0%, >0–9%, ≥9–79% and ≥79%), HLA mismatch (<2 or ≥2 mismatches), country of transplantation, year of transplantation, recipient age at transplantation, recipient sex, dialysis duration and primary renal disease.

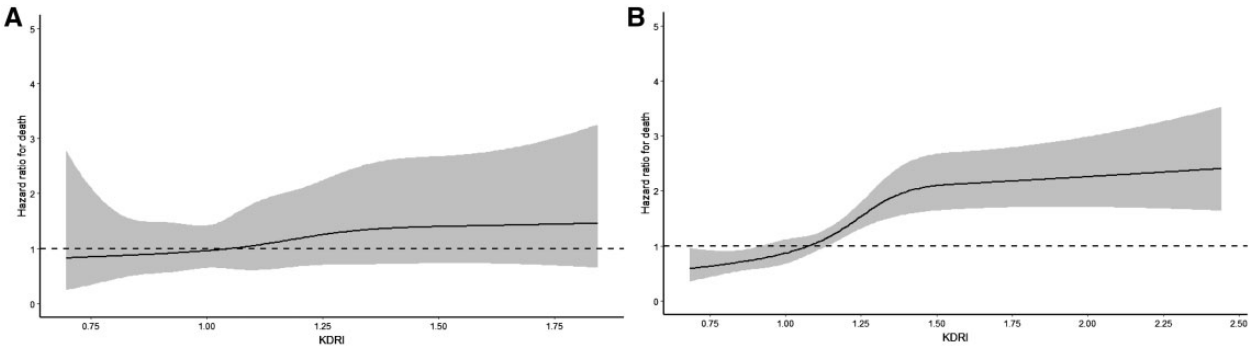


FIGURE 6: Effect of KDRI on the hazard of patient death for (**A**) very young recipients and (**B**) young recipients with 95% confidence bands. Adjusted for CIT, PRAs, HLA mismatch (<2 or ≥2 mismatches), country of transplantation, year of transplantation, recipient age at transplantation, recipient sex, dialysis duration and primary renal disease. Note the longer *x*-axis for B.

initial post-transplantation death rate was higher in the poorest functioning recipients compared with recipients with a higher functional status. Perez-Saez *et al.* [24] showed that adjusted patient survival was similar for older recipients (mean age 68.9 ± 5.8 years) receiving either older (≥75 years) or younger (<75 years) deceased donor kidneys. Although subgroup analysis showed that recipients <65 years had worse survival outcomes when receiving older (≥75 years) deceased donor kidneys. Importantly, receiving an older deceased donor kidney was associated with a significantly lower risk of death compared with waitlisted patients remaining on dialysis.

It is not clear if for younger recipients, in particular those with multiple comorbidities, survival after kidney transplantation with an older deceased donor kidney is superior to remaining on dialysis while waiting for a younger deceased donor kidney. In addition, the question regarding the delicate balance of survival benefit from transplantation, even with an older donor kidney, versus the increased risk of earlier graft failure resulting in increased sensitization and retransplantation needs to be addressed.

Deceased donor kidney quality is more than just donor age

In this study we focus on chronological donor age as a marker of kidney quality, i.e. nephron mass, although donor chronological age could be replaced by other scoring systems. We also presented the risk of graft failure and death by KDRI, where the link between KDRI score and increased risk was clear. The use of alternative scoring systems such as the KDRI [9] or histological scoring systems [25–27] in place of donor age may allow for the best kidneys from older deceased donors to be transplanted in younger transplant recipients appropriately. Therefore increased focus on validating and incorporating such scoring systems into transplant allocation models may allow for a clearer manner in which to identify better quality deceased donor kidneys. It may also help overcome the dilemma of

transplanting donor kidneys into younger recipients where large donor–recipient age gaps exist.

