ORIGINAL ARTICLE

Pre- and postdonation kidney function in donors of a kidney paired donation with unique criteria for donor glomerular filtration rate – a longitudinal cohort analysis

Jenny H. C. Chen[1,2], Peter Hughes[3,4], Claudia Woodroffe[1] & Paolo Ferrari[2,5,6]

1 Department of Nephrology and Transplantation, Prince of Wales Hospital, Sydney, NSW, Australia
2 Clinical School, University of New South Wales, Sydney, NSW, Australia
3 Department of Nephrology, Royal Melbourne Hospital, Parkville, Vic., Australia
4 University of Melbourne, Melbourne, Vic., Australia
5 Department of Nephrology, Ospedale Civico Lugano, Ente Ospedaliero Cantonale, Lugano, Switzerland
6 Biomedical Faculty, Università della Svizzera Italiana, Lugano, Switzerland

Correspondence
Paolo Ferrari MD, Department of Nephrology, Ospedale Civico Lugano, Ente Ospedaliero Cantonale, 6900 Lugano, Switzerland.
Tel.: +41 91 811 14 36;
fax: +41 91 811 12 60;
e-mail: paolo.ferrari@eoc.ch

SUMMARY

Baseline predonation estimated GFR (eGFR) appears to predict the risk of postdonation chronic kidney disease in live donors. New KIDGO guidelines recommend an eGFR ≥90 ml/min/1.73 m^2 as an acceptable level of glomerular filtration rate (GFR) for kidney donation. In the Australian Paired Kidney Exchange (AKX) program, all donors with a raw measured GFR (mGFR) ≥80 ml/min are deemed suitable for donation, but the significance of this selection indicator is unclear. We analysed the first 129 live donors in the AKX program with at least 1-year follow-up linking records in the AKX database and ANZDATA. There were 73 male and 56 female donors; mean (±SD) age was 53 ± 11 years. Predonation eGFR was 94 ± 13 ml/min/1.73 m^2, mGFR 99 ± 17 ml/min/1.73 m^2 and raw mGFR 108 ± 18 ml/min. Baseline eGFR was <80 ml/min/1.73 m^2 in 19 donors, and <90 ml/min/1.73 m^2 in 42 donors. At 1 year postdonation eGFR was 68 ± 15 ml/min/1.73 m^2 and the predicted eGFR at 30 years postdonation was on average 50 (29–83) ml/min/1.73 m^2. The hypothetical mean age at end-stage kidney disease was estimated to be 145 (95% CI 120–263) years. Over 30% of AKX live donors would have been excluded from donation using KDIGO guidelines. Using AKX donor guidelines, the majority of donors with predicted eGFR <30 ml/min/1.73 m^2 30-year postdonation were aged ≥50 years. Long-term outcome data on AKX donors with low eGFR will need careful monitoring.

Transplant International 2019; 32: 291–299

Key words
glomerular filtration rate, kidney paired donation, living donor kidney transplantation

Received: 27 March 2018; Revision requested: 22 May 2018; Accepted: 17 October 2018;
Published online: 8 November 2018

Introduction

Living donor kidney transplantation is known to be associated with favourable recipient outcomes compared with deceased donor kidney transplant. In Australia, living donor kidney transplantation accounts for nearly one-third of all kidney transplants [1]. Although the absolute risk of end-stage kidney disease (ESKD) of living donors after donation remains significantly lower than that of the general population [2], the relative risk of ESKD increases after donation compared with predonation [3,4]. There is widespread support for the use of a predonation glomerular filtration rate (GFR) threshold of 80 ml/min/1.73 m^2 in living donors [2,5–9] and

doi:10.1111/tri.13366

in some cases to consider acceptance of an age-dependent GFR thresholds as low as 50 ml/min/1.73 m^2 for donors older than 80 years [8]. Because of the concern on long-term consequences of living donation, integration of ESKD risk evaluation in the living kidney donor screening have recently been proposed [10–12], and a new screening strategy using ESKD risk calculators was included in the new recommendations on living kidney donor screening by the kidney disease improving global outcome group (KDIGO) [13]. These guidelines also recommend to routinely accept a living kidney donor with GFR of ≥90 ml/min/1.73 m^2 while candidates with GFR <60 ml/min/1.73 m^2 should not donate. This recommended predonation GFR value differs from previous thresholds found in the literature. Furthermore, the significance of these thresholds in older donors is unknown, given the well-recognized relationship between age and GFR as well as the uncertainty around the pathogenicity of age-related GFR decline [14,15].

Kidney paired donation (KPD) is an effective strategy to avoid antibody-incompatible live donor transplant as a result of the recipient having preformed donor-specific antibodies to human leucocyte antigen (HLA) or being blood group incompatible with their intended donor [16–19]. Adequate donor predonation renal function is essential to preserve graft survival and donor renal outcomes [20,21]. The Australian KPD program, also known as the Australian Paired Kidney Exchange (AKX) program, has adopted a practice for donor acceptance that requires donors to have a measured GFR of >80 ml/min, not corrected for body surface area (BSA) [18,19,22]. This is to provide reassurance to participating units and pairs that the recipient will receive a kidney with a minimum GFR of 40 ml/min [18,19,22]. Referring units have the discretion to accept or discard a living donor with an eGFR of <80 ml/min/1.73 m^2.

