

Outcomes in Kidney Transplant Recipients From Older Living Donors

Brian R. Englum,^{1,2} Matthew A. Schechter,¹ William D. Irish,^{1,3} Kadiyala V. Ravindra,^{1,4} Deepak S. Vikraman,^{1,4} Scott L. Sanoff,⁵ Matthew J. Ellis,⁵ Debra L. Sudan,^{1,4} and Uptal D. Patel^{2,5}



Background. Previous studies demonstrate that graft survival from older living kidney donors (LD; age >60 years) is worse than younger LD but similar to deceased standard criteria donors (SCD). Limited sample size has precluded more detailed analyses of transplants from older LD. **Methods.** Using the United Network for Organ Sharing database from 1994 to 2012, recipients were categorized by donor status: SCD, expanded criteria donor (ECD), or LD (by donor age: <60, 60–64, 65–69, ≥70 years). Adjusted models, controlling for donor and recipient risk factors, evaluated graft and recipient survivals. **Results.** Of 250,827 kidney transplants during the study period, 92,646 were LD kidneys, with 4.5% of these recipients (n = 4,186) transplanted with older LD kidneys. The use of LD donors 60 years or older increased significantly from 3.6% in 1994 to 7.4% in 2011. Transplant recipients with older LD kidneys had significantly lower graft and overall survival compared to younger LD recipients. Compared to SCD recipients, graft survival was decreased in recipients with LD 70 years or older, but overall survival was similar. Older LD kidney recipients had better graft and overall survival than ECD recipients. **Conclusions.** As use of older kidney donors increases, overall survival among kidney transplant recipients from older living donors was similar to or better than SCD recipients, better than ECD recipients, but worse than younger LD recipients. With increasing kidney donation from older adults to alleviate profound organ shortages, the use of older kidney donors appears to be an equivalent or beneficial alternative to awaiting deceased donor kidneys.

(*Transplantation* 2015;99: 309–315)

The number of patients on the kidney transplant waiting list in the United States continues to grow, with over 100,000 patients listed in 2014.¹ Despite efforts to expand the pool of kidney donors, organ availability has remained stagnant, and the average wait time for an adult patient has increased from 2.7 years in 1998 to 4.2 years in 2008.^{2,3} With increasing wait times and an aging U.S. population, transplant candidates have also been aging over time. Over 22,000 candidates 65 years or older were listed in 2014, nearly doubling their prevalence on the waitlist from 12% in 2002 to 20% by 2012.³

Living kidney donation holds great potential for recipients, even from older living donors. Living donors provide shorter wait times and better short- and long-term outcomes for their recipients compared with deceased donors.⁴ In addition, they expand the overall pool of organs, providing a benefit to all transplant candidates. Thus, older living kidney donation is likely to continue and become even more common as both the recipient and donor populations age.

Despite the growth in older donors, the safety and efficacy of using older living donor kidneys remain unclear. Although long-term studies have not demonstrated an additional mortality risk for living kidney donors,⁵ they have demonstrated an increased risk of end-stage renal disease, with the highest rates among older donors.⁶ Previous studies also indicate

Received 18 August 2014. Revision requested 10 November 2014.

Accepted 12 November 2014.

¹ Department of Surgery, Duke University Medical Center, Durham, NC.

² Duke Clinical Research Institute, Durham, NC.

³ CTI, Clinical Trial and Consulting Services, Raleigh, NC.

⁴ Division of Abdominal Transplantation, Duke University Medical Center, Durham, NC.

⁵ Department of Medicine, Division of Nephrology, Duke University Medical Center, Durham, NC.

The authors declare no funding or conflicts of interest.

B.R.E. participated in research design, writing of the article, performance of the research, contributed new reagents or analytic tools, and participated in data analysis. M.A.S. participated in research design. W.D.I. participated in research design, performance of the research, contributed new reagents or analytic tools, and participated in data analysis. K.V.R. participated in research design. D.S.V. participated

in research design. S.L.S. participated in research design, writing of the article, and performance of the research. M.J.E. participated in writing of the article. D.L.S. participated in research design and writing of the article. U.D.P. participated in research design, writing of the article, performance of the research, and contributed new reagents or analytic tools.

Correspondence: Brian Englum, MD, Department of Surgery, Duke University Medical Center, Box 3443 Medical Center, Durham, NC 27710. (brian.englum@duke.edu).

Supplemental digital content (SDC) is available for this article. Direct URL citations appear in the printed text, and links to the digital files are provided in the HTML text of this article on the journal's Web site (www.transplantjournal.com)

Copyright © 2015 Wolters Kluwer Health, Inc. All rights reserved.

ISSN: 0041-1337/15/9902-309

DOI: 10.1097/TP.0000000000000607

increased graft failure among recipients as donor age increases⁷⁻⁹; however, these studies have been conflicted and used varying definitions of older living donors. In an effort to better understand the impact of living kidney donation from older donors (≥ 60 years of age), we examine the temporal trends in the use of older living donors, evaluate donor and recipient characteristics of patients receiving these organs, and compare the outcomes of recipients of these organs based on donor type and age.

