Outcomes of Kidney Transplantation From Older Living Donors

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Background. The disparity between donor kidney availability and demand has increased utilization of kidneys from older living donors (OLD). We compared graft and patient outcomes of patients on maintenance dialysis after transplantation with OLD kidneys to those receiving younger live donor (YLD) kidneys and deceased donor (DD) kidneys.
Methods. Using Australia and New Zealand Dialysis and Transplant Registry, primary live and deceased donor renal transplant recipients aged 18 years or older between 1997 and 2009 were stratified into six groups: standard criteria deceased donor kidneys with total ischemic time of less than 12 hours (SCD, <12), SCD of 12 or greater, expanded criteria donor (ECD) less than 12, ECD of 12 or greater, YLD (LD, <60 years), and OLD kidneys (LD, ≥60 years). Preemptive and multiple-organ transplants were excluded.
Results. Of the 6,317 renal transplant recipients, 346 (5.5%) received OLD kidneys. Compared with kidneys from SCD of less than 12 hours, OLD kidneys were associated with a greater risk of death-censored graft failure (DCGF; adjusted HR 2.00; 95% confidence interval, 1.32–3.03) and inferior 5-year graft function (estimated glomerular filtration rate of 45 mL/min vs. 56 mL/min), although no increase in 5-year mortality (HR, 1.18; 95% confidence interval, 0.80–1.76). Outcomes for OLD kidneys were also inferior to YLD recipients, although modestly superior to ECD kidneys. Chronic allograft nephropathy was more commonly reported as the cause of DCGF among recipients of OLD kidneys than other donor types.
Conclusion. Patient survival was equal, but graft outcomes for recipients of OLD kidneys were inferior to those obtained with YLD and SCD kidneys. This study suggests that OLD kidneys should be utilized cautiously, cognizant of the fact that younger recipients may have a life expectancy in excess of the life of the transplanted kidney.

Keywords: ANZDATA, Donor type, Kidney transplant, Live donor, Deceased donor, Survival.

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Chronic kidney disease (CKD) and end-stage renal disease (ESRD) constitutes a major global public health problem. Kidney Health Australia estimates that approximately 1.7 million Australians over the age of 25 have CKD, with projected health expenditures of up to $12 billion by 2020 (*1*). In 2010, there were 1158 ESRD patients on the deceased donor transplant wait-list compared with only 550 deceased donor transplants being performed (*2*). The inability of donor kidney supply to match demand has led to increasing utilization of marginal donors, including kidneys from older living donors (OLD) and expanded criteria deceased donors (ECDs). In Australia, transplantation with kidneys from OLD and ECD has more than doubled over the last decade (*3, 4*).

The adverse impact of increasing donor age on renal allograft survival is well established for deceased donor kidney transplants (*5, 6*), but this has not been consistently observed in living-donor kidney transplantation. A recent study of the United States Renal Data System (USRDS) reported that variation in LD age between 18 and 64 years had minimal impact on renal allograft half-life (*7*). Similarly, data from the Organ Procurement Transplant Network/United Network for Organ Sharing (OPTN/UNOS) demonstrated that OLD kidneys (live-donor age, >55 years) achieved comparable graft survival (4-year graft survival, 78%) to young live donor (YLD) kidneys (81%) but superior survival compared with standard criteria deceased donor (SCD, 70%) and ECD kidneys (57%)

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among recipients aged 60 years or older (*8*), findings corroborated by another large single-center study (*9*). However, comparisons of long-term graft outcomes with kidneys from the various donor categories are lacking.

A key dilemma faced by some patients who are on maintenance dialysis, waiting for an offer of a deceased donor kidney, is whether to accept an offer of a kidney from an older, live donor. To inform this issue, the aim of this study was to compare graft and patient outcomes of nonpre-emptive kidney transplants from older living donors with younger living donors and deceased donors.

RESULTS

Baseline Characteristics

Of the 6,317 renal transplant recipients included in this study, 940 (14.9%) received SCD less than 12, 2,260 (35.8%) received SCD of 12 or greater, 214 (3.3%) received ECD less than 12, 702 (11.1%) received ECD of 12 or greater, 1,855 (29.4%) received YLD, and 346 (5.5%) received OLD kidneys. Baseline characteristics according to donor types are shown in Table 1. Recipients of LD kidneys were more likely to have spent a much shorter period on dialysis before first pretransplant and were less sensitized compared with recipients of SCD and ECD kidneys (40%–46% vs 10%–15% spent 1 year or lesser on dialysis pretransplant, respectively, and 4%–6% vs 10%–15% with PRA greater than 50%, respectively). Recipients of ECD or OLD kidneys were older compared with recipients of SCD and YLD kidneys (chi-square, $P<0.01$).

Donor Types and Delayed Graft Function

Compared with SCD less than 12, kidneys from SCD of 12 or greater, ECD less than 12, and ECD of 12 or greater were associated with a significantly higher risk of DGF in the adjusted model (adjusted odds ratio [OR], 1.36; 95% CI, 1.10–1.67; OR, 1.44; 95% CI, 1.02–2.07; and OR, 2.51; 95% CI, 1.97–3.20, respectively) (Fig. 1A). Expectedly, kidneys from YLD and OLD were associated with a significantly lower risk of DGF in the adjusted model (OR, 0.23; 95% CI, 0.17–0.31; and OR, 0. 31; 95% CI, 0.19–0.52, respectively). Higher BMI, diabetes, increasing dialysis duration pretransplant, increasing HLA mismatches, and earlier transplant era were associated with higher risk of DGF. There was no interaction between donor type and recipient age or other covariates and the risk of DGF.