The purpose of this study was to assess pre- and postdonation eGFR in donors participating in the AKX program, the proportion of donors satisfying the mGFR requirements that did not meet the new KDIGO guidelines of GFR ≥90 ml/min/1.73 m^2 or the previous clinical practice guidelines of ≥80 ml/min/1.73 m^2 and the relationship between age and eGFR level that may be considered acceptable for kidney donation.

Materials and methods

Study design

This study was a longitudinal cohort analysis of the first 129 living donor kidney transplants conducted through the AKX program between October 2010 and August 2015. All donors complied with the AKX Living Donor Evaluation Guidelines (http://www.donatelife.gov.au/akx-user-manual-August-2015-0). These do not allow donors with diabetes, but allow for enrolment of donors with impaired fasting glucose or impaired glucose tolerance at the discretion of the referring units. The program does not accept a registration for any donor who had a previous history of recurrent renal stone disease, but a remote history of a single kidney stone is acceptable. Basic donor demographics, including baseline serum creatinine, estimated GFR (eGFR) and measured GFR (mGFR) and other factors known to affect suitability to live kidney donation were retrieved from the AKX registry. Follow-up serum creatinine and eGFR at 1 year after donation were obtained from the Australia and New Zealand Dialysis and Transplant (ANZDATA) live donor registry.

Measurement of kidney function

All donors in the AKX program had raw mGFR ≥80 ml/min. The mGFR was measured using the slope-intercept method either after injection of Cr-51 EDTA (3 MBq) or Tc-99m DTPA (10 MBq) using at least three venous blood samples taken at between 2 and 5 h postinjection [23]. Although small systematic differences have been observed between GFR measurements obtained from EDTA and DTPA [24,25], these are sufficiently small to recommend DTPA as a suitable alternative radiopharmaceutical.

Statistical analysis

Statistical analysis was performed with STATA 13.1 (StataCorp. 2013; STATA Statistical Software, College Station, TX, USA: StataCorp LP). Data were expressed as numbers (percentages) for categorical data, means and standard deviations (SD) for normally distributed continuous data, with comparisons between age categories using chi-square test and analysis of variance (ANOVA), respectively, where appropriate. The predonation and postdonation eGFR was calculated using CKD-EPI equation [26]. We also compared the percentage of lost kidney function as follows: GFR difference (%) = (eGFR 1 year − eGFR baseline)/eGFR baseline. The annual decline in eGFR postdonation was derived by linear regression analysis of the postdonation eGFR of the cohort as a function of age, adjusted for the predonation body mass index (BMI), urine protein creatinine ratio (uPCR), presence of hypertension and prediabetes, defined as impaired fasting glucose or impaired

Transplant International 2019; 32: 291–299

Table 1. Baseline donor characteristics results are reported as mean ± SD or number (and percentage).

	Age groups (years)					
	Total (n = 129)	<40 (n = 16)	40–49 (n = 33)	50–59 (n = 37)	≥60 (n = 43)	P-value
Age (years)	53 ± 11	34 ± 4	45 ± 3	55 ± 3	64 ± 3	
Male gender (n, %)	73 (57%)	7 (44%)	18 (54%)	18 (49%)	30 (70%)	0.16
Weight (kg)	77 ± 14	73 ± 14	78 ± 17	77 ± 15	77 ± 9	0.61
Height (cm)	170 ± 10	172 ± 7	171 ± 11	168 ± 10	170 ± 9	0.41
BMI (kg/m^2)	26.6 ± 3.5	25.0 ± 4.0	26.7 ± 4.1	27.2 ± 3.3	26.6 ± 2.6	0.21
Blood pressure (mmHg)	123/75 ± 11/7	117/72 ± 8/6	121/76 ± 10/6	123/74 ± 13/9	126/75 ± 10/7	0.05/0.34
Hypertension (n, %)	23 (18%)	–	3 (9%)	8 (22%)	12 (28%)	0.04
Impaired glucose tolerance (n, %)	1 (0.8%)	–	1 (3%)	–	–	0.39
Impaired fasting glucose	7 (5%)	2 (13%)	–	1 (0.8%)	4 (3%)	0.15
Renal stones (n, %)	9 (7%)	–	–	5 (13%)	4 (9%)	0.09
uPCR (mg/mmol)	7.9 ± 4.6	7.6 ± 4.2	8.2 ± 4.2	7.3 ± 4.3	8.4 ± 5.2	0.71

BMI, body mass index; uPCR, urine protein creatinine ratio.

Impaired fasting glucose was defined as glucose levels of 5.6–6.9 mmol/l in fasting patients.

Impaired glucose tolerance was defined as 2-h glucose levels of 7.8–11.0 mmol/l on the 75-g oral glucose tolerance test.

glucose tolerance. The linearity was verified graphically and by multivariable fractional polynomial analysis (Fig. S1). The eGFR at 30 years postdonation was extrapolated by the average accumulated decline in eGFR (annual average decline multiplied by 29 years) from eGFR at 1 year postdonation. Moreover, the 95th percentile in annual eGFR decline was also used to estimate the predicted strongest loss in eGFR. Finally, the predicted age at ESKD (defined as eGFR <10 ml/min/1.73 m^2) was estimated as follows: age at ESKD = age at 1-year postdonation + (10 − eGFR at 1 year postdonation)/estimated annual eGFR decline postdonation. All P-values are two-sided and a P-value ≤0.05 was considered to be statistically significant. The 95% CI are for individual predictions.