METHODS

Data Source

Since 1987, the United Network for Organ Sharing has collected data from U.S. transplant centers using trained staff, data quality assessments, and site audits to provide high-quality data for the Standard Transplant Analysis and Research files.^{3,10} These data provide feedback to transplant centers on their risk-adjusted outcomes and have been used extensively for clinical research in transplant surgery.

Study Population

Isolated kidney transplants for adult recipients (age ≥ 18 years) from 1994 through March 2012 were analyzed. Cases were classified based on the donor type: standard criteria donor (SCD), expanded criteria donor (ECD),¹¹ and living donor (LD) by age group (<60, 60–64, 65–69, and ≥ 70 years).

Outcomes

Graft and overall recipient survival were the primary outcomes of this analysis. Secondary outcomes included short-term mortality, delayed graft function (DGF), time on dialysis since listing, and cause of graft failure and mortality. Time on dialysis accrued days on dialysis from the time of listing through death or censoring. When calculating percentage of dialysis-free days from time of waitlist, days on the waitlist before requiring dialysis were not included.

Statistical Analyses

Patients were categorized by kidney donor type as described above. Temporal trends in the annual rate of older LD use from 1994 to 2011 were analyzed using the Cochran-Armitage test. The LD estimated glomerular filtration rate (eGFR) was calculated based on the Modification of Diet in Renal Disease formula and normalized using mean GFR by age group.¹² Because donor eGFR is expected to decrease with age, we were concerned that unadjusted eGFR would not fully represent the stringent selection of older donors; therefore, observed to expected ratios were used to demonstrate normalized kidney function for age. Donor and recipient characteristics were evaluated by group using count and percentages for categorical variables and median and interquartile range for continuous variables. Differences were compared using Pearson χ^2 test and Kruskal-Wallis test for categorical and continuous variables, respectively.

Kaplan-Meier methods were used to evaluate long-term outcomes, including overall recipient survival and graft survival with outcomes right censored at 10 years. The log-rank test was applied to assess differences among the groups and pairwise comparisons for groups of interest. A Cox proportional hazards model was used to assess differential graft and overall survival. Because of the concerns that the

proportional hazards assumption was violated based on visual examination of log(-log) survival plots (see Appendix S1, SDC, <http://links.lww.com/TP/B115>), an adjusted accelerated failure time (AFT) survival analysis using the Weibull distribution was performed to assess for the relative hazards of these outcomes after controlling for known risk factors, including donor gender and race, and recipient age, sex, race, end-stage renal disease etiology, and HLA match.

Although previous analyses have controlled for donor renal function and recipient time on dialysis, these variables may be considered to be part of the causal pathway for graft and overall survivals. Waiting for a deceased donor kidney rather than using an elderly living donor almost certainly necessitates a long waitlist period during which a recipient would initiate or accrue substantial time on dialysis. In a similar fashion, GFR is known to decrease with age; therefore, the use of an elderly living donor inherently requires the recipient to accept a donor kidney with reduced function. In addition, baseline GFR is not reliable in deceased kidney donors, as they often have some degree of acute renal dysfunction that is expected to resolve. Thus, although the primary analyses excluded adjustment for these variables, we performed sensitivity analyses including them and using restricted cubic splines to evaluate the linear relationship of these variables with overall and graft survivals.

A final analysis examining the interaction of recipient age and donor groups was performed. Recipients were divided into broad categories (<40 years old, 40–59 years old, and ≥ 60 years old), and the AFT model was developed stratified by these age groups. An additional analysis of the overall cohort was performed including an interaction term between donor group and recipient age. The adjusted hazard ratios were then compared among the stratified analyses, using the *P* value from the interaction terms to assess statistically significant differences in the association of donor group and outcomes among different recipient age strata. *P* values less than 0.05 were considered significant, with type I error controlled at the level of comparison. R (v. 3.02; R Foundation for Statistical Computing, Vienna, Austria) was used for statistical analyses.

RESULTS

From January 1994 through March 2012, 250,827 patients met inclusion criteria, including 92,646 kidney transplants from living donors (36.9%). Of the cases from living donors, 95.5% ($n = 88,460$) were from living donors younger than 60 years, whereas 3.2% ($n = 3,002$), 1.0% ($n = 960$), and 0.2% ($n = 224$) were from older living donors with ages of 60 to 64 years, 65 to 69 years, and 70 years or older, respectively.