Donor Types and Acute Rejection

Compared with donor kidneys from SCD of less than 12, kidneys from OLD (OR, 1.47; 95% CI, 1.10–1.96) were associated with a significantly higher risk of acute rejection in the adjusted model, as were ECD of less than 12 (OR, 1.64; 95% CI, 1.18–2.28), ECD of 12 or greater (OR, 1.35; 95% CI, 1.07–1.69), and YLD (OR, 1.26; 95% CI, 1.03–1.53) (Fig. 1A). Younger recipients, higher BMI, increasing HLA mismatches, absence of induction therapy, PRA greater than 50%, and earlier transplant era were also associated with higher risk of acute rejection. There was no interaction between donor types and recipient age or other covariates and the risk of acute rejection.

Donor Types and Graft Failure

Compared with donor kidneys from SCD less than 12, kidneys from OLD (hazard ratio [HR], 1.50; 95% CI, 1.13–1.99), ECD less than 12 (HR, 1.46; 95% CI, 1.06–2.00) and ECD of 12 or greater (HR, 1.91; 95% CI, 1.56–2.34) were associated with a higher risk of overall graft failure in the adjusted model (Figs. 1B and 2A). There was no association between donor kidneys from SCD of 12 or greater (HR, 1.00; 95% CI, 0.83–1.19) and YLD (HR, 0.85; 95% CI, 0.70–1.04) and overall graft failure in the adjusted model. There were no statistically significant differences in the overall graft failure between kidneys from OLD and those from ECD, regardless of ischemic time (ECD less than 12 hr—HR, 0.97; 95% CI, 0.67–1.40; ECD of 12 hours or greater–HR, 1.27; 95% CI, 0.97–1.68). Younger recipients, indigenous recipients, PRA greater than 50%, increasing HLA mismatches, increasing dialysis duration, presence of CAD or CVD, and earlier transplant eras were associated with a greater risk of graft failure in the adjusted model. There was no interaction between donor types and recipient age or other covariates and overall graft failure.

The 5-year death-censored graft survival for recipients of SCD less than 12, SCD of 12 or greater, ECD less than 12, ECD of 12 or greater, YLD, and OLD were 93%, 93%, 87%, 84%, 93%, and 90%, respectively; whereas the 10-year death-censored graft survival were 85%, 83%, 71%, 68%, 86%, and 68%, respectively. Compared with donor kidneys from SCD less than 12, kidneys from OLD (HR, 2.00; 95% CI, 1.32–3.03), ECD less than 12 (HR, 2.06; 95% CI, 1.29–3.27), and ECD of 12 or greater (HR, 2.52; 95% CI, 1.82–3.49) and, but not kidneys from SCD of 12 or greater (HR, 1.03; 95% CI, 0.77–1.38) and YLD (HR, 0.93; 95% CI, 0.68, 1.28) were associated with a significantly higher risk of DCGF in the adjusted model. There were no statistically significant differences in the risk of DCGF between kidneys from OLD and those from ECD, regardless of ischemic time. Younger recipients, indigenous recipients, PRA greater than 50% and increasing HLA-mismatches were associated with a higher risk of DCGF in the adjusted model. Donor age was not an effect modifier of the association between donor groups and DCGF. There were no significant differences in the causes of DCGF between donor groups ($P=0.07$), although DCGF attributed to chronic allograft nephropathy was more common in recipients of OLD kidneys (75%), vascular and technical complications more common in recipients of ECD kidneys (28%) and noncompliance more common in recipients of YLD kidneys (13%).

Donor Types and All-Cause Mortality

The 5-year patient survival for recipients of SCD less than 12, SCD of 12 or greater, ECD less than 12, ECD of 12 or greater, YLD and OLD were 89%, 89%, 87%, 83%, 95%, and 90%, respectively; whereas the 10-year patient survival were 80%, 76%, 70%, 65%, 86%, and 78%, respectively (Figs. 1B and 2B). Compared with recipients of kidneys from SCD less than 12, kidneys from OLD (HR, 1.18; 95% CI, 0.80–1.76), and ECD less than 12 (HR, 1.12; 95% CI, 0.73, 1.74) had similar mortality, whereas kidneys from ECD of 12 or greater (HR, 1.49; 95% CI, 1.15–1.93) had a greater risk of all-cause mortality in the adjusted model. There were no associations between other donor groups and all-cause mortality. Older recipients, indigenous recipients, smokers, presence of CAD or CVD, PRA greater than 50%, increasing HLA-mismatches, increasing dialysis duration and earlier transplant

TABLE 1. Baseline characteristics of renal transplant recipients stratified by donor types

