ORIGINAL ARTICLE

Lifetime risk of end-stage kidney disease in living donors for paediatric kidney transplant recipients in Australia and New Zealand – a retrospective study

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SUMMARY

Living kidney donors (LKD) for paediatric kidney transplant recipients (KTR) have a heightened motivation to donate for emotional reasons and the clear health benefits to the KTR. We hypothesized that the cohort of LKD for paediatric KTR (LKD-P) includes motivated young parents with a higher lifetime end-stage kidney disease (ESKD) risk compared to adult KTR (LKD-A). Data from the Australia and New Zealand Dialysis and Transplant LKD Registry (2004–2015) was analysed to compare baseline characteristics and predonation ESKD risk in LKD-P ($n = 315$) versus LKD-A ($n = 3448$). LKD-P were younger (median age 42 vs. 50 years; $P < 0.001$) and had a marginally higher lifetime ESKD risk (median 0.44% vs. 0.40%; $P < 0.01$), with a similar proportion of LKD exceeding 1% risk threshold (5.4% vs. 5.6%; P = NS). Compared to grandparents as LKD-P, parents (median age 41 vs. 59 years; $P < 0.001$) had a higher lifetime ESKD (0.44% vs. 0.25%; $P < 0.001$). Although unique benefits to paediatric KTR justify the minor increase in lifetime ESKD risk in young parents, carefully selected grandparents are an alternative LKD-P option, allowing parents to donate for subsequent transplants.

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Introduction

Kidney transplantation not only offers a survival advantage for children with end-stage kidney disease (ESKD) compared with remaining on dialysis [1,2] but also unique benefits for growth [3] and cognitive development [4]. Living kidney donors (LKD) facilitate timely (often pre-emptive) transplantation and superior outcomes over deceased donors [5]. Therefore, young parents have heightened motivation to become LKD for their children. In an interdependent relationship, there are also tangible psychosocial benefits to parents as LKD after successful kidney transplantation [6]. These benefits need to be balanced against the accumulating

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evidence for increased ESKD risk in LKD compared with healthy nondonors [7,8]. The recently published Kidney Disease Improving Global Outcomes (KDIGO) guideline [9] recommends the use of a multiparameter prediction tool such as the one developed by Grams *et al.* [10] to estimate the lifetime predonation risk of ESKD, as well as an acceptance risk threshold of 1.0–1.5% (projecting to a postdonation risk of approximately 5%). However, parents as LKD for paediatric kidney transplant recipients (KTR) are usually younger with anticipated higher lifetime ESKD risk postdonation [11] for whom risk prediction may be imprecise, and risk factors poorly captured [12]. This scenario presents a complex clinical scenario balancing optimal donor well-being, the emotional implications of parent-to-child donation and expected health benefits for the child with ESKD.

Paediatric KTR often have multiple LKD candidates, and the overwhelming majority will require re-transplantation later in their lifetime. Older grandparents are an alternative LKD option that mitigates the increased risk of ESKD in young parents as LKD and allows parents to donate for later subsequent re-transplantation if required. However, grandparents generally have inferior HLA matching, which increases the risk of broad sensitization and compromises the prospects and outcome of re-transplantation [13]. While the registry data are conflicting for older LKD offering either similar [14] or inferior [15] graft outcomes in the general adult KTR population, smaller studies have shown that carefully selected grandparents [16] and older LKD [17] may offer comparable graft outcomes for paediatric KTR.

To address these complex issues, we retrospectively compared baseline characteristics and ESKD risk profile of LKD for paediatric KTR (LKD-P) with those for adult KTR (LKD-A) using data from the Australia and New Zealand Dialysis and Transplant (ANZDATA) Registry between 2004 and 2015. Predonation ESKD risk estimates were generated and compared using the prediction tool by Grams *et al.* [10]. We hypothesized that younger LKD-P with higher ESKD risk was more often accepted compared with LKD-A due to the unique benefits to paediatric KTR and parent LKD-P. The risk of ESKD and HLA mismatches from grandparents and parents for LKD-P were compared.

Materials and methods

Study population

Three thousand nine hundred and sixty-nine LKD who donated between 2004 and 2015 were identified from the ANZDATA LKD Registry (http://anzdata.org.au), after excluding 10 nondirected altruistic LKD. Figure S1 illustrates those who were categorized into the *complete data cohort* ($n = 599$, no missing baseline data, and all 10 variables within range for the ESKD risk calculation), and those who qualified for the *imputed data cohort* ($n = 3164$). The imputed data cohort captured LKD with the three missing variables (urine albumin:creatinine ratio (uACR) and/or body mass index (BMI) and/or diabetes status), primarily due to unreported uACR. LKD from these two cohorts were then combined in the analysis. Those with the other seven variables (age, gender, race, estimated glomerular filtration rate (eGFR), systolic blood pressure (SBP), anti-hypertensive requirement and smoking history) missing or variables out of the risk calculation range, were excluded. This approach had been adopted for the original modelling of the ESKD risk calculator [10]. Of the 3763 LKD in the combined cohort, 315 and 3448 were LKD-P (KTR age < 18 years) and LKD-A (KTR age ≥ 18 years), respectively.

Data collection

In addition to the 10 above-mentioned variables, additional baseline demographic data were studied. These included LKD's relationship to KTR, diastolic BP (DBP), measured GFR (mGFR), KTR's age and HLA mismatches (comparing direct donation from grandparent LKD-P vs. parent LKD-P only). For LKD [$n = 164$ (4.4%)] who participated in Kidney Paired Donation (KPD), the Australian Kidney Exchange (AKX) program database was linked with the ANZDATA registry, and baseline characteristics of the originally intended LKD (rather than the matched KPD LKD) were analysed. The relationship of the originally intended LKD with the KTR was not recorded. The CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) equation was used to calculate eGFR. uACR is expressed as both mg/mmol and mg/g.

Estimation of predonation ESKD risk

Projected 15-year and lifetime predonation ESKD risk estimates were calculated by the prediction tool previously published [10], using an implementation in R (R Foundation for Statistical Computing, Vienna, Austria). For the imputed data cohort, median values for missing uACR and/or BMI in LKD-A and LKD-P, and/or no diabetes for missing diabetes status, were imputed. For

Table 1. