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Research paper

US deceased kidney transplantation: Estimated GFR, donor age and KDPI association with graft survival

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ABSTRACT

Background: Despite a significant shortage of kidneys for transplantation in the US, kidneys from older deceased donors are infrequently transplanted. This is primarily over concern of graft quality and transplant durability.
Methods: The US national transplant database (2000–2018) was assessed for deceased donor kidney transplant patient and graft survival, graft durability and stratified by donor age (<65 years>), Kidney Donor Profile Index (KDPI) and estimated glomerular filtration rate (GFR) one year post-transplantation (eGFR-1) were calculated.
Findings: Recipients of kidneys transplanted from deceased donors >65 years had a lower eGFR-1, (median 39 ml/min) than recipients of younger donor kidneys (median 54 ml/min). However, death-censored graft survival, stratified by eGFR-1, demonstrated similar survival, irrespective of donor age or KDPI. The durability of kidney survival decreases as the achieved eGFR-1 declines. KDPI has a poor association with eGFR-1 and lesser for graft durability. While recipients of kidneys > 65 years had a higher one year mortality than younger kidney recipients, recipients of kidneys > 65 years and an eGFR-1 <30 ml/min, had a lower survival than an untransplanted waitlist cohort ($p<0.001$).
Interpretation: The durability of kidney graft survival after transplantation was associated with the amount of kidney function gained through the transplant (eGFR-1) and the rate of graft loss (return to dialysis) was not significantly associated with donor age. 24.9% of recipients of older donor kidneys failed to achieve sufficient eGFR-1 providing a transplant survival benefit. While there is significant benefit from transplanting older kidneys, better decision-making tools are required to avoid transplanting kidneys that provide insufficient renal function.
Funding: None.

1. Introduction

Kidney transplantation is the optimal treatment for many people with renal failure. In 2019, the greatest number of deceased organ donations were performed in the US (11,870) resulting in 16,534 deceased kidney transplants [1]. However, when juxtaposed against the 500,000 people requiring dialysis [2] and 93,000 on the national kidney transplant waitlist [1], the need for kidneys is striking. The HRSA sponsored, Deceased Donor Potential study suggested that 38,000 deceased donors was feasible, but an expanded use of older donors would be required [3]. While older donor kidneys are frequently transplanted in Europe [4,5], it is less frequent in the US. The US transplant and recipient community has concern about the quality and durability of kidneys from older donors, in part due to the known decline of glomerular filtration and kidney damage with increasing age [6–9]. Presently, over 50% of kidneys retrieved from donors over 65 years are not transplanted [1]. In 2019, only 646 of 11,152 US deceased kidney donors were >65 years (5.8%) and fewer than half of the kidneys (298) were transplanted.

Kidney transplantation intends to provide durable relief from dialysis. From a multinational, >13,000 transplant study, the amount of renal function (estimated glomerular filtration rate at a year post-

Abbreviations: AUC, area under curve; CKD, chronic kidney disease; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration Equation; CI, Confidence Interval; CPRA, calculated panel-reactive antibody; DCD, donation after circulatory death; eGFR, estimated glomerular filtration rate; eGFR-1, one year after transplantation; ESRD, end stage renal disease; HHS, Department of Health and Human Services of the US government; HRSA, Health Resources and Services Administration, Agency within HHS; KDIGO, Kidney Disease Improving Global Outcomes; KDPI, kidney donor profile index; KDRI, kidney donor risk index; OPTN, Organ Procurement and Transplantation Network

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Research in Context

Evidence before this study

Despite is a global shortage of kidneys for transplantation, the use of older deceased donor kidneys is heterogeneous. European countries frequently transplant kidneys from deceased donors over 60–65 years of age (NHS, Eurotransplant, CNT and ONT annual reports), whereas the US has a much lower use (OPTN annual report). This is predominantly thought to be due to uncertain kidney quality and durability of graft function.

Added value of this study

Analysis of the US donor and transplant database demonstrated that the durability of kidney transplants from deceased donors > 65 years was similar to younger donor kidneys when stratified by estimated glomerular filtration rate after one year (eGFR-1) and that durability decreases as eGFR-1 decreases. Importantly, the recipient survival benefit was lost when the older kidney failed to supply an eGFR-1 > 30 ml/min.

Implications of all the available evidence

A kidney transplant should provide sufficient function to provide the recipient a survival benefit. This analysis suggests an eGFR-1 > 30 ml/min is required (in the US), but global applicability needs to be assessed. The loss of GFR with age is known to occur and its impact upon transplanting older kidneys is substantial for risk assessment.

transplantation, eGFR-1) was associated with 10-year kidney survival [10]. Lesser eGFR-1 had increasing rates of graft failure, but did not specifically address the impact of deceased donor age upon graft survival. Do older kidneys fail quicker? This analysis focuses upon deceased donor age, estimated graft function after one year and long-term graft failure.

2. Methods

2.1. Data and construction of cohorts

This study used the Organ Procurement and Transplantation Network (OPTN) database that includes information on donors, waitlisted candidates, and transplant recipients in the U.S., and has been described elsewhere [1]. The Health Resources and Services Administration (HRSA), U.S. Department of Health and Human Services provides oversight to the activities of the OPTN contractor. IRB exemption was obtained from the US Department of Health and Human Services Health Resources and Services Administration (HRSA) under the Public Benefit and Service program exemption of the Common Rule. The de-identified database was queried for the outcomes of adult deceased donor kidney transplants in first kidney-alone transplants occurring between 01/01/2000 and 12/31/2018 (Table 1). 139,363 kidney transplants met this criteria; a small number were excluded (N = 1006, 0.7%) for one or more missing data elements. Kidney graft failure is recorded when the recipient either returned to dialysis, the graft was removed or at recipient death. As the study intent is the assessment of age upon graft durability, recipients with grafts surviving one year had the eGFR calculated using the CKD_EPI equation [11]. The current assessment of kidney quality, the Kidney Donor Risk Index [12] was calculated, with a subsequent conversion to KDPI (Kidney Donor Profile Index, with higher percentiles predicting worse function). The eGFR-1 calculation was made from the closest data point, within a 90 day window, of the actual "one year transplant anniversary". 20,561 records (14.8%) did not have a creatinine measurement within 90 days of the "one-year transplant anniversary", but within this group were 97% of one-year graft failures. While eGFR-1 after transplant is a continuous outcome; for outcome comparisons, the eGFR-1 were categorized by the 2012 KDIGO Chronic Kidney Disease criteria [13]: eGFR-1 >45 ml/min (CKD 3a), eGFR-1 30–44 ml/min (CKD 3b) and eGFR-1 < 30 ml/min (CKD 4/5). An eGFR-1 >60 ml/min (CKD 2 and CKD 1) from older donor kidneys were few and are included in the > 45 ml/min group.