	SCD<12 (n=940)	SCD≥12 (n=2260)	ECD<12 (n=214)	ECD≥12 (n=702)	YLD (n=1855)	OLD (n=346)	*P*
Donor age	36.3±14.7	36.6±14.9	63.0±6.6	63.5±6.7	45.2±9.4	64.5±4.2	<0.001
Donor male	59.3	59.4	55.1	55.1	42.0	47.1	<0.001
Donor hypertension[#]	7	9	54	64	6	28	<0.001
Recipient age							<0.001
18–30 years	10.7	9.5	8.9	6.6	23.7	10.4	
>30–40 years	15.9	16.8	15.4	14.1	19.9	23.4	
>40–50 years	28.1	26.5	22.0	24.5	25.4	15.3	
>50 years	45.3	47.1	53.7	54.8	31.0	50.9	
Recipient male	62.0	62.7	65.0	64.4	62.7	56.6	0.233
Indigenous recipients	6.0	10.8	6.5	10.7	6.8	3.2	<0.001
ESRD cause							0.022
Diabetic nephropathy	9.0	10.4	8.9	10.4	8.1	9.0	
Glomerulonephritis	45.4	46.9	50.5	45.2	49.2	45.7	
Cystic	16.7	15.3	12.6	15.7	13.5	15.9	
Vascular/hypertension	4.3	5.0	7.0	5.7	4.0	6.9	
Initial pretransplant dialysis modalities							0.003
PD-PD	16.1	16.8	9.8	14.2	18.1	17.3	
PD-HD	9.8	9.3	12.6	12.3	7.1	9.0	
HD-HD	65.5	64.5	69.6	63.7	66.4	65.0	
HD-PD	8.6	9.3	7.9	9.8	8.4	8.7	
Time on dialysis							<0.001
0–1 year	14.7	13.2	10.3	10.7	45.6	39.6	
>1–3 years	39.8	39.9	29.9	36.0	36.1	40.8	
>3–5 years	22.0	21.2	21.5	23.9	11.4	17.1	
>5 years	23.5	25.8	38.3	29.3	7.0	2.6	
Recipient BMI >30 kg/m^2	17.3	21.2	16.3	17.6	16.8	16.5	0.003
HLA-MM	3.2±1.6	3.2±1.7	3.6±1.6	3.2±1.7	3.0±1.6	3.4±1.5	<0.001
Peak PRA >50%	9.6	12.1	10.3	15.0	6.1	4.1	<0.001
Recipient diabetes (yes)	13.5	13.6	12.1	14.2	10.0	11.8	0.007
Recipient nonsmoker	52.2	52.6	53.7	52.5	61.1	61.0	<0.001
Recipient CVD (yes)	3.7	3.1	1.4	3.3	2.7	5.2	0.115
Recipient CAD (yes)	8.2	10.5	10.3	11.4	9.4	13.6	0.052
Transplant era							<0.001
1997–2000	24.4	32.5	20.1	26.2	23.6	17.1	
2001–2003	19.0	25.5	15.9	18.7	22.9	21.4	
2004–2006	24.5	21.5	24.3	26.5	25.1	24.9	
2007–2009	32.1	20.4	39.7	28.6	28.5	36.7	
Received induction (yes)	49.0	40.6	51.9	51.7	47.9	58.4	<0.001

Data expressed as proportion or as mean±SD (for HLA-mismatches and donor age). [#]Restricted to data between 2004 and 2009 (data on LD hypertension collected from 2004). PD-PD = initial and pretransplant peritoneal dialysis, PD-HD = initial peritoneal dialysis and pretransplant hemodialysis, HD-HD = initial and pretransplant hemodialysis, HD-PD = initial hemodialysis and pretransplant peritoneal dialysis, ESRD = end-stage renal disease, BMI = body mass index, HLA-MM = human leukocyte antigen mismatches, PRA = panel reactive antibodies, CAD = coronary artery disease, CVD = cerebrovascular disease.

era were associated with a higher risk of all-cause mortality. Donor age was not an effect modifier of the association between donor group and all-cause mortality.

Donor Types and Estimated Glomerular Filtration Rate (eGFR) at 1 and 5 Years

Mean donor eGFR was 110 mL/min in the SCD less than 12 group, 105 mL/min in SCD of 12 or greater group, 89 mL/min in the YLD group, 87 mL/min in the ECD less than 12 hour group, 81 mL/min in both ECD≥12 h and OLD groups at baseline ($P<0.01$) (Fig. 3). In a subanalysis of donor types, mean donor age and proportion of donor hypertension were significantly higher in donors of ECD and OLD kidneys compared with donors of SCD and YLD kidneys (Table 1). There was a greater proportion of male donors in the DD groups (59% SCD<12, 59% SCD≥12, 55% ECD<12, and 55% ECD12) compared white YLD (42%) and OLD (47%) groups ($P<0.01$) but donor BMI was similar in all donor groups. The recipient 1 and 5 years' eGFR were comparable between kidneys from YLD, SCD less than 12 and SCD of 12