Older living kidney donation increased dramatically over the study period, accounting for 97 cases annually in 1994, but over 400 cases by 2011 (Figure 1). Older kidney donors also comprised a growing proportion of living kidney donation, increasing from 3.6% in 1994 to 7.4% in 2011 ($P < 0.001$). The increase was mostly observed in the 60- to 69-year-old age group, whereas the contribution of those 70 years or older remained relatively constant. As donor age increased, eGFR decreased, with 18% of donors 70 years or older having an eGFR less than 60 mL/min/1.73 m² (Figure 2A). When normalized for age, however, older donors

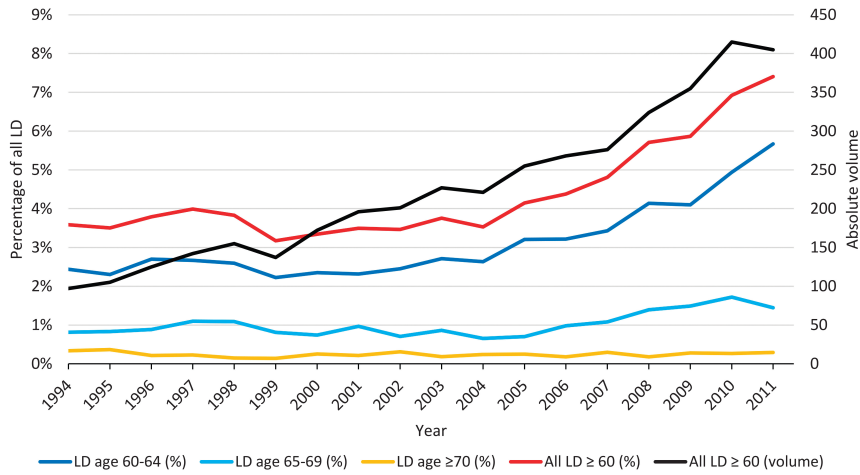


FIGURE 1. Temporal trends in older LD use. Cochran-Armitage trend test for change in use of older living donors over time: $P < 0.001$.

actually had better than expected kidney function compared to their younger counterparts (Figure 2B).

As expected, the age of kidney recipients increased as donor age increased, with median age of 40 years for recipients of younger than 60 years LD, whereas median recipient ages were 58, 62, and 65 years for donor age groups 60 to

64 years, 65 to 69 years, and 70 years or older, respectively ($P < 0.001$; Table 1). At the time of transplant, recipients of living donors in all age groups were less likely to be on dialysis than recipients of deceased donor kidneys. In addition, days on dialysis while on the transplant waiting list were dramatically lower for recipients of LD kidneys.

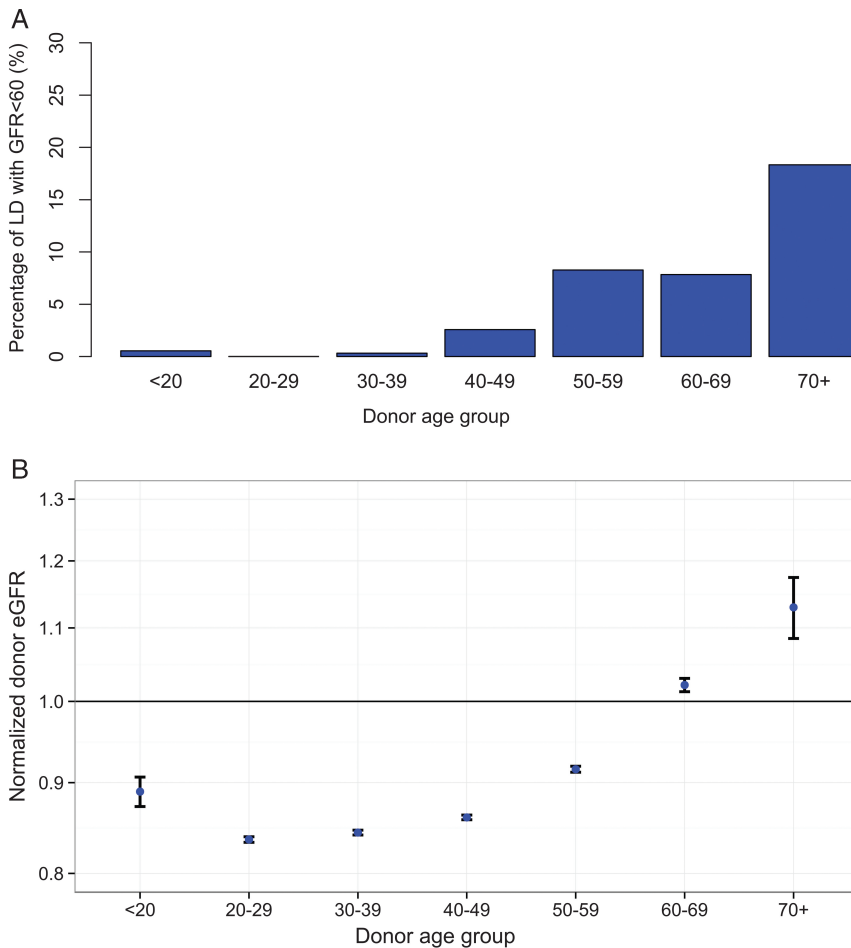


FIGURE 2. A, Living donors with an eGFR less than 60 mL/min/1.73 m² by donor age group. B, Living donor eGFR normalized to mean GFR by age group. Blue points represent point estimates, and error bars represent 95% confidence intervals.