To assess transplant survival benefit of recipients with a kidney from a deceased donor >65 years, patients with a functioning kidney at one year were compared to the survival of a matched cohort of waitlisted, but not transplanted candidates. This used propensity-matching procedures developed by Ho et al. [14] including candidate sex, age, race, diagnosis, CPRA, BMI, height, and ESRD time of the kidney recipients and waitlist candidates (details in Supplement).

2.2. Statistical analysis

Outcomes of deceased donor (>65 years) kidney recipients with a functioning graft at one year were stratified by demographics and grouped by the recipients' eGFR-1. Kruskal-Wallis (for continuous data elements) and Chi-Squared tests (for categorical data elements) were used to determine significance of differences between transplant groups. 5 and 10 year Kaplan-Meier (95% confidence intervals) graft survival, with and without death censoring, was performed: using donor age (18–64 and 65+), donor KDPI (0–85, 86+), and eGFR-1 (<30, 31–44 and >45 ml/min). As death and graft loss during the first year precluded the eGFR-1 calculation, a separate analysis of recipients with first-year graft failure was performed.

A logistic regression model was used to assess donor/recipient variables associated with eGFR-1 greater or less than 45 ml/min. Multiple imputation—using 37 separate imputations to predict missing values (common among earlier transplants)—was necessary as OPTN data elements and collection policies changed over time (details in Supplement). Continuous predictors were parametrized using restricted cubic splines each, having three knots at the 10th, 50th (i.e., the median) and 90th percentiles of the respective data. Starting from a "full model" involving all of the imputed modelling data elements, a backwards variable selection procedure was used to remove predictors from the model until the Aikake Information Criteria (AIC) could not be further reduced. All analyses were performed using the R statistical software and associated packages [15,16].

2.3. Role of funding source

There was no funding source for this study. GV had access to the full dataset and all the authors decided to submit the manuscript for publication.

3. Results

3.1. Demographics of donors and recipients of kidneys from deceased donors greater or less than 65 years

Deceased donors over the age of 65 had a median KDPI of 92% (86%–96%; KDRI 1.90–2.36) compared to 41% (19%–63%; KDRI 0.94–1.45) for those under 65 years (Table 2). Donors >65 were more likely to be female, with fewer donations after circulatory death (DCD). Allocation policy intends to match organ potential with recipient need, so recipients of older kidneys were expected to differ from recipients of younger kidneys. The recipients of kidneys >65 years were older, median age of 65 (vs 54) years and had a higher prevalence of diabetes as the cause for ESRD. There was a higher use of dual kidney transplants with donors >65.

Table 1
Data from the OPTN database: criteria and exclusions.

Cohort	Inclusion Criteria	Number of Records
All kidney transplants during 2000–2018		298,394
Initial Cohort	*Adult deceased donor (18+ y.o.)* *Kidney-alone transplant* *No previous transplant* *Deceased-donor kidney*	139,363
Reduced Cohort	*Must have all data elements to compute eGFR (creatinine, age, sex, race, height)*	138,358
Reduced Cohort with eGFR-1	*Must have measured post-transplant creatinine within 90 days of 1-year after transplant*	118,802*
Reduced Cohort with eGFR-1 and Received Elderly-Donor Kidney	*Donor age 65+*	4615
Final Cohort	*Must not have experienced graft failure or death within first year posttransplant*	4545

* Among 19,556 patients excluded for not having a 1-year eGFR (+/- 90 days), nearly half (9248, 47.3%) could not contribute a measured eGFR because the patient experienced death or graft failure during the first year. An additional 1348 patients did not die or experience graft loss, but were otherwise lost to follow-up before they could contribute a measured creatinine within the 90-day period. The remaining 8960 had creatinine measurements taken at times that were too distant from the 1-year anniversary to be included in the study (e.g., 7127 measurements recorded at the 1-year follow-up visit were measured during the first 9 months after transplant).

Table 2
Demographic comparison of adult, deceased-donor, kidney-only, first transplants occurring between 01/01/2000 and 12/31/2018 by donor age >65 years.

	Donor Age 0–64	Donor Age >65	p-value
N (Transplants)	133,502	5861	—
Donor KDPI (median, IQR)	41% (19% - 63%)	92% (86% - 96%)	< 0.0001
Donor KDRI (median, IQR)	1.17 (0.94 - 1.45)	2.11 (1.90 - 2.36)	< 0.0001
Donor Sex: Female	53,023 (39.7%)	3104 (53.0%)	< 0.0001
Donor Creatinine (mg/dL; median, IQR)	1.00 (0.70 - 1.30)	0.90 (0.70 - 1.20)	< 0.0001
Donor Type: DCD	18,260 (13.7%)	142 (2.4%)	< 0.0001
Donor Cigarette Use: > 20 Pack-Years	39,059 (29.3%)	1796 (30.6%)	0.023
Share Type: Local Donor	100,320 (75.1%)	4122 (70.3%)	< 0.001
Candidate Sex: Female	51,909 (38.9%)	2199 (37.5%)	0.037
Candidate Race: White	56,829 (42.6%)	2759 (47.1%)	< 0.001
Candidate Race: Black	44,298 (33.2%)	1779 (30.4%)	
Candidate Race: Hispanic	21,238 (15.9%)	770 (13.1%)	
Candidate Race: Asian	8060 (6.0%)	446 (7.6%)	
Candidate Race: Other	3076 (2.3%)	107 (1.8%)	
Candidate BMI (kg/m^2; median, IQR)	27.5 (23.9 - 31.7)	27.3 (24.1 - 31.0)	0.019
Candidate DX at Listing: Diabetes	36,715 (27.5%)	2149 (36.7%)	< 0.0001
Candidate DX at Listing: Glomerular Diseases	27,277 (20.4%)	716 (12.2%)	
Candidate DX at Listing: Hypertensive Nephrosclerosis	33,974 (25.4%)	1655 (28.2%)	
Candidate DX at Listing: Polycystic Kidneys	11,236 (8.4%)	434 (7.4%)	
Candidate DX at Listing: Other	24,300 (18.2%)	907 (15.5%)	
Candidate PVD: Yes	8277 (6.2%)	422 (7.2%)	0.0040
Delayed Graft Function: Yes	34,759 (26.0%)	1773 (30.3%)	< 0.0001
Candidate Total Serum Albumin at Listing (g/dL; median, IQR)	4.0 (3.6 - 4.3)	4.0 (3.6 - 4.3)	0.19
Candidate ESRD Time (days; median, IQR)	944 (435 - 1605)	789 (370 - 1324)	< 0.0001
Transplant Type: Dual/En-Bloc	1256 (0.9%)	790 (13.5%)	< 0.0001
Cold Ischemic Time at Transplant (hours; median, IQR))	17.0 (11.5 - 23.0)	18.0 (13.0 - 24.0)	< 0.0001
Recipient Age at TX (years)	54 (43 - 62)	65 (58 - 70)	< 0.0001