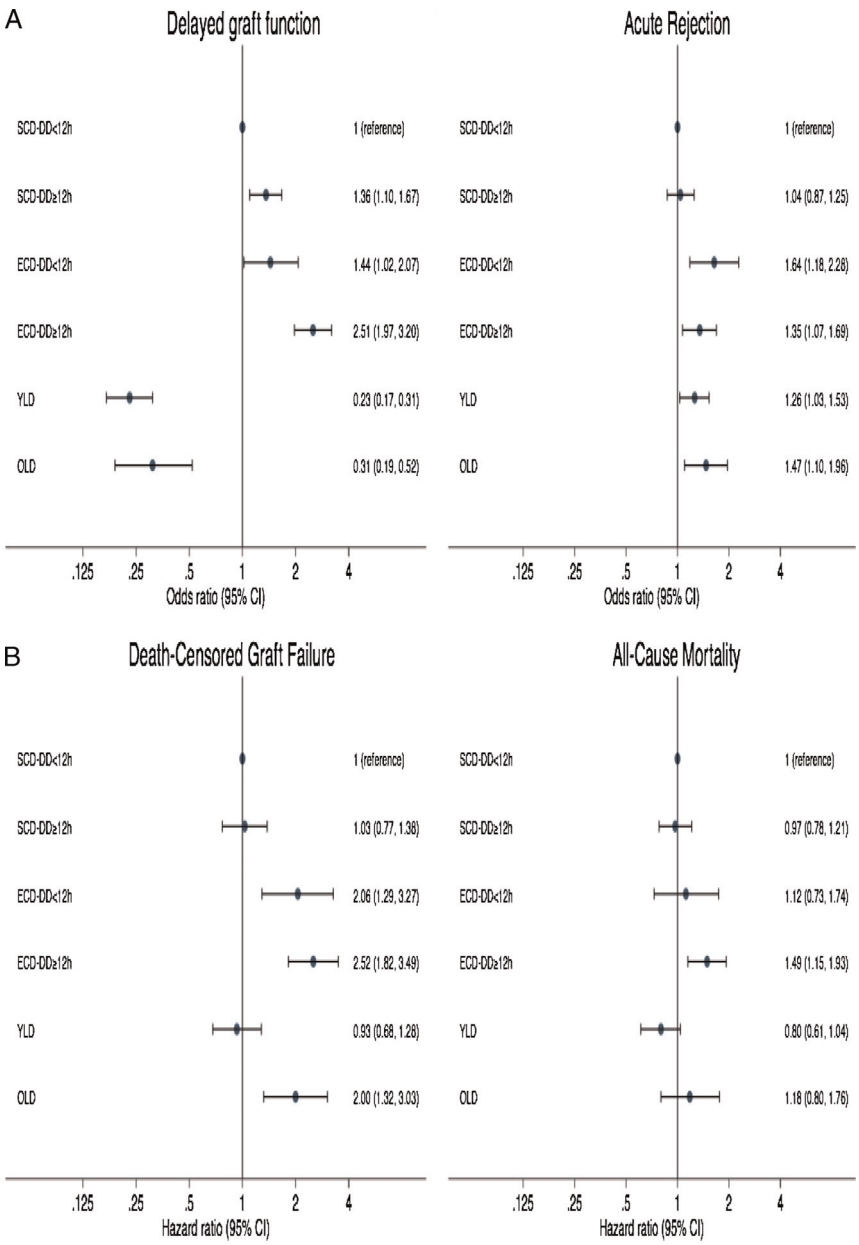


FIGURE 1. A, Forest plots of donor types and adjusted odds ratios for acute rejection and delayed graft function. B, Forest plots of donor types and adjusted hazard ratios for death-censored graft failure and all-cause mortality.

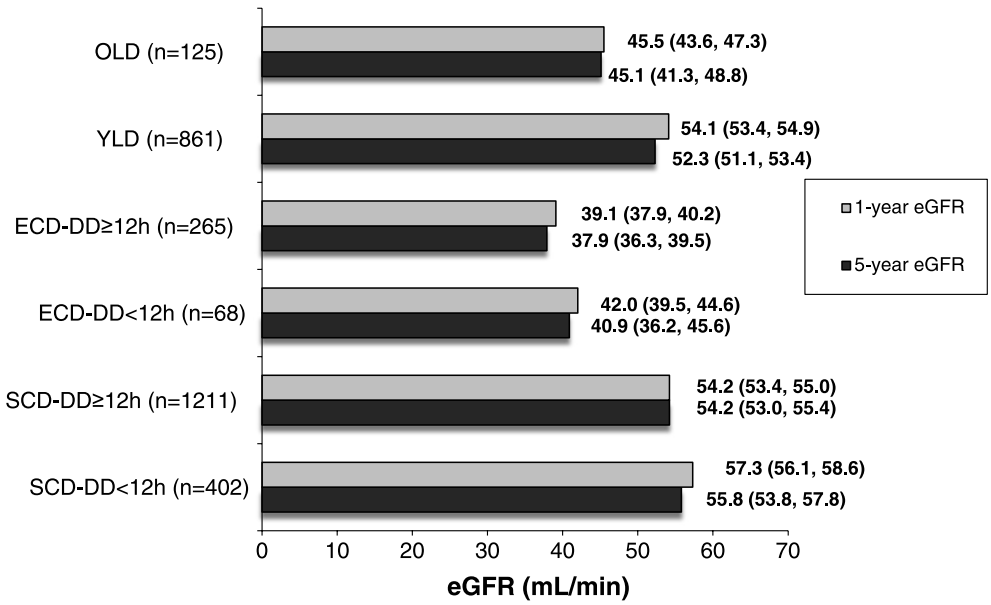
or greater and higher compared with the remaining 3 groups in the unadjusted and adjusted models. One and five-year eGFR in recipients of OLD kidneys were higher compared to recipients of ECD kidneys but lower than recipients of SCD and YLD kidneys (Fig. 3). The inclusion of donor eGFR in the adjusted model did not change our study findings.

Sensitivity Analyses

In a separate analysis, we examined the association between donor groups and graft failure excluding recipients with early graft failure (i.e., graft failed <7 d). Compared with donor kidneys from SCD less than 12, kidneys from OLD (HR, 1.54; 95%CI 1.14, 2.08), ECD less than 12 (HR, 1.39; 95% CI, 1.01, 1.96) and ECD≥12 (HR 1.83, 95%CI 1.47, 2.28) were associated with a significantly higher risk of graft failure in the fully adjusted multivariate analyses ($P<0.01$). Compared with donor kidneys from SCD less than 12, kidneys from OLD (HR, 2.16; 95% CI 1.37–3.41), ECD less than 12 (HR 1.81, 95%CI 1.03, 3.16) and ECD≥12 (HR 2.52, 95%CI 1.75, 3.63) were associated with a significantly higher risk of DCGF after adjusting for the effects of age, gender, cause of ESRD, initial and pre-transplant dialysis modality, peak PRA, dialysis duration pre-transplant, diabetes, smoking history and coronary artery disease ($P<0.01$).