TABLE 1.
Donor and recipient characteristics by donor type

	Deceased donors		Living donors				P
	SCD	ECD	<60	60-64	65-69	≥70	
N	132,561 (52.9%)	25,610 (10.2%)	88,460 (35.3%)	3,002 (1.2%)	960 (0.4%)	224 (0.1%)	
Donor							
Age, y	34 (21, 46)	60 (55, 64)	40 (31, 47)	61 (60, 63)	66 (65, 67)	71 (70, 73)	<0.001
Female	51,037 (38.5%)	13,150 (51.3%)	52,302 (59.1%)	1,881 (62.7%)	593 (61.8%)	106 (47.3%)	<0.001
Race/ethnicity							<0.001
White	95,139 (71.9%)	19,311 (75.5%)	61,299 (69.3%)	2,548 (84.9%)	830 (86.5%)	206 (92.4%)	
Black	16,250 (12.3%)	2,918 (11.4%)	11,874 (13.4%)	153 (5.1%)	32 (3.3%)	2 (0.9%)	
Hispanic	16,847 (12.7%)	2,376 (9.3%)	11,162 (12.6%)	178 (5.9%)	53 (5.5%)	8 (3.6%)	
Other	4,140 (3.1%)	981 (3.8%)	4,072 (4.6%)	122 (4.1%)	45 (4.7%)	7 (3.1%)	
BMI, kg/m ²	25 (22, 29)	27 (24, 31)	27 (24, 30)	26 (24, 29)	26 (24, 29)	26 (24, 28)	<0.001
Recipient							
Age, y	50 (39, 59)	59 (50, 65)	46 (35, 56)	58 (40, 63)	62 (43, 67)	65 (46, 71)	<0.001
Female	52,520 (39.6%)	9,511 (37.1%)	35,876 (40.6%)	1,185 (39.5%)	387 (40.3%)	97 (43.3%)	<0.001
Race/ethnicity							<0.001
White	67,265 (50.7%)	12,859 (50.2%)	59,430 (67.2%)	2,476 (82.5%)	797 (83%)	198 (88.4%)	
Black	39,128 (29.5%)	7,752 (30.3%)	13,093 (14.8%)	192 (6.4%)	49 (5.1%)	6 (2.7%)	
Hispanic	16,999 (12.8%)	2,936 (11.5%)	11,274 (12.7%)	187 (6.2%)	58 (6%)	8 (3.6%)	
Other	9,169 (6.9%)	2,063 (8.1%)	4,659 (5.3%)	147 (4.9%)	56 (5.8%)	12 (5.4%)	
BMI, kg/m ²	26 (23, 31)	27 (24, 31)	26 (23, 30)	26 (23, 30)	27 (23, 31)	25 (22, 28)	<0.001
Primary diagnosis							<0.001
Diabetes	29,129 (22.4%)	7,659 (30.3%)	19,052 (21.9%)	741 (25.1%)	239 (25.2%)	40 (18.2%)	
Glomerular disease	32,129 (24.7%)	4,581 (18.2%)	26,728 (30.7%)	719 (24.3%)	217 (22.9%)	50 (22.7%)	
Other	69,055 (53%)	12,996 (51.5%)	41,230 (47.4%)	1,496 (50.6%)	493 (51.9%)	130 (59.1%)	
Dialysis at time of transplant	117,916 (89.9%)	23,178 (91.4%)	61,800 (71.1%)	1,940 (65.5%)	602 (63.7%)	136 (61.5%)	<0.001
Days on dialysis while on transplant waitlist	419 (142, 931)	477 (142, 966)	0 (0, 184)	0 (0, 190)	0 (0, 160)	0 (0, 147)	<0.001
Previous kidney transplant	18,058 (13.6%)	1,930 (7.5%)	8,896 (10.1%)	249 (8.3%)	75 (7.8%)	30 (13.4%)	<0.001
HLA mismatch ≥ 5	49,503 (37.6%)	12,139 (47.7%)	20,703 (23.8%)	875 (29.6%)	300 (31.9%)	67 (30.6%)	<0.001
Peak PRA							
<20%	82,717 (86.6%)	16,058 (91.4%)	33,295 (91.2%)	1,116 (92.6%)	343 (92.5%)	66 (89.2%)	<0.001
20%-80%	8,922 (9.3%)	1,186 (6.8%)	2,539 (7%)	70 (5.8%)	21 (5.7%)	5 (6.8%)	<0.001
>80%	3,896 (4.1%)	321 (1.8%)	660 (1.8%)	19 (1.6%)	7 (1.9%)	3 (4.1%)	<0.001

Values represent count (%) for categorical variables and median (IQR) for continuous data. IQR, interquartile range; BMI, body mass index; PRA, panel reactive antibody.

Thirty-day mortality was also lower in those receiving living kidney donation. Although DGF was more common in recipients of older living donor kidneys, rates of DGF were dramatically lower than among recipients of deceased donor kidneys (Table 2). From the time of listing through 10 years of posttransplant follow-up, recipients of living donor kidneys spent a greater percentage of their time free from dialysis (>95% for all groups) compared to the ECD group (65%) and the SCD group (73%; $P < 0.001$). Among those with graft failure, recipients of LD ≥70 had less chronic rejection but higher rates of graft thrombosis and infection. Cardiovascular, cerebrovascular, and infectious causes of death occurred more often among recipients of LD 70 years or older (Table 2).