3.2. Spectrum of deceased kidney transplant function stratified by donor age, KDPI and eGFR-1

Deceased kidney recipients demonstrated the expected decline in eGFR-1, as donor age increased (Fig. 1). The median recipient eGFR-1 after <45 year donor kidney transplant was 60 ml/min with 80% of recipients obtaining at least CKD 3a, (eGFR-1 >45 ml/min) and 95% of recipients better than CKD 3b (>30 ml/min). Kidney recipients from donors 46–64 years had a median eGFR-1 of 46 ml/min with 55% of obtaining at least CKD 3a and an additional 31.5% CKD 3b. However, recipients of kidneys from deceased donors >65 years had a median eGFR-1 of only 39 ml/min, with 35.6% of recipients gaining CKD 3a, 39.4% CKD 3b and 24.9% CKD 4 or 5 (>45, 30–44 and <30 ml/min, respectively). There were minimal KDRI/KDPI clinical differences between the three eGFR-1 ranges for recipients of >65 year kidneys (Table 3). The KDPI was 92% for recipients with one year eGFR-1 >45 ml/min (CKD3a), 93% for 30–44 ml/min (CKD 3b) and 94% for <30 ml/min (CKD 4/5). Recipients with the lower eGFR-1 (< 30 ml/min); trended towards being female and more frequently black. Asians and Hispanics were more common with the higher eGFR-1. Diabetes-related ESRD and a longer duration of dialysis was more common in the higher eGFR groups. While statistically significant as categorical features, there were few clinical distinctions between these groups.

As recipient comorbidities affect patient survival, death censoring was used to discern the impact of eGFR-1 upon the duration of graft survival. Death-censored 5 and 10-year graft survival (95% CI) for recipients of >65 year donor kidneys (KDPI 92%) and an eGFR-1 >45 ml/min was 94% (92.2%–94.9%) and 77% (73.4%–80.4%). This was nearly identical to the 5 and 10-year survival (93% [93.2%–93.6%] and 80% [79.9%–80.8%]) observed in recipients of younger kidneys (KDPI 41%) (Fig. 2a). These outcomes are striking as the younger donor group includes the >30,000 transplants from donors <45 years and an eGFR-1> 60 ml/min. A similar pattern was seen in eGFR-1 of 31–44 ml/min (CKD 3b) recipients, with 5 and 10-year death-censored graft survival from “older” and “younger” kidney donors being similar, 89% (87.3%–90.6%) and 63% (59.5%–66.4%) vs 86% (85.5%–86.4%) and 65% (64.1%–65.8%) graft function

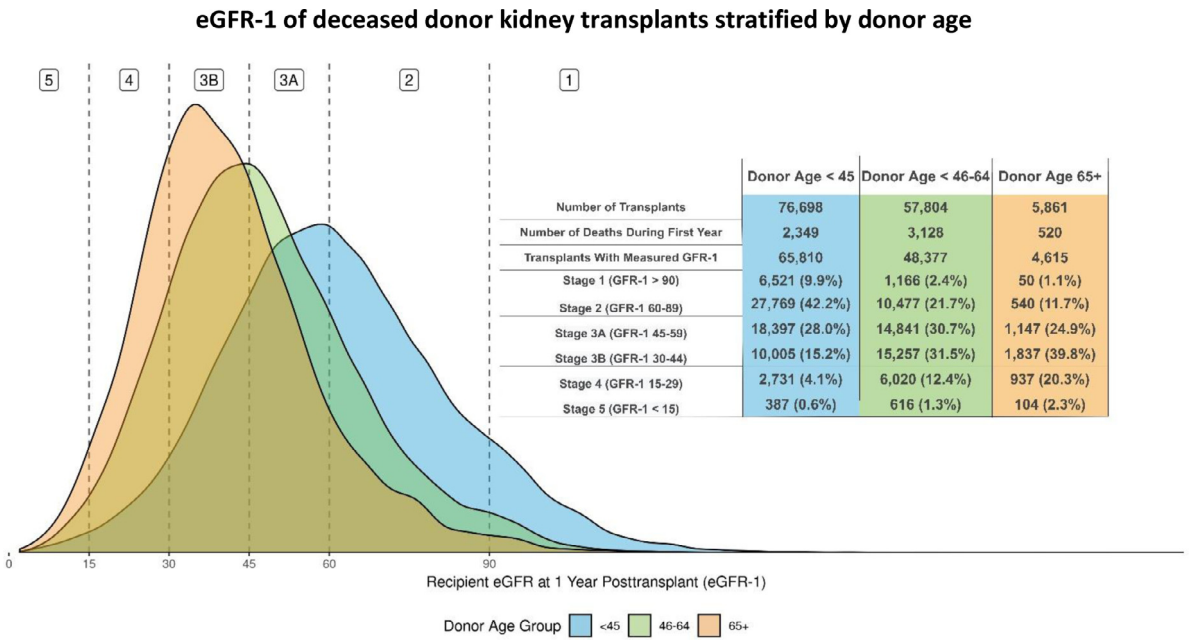

Fig. 1. Distribution of eGFR-1 observed in adult deceased donor kidney transplant recipients segregated by donor age. <45 years (blue), <46–64 years (green) and 65+ years (orange).