DISCUSSION

In this study, recipients of OLD kidneys had a 2-fold increased risk of DCGF and inferior graft function (both at



**p<0.01 GLM model (number of recipients in each group correspond to the number of recipients at the 5 year time-point), corresponding numerical data expressed as mean (95%CI). eGFR = estimated glomerular filtration rate, calculated by Modification of Diet in Renal Disease equation. Model adjusted for donor and recipient gender, recipient age, race, BMI, cause ESRD, PRA, HLA-mismatches, diabetes, CVD, CVD, time on dialysis, pre transplant dialysis modality, transplant era, transplant state/country and induction therapy.*

FIGURE 2. A, Kaplan Meier survival curve of death-censored graft survival with corresponding number at risk table (log-rank, P <0.001). B, Kaplan Meier survival curve of all-cause mortality with corresponding number at risk table (log-rank, P <0.001).

1 and 5-year) compared with recipients of SCD and YLD kidneys despite a lower risk of DGF. Graft survival was similar among recipients of OLD and ECD kidneys. Compared with recipients of SCD kidneys, recipients of OLD, YLD, and ECD kidneys had over a 20% greater risk of acute rejection.

Our findings contrast with an analysis of OPTN/UNOS data where OLD kidneys (defined as donor age greater than 55 years) had similar graft survival compared with YLD kidneys (defined as donor age ≤55 years), and both had superior graft and patient survival compared with SCD and ECD kidneys transplanted into recipients aged 60 years or leather. However, similar to our study findings, recipients of OLD and ECD have lower eGFR at 1 year compared with recipients of SCD and YLD (P<0.001). It is surprising that in our study, donor eGFR was higher in the SCD groups compared with both YLD and OLD groups and may reflect that YLD and OLD were older, more likely to be female with a greater proportion of OLD having hypertension compared with SCD, all of which may be associated with lower donor kidney function (*10, 11*). Although the MDRD-derived eGFR was derived from people with CKD rather than healthy donors and has not been validated for those with eGFR greater than 60 mL/min/1.73 m^2, use of MDRD-eGFR provided an opportunity to directly compare renal function between donor types (LD and DD).

Studies on outcomes of recipients of young versus old live-donor kidneys have reported conflicting results. While some have observed poorer graft and patient survival with OLD kidneys compared with YLD kidneys (*12, 13*), there have been large single-center studies showing no difference (*14*). A single-center study by De La Vega L et al reported comparable 3-year graft and patient survivals in recipients of YLD and OLD kidneys despite lower predonation GFR in OLD kidneys compared with YLD kidneys (94 versus 108 mL/min) (*15*). In another single-center study of 1,063 LD transplant recipients, increasing LD age (especially >60 years) was associated with a reduction in graft survival, and this was more apparent beyond 4 years posttransplantation (*13*). In addition, >the impact of LD age on graft outcomes was conditional on recipient age, such that allocation of an OLD kidney had a greater adverse impact on younger but not older recipients. This, however, contrasted against the findings observed in a recent ANZDATA registry analysis (*16*). Similar to our study, a single-center study of 462 LD kidney transplants found that recipients of OLD kidneys older than 50 years had greater than 10 mL/min/1.73 m^2 reduction in 5-year recipient GFR compared with recipients of YLD kidneys aged 50 years or younger (*9*).

Despite recipients of OLD kidneys having a higher risk of DCGF compared with recipients of SCD and YLD kidneys, we found that recipients of kidneys from OLD and ECD less than 12 hours had similar risk of mortality to SCD and YLD kidneys, whereas kidneys from ECD of 12 or greater was associated with a higher risk of all-cause mortality. This observation may reflect a type II error with small numbers in the ECD less than 12 and OLD groups and additional confounder with recipients of kidneys from ECD of 12 or greater having poorer recipient graft function, which is independently associated with a greater risk of mortality (*17, 18*).

Several studies have noted that the adverse impact of increasing donor age on graft survival increases with duration of follow up; this may partly explain the discrepancy between

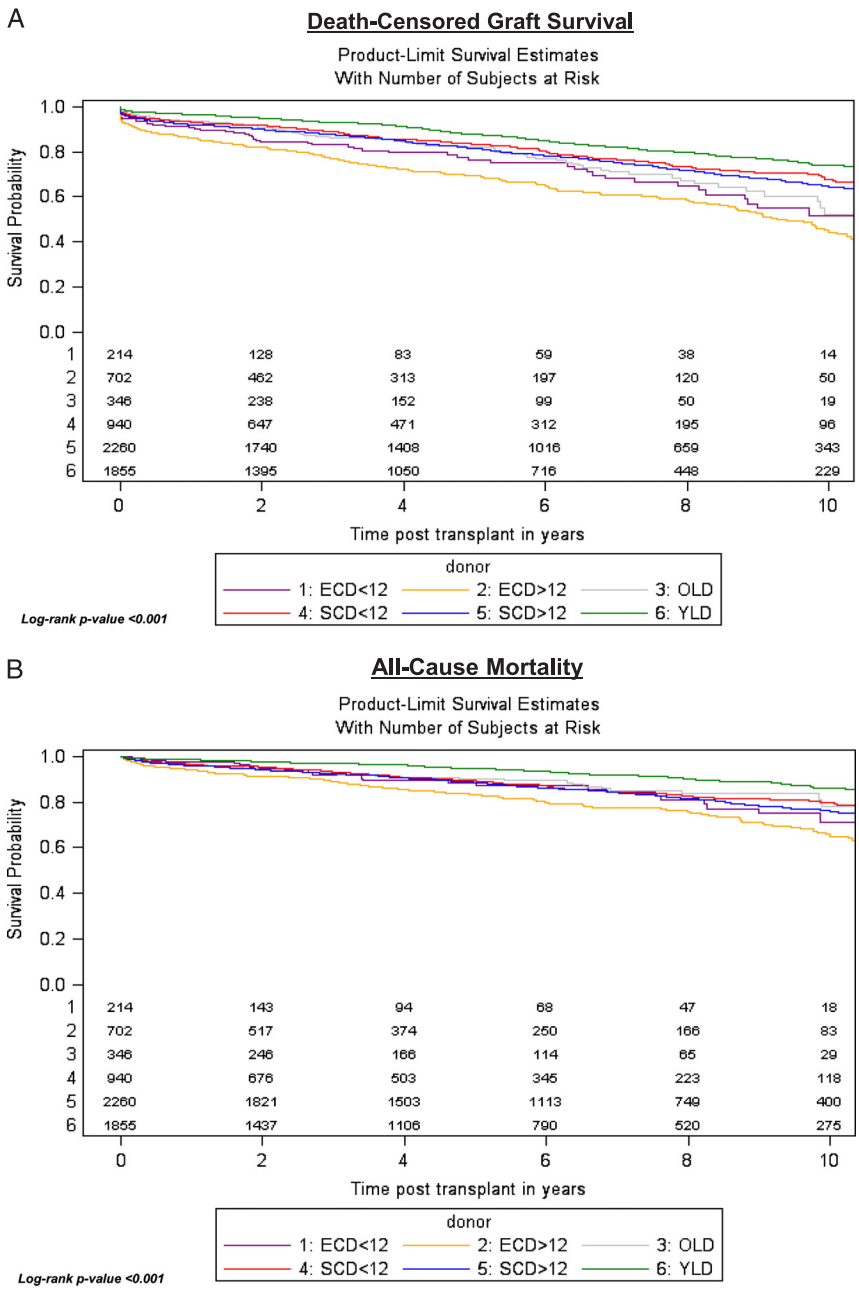


FIGURE 3. Bar graph of recipients' eGFR at 1 and 5 years stratified by donor type.

our findings and studies in which the follow-up posttransplant period was shorter (*15, 19*). In addition, differences in the definitions of YLD and OLD kidneys and the focus on elderly recipients in other studies may contribute to the discrepant findings. In an analysis from the Scientific Registry of Transplant Recipients (SRTR) database, recipients of kidneys from LD of all ages had lower all-cause mortality than recipients of DD kidneys. However, the authors did not examine the association between LD age and graft survival (*20*). In contrast to most published studies, we found that OLD kidneys were associated with inferior graft outcomes compared with both YLD kidneys and SCD kidneys. Despite a lower incidence of DGF and superior graft function, graft and patient survival from OLD kidneys were no better than those observed with ECD kidneys. Although live donor hypertension data were only available from 2004, a much greater proportion of old live donors had hypertension (29%) in our study, than reported in the study based on OPTN/UNOS data by Gill et al (0.5% of YLD and 3.3% of OLD with hypertension) (*8*). This may in part explain poorer graft outcomes associated with OLD kidneys compared with SCD and YLD kidneys in our study, but this requires further investigation. Consistent with older donor kidneys having diminished functional renal reserve, lower nephron mass, and/or number, both our study and the UNOS registry study by Gill J et al observed lower 1 and 5-year eGFR with OLD and ECD kidneys compared with YLD and

SCD kidneys (*8*). In our analysis, we excluded preemptive LD grafts as it is well established that this group of recipients generally have a more favorable graft outcomes (*21*). In addition, we performed sensitivity analysis evaluating the effects of excluding early graft failure (80%–90% attributed to vascular and technical complications that may not necessarily reflect donor quality) on graft outcome; exclusion of these kidneys from the analysis did not appreciably change our study findings.

In contrast to the study by Serur D et al (*22*), we found that ECD kidneys, YLD and OLD kidneys were all associated with a higher risk of acute rejection compared with SCD kidneys. It has been proposed that the susceptibility to injury of older donor kidneys may enhance immunogenicity, eliciting a greater host immune response than younger donor kidneys (*23*). In our study, a greater proportion of recipients receiving YLD kidneys were considerably younger; a recognized association with acute rejection (*24*). Initial immunosuppression was similar between donor groups and was not a reason for the differences in the risk of acute rejection (data not shown). Consistent with our published data, younger recipients had significantly higher risk of DCGF, which may be explained by the higher risk of acute rejection and lower risk of death with functioning graft (*18*). ANZDATA collects information on immunosuppressive drug doses but not therapeutic levels, which could contribute to the study findings. The lack of difference in the severity and types of acute rejections (including vascular rejection) between donor groups (data not shown) indirectly suggests that recipients of ECD, YLD, and OLD kidneys were not at greater immunologic risk compared with recipients of SCD kidneys, although data on pretransplant donor-specific antibodies is not collected by ANZDATA.

The strengths of this study are the large sample size, and inclusion of all renal transplant recipients in Australia and New Zealand during the study period except for preemptive LD and all repeat transplants. The study's limitations include limited depth of data collection, as ANZDATA does not collect some donor risk factors such as severity of donor comorbidities, patient compliance, individual unit management, biopsy reports confirming acute rejection and has limited availability of pretransplant clinical and laboratory data, details of immunosuppression and the presence of donor-specific antibodies. Despite adjustment for a large number of donor, recipient, and transplant-related characteristics, the possibility of residual confounding could not be excluded.

The inability to transplant all ESRD patients with optimal donor kidneys, and acceptance of more marginal recipients make it important to understand short- and long-term outcomes associated with kidneys from different donor types. The increasing use of OLD kidneys emphasizes the importance of determining the effect of LD age on graft and/or patient outcomes, and the comparison of these with outcomes from deceased donor kidney transplantation. Our study indicates that LD age is a critical factor for longer-term graft survival in renal transplantation, suggesting that progressive age-related changes may be harmful to the longevity of both DD and LD grafts.

Although OLD kidneys may have inferior long-term death-censored graft survival compared with SCD kidneys and YLD kidneys, the shortage of deceased donor kidneys coupled with the increasing number of ESRD patients on the transplant waiting list make suitable OLD kidneys important options for patients on dialysis. As is the case with ECD kidneys, acceptance of kidneys from OLD still confers a significant survival advantage over maintenance dialysis. Nevertheless, this study does suggest that OLD kidneys should be utilized cautiously, and should consider the likelihood of a longer life expectancy in younger recipients and availability and waiting time of deceased donor transplants.

MATERIALS AND METHODS

Study Population

Using the Australia and New Zealand Dialysis and Transplant (ANZDATA) Registry, all primary live and deceased donor renal transplant recipients age 18 years or older in Australia and New Zealand between 1997 and 2009 were included. Multiple-organ transplant recipients were excluded from this study. Given that the primary aim of the study was to assess the association between donor types and transplant outcomes in patients on maintenance dialysis, recipients who received preemptive transplantation were also excluded from the analyses. Less than 1% of renal transplant recipients had missing clinical outcome data and were excluded from analysis (n=56).

Renal transplant recipients were categorized into 6 groups depending on their donor type—standard criteria deceased donor kidneys with total ischemic time of less than 12 hours (SCD<12), standard criteria deceased donor kidneys with total ischemic time of 12 hours or greater (SCD≥12), expanded criteria deceased donor kidneys with total ischemic time of less than 12 hours (ECD<12), expanded criteria deceased donor kidneys with total ischemic time of 12 hours or greater (ECD≥12), YLD kidneys (live-donor kidneys <60 years), and OLD kidneys (live-donor kidneys ≥60 years). ECD kidneys are defined as deceased donors older than 60 years or deceased donors older than 50 years with any 2 of the 3 following criteria: (1) hypertension, (2) cerebrovascular cause of brain death, or (3) pre-retrieval serum creatinine greater than 133 μmol/L (*25*). There were 632 YLD (25% of overall YLD grafts) and 146 OLD (29% of overall OLD grafts) preemptive transplants that were excluded from analysis.

Data Collection

Recorded baseline data included donor gender; recipients' characteristics including age (categorized as 18–30, >30–40, >40–50, and >50 years), sex, race (indigenous and nonindigenous), cause of ESRD (categorized as diabetic nephropathy, glomerulonephritis, cystic disease, vascular/hypertensive disease, or others), initial and pretransplant dialysis modality (categorized as initial and pretransplant peritoneal dialysis [PD-PD], initial PD and pretransplant hemodialysis [PD-HD], initial and pretransplant HD [HD-HD] and initial HD and pretransplant PD [HD-PD]), peak panel reactive antibody (PRA; categorized as 0%–10%, 11%–50%, and >50%), dialysis duration pretransplant (categorized as 0–1, >1–3, >3–5, and >5 years on dialysis), diabetes, coronary artery disease (CAD), cerebrovascular disease (CVD), and smoking history (categorized as current smokers, former smokers, or nonsmokers), and transplant-related characteristics including the use of induction antibody therapy (including interleukin-2 receptor antibody or T cell depleting agents), transplant era and transplant state or country. Transplant era was divided into four groups for analysis (i.e., 1997–2000, 2001–2003, 2004–2006, and 2007–2009) and transplant state or country into six groups (i.e., South Australia/Northern Territory, Victoria/Tasmania, New South Wales/Australia Capital Territory, Western Australia, Queensland and New Zealand). The number of HLA-mismatches (0–6 mismatches) was modeled as a continuous variable in the analysis.

Clinical Outcomes

The primary clinical outcomes of this study were delayed graft function (DGF; defined as requiring dialysis within the first 72 hours posttransplantation), acute rejection occurring in the first 6 months posttransplant, estimated glomerular filtration rate (eGFR, calculated by modification of diet in renal disease equation) (*26*), overall graft failure (defined as death or returned to dialysis), death-censored graft failure (DCGF), and death. Data on acute rejection

were collected from 1997. The reporting of acute rejection is voluntary, with the majority being biopsy proven and coded according to Banff classification. The outcome data of all recipients were censored at 31st December 2009.