In analyses of unadjusted graft survival, recipients had decreasing graft survival with increasing donor age (Figure 3A). Those receiving kidneys from donors younger than 65 years had higher survival rates than recipients of SCD kidneys ($P < 0.001$ for SCD vs LD 60–64 years). Recipients from LD 65 to 69 years had equivalent graft survival to those from SCD kidneys ($P = 0.66$). Recipients of LD 70 years or older appeared to have worse graft survival than SCD recipients

but failed to reach statistical significance ($P = 0.12$). Recipients of ECD kidneys had the highest rates of graft failure.

After adjustment for known risk factors, donor age continued to be significantly associated with graft failure. Recipients of LD younger than 60 years old had improved graft survival compared to recipients of SCD donors (Figure 4A). Grafts from LD 60 to 64 years and LD 65 to 69 years old had similar survival to SCD kidneys, whereas those of LD 70 years or older had worse graft survival than SCD grafts ($P < 0.001$). The ECD recipients had the worst graft survival, although not statistically different from the LD 70 years or older recipients (adjusted hazard ratio [HR], 0.88; 95% confidence interval [95% CI], 0.66–1.17; $P = 0.38$).

Unadjusted overall survival trends were similar to those of graft survival, with a gradient of worsening survival among older donor groups. Patients who received kidneys from donors younger than 65 years had increased long-term graft survival compared to SCD recipients (Figure 3B; $P < 0.001$ for SCD vs LD 60–64 years). Recipients from LD 65 years or older had worse survival than SCD recipients ($P = 0.04$ for SCD vs LD 65–69 years; $P = 0.01$ for SCD vs LD ≥ 70 years). After accounting for recipient age and other confounders in

TABLE 2.
Outcomes by donor type

	Deceased donors		Living donors				P
	SCD	ECD	<60	60-64	65-69	≥70	
N	132,561 (52.9%)	25,610 (10.2%)	88,460 (35.3%)	3002 (1.2%)	960 (0.4%)	224 (0.1%)	
Short-term outcomes							
Delayed graft function	30,755 (23.3%)	8485 (33.2%)	3884 (4.4%)	150 (5%)	66 (6.9%)	16 (7.2%)	<0.001
Death –30 days	1463 (1.1%)	421 (1.7%)	359 (0.4%)	11 (0.4%)	5 (0.5%)	2 (0.9%)	<0.001
Long-term outcomes							
Dialysis-free time since listing	73% (44%-92%)	65% (32%-87%)	98% (82%-100%)	98% (78%-100%)	98% (79%-100%)	99% (77%-100%)	<0.001
Cause of graft failure							
Chronic rejection	11,368 (42.2%)	2888 (40.6%)	5810 (43.8%)	183 (40.2%)	82 (49.4%)	13 (26.5%)	<0.001
Acute rejection	4388 (16.3%)	973 (13.7%)	2000 (15.1%)	64 (14.1%)	16 (9.6%)	10 (20.4%)	
Primary failure	1919 (7.1%)	831 (11.7%)	581 (4.4%)	23 (5.1%)	9 (5.4%)	0 (0%)	
Graft thrombosis	1,532 (5.7%)	374 (5.3%)	807 (6.1%)	32 (7%)	8 (4.8%)	6 (12.2%)	
Recurrent disease	1331 (4.9%)	214 (3%)	1035 (7.8%)	28 (6.2%)	9 (5.4%)	3 (6.1%)	
Infection	973 (3.6%)	350 (4.9%)	349 (2.6%)	12 (2.6%)	8 (4.8%)	5 (10.2%)	
Noncompliance	741 (2.8%)	88 (1.2%)	379 (2.9%)	6 (1.3%)	0 (0%)	0 (0%)	
Other	3732 (13.9%)	1115 (15.7%)	1790 (13.5%)	87 (19.1%)	29 (17.5%)	11 (22.4%)	
Cause of death							
Cardiovascular	4244 (22.5%)	1150 (22.8%)	1792 (22.1%)	70 (20.2%)	26 (17.4%)	11 (28.2%)	<0.001
Infection	3981 (21.1%)	1255 (24.9%)	1426 (17.6%)	62 (17.9%)	24 (16.1%)	11 (28.2%)	
Malignancy	1733 (9.2%)	435 (8.6%)	957 (11.8%)	40 (11.6%)	18 (12.1%)	2 (5.1%)	
Cerebrovascular	809 (4.3%)	185 (3.7%)	379 (4.7%)	15 (4.3%)	6 (4%)	4 (10.3%)	
Other	7363 (39.1%)	1838 (36.5%)	3233 (39.9%)	147 (42.5%)	68 (45.6%)	10 (25.6%)	

Cause of graft failure and death are among those with those outcomes.

an adjusted AFT analysis, we found that recipients of kidneys from LD younger than 60 years and LD 60 to 64 years demonstrated improved overall survival compared to those receiving SCD grafts (Figure 4B). Recipients of LD 65 to 69 years and LD 70 years or older had similar overall survival compared to SCD recipients. The ECD recipients continued to have the worst overall survival, even when compared to the LD 70 years or older (adjusted HR, 0.78; 95% CI, 0.62–0.98; $P = 0.03$). Results of both adjusted graft survival and overall survival were similar in adjusted Cox proportional hazards models (see Appendix S2, SDC, <http://links.lww.com/TP/B115>).