Table 3
Demographics of > 65 year Deceased Donor kidney transplants surviving one year and stratified by eGFR-1.

	Recipient eGFR-1			p-value
	<30 ml/min	31–44 ml/min	>45 ml/min	
Number	1133	1792	1620	
Donor KDPI (median, IQR)	94% (88% - 97%)	93% (87% - 96%)	92% (86% - 96%)	< 0.0001
Donor KDRI (median, IQR)	2.16 (1.93 - 2.43)	2.11 (1.90 - 2.33)	2.07 (1.86 - 2.30)	< 0.0001
Donor Sex: Female	598 (52.8%)	977 (54.5%)	842 (52.0%)	0.26
Donor Creatinine (mg/dL; median, IQR)	1.00 (0.80 - 1.29)	0.90 (0.70 - 1.20)	0.90 (0.70 - 1.20)	< 0.0001
Donor Type: DCD	42 (3.7%)	39 (2.2%)	25 (1.5%)	0.0020
Donor Cigarette Use: > 20 Pack-Years	42 (3.7%)	39 (2.2%)	25 (1.5%)	0.063
Share Type: Local Donor	801 (70.7%)	1274 (71.1%)	1138 (70.2%)	0.87
Candidate Sex: Female	487 (43.0%)	686 (38.3%)	572 (35.3%)	< 0.0001
Candidate Race: White	486 (42.9%)	885 (49.4%)	755 (46.6%)	< 0.0001
Candidate Race: Black	492 (43.4%)	528 (29.5%)	347 (21.4%)	
Candidate Race: Hispanic	90 (7.9%)	223 (12.4%)	298 (18.4%)	
Candidate Race: Asian	53 (4.7%)	123 (6.9%)	177 (10.9%)	
Candidate DX at Listing: Diabetes	377 (33.3%)	653 (36.4%)	637 (39.3%)	0.024
Candidate DX at Listing: Glomerular Diseases	138 (12.2%)	236 (13.2%)	194 (12.0%)	
Candidate DX at Listing: Hypertensive Nephrosclerosis	363 (32.0%)	478 (26.7%)	427 (26.4%)	
Candidate DX at Listing: Polycystic Kidneys	94 (8.3%)	140 (7.8%)	123 (7.6%)	
Candidate PVD: Yes	72 (6.4%)	123 (6.9%)	123 (7.6%)	0.49
Delayed Graft Function: Yes	400 (35.3%)	454 (25.3%)	304 (18.8%)	< 0.0001
Candidate Total Serum Albumin at Listing (g/dL; median, IQR)	3.9 (3.6 - 4.3)	4.0 (3.7 - 4.3)	4.0 (3.6 - 4.3)	0.21
Candidate ESRD Time (days; median, IQR)	744 (383 - 1268)	791 (356 - 1355)	825 (418 - 1361)	0.0080
Transplant Type: Dual/En-Bloc	99 (8.7%)	183 (10.2%)	349 (21.5%)	< 0.0001
Cold Ischemic Time (hours; median, IQR)	18.0 (13.0 - 24.0)	18.0 (13.1 - 23.7)	17.6 (12.8 - 24.0)	0.15
Recipient Age at TX (years; median, IQR)	64 (58 - 69)	65 (58 - 70)	65 (59 - 70)	0.041

respectively. For recipients with eGFR-1 <30 ml/min (CKD 4/5), the 5 and 10 year death-censored kidney function was lower, 62% (59.3% - 65.8%) and 36% (31.5%–40.3%), from >65 year kidneys, but still similar to younger kidneys. The donor KDPI had a poor correlation with 5 and 10-year graft survival contrasted to eGFR-1 (Fig. 3), only kidneys with a KDPI >95% had statistically significant lower graft survival.

3.3. Long-term graft survival, including patient death

The median recipient age of >65 year deceased kidneys was 65 (IQR = 58–70) years, over a decade older than the median age (54 years, IQR = 43–62) of recipients of younger grafts. It is expected that older recipients would die more frequently than younger recipients. When recipient death is included as a cause of graft loss, the graft survival was lower in the recipients of kidneys > 65 years. Graft survival that includes recipient death with deceased donors aged less or greater than 65 years was; 86% (85.6%–86.1%) vs 78% (75.3%–79.7%), 76% (75.6%–76.8%) vs 74% (71.6%–76.0%) and 51 (50.4%–52.5%) vs 48% (45.3%–51.5%); if the eGFR-1 was >45, 30–44 or <30 ml/min. (Fig. 2b).

3.4. One year patient and graft survival

eGFR-1 calculations can only be made when the patient and graft survive for a year. Younger recipients (< 65 years, median age 54