Statistical Analyses

Comparisons of baseline characteristics between donor types were made using chi-square test. Recipient eGFR at 1 and 5 years posttransplant were compared using unadjusted and adjusted generalized linear model (GLM) and data expressed as mean±95% confidence interval (95% CI). Predictors of DGF and acute rejection at 6 months were modeled by adjusted and unadjusted binary logistic regression analysis. Graft and patient survival were examined using Cox proportional hazard regression analysis. Results were expressed as hazard ratio (HR) or as odds ratio (OR) with 95% CI. The covariates included in the logistic regression and time-dependent Cox regression models were donor sex, recipients' characteristics (including age, race, sex, cause of ESKD, initial and pretransplant dialysis modality, peak PRA, dialysis duration pretransplant, diabetes, smoking history, and CAD) and transplant-related characteristics (including induction therapy, transplant era, and transplant state/country). Effect modification between donor types with covariates and outcomes were examined. Sensitivity analysis was constructed to examine the association between donor types and graft and patient outcomes excluding failed graft within 7 days of transplantation.

Statistical evaluation was performed using SSPS V10 statistical software program (SPSS Inc., North Sydney, Australia). A $P<0.05$ was considered statistically significant.

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REFERENCES

1. Chadban S, Briganti E, Kerr P, et al. Prevalence of kidney damage in Australian adults: The AusDiab Kidney Study. *J Am Soc Nephrol* 2003; 14: S131.
2. Clayton P, Campbell S, Hurst K, et al. Transplantation. In: McDonald S, Excell L, Livingston B, eds. *ANZDATA Registry 34th Annual Report 2011*. Adelaide: 2011.
3. Excell L, Marion V, Russ G. *ANZOD Registry Report 2012. ANZOD Registry Report*. Adelaide: ANZDATA Registry and ANZOD Registry; 2012.
4. Excell L, Hee K, Russ G. ANZOD Registry Report 2007. In: Excell L, Hee K, Russ G, eds. *ANZOD Registry Report*. Adelaide: 2007.
5. Basar H, Soran A, Shapiro R, et al. Renal transplantation in recipients over the age of 60: the impact of donor age. *Transplantation* 1999; 67: 1191.
6. Laging M, Kal-van Gestel J, van de Wetering J, et al. The relative importance of donor age in deceased and living donor kidney transplantation. *Transpl Int* 2012; 25: 1150.
7. Chang P, Gill J, Dong J, et al. Living donor age and kidney allograft half-life: implications for living donor paired exchange programs. *Clin J Am Soc Nephrol* 2012; 7: 835.
8. Gill J, Bunnapradist S, Danovitch G, et al. Outcomes of kidney transplantation from older living donors to older recipients. *Am J Kidney Dis* 2008; 52: 541.
9. Balachandran V, Aull M, Charlton M, et al. Kidneys from older living donors provide excellent intermediate-term outcomes after transplantation. *Transplantation* 2012; 94: 499.
10. Dols L, Kok N, Roodnat J, et al. Living kidney donors: impact of age on long-term safety. *Am J Transplant* 2011; 11: 737.
11. Kawamoto R, Kohara K, Tabara Y, et al. An association between metabolic syndrome and the estimated glomerular filtration rate. *Intern Med* 2008; 47: 1399.
12. Naumovic R, Djukanovic L, Marinkovic J, et al. Effect of donor age on the outcome of living-related kidney transplantation. *Transpl Int* 2005; 18: 1266.
13. Noppakun K, Cosio F, Dean P, et al. Living donor age and kidney transplant outcomes. *Am J Transplant* 2011; 11: 1279.
14. Johnson S, Khwaja K, Pavlakis M, et al. Older living donors provide excellent quality kidneys: a single center experience (older living donors). *Clin Transplant* 2005; 19: 600.
15. De La Vega L, Torres A, Bohorquez H, et al. Patient and graft outcomes from older living kidney donors are similar to those from younger donors despite lower GFR. *Kidney Int* 2004; 66: 1654.
16. Ferrari P, Lim W, Dent H, et al. Effect of donor-recipient age difference on graft function and survival in live-donor kidney transplantation. *Nephrol Dial Transplant* 2011; 26: 702.
17. Kasiske B, Israni A, Snyder J, et al. The relationship between kidney function and long-term graft survival after kidney transplant. *Am J Kidney Dis* 2011; 57: 466.
18. Lim W, Chang S, Chadban S, et al. Donor-recipient age matching improves years of graft function in deceased-donor kidney transplantation. *Nephrol Dial Transplant* 2010; 25: 3082.
19. Prommool S, Jhangri G, Cockfield S, et al. Time dependency of factors affecting renal allograft survival. *J Am Soc Nephrol* 2000; 11: 565.
20. Molnar M, Streja E, Kovesdy C, et al. Age and the associations of living donor and expanded criteria donor kidneys with kidney transplant outcomes. *Am J Kidney Dis* 2012; 59: 841.
21. Milton C, Russ G, McDonald S. Pre-emptive renal transplantation from living donors in Australia: Effect on allograft and patient survival. *Nephrology* 2008; 13: 535.
22. Serur D, Saal S, Wang J, et al. Deceased-donor kidney transplantation: improvement in long-term survival. *Nephrol Dial Transplant* 2011; 26: 317.
23. Halloran P, Homik J, Goes N, et al. The ''injury response'': a concept linking non-specific injury, acute rejection, and long-term transplant outcomes. *Transplant Proc* 1997; 29: 79.
24. Tullius S, 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.
25. Metzger R, Delmonico F, Feng S, et al. Expanded criteria donors for kidney transplantation. *Am J Transplant* 2003; 3: 114.
26. Levey A, Bosch J, Lewis J, et al. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. *Ann Intern Med* 1999; 130: 461.