Several sensitivity analyses were performed to examine the role of preoperative dialysis and baseline renal function among living donors. In unadjusted analyses, pretransplant time on dialysis was strongly associated with overall and graft survivals. This relationship was most pronounced over the first 200 days of pretransplant dialysis (HR for mortality, 1.19 per 100 days of dialysis; 95% CI, 1.18–1.19; HR for graft failure, 1.18 per 100 days of dialysis; 95% CI, 1.16–1.19); however, after 200 days of dialysis, the hazard ratios were smaller (HR for mortality, 1.004 per 100 days; HR for graft failure, 1.01 per 100 days; all P values < 0.001). These results were similar, although not as pronounced in adjusted analysis (see Appendix S3, SDC, <http://links.lww.com/TP/B115>).

Living donor eGFR did not demonstrate a strong association with overall recipient survival in unadjusted or adjusted analyses. Even in graft survival, only the lowest eGFR category (≥ 150 mL/min/1.73 m², 120–149, 90–119, 60–89, and <60) demonstrated an association with worse graft survival (HR, 1.32; 95% CI, 1.01–1.71) after adjustment

(see Appendix S4, SDC, <http://links.lww.com/TP/B115>). Neither the adjustment for days on dialysis nor donor eGFR substantially changed the association between donor groups and outcomes.

Finally, analyses examining interactions between donor group and recipient age were performed to determine whether the differences in outcomes by donor group held true in both young and elderly recipients. Overall, the results were similar to the primary analyses. Graft failure was elevated in patients across all age groups with ECD donors, but it was most pronounced in recipients younger than 60 years (adjusted HR, 1.92 vs 1.61 in <40 years; interaction P value = 0.001). The adjusted HR for graft failure from LD 70 years or older was higher among recipients younger than 40 years compared to those 60 years or older (adjusted HR [95% CI], 2.00 [1.08–3.73] vs 1.46 [0.92–2.32]); however, this difference was not statistically significant (interaction P value = 0.40).

DISCUSSION

With an aging U.S. population, both the pool of older kidney transplant candidates and donors is likely to increase, leading to a potential increase in the use of older living kidney donors. This study demonstrates that such trends are already in progress, with a doubling in the use of older (age, ≥ 60 years) kidney donors from 1994 to 2011. Our study is the first to focus on both graft and patient survivals among specific age groups over the age of 60 years, and we demonstrate that although increasing LD age groups were associated with decreased recipient overall and graft survivals, outcomes remain superior to

those among recipients of ECD kidneys and at least equivalent to those among recipients of standard criteria deceased donor kidneys. With a critical shortage of donor kidney availability, the current study supports continued use of older living donor kidneys as a means to avoid dialysis and maintain reasonable long-term outcomes. In addition, this study establishes the importance of this growing source of donor organs and sets the stage for further research in this area as we move to a new Kidney Donor Profile Index–based evaluation system.

With developments in renal transplantation, such as the use of incompatible renal transplant, paired kidney exchange programs, and altruistic donors, there is increased potential for the use of living kidney transplantation. Although previous research has demonstrated superior outcomes for recipients of living kidney donation compared to deceased kidney donation,⁴ the benefits of using older living donor remains less clear. Single center studies have evaluated the outcomes after older kidney donation, finding no significant differences between younger and older donors. These studies were underpowered to make substantial claims about differences between age groups and were forced to create broad classifications of older donors due to small sample sizes.^{8,13-15} Other studies examining United Network for Organ Sharing data have found decreased graft and overall survival for recipients of older living donor kidneys; however, most studies have found that these older living donor kidneys perform as well or better than deceased donor kidneys.^{9,16-18} In an examination of living donors 70 years or older, Berger et al¹⁸ found no significant differences in short-term graft failure or recipient survival