Results

Baseline characteristics

There were 73 male and 56 female donors; mean (±SD) age was 53 ± 11 years. The cohort was categorized into four age groups: <40, 40–49, 50–59, ≥60 years, a third of donors were aged 60 years or over (n = 43, 33%). Mean BMI was 26.6 ± 3.5 kg/m^2 and 23 donors (18%) had BMI >30 kg/m^2. Mean blood pressure (±SD) was 123/75 ± 11/7 mmHg. There were 23 donors (18%) with controlled hypertension, and the proportion increased by age group with 28% of those over 60 years of age diagnosed with hypertension. All donors with hypertension had well-controlled blood pressure. Eight donors (6%) were classified has having prediabetes (either impaired fasting glucose or impaired glucose tolerance) and nine donors (7%) had a history of nonrecurrent kidney stones. Mean uPCR was 7.9 ± 4.6 mg/mmol, and maximum uPCR was 20 mg/mmol. All donors had complete 12 months follow-up information. Basic demographic data of participating donors by age-group is summarized in Table 1.

Baseline renal function

The uncorrected mGFR by age groups ranged from 121 ± 17 ml/min in donors <40 years to 99 ± 13 ml/min in those ≥60 years (P < 0.001; Fig. 1). The mean corrected mGFR decreased with age on average by −0.69 ml/min/1.73 m^2 (95% CI 0.44–0.96) per year and ranged from 112 ± 17 ml/min/1.73 m^2 in donors <40 years to 90 ± 13 ml/min in those ≥60 years (P < 0.001). Baseline eGFR by CKD-EPI was lower than mGFR in all age groups, ranging from 104 ± 14 ml/min/1.73 m^2 in donors <40 years, to 85 ± 10 ml/min/1.73 m^2 in those ≥60 years (P < 0.001; Table 2, Fig. 1). The age-related decline averaged 0.64 ml/min/1.73 m^2 (95% CI 0.39–0.89) per year. In 19 donors baseline eGFR was <80 ml/min/1.73 m^2, and in 42 it was <90 ml/min/1.73 m^2.

Postdonation renal function

At 1-year after kidney donation, the mean eGFR by CKD-EPI was 68 ± 15 ml/min/1.73 m^2. For donors aged <40 years, mean postdonation eGFR was 84 ± 18 ml/min/1.73 m^2, 73 ± 14.4 ml/min/1.73 m^2

Table 2. Measured and calculated glomerular filtration rate (GFR) at baseline, calculated GFR at 12 months and extrapolated estimated GFR at 30 years after kidney donation.

	Age groups (years)					
	Total (n = 129)	<40 (n = 16)	40–49 (n = 33)	50–59 (n = 37)	≥60 (n = 43)	*P*-value
Measured GFR						
Raw (ml/min)	108 ± 18	121 ± 17	116 ± 15	107 ± 19	99 ± 13	<0.001
Corrected (ml/min/1.73 m^2)	99 ± 18	112 ± 17	106 ± 17	98 ± 18	90 ± 13	<0.001
Predonation eGFR						
eGFR (ml/min/1.73 m^2)	94 ± 13	104 ± 14	101 ± 9	92 ± 11	85 ± 10	<0.001
eGFR <80 (n, %)	19 (15%)	1 (6%)	–	5 (13%)	13 (30%)	<0.005
eGFR <90 (n, %)	42 (33%)	3 (19%)	4 (12%)	16 (43%)	19 (44%)	<0.01
eGFR 12 months post-donation						
eGFR (ml/min/1.73 m^2)	68 ± 15	84 ± 18	73 ± 14	66 ± 15	61 ± 10	<0.001
eGFR<60 (n, %)	39 (30%)	2 (12%)	6 (18%)	12 (32%)	19 (44%)	<0.05
eGFR Difference between predonation and 12-month postdonation eGFR						
Absolute reduction (ml/min/1.73 m^2, 95% CI)	25 (23–27)	20 (16–25)	28 (24–32)	26 (22–30)	24 (22–27)	0.089
Relative reduction (%, 95% CI)	27 (25–29)	20 (16–25)	28 (24–32)	28 (25–32)	28 (25–31)	0.047
eGFR 30 years postdonation						
eGFR (ml/min/1.73 m^2, 95% CI)	50 (29–83)	63 (35–99)	52 (35–86)	46 (29–78)	43 (25–59)	<0.001
eGFR <30 (n, %)	9 (7%)	–	1 (3%)	3 (8%)	5 (12%)	0.32

Results are reported as mean ± SD or 95% confidence interval or number (and percentage), respectively.

for donors aged 40–49 years, 66 ± 14 ml/min/1.73 m^2 for donors aged 50–59 years, and 61 ± 0.2 ml/min/1.73 m^2 for donors aged ≥60 years (Table 2, Fig. 2). The absolute eGFR difference 12 months postdonation was −25.2 ± 10.4 ml/min/1.73 m^2. The percentage change in eGFR at 1-year averaged −27.2 ± 10.5% (Fig. 3) and in 75% of donors postdonation eGFR dropped by ≤35% compared with predonation. The eGFR 1-year postdonation was <60 ml/min/1.73 m^2 in 39 donors (range 41–59.9 ml/min/1.73 m^2). Of these, 17 donors had a predonation eGFR <80 ml/min/1.73 m^2 and 29 donors an eGFR of <90 ml/min/1.73 m^2.

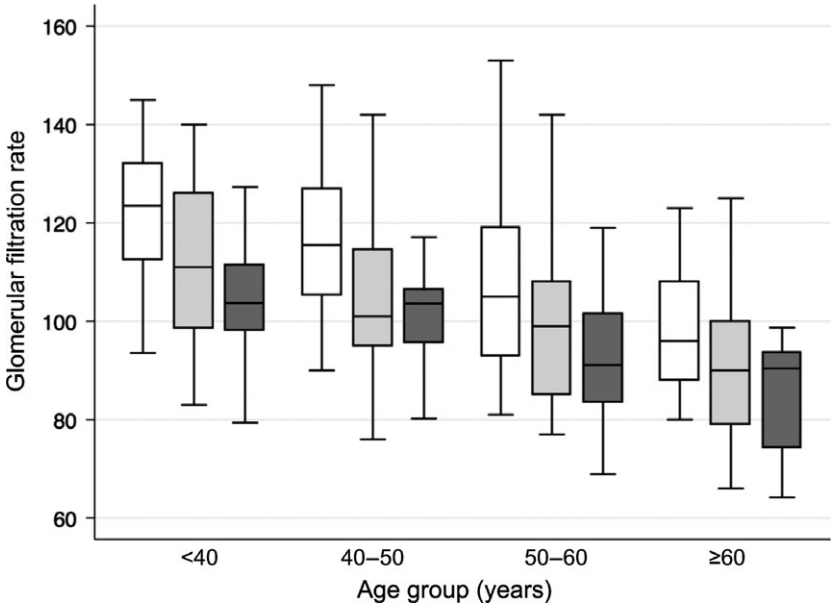

Figure 1 Predonation glomerular filtration rate glomerular filtration rate (GFR) by age groups: measured GFR not corrected for body surface are in ml/min (white boxes), corrected measured GFR in ml/min/1.73 m^2 (light grey boxes) and estimated GFR by CKD-EPI in ml/min/1.73 m^2 (dark grey boxes).

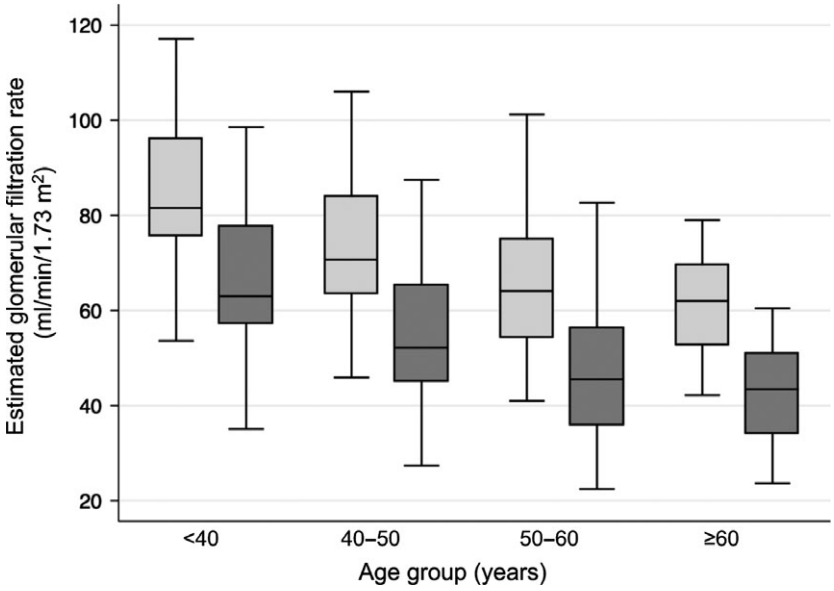

Figure 2 Postdonation glomerular filtration rate (eGFR) by age groups: eGFR at 1-year post-donation (light grey boxes) and predicted eGFR at 30 years post-donation (dark grey boxes).

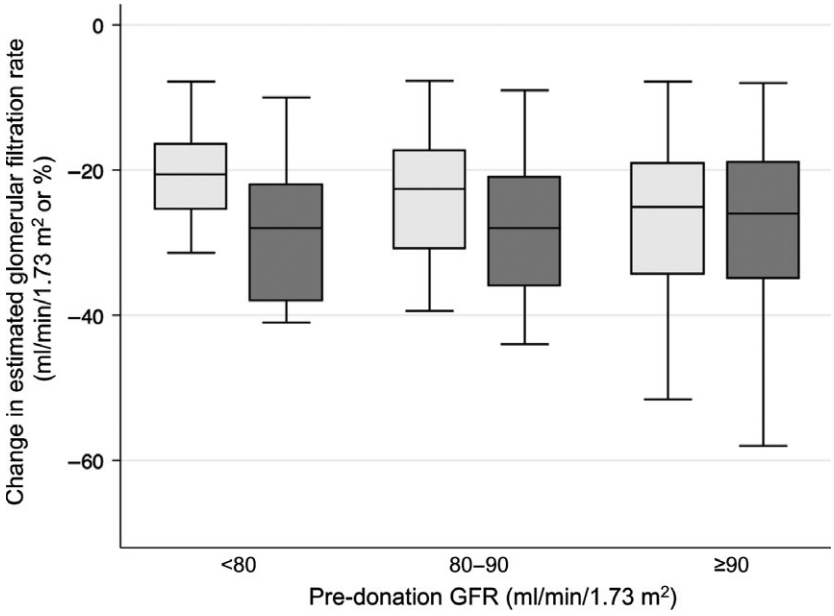

Figure 3 Difference between pre- and 1-year postdonation glomerular filtration rate (eGFR) by predonation eGFR groups: absolute eGFR difference (light grey boxes) and percentage eGFR difference (dark grey boxes).

Prediction of postdonation long-term eGFR and ESKD risk

The adjusted age-related eGFR 1 year postdonation declined on average by −0.64 ml/min/1.73 m^2 (95% CI 0.39–0.89) for every year increase in age. Based on the observed eGFR at 1-year after kidney donation, the predicted eGFR at 30 years postdonation for the entire cohort was 50 ml/min/1.73 m^2 (95% CI 43–57). The predicted eGFR 30 years postdonation by age group is shown in Fig. 2. Donors were older in the group with predonation eGFR <80 ml/min/1.73 m^2 (59 ± 8 years), compared with those in the eGFR 80–90 group (54 ± 10 years) or >90 ml/min/1.73 m^2 group

(51 ± 11 years; $P < 0.01$). The predicted eGFR 30 years postdonation was lower in donors with eGFR <80, (32 ml/min/1.73 m^2, 95% CI 22–49), compared with those with eGFR 80–90 (42 ml/min/1.73 m^2, 95% CI 32–56) or >90 ml/min/1.73 m^2 (55 ml/min/1.73 m^2, 95% CI 36–87) at the time of donation (Fig. 4). When the predicted loss of eGFR at 30 years was estimated using the 95th percentile, rather than average, of the annual eGFR decline, this revealed that 30 donors (23%) would achieve an eGFR <30 ml/min/1.73 m^2 and four donors would achieve an eGFR <20 ml/min/1.73 m^2 although none would have a predicted eGFR <15 ml/min/1.73 m^2 (CKD-stage 5) 30 years postdonation. Of the 30 donors with 30 years postdonation predicted eGFR <30 ml/min/1.73 m^2 (CKD-stage 4) 26 were aged 50 years or over at time of donation. The hypothetical mean age at ESKD was estimated to be 125 years (95% CI 107–200) in donors with baseline eGFR <80, compared with 135 years (95% CI 113–235) in those with eGFR 80–90 and 153 years (95% CI 124–284) in those with eGFR >90 ml/min/1.73 m^2 ($P = <0.001$).

Discussion

Our study is an analysis of Australian practices on the selection of living kidney donors with a particular focus on the predonation uncorrected mGFR threshold that is used to define acceptance into the AKX program and the significance with regard to pre- and postdonation eGFR.

The first key observation of this study is that by adopting the newly recommended KDIGO minimal eGFR threshold of 90 ml/min/1.73 m^2 [13] for unrestricted donor acceptance, 33% of our donors would be considered high risk or unsuitable depending on the adherence to, and interpretation of the guidelines. Using the more widely established minimal acceptable threshold of 80 ml/min/1.73 m^2 [2,5–9], there were still 15% of donors who had an eGFR <80 ml/min/1.73 m^2, who donated a kidney and 95% of these were older than 50 years of age. The AKX does not prescribe a minimum donor eGFR, as the decision on long-term donor risk related to baseline kidney function is left to participating units. However, AKX mandates that all donors undergo a measurement of GFR by nuclear method and donors who have an uncorrected mGFR of <80 ml/min are excluded from donating in the program. This rule was chosen to guarantee that recipients can be assured that they will receive an organ of good quality and a mGFR of at least 40 ml/min, which will provide in all instances an adequate allograft function, independently of donor age [27]. It's also important to stress that all donors also undergo nuclear split function studies prior to donation [28]. For donors with mGFR 80–90 ml/min, the donated kidney right/left split must be 50 ± 5%. The observation that 15% of donors in our study were accepted despite an eGFR <80 ml/min/1.73 m^2 could have several reasons. First, nuclear mGFR studies were reported to referring clinicians with both uncorrected and corrected mGFR, and corrected mGFR was on average 5.7 ± 1.9 ml/min/

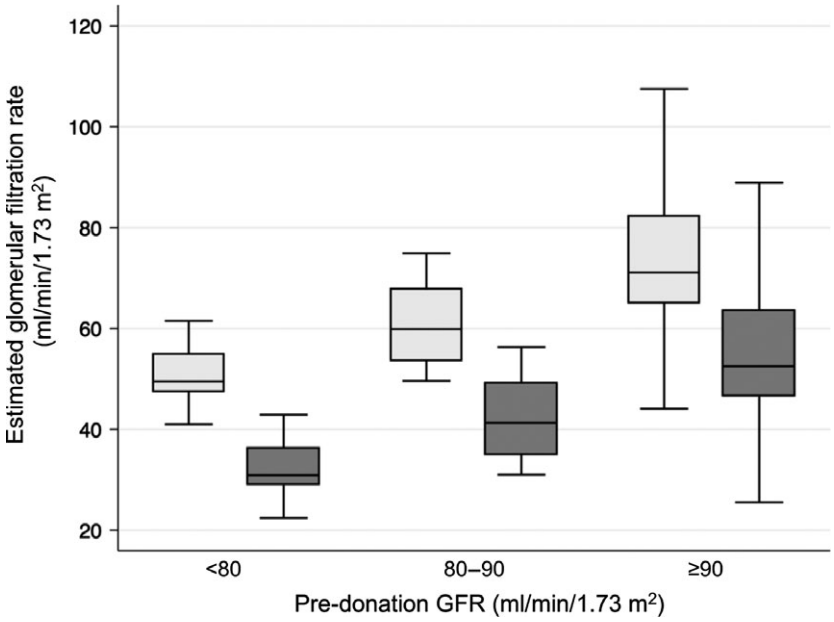

Figure 4 Postdonation glomerular filtration rate (eGFR) by predonation eGFR groups: eGFR at 1year post-donation (light grey boxes) and predicted eGFR at 30 years postdonation (dark grey boxes).

1.73 m^2 higher than eGFR ($P < 0.001$) in this cohort. Indeed, corrected mGFR was ≥80 ml/min/1.73 m^2 in 14 out of 19 cases of donors with eGFR <80 ml/min/1.73 m^2. Second, because donors with eGFR <80 ml/min/1.73 m^2 were almost exclusively older than 50 years of age, acceptance of lower eGFR may reflect some units policies tolerating a more liberal approach that takes into account GFR thresholds lower than 80 ml/min/1.73 m^2 for older donors [8]. The recent KDIGO recommendations recognizes also in the setting of live donors that 90 ml/min/1.73 m^2 is part of the CKD classification and defines stage 1. However, in our view, it is misleading to discount donor's age from the evaluation of predonation renal function, rather this decision should consider whether the donor candidate has a GFR value within the range of values similar to those of age-matched healthy individuals, as well as taking into consideration other factors. In fact, all things being equal, the life-time risk of ESKD in a 35 year old donor with eGFR 95 ml/min/1.73 m^2 is higher than that of a 65 year old donor with eGFR 70 ml/min/1.73 m^2 (0.39% vs. 0.15%) [10]. Therefore, ignoring the physiological age-related decline in kidney function may have important implications for selecting living kidney donors.

The second key observation of our analysis is that kidney donation has acceptable short-term functional consequences, even for donors with low predonation GFR (<80 ml/min/1.73 m^2). The relative change in eGFR in elderly donors with lower eGFR is similar to the one observed in younger donors with higher eGFR. Notably, the level of predonation eGFR does not influence the relative postdonation GFR loss, with a relative reduction in less than one-third for all ages and baseline GFR groups, suggesting that the ability to compensate the postnephrectomy loss of renal function in older donors is similar to that of younger ones, as previously reported by others [29].

The third key observation of this study is that the hypothetical age of reaching ESKD in our donor population is always far beyond any of the donors expected life expectancy, regardless of predonation eGFR, age or gender, even though donors with predonation eGFR <80 ml/min/1.73 m^2 will reach ESKD 20–25 years earlier than those with predonation eGFR ≥90 ml/min/1.73 m^2. Finally, in addition to the hypothetical age of reaching ESKD, estimation of eGFR 30 years postdonation could be an even more important long-term prognostic marker after kidney donation, since low eGFR has been associated with cardiovascular morbidity and mortality [30]. Among the 30 donors who are predicted to reach stage 4 CKD after 30 years, 87% of them would be over 90 years of age at the time their eGFR would drop <30 ml/min/1.73 m^2. The predicted incidence of CKD stage 4 in donors reaching 90 years of age is threefold higher than that reported in a geriatric population over 85 years of age [31]. Interestingly, the presence of complications such as anaemia, an elevated PTH or an elevated serum phosphorus level are uncommon in the very elderly with reduced kidney function [32,33], thus suggesting that the low eGFR in older age without other evidence of kidney damage may not necessarily represent disease.

It is essential to keep in mind that the donor eligibility criteria of the AKX program introduce a selection bias because of the competing interests between quality of the donated kidney and donor safety. For a donor to be accepted, the AKX program must guarantee that the quality of the kidney being offered is sufficiently high, with at least an absolute mGFR of 40 ml/min, in order to reassure the transplanting unit that they can accept the organ that is donated to their recipient. Thus, all stakeholders in Australia agreed on a minimum absolute mGFR of 80 ml/min (with less than 55/45 split function if GFR <90). On the other hand, the program's donor eligibility guidelines do not prescribe an actual minimum eGFR for the donor acceptance and this is left at the discretion of the unit that has assessed the donor. Each unit may have a different threshold of a minimum corrected eGFR at which they accept or refuse donor. Generally a tendency to more conservative approach about the lower limit of eGFR in favour of the donor is observed, regardless of mGFR. Therefore, donors with an acceptable mGFR by AKX criteria may not be accepted for donation if their eGFR is low, more so in younger donors, rather than older donors. Thus, although all donors in this study had an absolute mGFR >80 ml/min, only one donor aged 50 years or younger had predonation a eGFR <80 ml/min/1.73 m^2. Interestingly, this donor had a corrected mGFR of 92 ml/min/1.73 m^2. This aspect is important, because we do not advocate that a threshold of mGFR >80 ml/min, regardless of eGFR is safe for the donor.

Obviously, even in the healthy nondonor population the individual lifetime risk of developing advanced-stage CDK or ESKD is greater than 0%, if variability is properly taken into account. The individual predonation projected risk of ESKD in the absence of kidney donation can be estimated using the model proposed by Grams *et al.* [10] developed for adults in the United States. It does not take into account any added risk a donor might incur because of the nephrectomy or resultant single kidney status. However, currently there

are no accurate tools to predict the lifetime postdonation risk of ESKD according to predonation donor candidate's characteristics and postdonation eGFR. Our study has some limitations. First, the sample size is relatively small and the follow-up is limited to 1-year postdonation. Nevertheless, it has been demonstrated that single kidney function remains stable from early (median, 0.8 years) to late (median, 6.1 years) after kidney donation [34]. Second, our donor cohort may not be representative of the broad population of live donors. In the AKX program, in addition to require an uncorrected mGFR ≥80 ml/min for donor candidates to be accepted, the program strictly excludes patients with urinary protein/creatinine ratio >20 mg/mmol, age ≥70 years, BMI >35 kg/m^2, diabetes mellitus, treated hypertension requiring >2 agents to control, which differs from the risk-profile of the general donor population in Australia [35], and, consequently, our data may not be sufficiently generalizable. Nevertheless, in relation to age and GFR our cohort is similar to many other previously studied cohorts of healthy individuals [36–38]. In conclusion, data from the Australian KPD living donor cohort, selected based on a raw mGFR of at least 80 ml/min, demonstrates that kidney donation has acceptable short-term functional consequences, even for donors with low predonation eGFR (<80 ml/min/1.73 m^2), with 75% of donors showing a drop of ≤35% in postdonation eGFR compared with predonation and 70% having an eGFR ≥60 ml/min/1.73 m^2 at 1-year postdonation. Over 30% of these donors accepted in the AKX program would have been excluded from live kidney donation using KDIGO guidelines. Prediction of long-term kidney function indicate that up to 23% of donors who meet the AKX kidney function acceptance criteria would reach an eGFR of <30 ml/min/1.73 m^2 30-year postdonation and that the majority of these donors were aged ≥50 years, reaching CKD stage 4 at a median age of 90 years (95% CI 74–102). Although these data are reassuring, long-term outcome data on AKX donors with low eGFR will need careful monitoring.

Funding

The authors have declared no funding.

Conflict of interest

The authors have declared no conflicts of interest.

Acknowledgements

The authors acknowledge the support of the Australian Organ and Tissue Donation and Transplantation Authority for the funding of the National Paired Kidney Donation program. The authors thank the collaboration of all participating transplant centres, in particular surgeon and theatre staff for agreeing sometime to a very early morning donor surgery start or a late night transplant.

Authorship

JHCC and PF: participated in research design. JHCC, PH and PF: participated in the writing of the paper; JHCC, PH, CW and PF: participated in the performance of the research. JHCC, PH, CW and PF: participated in data analysis.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1. Linear regression analysis (with 95% CI), locally weighted scatterplot smoothing (Lowess) and multivariable fractional polynomial analysis confirming linearity of the relationship between eGFR decline at 1 year after donation in relation to age.

REFERENCES

1. ANZDATA. Registry: 38th Report, Chapter 9: Kidney Donors. *Australia and New Zealand Dialysis and Transplant Registry*: 1–11, 2016.
2. Ibrahim HN, Foley R, Tan L, *et al.* Long-term consequences of kidney donation. *N Engl J Med* 2009; **360**: 459.
3. Mjoen G, Hallan S, Hartmann A, *et al.* Long-term risks for kidney donors. *Kidney Int* 2014; **86**: 162.
4. Muzaale AD, Massie AB, Wang MC, *et al.* Risk of end-stage renal disease following live kidney donation. *JAMA* 2014; **311**: 579.
5. Davis CL, Delmonico FL. Living-donor kidney transplantation: a review of the current practices for the live donor. *J Am Soc Nephrol* 2005; **16**: 2098.
6. Cohney S, Kanellis J, Howell M. Cari: the CARI guidelines. Donor renal function. *Nephrology* 2010; **15**(Suppl. 1): S137.
7. Mandelbrot DA, Pavlakis M. Living donor practices in the United States. *Adv Chronic Kidney Dis* 2012; **19**: 212.

8. Andrews PA, Burnapp L, Manas D, Bradley JA, Dudley C, British Transplantation, S, Renal, A. Summary of the British Transplantation Society/Renal Association U.K. guidelines for living donor kidney transplantation. *Transplantation* 2012; **93**: 666.
9. Abramowicz D, Cochat P, Claas FH, *et al.* European Renal Best Practice Guideline on kidney donor and recipient evaluation and perioperative care. *Nephrol Dial Transplant* 2015; **30**: 1790.
10. Grams ME, Sang Y, Levey AS, *et al.* Chronic Kidney Disease Prognosis, C: kidney-failure risk projection for the living kidney-donor candidate. *N Engl J Med* 2016; **374**: 411.
11. Ibrahim HN, Foley RN, Reule SA, *et al.* Renal function profile in white kidney donors: the first 4 decades. *J Am Soc Nephrol* 2016; **27**: 2885.
12. Massie AB, Muzaale AD, Luo X, *et al.* Quantifying postdonation risk of ESRD in living kidney donors. *J Am Soc Nephrol* 2017; **28**: 2749.
13. Lentine KL, Kasiske BL, Levey AS, *et al.* KDIGO clinical practice guideline on the evaluation and care of living kidney donors. *Transplantation* 2017; **101**: S1.
14. Delanaye P, Schaeffner E, Ebert N, *et al.* Normal reference values for glomerular filtration rate: what do we really know? *Nephrol Dial Transplant* 2012; **27**: 2664.
15. Denic A, Mathew J, Lerman LO, *et al.* Single-nephron glomerular filtration rate in healthy adults. *N Engl J Med* 2017; **376**: 2349.
16. Segev DL, Gentry SE, Warren DS, Reeb B, Montgomery RA. Kidney paired donation and optimizing the use of live donor organs. *JAMA* 2005; **293**: 1883.
17. de Klerk M, Witvliet MD, Haase-Kromwijk BJ, Claas FH, Weimar W. A highly efficient living donor kidney exchange program for both blood type and crossmatch incompatible donor-recipient combinations. *Transplantation* 2006; **82**: 1616.
18. Ferrari P, Fidler S, Wright J, *et al.* Virtual crossmatch approach to maximize matching in paired kidney donation. *Am J Transplant* 2011; **11**: 272.
19. Ferrari P, Weimar W, Johnson RJ, Lim WH, Tinckam KJ. Kidney paired donation: principles, protocols and programs. *Nephrol Dial Transplant* 2015; **30**: 1276.
20. Hawley CM, Kearsley J, Campbell SB, *et al.* Estimated donor glomerular filtration rate is the most important donor characteristic predicting graft function in recipients of kidneys from live donors. *Transpl Int* 2007; **20**: 64.
21. Levey AS, Inker LA. GFR evaluation in living kidney donor candidates. *J Am Soc Nephrol* 2017; **28**: 1062.
22. Cantwell L, Woodroffe C, Holdsworth R, Ferrari P. Four years of experience with the Australian kidney paired donation programme. *Nephrology* 2015; **20**: 124.
23. Chantler C, Garnett ES, Parsons V, Veall N. Glomerular filtration rate measurement in man by the single injection methods using 51Cr-EDTA. *Clin Sci* 1969; **37**: 169.
24. Fleming JS, Wilkinson J, Oliver RM, Ackery DM, Blake GM, Waller DG. Comparison of radionuclide estimation of glomerular filtration rate using technetium 99m diethylenetriaminepentaacetic acid and chromium 51 ethylenediaminetetraacetic acid. *Eur J Nucl Med* 1991; **18**: 391.
25. Biggi A, Viglietti A, Farinelli MC, Bonada C, Camuzzini G. Estimation of glomerular filtration rate using chromium-51 ethylene diamine tetra-acetic acid and technetium-99m diethylene triamine penta-acetic acid. *Eur J Nucl Med* 1995; **22**: 532.
26. Levey AS, Stevens LA, Schmid CH, *et al.* A new equation to estimate glomerular filtration rate. *Ann Intern Med* 2009; **150**: 604.
27. Ferrari P, Lim W, Dent H, McDonald SP. Effect of donor-recipient age difference on graft function and survival in live-donor kidney transplantation. *Nephrol Dial Transplant* 2011; **26**: 702.
28. Patankar K, Low RS, Blakeway D, Ferrari P. Comparison of computer tomographic volumetry versus nuclear split renal function to determine residual renal function after living kidney donation. *Acta Radiol* 2014; **55**: 753.
29. Tan JC, Busque S, Workeneh B, *et al.* Effects of aging on glomerular function and number in living kidney donors. *Kidney Int* 2010; **78**: 686.
30. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med* 2004; **351**: 1296.
31. Formiga F, Ferrer A, Cruzado JM, *et al.* Geriatric assessment and chronic kidney disease in the oldest old: the Octabaix study. *Eur J Intern Med* 2012; **23**: 534.
32. Ferrari P, Xiao J, Ukich A, Irish A. Estimation of glomerular filtration rate: does haemoglobin discriminate between ageing and true CKD? *Nephrol Dial Transplant* 2009; **24**: 1828.
33. Van Pottelbergh G, Vaes B, Jadoul M, Mathei C, Wallemacq P, Degryse JM. The prevalence and detection of chronic kidney disease (CKD)-related metabolic complications as a function of estimated glomerular filtration rate in the oldest old. *Arch Gerontol Geriatr* 2012; **54**: e419.
34. Lenihan CR, Busque S, Derby G, Blouch K, Myers BD, Tan JC. Longitudinal study of living kidney donor glomerular dynamics after nephrectomy. *J Clin Invest* 2015; **125**: 1311.
35. Clayton PA, Saunders JR, McDonald SP, *et al.* Risk-factor profile of living kidney donors: the Australia and New Zealand dialysis and transplant living kidney donor registry 2004–2012. *Transplantation* 2016; **100**: 1278.
36. Back SE, Ljungberg B, Nilsson-Ehle I, Borga O, Nilsson-Ehle P. Age dependence of renal function: clearance of iohexol and p-amino hippurate in healthy males. *Scand J Clin Lab Invest* 1989; **49**: 641.
37. Hoang K, Tan JC, Derby G, *et al.* Determinants of glomerular hypofiltration in aging humans. *Kidney Int* 2003; **64**: 1417.
38. Pottel H, Delanaye P, Weekers L, *et al.* Age-dependent reference intervals for estimated and measured glomerular filtration rate. *Clin Kidney J* 2017; **10**: 545.