Safety and Efficacy of Kidney Transplants From Older Adult Living Donors: A Comparative Analysis of Donor and Recipient Outcomes

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Abstract

Objectives: **We investigated the safety of donor nephrectomy from older adult donors (age ≥60 years), as well as long-term donor, recipient, and graft outcomes.**
Materials and Methods: **We retrospectively analyzed data from 307 living donor kidney transplants from 1996 to 2016 and defined 2 cohorts based on donor age. Cohort A comprised donors aged 60 years and older, and cohort B comprised donors from 18 to 59 years old. We recorded donor and recipient perioperative complications, outcomes, and survival rates and used SPSS and MedCalc statistical software programs for data analyses.**
Results: **The mean follow-up period for donor-recipient pairs in cohort A was 97 months (SD, 25.1 months) with median 108 months (IQR, 92-108 months) and in cohort B was 100.57 months (SD, 25.45 months) with median 120 months (IQR, 84-120 months). Mean donor age in cohort A was 64.13 years (SD, 3.78 years) with median 63 years (IQR, 61-66.5 years) and in cohort B was 41.08 years (SD, 9.15 years) with median 41 years (IQR, 34.5-48 years) (*P* < .001, cohort A vs B). Mean recipient age in cohort A was 47.65 years (SD, 14.26 years) with median 48.5 years (IQR, 35.5-61 years) and in cohort B was 43.55 years (SD, 13.15 years) with median 40.5 years (IQR, 33.5-54 years) (*P* < .001, cohort A vs B). Both cohorts showed no significant differences in perioperative donor and recipient complications. Renal function (measured as estimated glomerular filtration rate) in remaining native kidneys of cohort A showed no significant decline during median 8-year follow-up (*P* = .089 and *P* < .414, respectively). There were no significant differences in survival rates for donors, recipients, and grafts.**
Conclusions: **Living donor kidney transplant from older adult donors is safe and effective with good long-term patient and allograft survival.**

Key words: *Estimated glomerular filtration rate, Graft survival, Living donor kidney transplant*

Introduction

Kidney transplant is considered the gold standard treatment for patients with end-stage renal disease. Despite attempts by the transplant community to increase the number of available donor organs,[1-4] the gap between organ supply and demand remains large.[5] There have been major improvements in outcomes of deceased donor transplants, including improvements in the process of donation and procurement,[6] the use of organs from extended criteria donors,[1,7] better utilization of organs from deceased pediatric donors,[8] dual-kidney transplants,[9,10] use of kidneys from donors after cardiac death, and recent favorable changes in the laws governing the opt-out system.[11] For living donor renal transplants, the recently established National Kidney Sharing Scheme is a major recent advancement.[12]

Age is an important factor for assessment of living donor suitability, and older donors may be considered marginal.[13,14] Although age above 60 years is not considered an absolute contraindication for transplant, it remains an unfavorable factor.[15,16] The global population is aging,[17] and this swing in population dynamics has changed the demographics of potential donors. Therefore, it is important to understand the effects of these donor characteristics on transplant outcomes. Here, we describe our experience with living donor kidney transplants

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from donors 60 years old and older, with a focus on donor safety and long-term survival.

Materials and Methods

We retrospectively analyzed the data for the living donor kidney transplant program at St George's University Hospitals NHS Foundation Trust in London from 1996 to 2016. A total of 564 living donor kidney transplants were performed during this period, and 101 of these transplants were from donors aged 60 years or older. Of these 101 older adult donor transplants, there were 72 for which the required data were available; this group was defined as study cohort A. The primary reasons for exclusion were lack of complete follow-up data on graft outcome (n = 13), participation in the National Kidney Sharing Scheme (n = 6), and lack of availability of predonation and postdonation medical records (n = 10).

We recorded donor and recipient demographics and baseline characteristics and analyzed the following donor outcomes: postoperative complications, predonation and postdonation renal function, and donor survival. We also analyzed the following recipient outcomes from those kidneys: postoperative complications, graft function, recipient survival, and graft survival. Graft failure was defined as either (1) return to dialysis or (2) preemptive transplant. For standardization, all renal functions were recorded as estimated glomerular filtration rates (eGFR) calculated with the Chronic Kidney Disease Epidemiology Collaboration equation. We compared these results with results from our standard-criteria adult living donor kidney transplants from donors aged 18 to 59 years (control cohort B). During the same period (1996-2016), there were 463 living donor renal transplants performed in cohort B. Exclusion criteria were altruistic donation, National Kidney Sharing Scheme participation, and unavailability of required study data (for example, due to loss of follow-up or transfer of care to other hospitals), after which there remained 235 patients in cohort B. The mean follow-up period (and the corresponding median value) for the donor-recipient pairs in cohort A was 97 months (SD, 25.1 months) with median 108 months (IQR, 92-108 months) and in cohort B was 100.57 months (SD, 25.45 months) with median 120 months (IQR, 84-120 months).

We used the SPSS and MedCalc software statistical programs for data analyses. Baseline characteristics and postdonation outcomes were compared with a *t* test, the Fisher exact test, chi-square test, or the Mann-Whitney U test, as appropriate. We used box-whisker plots to present the data (mean values, SD, and SEM). We used Kaplan-Meier estimates for survival analyses and a log-rank test for differences in survival. Recipient and graft survival analyses were performed for cohorts A and B and represented participants of the present study population with full follow-up datasets (n = 307), as well as overall living donor transplants performed during the same period (n = 564).

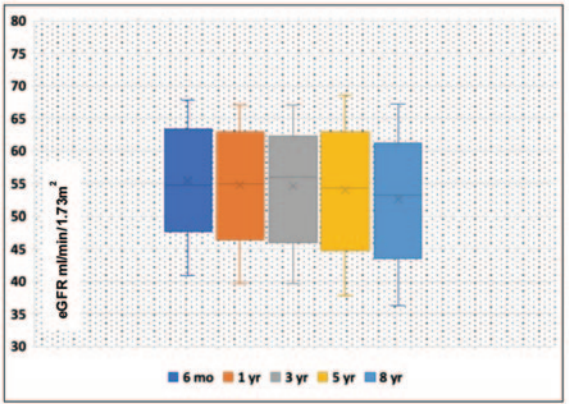
This study was in compliance with local ethical and data protection policies and is registered with the audit department of the St George's University Hospitals NHS Foundation Trust (No. DB 326 Jan 2014), and the online assessment tool confirmed that NHS HRA/REC approval was not required.

Results

Donor demographics and outcomes

These are presented in Table 1, Table 2, Table 3, and Figure 1. The mean donor age in cohort A was 64.13 years (SD, 3.78 years) with median 63 years (IQR, 61-66.5 years) and in cohort B was 41.08 years (SD, 9.15 years) with median 41 years (IQR, 34.5-48 years). Female donors provided more than half of the organs in both groups (Table 1). There were 39 donations (54%) from related donors in cohort A compared with 185 (78%) in cohort B ($P < .001$). There were also significantly more parental and spouse donations in cohort A compared with cohort B ($P = .002$ and $P = <.001$, respectively). However, there were significantly more donations from siblings and children in cohort B compared with cohort A ($P < .001$ and $P \leq 0.004$, respectively) (Table 2).

Figure 1. Postdonation Estimated Glomerular Filtration Rate of Native Kidney in Older Adult Donors (Cohort A)



Abbreviations: eGFR, estimated glomerular filtration rate

The pre-donation mean eGFR in cohort A was 86.73 mL/min/1.73 m^2 (SD, 11.56 mL/min/1.73 m^2) and in cohort B was 93.51 mL/min/1.73 m^2 (SD, 13.42 mL/min/1.73 m^2) (P < .001). The median eGFR in cohort A was 87 mL/min/1.73 m^2 (IQR, 80-97 mL/min/1.73 m^2) and in cohort B was 94 mL/min/1.73 m^2 (IQR, 85-101 mL/min/1.73 m^2). The postdonation mean eGFR values between the 2 cohorts were also significantly different at 2, 6, 12, 36, and 60 months (Table 1). The function of the remaining native donor kidneys in cohort A donors (study population) was further investigated, and there was no significant deterioration in eGFR from 6 months to 8 years after kidney donation (P = .089) (Figure 1).