Limitations

Although we have shown the 10-year survival outcomes of 6448 allografts with a combined follow-up time of 46 982 years across six European countries, this study is bound to the traditional limitations associated with observational studies. The very young and young recipients receiving older donor kidneys may be in a physiologically worse state than their counterparts receiving younger donor kidneys. This may explain the reasons why they received the older donor kidneys in the first place and as such this study is limited by confounding by indication. Although we adjusted for recipient factors that could influence graft and patient survival, such as primary renal disease, there are many known recipient factors that can influence survival, such as comorbidities and unknown recipient factors, that we are unable to account for in our analysis. Transplant outcomes are defined as more than just graft and patient survival outcomes; it is important to know what the current risks of delayed graft function and rejection associated with the older donor kidneys are. It is well known that older deceased donor kidneys are associated with delayed graft function and acute rejection in younger recipients [16], though given the improvements in transplantation medicine this may be less of a problem than in prior years. However, we do not have data on delayed graft function or acute rejection. In addition, viewing these results in combination with knowledge of the recipients' comorbidities and immunosuppression regimes may help form a better overview of how best to clinically proceed with older deceased donor kidneys in younger recipients; however, we do not have access to this information.

CONCLUSION

Very young and young recipients of older donor kidneys have worse outcomes compared with recipients of younger donor kidneys, translating into both reduced graft and patient survival. It is clear that these recipients should, as far as possible, receive younger donor kidneys. However, it is also clear from the fact that we were able to perform this study that very young and young recipients do receive older donor kidneys. With the increasing age of deceased donors this may occur more frequently in the future. As such, we should be aware of their outcomes in order to counsel potential recipients appropriately in a fair and thorough manner. The question that now requires revisiting is whether, for these very young recipients, there is a survival benefit in accepting an older deceased donor kidney, or are they better off remaining on dialysis while awaiting a younger (better quality) kidney?

SUPPLEMENTARY DATA

Supplementary data are available at ndt online.

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AUTHORS' CONTRIBUTIONS

Each author contributed important intellectual content during manuscript drafting or revision and accepts accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved.

CONFLICT OF INTEREST STATEMENT

The funders of this study had no role in study design; collection, analysis and interpretation of data; writing the report and the decision to submit the report for publication. There are no conflicts of interest. The results presented in this paper have not been published previously in whole or part, except in abstract format.

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APPENDIX 1

KDRI calculation, donor factors and model coefficients as described by Rao *et al.* [9]

Table A1. Additional data sources and number of recipients provided by country or region

Donor characteristic	Applies to:	KDRI coefficient ('Beta')	KDRI 'XBeta' component
Age (integer years)	All donors	0.0128	0.0128 × (age-40)
	Donors <18 years of age	−0.0194	−0.0194 × (age-18)
	Donors >50 years of age	0.0107	0.0107 × (age-50)
Height (cm)	All donors	−0.0464	−0.0464 × (hgt-170)/10
Weight (kg)	All donors with weight <80 kg	−0.0199	−0.0199 × (wgt-80)/5
Ethnicity	African American donors	0.1790	0.1790
History of hypertension	Hypertensive donors	0.1260	0.1260
History of diabetes mellitus	Diabetic donors	0.1300	0.1300
Cause of death	Donors with cause of death as a cerebrovascular event	0.0881	0.0881
	All donors	0.2200	0.2200 × (creat-1.0)
Serum creatinine	Donors with creatinine >1.5 mg/dL	−0.2090	−0.2090 × (creat-1.5)
Hepatits C status	Hepatits C-positive donors	0.2400	0.2400
Donation after circulatory status	Donation after circulatory death donors	0.1330	0.1330

$KDRI_{exp} = \exp(-0.0194 \times I[\text{age} < 18\ \text{yr}] \times [\text{age} - 18\ \text{yr}] + 0.0128 \times [\text{age} - 40\ \text{yr}] + 0.0107 \times I[\text{age} > 50\ \text{yr}] + 0.179 \times I[\text{race} = \text{African American}] + 0.126 \times I[\text{hypertensive}] + 0.130 \times I[\text{diabetes}] + 0.220 \times [\text{SCr} - 1\ \text{mg/dL}] - 0.209 \times I[\text{SCr} > 1.5\ \text{mg/dL}] \times [\text{SCr} - 1.5\ \text{mg/dL}] + 0.0881 \times I[\text{cause of death} = \text{CVA}] - 0.0464 \times [\{\text{height} - 170\ \text{cm}\}/10] - 0.0199 \times I[\text{weight} < 80\ \text{kg}] \times [\{\text{weight} - 80\ \text{kg}\}/5] + 0.133 \times I[\text{donation after cardiac death}] + 0.240 \times I[\text{hepatitis C}]$, where $I = 1$ if the condition is true and $I = 0$ if the condition is false. CVA, cerebrovascular accident; SCr, serum creatinine.