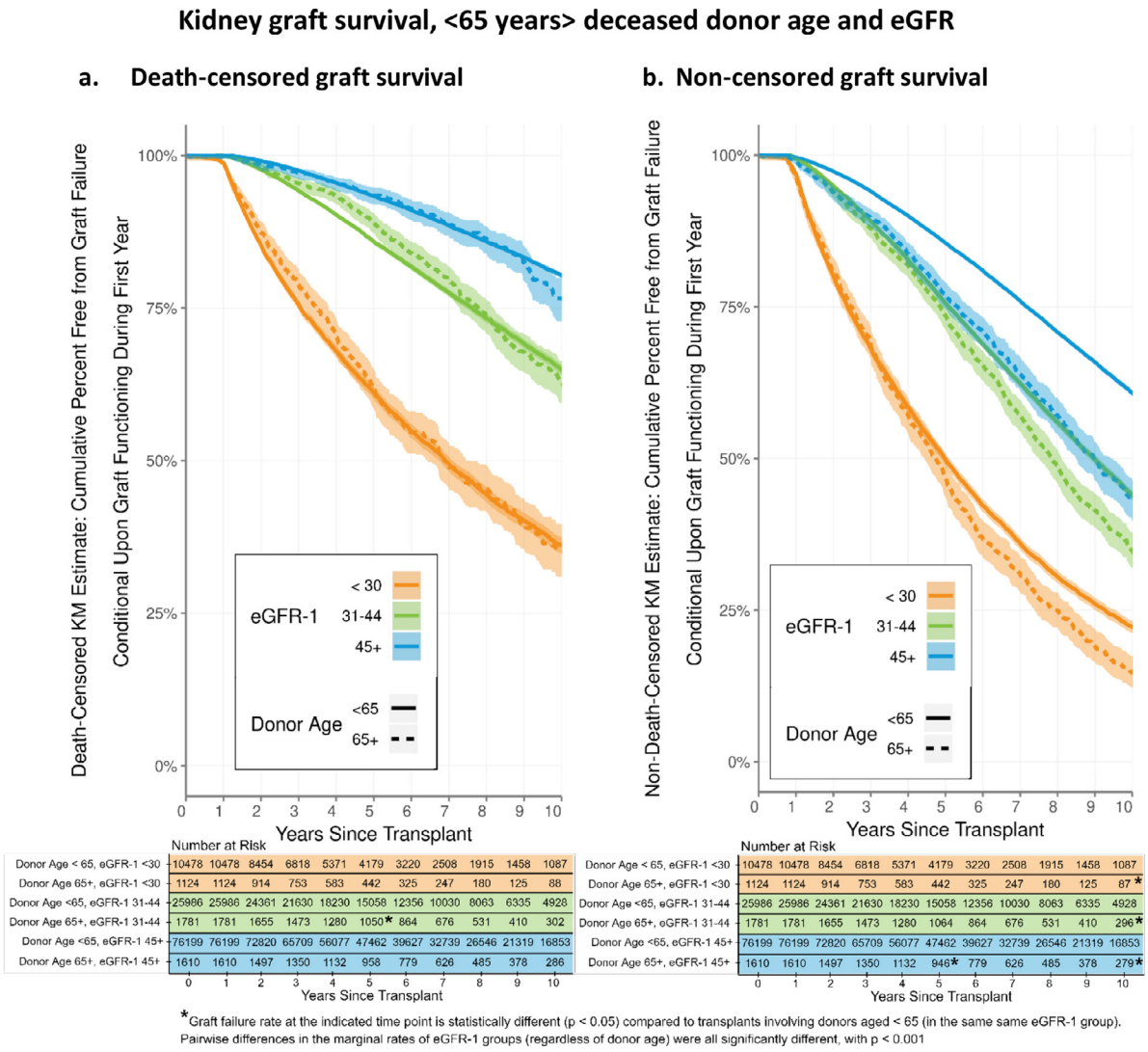

Fig. 2. Death-censored (a) and non-death-censored (b) Kaplan-Meier Graft Failure Rates (95% CIs) categorized by deceased donor age and recipient eGFR-1. Solid lines kidney transplants from donors < 65 years, dashed lines were from donors over 65 years. Solid lines incorporate the 95% CI. Renal function stratified <30 ml/min (orange), 31–44 ml/min (green) and >45 ml/min (blue).

years) receiving a kidney from a deceased donor <65 years had an aggregate one-year graft survival rate of 93.0%, with a 3.34% one year mortality. All but 0.8% of the deaths occurred with a functioning graft (Table 4). In contrast, the older recipients of kidneys >65 years were over a decade older with a one-year graft survival of 84.4% and a 10.7% one-year mortality (7.08% died with a functioning graft and 3.6% died after the kidney failed).

There were no clinically relevant differences of measured organ quality (KDPI 93 vs 92, $p<0.001$) or recipient characteristics between the older recipients that died or survived (Table 5). A higher rate of delayed graft function was observed in non-survivors, 48.3 vs 28.5%. The vast majority of deaths were attributed to cardiac events, stroke or infection. There were the expected statistical associations with death (slight increase in age, slightly higher KDRI), but clinical predictions of survival or death within first year was not possible from the OPTN data.

3.5. Survival benefit stratified by eGFR-1

A successful kidney transplant should confer some form of (survival) benefit compared to remaining on the waitlist. To determine long-term benefit of eGFR-1, the survival curves were superimposed upon the survival point when eGFR-1 was calculated. Kidney recipients from a deceased donor >65 years (older, median age 65) had a 91.1% graft survival and 95.9% of recipients of <65 year kidneys were alive after one year with a surviving graft. The recipients of *a* >65 year kidney achieving an eGFR-1 of >45, 30–44 and <30 ml/min had a 5-year survival of 72.5% (70.5%–74.3%), 71.9% (70.0%–73.7%) and 58.8% (56.0%–61.4%) (Fig. 3) after transplantation. The cohort of similar candidates remaining on the waitlist had a 68.4% (66.0%–71.0%) 5-year survival (Fig. 4). The recipients of *a* >65 year old kidneys achieving an eGFR-1 of 30–44 or >45 ml/min demonstrated no significant survival benefit after Bonferroni correction at 5 or 10 years post-transplant (statistical comparisons for each eGFR-1 group at each time point used Bonferroni-adjusted α-levels of 0.05/6 = 0.008), although the overall survival trended better than the waitlist cohort (Supplement). Recipients with an eGFR-1 <30 ml/min, never achieved survival equivalence (p <0.001).

3.6. Logistic regression predicting achievement of eGFR-1> 45

A logistic regression model was used to determine, among recipients of donor kidneys 65 or older, which factors best predicted achievement of eGFR-1 >45 ml/min. A final model considering donor

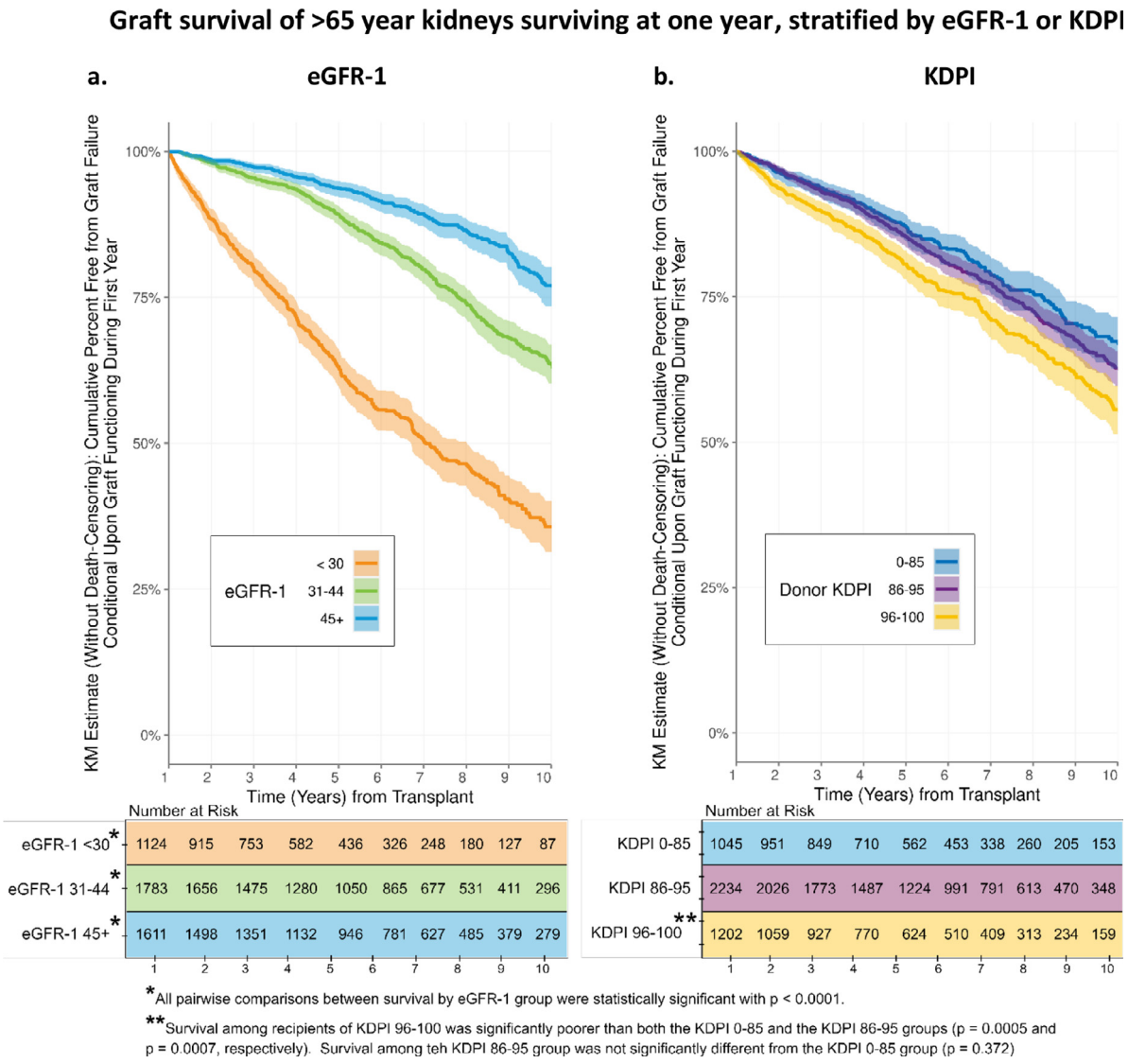

Fig. 3. Kaplan-Meier Graft Failure Rates (95% CIs) of deceased donor >65 years, kidney transplants surviving one year, subsequent graft survival is stratified by either a) recipient eGFR-1 or b) donor KDPI. eGFR stratifications: <30 ml/min (orange), 31–44 ml/min (green), >45 ml/min (blue). KDPI stratifications, 0–85% (blue), 86–95% (purple) and 96–100% (gold).

Table 4
One-Year Patient Death and Graft Failure Rates, With and Without Inclusion of Deaths with a Functioning Graft. Categorized by Donor Age and Recipient Age.

	Graft Failure Rate (Includes Patient Deaths)		Graft Failure Rate (Excluding Deaths with a Functioning Graft)		Patient Death Rate	
	Donors 18–64 (*N* = 133,502)	Donors 65+ (*N* = 5861)	Donors 18–64 (*N* = 133,502)	Donors 65+ (*N* = 5861)	Donors 18–64 (*N* = 133,502)	Donors 65+ (*N* = 5861)
Recipients 0–64 (*N* = 111,300)	$\frac{7643}{108407} = 7.05\%$	$\frac{431}{2894} = 14.9\%$	$\frac{4915}{108407} = 4.53\%$	$\frac{290}{2894} = 10.0\%$	$\frac{3624}{108407} = 3.34\%$	$\frac{202}{2894} = 6.98\%$
Recipients 65+ (*N* = 28,063)	$\frac{2692}{25095} = 10.7\%$	$\frac{464}{2967} = 15.6\%$	$\frac{1294}{25095} = 5.16\%$	$\frac{254}{2967} = 8.56\%$	$\frac{1853}{25095} = 7.38\%$	$\frac{318}{2967} = 10.7\%$

type, KDPI, BMI, diagnosis, ESRD time, transplant type, insurance type, and clinical infections resulted in only a moderate-to-weak ability to discriminate those with eGFR-1 >45 from those who did not reach this threshold (AUC = 0.649). Although the overall model performance was lacking, recipients of dual transplants had over 3 times (3.63, 3.01 – 4.38) greater odds of achieving eGFR-1 compared to single-KI recipients.

4. Discussion

This analysis reconfirms the association between the amount of transplant kidney function after a year (eGFR-1) and ten-year kidney allograft survival. Importantly, kidneys from deceased donors over 65 years did not have accelerated graft loss when stratified by eGFR-1. The recipient of a donor kidney > 65 years and obtaining an eGFR-

Table 5
Deceased-Donor Kidney Transplants from Deceased Donors >65 years; Patient Status (Alive/Deceased) During the First Year.