There were no significant differences in perioperative complications in both cohorts (Table 3). The mean hospital stay in both groups was 3 days with no significant difference (P = .542).

Recipient demographics and outcome

There was a higher proportion of male recipients in both groups: 59% of cohort A and 62% of cohort B. The mean recipient age in cohort A was 47.65 years (SD, 14.26 years) with median 48.5 years (IQR, 35.5-61 years) and in cohort B was 43.55 years (SD, 13.15 years) with median 40.5 years (IQR, 33.5-54 years) (P< .001, cohort A vs cohort B). Preemptive transplants and 2 human leukocyte antigen DR mismatch transplants were more common in recipients of organs from cohort A donors than from cohort B donors (P < .042 and P <. 009, respectively) (Table 4). These findings reflect a trend for spousal donation at older age. There were no significant differences in postoperative complications and outcomes between the 2 groups (Table 5).

Table 1. Comparison of Basic Donor Demographics and Postdonation Outcomes

	Cohort A (≥60 y) (N = 72)		Cohort B (18-59 y) (N = 235)		*P*
	Mean	SD	Mean	SD	
Age, y	64.13	3.78	41.08	9.15	<.001
BMI	26.76	3.89	27.69	4.91	.142
eGFR, mL/min/1.73 m^2					
Predonation	86.73	11.56	93.52	13.42	<.001
2 wk postdonation	54.84	12.74	58.95	9.20	<.003
6 mo postdonation	54.35	12.31	58.05	9.17	.006
1 y postdonation	53.30	11.75	56.80	8.56	.006
3 y postdonation	52.73	11.69	56.48	9.67	<.007
5 y postdonation	51.33	11.86	55.43	9.52	<.003
Hospital stay, d	3.53	3.42	3.55	3.35	.965

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); eGFR, estimated glomerular filtration rate

Table 2. Relationship of Donors to Recipients

	Cohort A (≥60 y) (N = 72)	Cohort B (18-59 y) (N = 235)	*P*
Related donor, No. (%)	39 (54)	185 (78.7)	<.001
Parent	27 (37.5)	49 (20.8)	.002
Sibling	8 (11.1)	93 (39.5)	<.001
Daughter/son	1 (1.4)	39 (16.5)	<.001
Other[a]	3 (4.1)	4 (1.7)	.102
Unrelated donor, No. (%)	33 (46)	50 (21.2)	<.001
Spouse/partner	25 (34.7)	37 (15.7)	<.001
Other[b]	8 (11.1)	13 (5.5)	.076

[a]Half-sister/brother, grandchild, or grandparent. [b]Uncle/aunt, niece/nephew, or cousin.

Table 3. Comparison of Donor Perioperative Complications

Donor Complication	No. of Donors (%)		*P*
	Cohort A (≥60 y) (N = 72)	Cohort B (18-59 y) (N = 235)	
Conversion[a]	1 (1.38)	4 (1.7)	.429
Reexploration[b]	1 (1.38)	3 (1.27)	.469
Hemorrhage[c]	2 (2.77)	5 (2.12)	.371
Chest infection[d]	2 (2.77)	7 (2.97)	.467
Wound infection[d]	4 (5.55)	13 (5.53)	.494
UTI[d]	3 (4.16)	9 (3.82)	.446
VTE[e]	1 (1.38)	3 (1.27)	.469

Abbreviations: UTI, urinary tract infection; VTE, venous thromboembolism Values are No. of donors (%). The proportions were compared with the chi-square test or the Fisher exact test. [a]Laparascopic to open. [b]Wound reexploration. [c]More than 500 mL blood loss. [d]Required antibiotics. [e]VTE within 90 days of surgery.