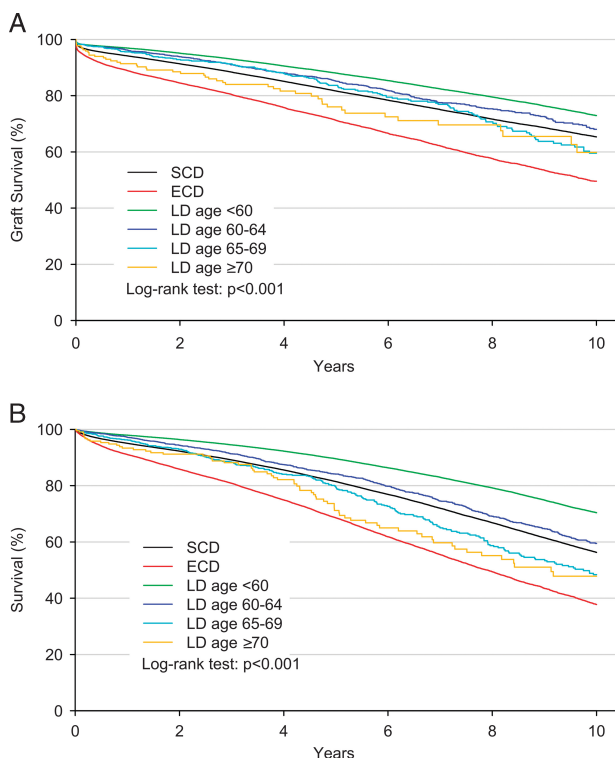


FIGURE 3. A, Death-censored graft survival of isolated kidney transplants by donor type. Log-rank test evaluated difference in graft survival among all groups. B, Overall survival of isolated kidney transplants by donor type. Log-rank test evaluated difference in survival among all groups.

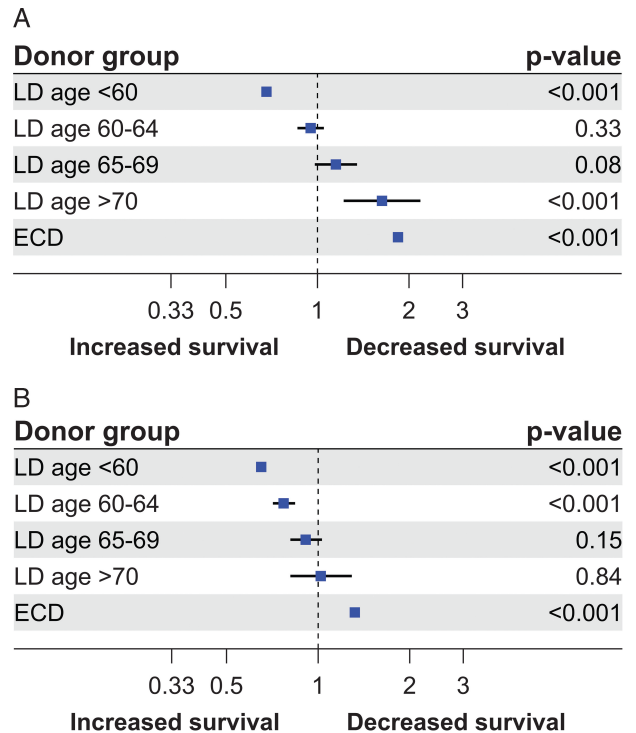


FIGURE 4. A, Adjusted hazard ratios for graft survival by donor type. Accelerated failure time model with Weibull distribution was used to adjust for donor sex and race, and recipient age, gender, race, end-stage renal disease etiology, and HLA match. Reference group, SCD recipients. B, Adjusted hazard ratios for overall survival by donor type. Accelerated failure time model with Weibull distribution was used to adjust for donor gender and race, and recipient age, gender, race, end-stage renal disease etiology, and HLA match. Reference group, SCD recipients.

when comparing these patients to recipients of 50- to 59-year-old deceased donors. Conversely, Gill et al compared older living donor kidneys to kidneys from deceased donors less than 55 years old, finding similar graft failure for recipients from living donors aged 55 to 64 years, but worse outcomes when donors were 65 years or older.

The current study adds to previous reports by demonstrating the significant temporal trend in the use of older living kidney donors, with more than 7% of living donors being over the age of 60 years in 2011. As expected, older donors offer kidneys with decreased eGFR compared to younger living donors. The GFR is expected to decrease with age, and extrapolated data from normal subjects demonstrated that men in their 20s have an expected eGFR greater than 120 mL/min/1.73 m², whereas men in their 70s have an expected eGFR of 70 mL/min/1.73 m².¹² Our analyses normalized the eGFR using observed to expected ratios. When age normalized, older donors had better than expected eGFR, potentially indicating a more stringent selection process for these potential donors.

Despite this selection process, older LD kidneys had decreased graft survival, compared to younger LD kidneys. When compared to SCD and ECD kidneys, these older living donor kidneys performed favorably. Although graft failure was significantly increased in kidneys from donor 70 years or older, these patients did not have worse overall survival, potentially related to decreased time spent on dialysis while awaiting an available kidney. Previous studies have chosen

to control for pretransplant dialysis time when analyzing long-term outcomes.¹⁶ Decreased dialysis exposure is an inherent advantage of living donor transplantation and a potential part of the causal pathway for long-term outcomes in this patient population; therefore, our primary analyses did not adjust for this factor. In sensitivity analyses accounting for these differences, significant associations with outcomes were observed but did not dramatically alter the results of living donor age. We also compared outcomes to a broad group of deceased donor recipients more representative of those seen when making clinical decisions about kidney transplantation. These deceased donor groups also have a strong relation to how donors will be evaluated moving forward, although further research will be needed to evaluate the use of older living donors as the Kidney Donor Profile Index–based evaluation system changes kidney allocation.