	Recipient Survived First Year Posttransplant	Recipient Death During First Year Posttransplant	p-value
N	5341	520	
Donor KDPI	92% (86% - 96%)	93% (87% - 97%)	< 0.001
Donor KDRI	2.11 (1.90 - 2.36)	2.16 (1.93 - 2.43)	< 0.001
Donor Sex: Female	2833 (53.0%)	271 (52.1%)	< 0.001
Donor Creatinine	0.90 (0.70 - 1.20)	1.00 (0.80 - 1.21)	< 0.001
Donor Type: DCD	128 (2.4%)	14 (2.7%)	0.115
Donor Cigarette Use: > 20 Pack-Years	1632 (30.6%)	164 (31.5%)	< 0.001
Share Type: Local Donor	3747 (70.2%)	375 (72.1%)	< 0.001
Candidate Sex: Female	2021 (37.8%)	178 (34.2%)	< 0.001
Candidate Race: White	2488 (46.6%)	271 (52.1%)	< 0.001
Candidate Race: Black	1629 (30.5%)	150 (28.8%)	
Candidate Race: Hispanic	709 (13.3%)	61 (11.7%)	
Candidate Race: Asian	414 (7.8%)	32 (6.2%)	
Candidate BMI	27.30 (24.20 - 31.00)	27.10 (24.00 - 31.22)	< 0.001
Candidate DX at Listing: Diabetes	1948 (36.5%)	201 (38.7%)	< 0.001
Candidate DX at Listing: Glomerular Diseases	675 (12.6%)	41 (7.9%)	
Candidate DX at Listing: Hypertensive Nephrosclerosis	1488 (27.9%)	167 (32.1%)	
Candidate DX at Listing: Polycystic Kidneys	410 (7.7%)	24 (4.6%)	
Candidate PVD: Yes	375 (7.0%)	47 (9.0%)	< 0.001
Delayed Graft Function: Yes	1522 (28.5%)	251 (48.3%)	< 0.001
Candidate Total Serum Albumin at Listing	4.0 (3.6 - 4.3)	3.9 (3.5 - 4.2)	< 0.001
Candidate ESRD Time (days)	789 (375 - 1328)	784 (328 - 1305)	0.024
Transplant Type: Dual/En-Bloc	719 (13.5%)	71 (13.7%)	< 0.001
Cold Ischemic Time	18.00 (13.00 - 24.00)	18.89 (13.32 - 24.13)	< 0.001
Recipient Age at TX	64 (58 - 70)	66 (61 - 71)	< 0.001

1 >45 ml/min had 5 and 10-year graft survival (barring death of the recipient) similar to younger recipients receiving younger kidneys and obtaining a similar eGFR-1. Dual transplants more often provided an eGFR-1 >45 ml/min. However, differences in death or graft failure were not observed with the only significant stratification being amount of eGFR provided.

Kidney transplantation is a superior therapy for ESRD contrasted to dialysis [2,17]. Transplanting lower quality kidneys using the "extended criteria donor" [18] definition or the "high KDPI" kidney [19] has demonstrated a consistent survival benefit after the risks of the peri-operative period have passed. The iBOX score reliably predicts outcomes, but is dependent upon information not within the OPTN database (post-transplant biopsy results and alloantibodies) [20]. The first year risks to recipients of greater> 65 year kidneys ("older" kidneys go to older recipients, mimicking the "old to old" European program) is substantial, with a lower 1-year survival than remaining on the waitlist (89.3 vs 97%), consistent with prior reports [21–25]. If the transplanted kidney provided at least 30 ml/min eGFR-1 (better than CDK3b), the five year survival was similar and trended better than the waitlist cohort. However, recipients of older kidneys and an eGFR-1< 30 ml/min, *never* achieved similar survival observed in the cohort group.

Young adult deceased donor kidneys have long been the "standard", providing predictable transplant outcomes. Accordingly, over 60% of US adult deceased kidney transplants use kidneys from deceased donors under 45 years [2], but more (quality) kidneys are needed. In 2018, there were >2.8 million deaths in the US and fewer than 170,000 deaths occurred in adults <45 years. Over 900,000 deaths were in people 55–75 years [26]. Despite greater than five-fold more deaths, kidneys from this older age group accounts for only 16% of kidney transplants. Additionally, over 40% of the kidneys retrieved from older donors were not transplanted (discarded). 543,778 deaths occurred in individuals 65–74 years, yet only 298 kidneys were transplanted. From this analysis, it is likely that many of these deaths could have provided kidneys with excellent long-term dialysis relief.

Analysis of the US transplant experience from almost 20 years of OPTN data has inherent limitations. While most data are very reliable {patient and graft survival, age and gender, KDPI), there are issues with completeness and timing of data entry (of 138,358 recipients, 6% did not have data for an eGFR-1 calculation within the ninety-day window), historical and added/differing medical elements can produce variance. The large transplant numbers mitigate the inherent internal data vagaries. Medical care, donor/recipient characteristics and immunosuppression have gradually changed over time, but have not created "transplant eras". Center criteria for organ and recipient selection are highly individualistic, and not available. All these add to outcomes variability.

Despite these uncertainties, the large number of transplants minimizes the vagaries and permits the basic questions to be addressed: is the duration of kidney graft function significantly impacted by donor age and can eGFR-1 serve as a metric to supplement (not replace) one-year graft survival? In the absence of recipient death, kidney donor age is not associated with accelerated graft loss and eGFR-1 was a good surrogate for 5 and 10-year graft function, independent of donor age. This analysis reinforces that death within the first year remains a major barrier to survival benefit for older candidates. As the >65 year recipient of a live donor kidney only has a 2.7% one mortality [27], there should be an expectation that the risk/benefit relationship could be modified. Failure to reach a specified degree of kidney function is deleterious and should be candidate specific. This analysis focused upon graft survival from older kidneys (usually put into older recipients) and didn't address the quality of life issues for all recipients; when poor graft function results in repeated hospitalizations, biopsies, immunosuppression modifications and infections. Achieving sufficient kidney function is an important outcome.