Table 4. Comparison of Baseline Recipient Characteristics Between Cohort A Donors and Cohort B Donors

Recipient Variable	Cohort A (≥60 y) (N = 72)		Cohort B (18-59 y) (N = 235)		*P*
	Mean	SD	Mean	SD	
Age, y	50.81	14.36	42.98	16.16	<.001
BMI	27.66	4.81	28.29	5.45	.379
Dialysis duration, mo	12.61	10.39	10.58	9.68	.127
WIT, min	4.70	2.87	4.78	2.83	.834
CIT, min	104.68	74.81	110.11	83.09	.564
Hospital stay, d	6.49	2.31	6.65	2.16	.770
Complication, No. (%)					
Preemptive transplant	23 (32)		52 (22)		<.042
HLA-2 DR MM	19 (26)		33 (14)		<.009

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CIT, cold ischemia time; HLA-2 DR MM, human leukocyte antigen DR mismatch; WIT, warm ischemia time

Table 5. Comparison of Recipient Postoperative Complications

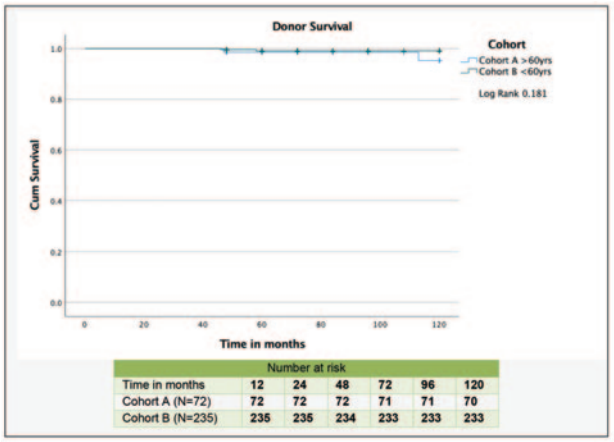
Recipient Complication	No. of Recipients (%))		*P*
	Cohort A (≥60 y) (N = 72)	Cohort B (18-59 y) (N = 235)	
Hemorrhage[a]	3 (4.1)	9 (3.82)	.446
Chest infection[b]	2 (2.7)	7 (2.97)	.467
UTI[b]	2 (2.7)	8 (3.4)	.399
Collections[c]	3 (4.1)	7 (2.97)	.307
DGF[d]	4 (5.5)	13 (5.53)	.494
Rejection[e]	7 (9.7)	16 (6.8)	.203

Abbreviations: DGF, delayed graft function; UTI, urinary tract infection Proportions were compared with the chi-square and the Fisher exact test. [a]Perioperative blood loss required transfusion. [b]Treated with antibiotics during first admission. [c]Required surgical or radiological intervention for lymphocele, urinoma, hematoma. [d]DGF dialysis required in week 1 after surgery. [e]Biopsy-proven rejections, including cellular and vascular in year 1 after transplant.