Along with overall survival that was better than ECD kidney recipients and equal to or better than SCD kidney recipients, recipients of older living donor kidneys spent a dramatically smaller proportion of their postlisting lives on dialysis compared to those awaiting deceased donor kidneys. This finding has significant implications for quality of life and cost and will require further inquiry.

The current study must be understood in the context of limitations of an observational study, with the inherent possibility of selection bias and unmeasured confounders. Even with the largest sample of older donors currently published, the small number of patients in the highest donor age groups may lead to uncertainty in these estimates. To fully assess the risk-benefit ratio of using older kidney donors, detailed information on the outcomes of donors after nephrectomy would be needed, which was unavailable for the current analyses. Finally, our study was not able to examine the impact of older donor use on the overall kidney donation pool; therefore, downstream advantages of this expansion of the supply of transplant kidneys could not be estimated.

In conclusion, we found a substantial increase in the use of older living kidney donation in the United States over the last 20 years, a trend that will likely continue given current demographic shifts and organ shortages. Recipients of older donors appear to have increased graft failure and long-term mortality compared to cases of younger living kidney donation; however, these recipients appear to do as well or better than recipients of SCD or ECD kidneys. Although further research will be needed to fully assess the causes and implications of these findings, the comparable long-term outcomes of kidneys from older living donors compared to SCD or

ECD kidneys with the short-term advantages of avoiding dialysis promote the expanded use of this resource.

REFERENCES

1. Organ Procurement and Transplantation Network. OPTN National Data Reports: Kidney; 2014 [accessed 7/18/2014]. Available from: <http://optn.transplant.hrsa.gov/latestData/step2.asp>.
2. Knoll G. Trends in kidney transplantation over the past decade. *Drugs*. 2008;68(Suppl 1):3–10.
3. *Organ Procurement and Transplantation Network (OPTN) and Scientific Registry of Transplant Recipients (SRTR). OPTN / SRTR 2012 Annual Data Report*. Rockville, MD: Department of Health and Human Services, Health Resources and Services Administration, Healthcare Systems Bureau, Division of Transplantation; 2013.
4. Terasaki PI, Cecka JM, Gjertson DW, Takemoto S. High survival rates of kidney transplants from spousal and living unrelated donors. *N Engl J Med*. 1995;333:333–336.
5. Segev DL, Muzaale AD, Caffo BS, et al. Perioperative mortality and long-term survival following live kidney donation. *JAMA*. 2010;303:959–966.
6. Muzaale AD, Massie AB, Wang MC, et al. Risk of end-stage renal disease following live kidney donation. *JAMA*. 2014;311:579–586.
7. Sapir-Pichhadze R, Young A, Joseph Kim S. Living donor age and kidney transplant outcomes: an assessment of risk across the age continuum. *Transpl Int*. 2013;26:493–501.
8. Noppakun K, Cosio FG, Dean PG, Taler SJ, Wauters R, Grande JP. Living donor age and kidney transplant outcomes. *Am J Transplant*. 2011;11:1279–1286.
9. 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;7:835–841.
10. Daily OP, Kauffman HM. Quality control of the OPTN/UNOS Transplant Registry. *Transplantation*. 2004;77:1309;author reply –10.
11. Pascual J, Zamora J, Pirsch JD. A systematic review of kidney transplantation from expanded criteria donors. *Am J Kidney Dis*. 2008;52:553–586.
12. National Kidney Foundation. Kidney Disease Outcomes Quality Initiative Guidelines Part 4: Definition and Classification of Stages of Chronic Kidney Disease 2002 [accessed 11/4/2014]. Available from: http://www2.kidney.org/professionals/KDOQI/guidelines_ckd/p4_class_g1.htm.
13. De La Vega LS, Torres A, Bohorquez HE, et al. Patient and graft outcomes from older living kidney donors are similar to those from younger donors despite lower GFR. *Kidney Int*. 2004;66:1654–1661.
14. Basar H, Soran A, Shapiro R, et al. Renal transplantation in recipients over the age of 60: the impact of donor age. *Transplantation*. 1999;67:1191–1193.
15. Balachandran VP, Aull MJ, Charlton M, et al. Kidneys from older living donors provide excellent intermediate-term outcomes after transplantation. *Transplantation*. 2012;94:499–505.
16. Gill JS, Gill J, Rose C, Zalunardo N, Landsberg D. The older living kidney donor: Part of the solution to the organ shortage. *Transplantation*. 2006;82:1662–1666.
17. Gill J, Bunnapradist S, Danovitch GM, Gjertson D, Gill JS, Cecka M. Outcomes of kidney transplantation from older living donors to older recipients. *Am J Kidney Dis*. 2008;52:541–552.
18. Berger JC, Muzaale AD, James N, et al. Living kidney donors ages 70 and older: recipient and donor outcomes. *Clin J Am Soc Nephrol*. 2011;6:2887–2893.