Tools to predict perioperative survival and subsequent durability of graft survival need attention. This analysis confirms the benefit and the uncertainty of transplanting older donor kidneys. The benefit is real, over three quarters of recipients achieved survival equivalence and many more would have survival benefit, if one year mortality was similar to age-matched live donor recipients. However, almost a quarter of older donor kidney transplant recipients had a survival outcome that was worse than the waitlist cohort. The differential use of "older" kidneys between the US and Europe appears to center upon acceptance of perceived risk vs. probable benefit. There should

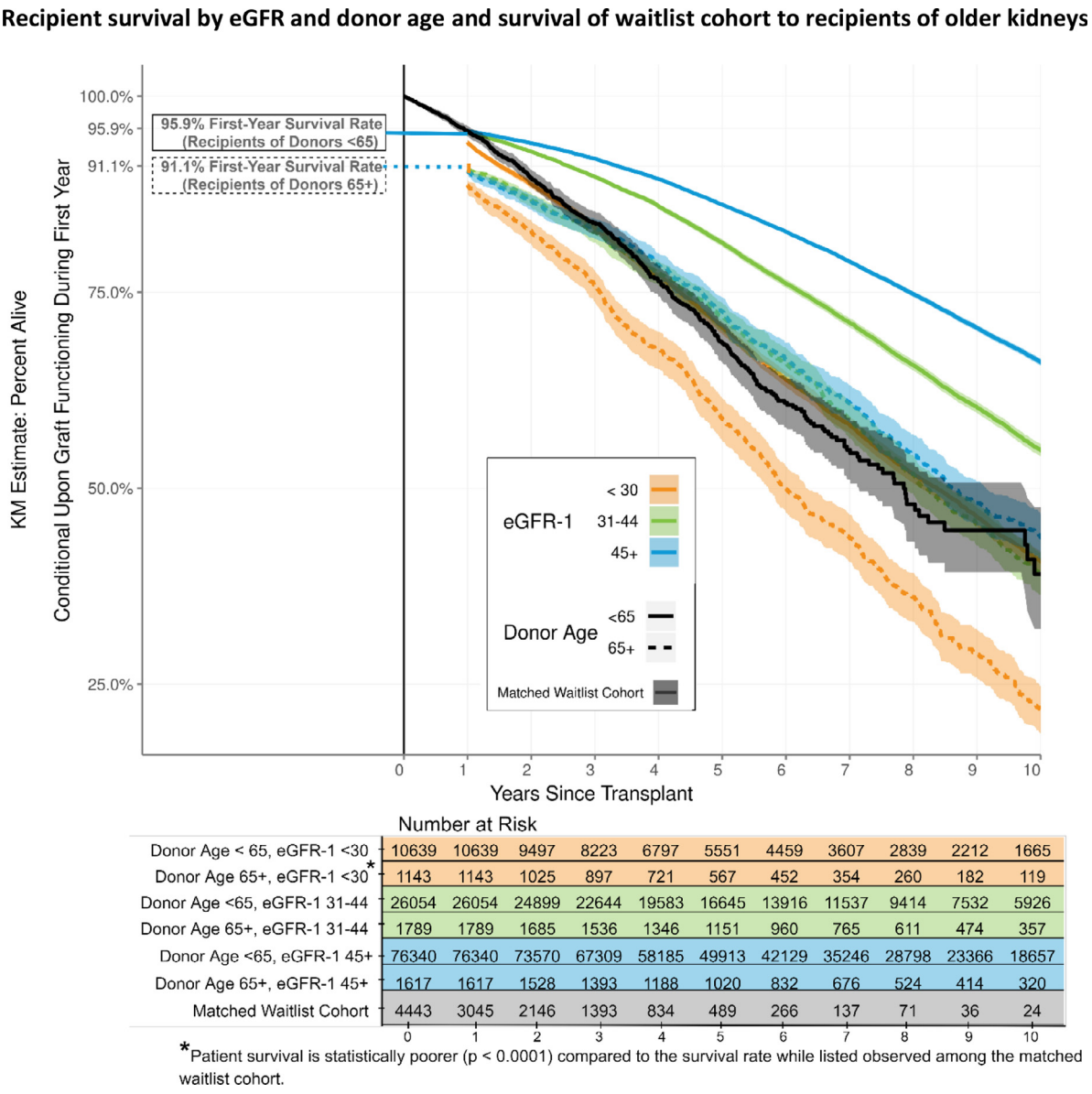

Fig. 4. Kaplan-Meier recipient survival (95% CIs) stratified by deceased donor age and the amount of recipient eGFR-1 (<30 ml/min (orange), 31–44 ml/min (green) and >45 ml/min (blue)). Survival of non-transplanted cohort of candidates awaiting kidney transplant, who were matched to recipients of >65 year kidneys, is shown (solid black line). Because the measurements of eGFR after one year necessitates survival for the first year, KM estimates begin at the observed one-year survival rate observed for each donor age group. The cohort survival was 100% at the time of matching with recipients.

be methods to clarify the risk/benefit decisions necessary for acceptance of older donor kidneys for transplantation. Others have used kidney volumes [28,29], histology [30,31], deceased donor ICU management [32,33] or pumping characteristics [34,35] to aid quality assessment. While each may have marginal univariate predictability, it is probable that machine-learning algorithms could to improve reliability.

This analysis puts quantitative measures onto outcomes that are clinically obvious to clinicians. Older donor kidneys can provide excellent long-term outcomes, but are presently unpredictable. The OPTN definition of one-year graft survival does predict long-term function, but the data includes the ability to calculate eGFR-1, which is a good surrogate for 10-year graft survival (off dialysis). Transplantation is a predictable ESRD treatment, but increasing demand requires more kidneys that provide similar outcomes as seen with kidneys from younger donors. Older donor kidneys can provide excellent long-term function (eGFR-1 >45 ml/min) and should be available in larger numbers. However, better predictive tools are required to assess renal function.

Declaration of Competing Interest

TP is a Board member of an Organ Procurement Organization (Lifesource). All the other authors declare no conflicts of interest.

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Data sharing

This study used the Organ Procurement and Transplantation Network (OPTN) database that includes information on donors, wait-

listed candidates, and transplant recipients in the U.S., and has been described at https://optn.transplant.hrsa.gov/data/about-data/. The Health Resources and Services Administration (HRSA), U.S. Department of Health and Human Services provides oversight to the activities of the OPTN contractor. All data used in this study are publicly available from the OPTN. Processes to obtain the data are enunciated on the OPTN website, found here: https://optn.transplant.hrsa.gov/data/request-data/data-request-instructions/.

Contributors

TP and GV developed the initial hypothesis. GV and RC collected, organized and performed final statistical analysis of data. TP, GV, RC and DK analyzed data and generated conclusions. TP was primary author of manuscript and incorporated edits and suggestions from GV, RC and DK. There is agreement amongst all authors about the content and interpretation.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.eclinm.2021.100980.

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