Survival analyses

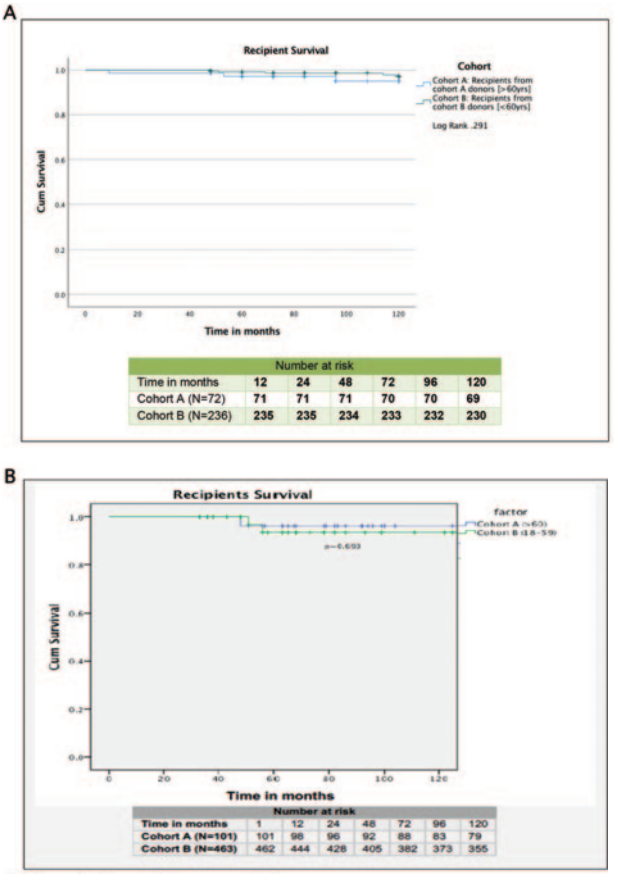
The mean follow-up period for transplant pairs in cohort A was 97 months (SD, 25.1 months) and for cohort B was 100.57 months (SD, 25.45 months). There was no significant difference in donor survival between the 2 cohorts (Figure 2). In cohort A, 1 donor died from multiple trauma after a road traffic accident at year 4. In cohort B, 2 donors died after 5 years (1 with myocardial infarction at age 53 years, and 1 with multiple trauma from an accident at age 57 years). Analyses of rates of recipient survival and graft survival from 307 transplants included in cohorts A and B did not show any significant differences (Figure 3A and Figure 4A); likewise, comparison of available data from the entire cohort of 564 living donor transplants showed no significant differences between the 2 cohorts (Figure 3B and Figure 4B). We further investigated the function of renal transplants from cohort A donors by recording their eGFR at 6, 12, 36, and 60 months (Figure 5). There was no significant decline in eGFR when compared at 6 months and 5 years after transplant (P = .414).

Figure 2. Kaplan-Meier Donor Survival Analysis



Abbreviations: Cum, cumulative

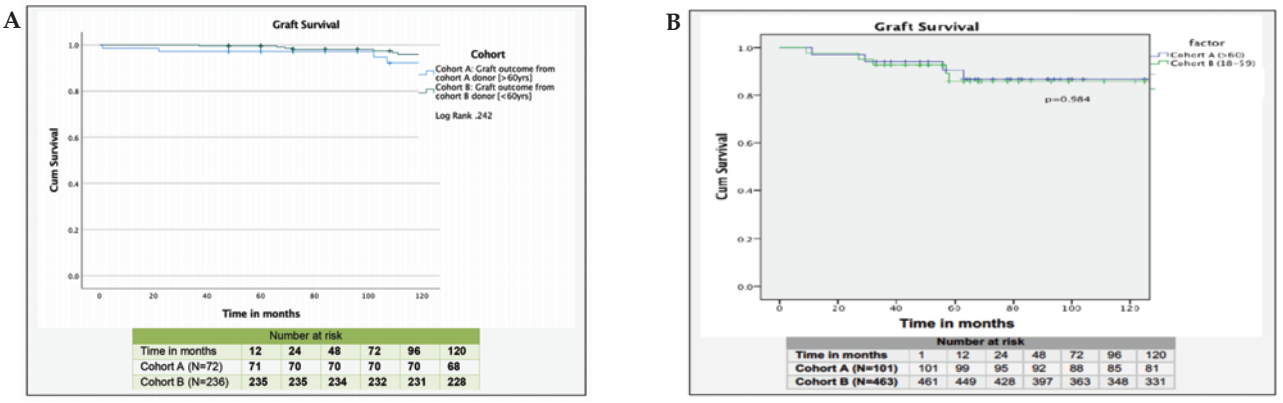
Figure 3. Kaplan-Meier Recipient Survival Analysis



Abbreviations: Cum, cumulative

(A) Kaplan-Meier recipient survival analysis of the study cohort (n = 307). **(B)** Kaplan-Meier recipient survival analysis of the overall cohort (n = 564).

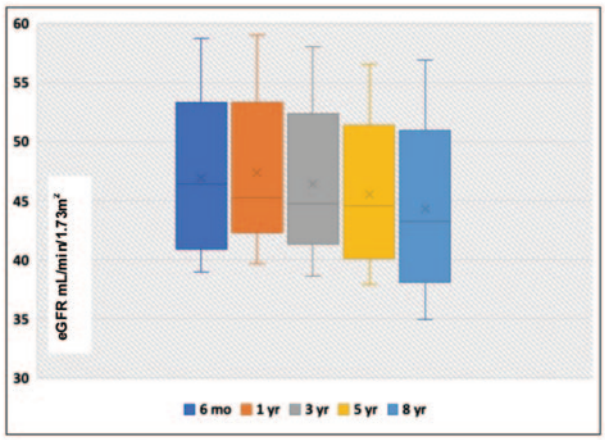
Figure 4. Kaplan-Meier Graft (Death-Censored) Survival Analysis



Abbreviations: Cum, cumulative

(A) Kaplan-Meier graft (death-censored) survival analysis of the study cohort (n = 307). **(B)** Kaplan-Meier graft (death-censored) survival analysis of the overall cohort (n = 564).

Figure 5. Recipient Estimated Glomerular Filtration Rate Measurements From Older Adult Donor Allografts (N = 72)



Abbreviations: eGFR, estimated glomerular filtration rate

Discussion

The United Nations Department of Economic and Social Affairs has predicted that the rate of population aging in the 21st century will exceed the rate observed in the 20th century.[17] In the United Kingdom alone, the number of people who are 60 years old and older exceeds the number people less than 18 years old. There are nearly 14.7 million people aged 60 years and older, of which 11 million are 65 years or older.[18-20] This shift in population dynamics has created substantial challenges. One such challenge is consideration of living older adult donors for solid-organ transplants.

For transplants from older adult kidney donors, there are 2 major concerns: donor safety and allograft outcomes. Donor safety remains the priority in any living donor kidney transplant program. In normal renal physiology, with advancing age, there is reduction in the proportion of functioning glomeruli and mean glomerular volume.[21,22]

In our study, we followed postdonation eGFR of older adult living donors at different time intervals and did not find any significant decline in eGFR at 5 years after donation (P = .481) (Figure 1). These findings are similar to studies from Oikawa and colleagues[23] and Toyoda and colleagues,[24] but our study included a significantly larger cohort of patients with a longer mean follow-up period.

Another factor that disfavors the use of older adult donors is the risk of potential complications known to be associated with older age. According to a retrospective cross-sectional analysis of 6320 cases by Friedman and colleagues,[25] there was a higher incidence of complications among older donors (41.3 vs 39.7 years; $P < .001$). In our study the mean age of older donor was much higher (64.13 vs 41.08 years; $P < .001$). Although our cohort was smaller, the postoperative complications and duration of hospital stay in older donors were not significantly different compared with younger donors.

In addition to donor safety, another major concern is allograft outcome, ie, the function of the donated kidney in the recipient after transplant. The superiority of living donor transplant versus deceased donor transplant is well established.[24,26] In a meta-analysis of 31 studies, Iordanous and colleagues[27] described less favorable 5-year graft outcomes and patient outcomes in recipients of grafts from older donors. On the contrary, although Jeong and colleagues[28] described early lower graft functions in older donors compared with younger donors, there was no significant difference in graft survival at 1 year. In our study there was no significant difference over 10 years in the mean graft survival between the 2 groups, which is comparable to the results published by Toyada and colleagues.[24] In addition, we observed no significant decline in the posttransplant eGFR of these kidneys in recipients (Figure 5). In this analysis, we provide evidence that kidneys from suitable older living donors have good long-term allograft outcomes.

We do recognize that our study is limited by the retrospective design. However, a prospective study with long-term follow-up may be difficult to organize because of the time constraints, and therefore this retrospective analysis of prospectively collected data will provide useful information regarding donor safety and residual renal functions, as well as posttransplant allograft outcomes.

Conclusions

We believe that living donor renal transplants from older donors are a valuable resource. Although these older adult donors require rigorous pre-donation workup to exclude significant medical comorbidities, kidney donation from carefully selected older adults is not only safe but also results in good long-term allograft survival.

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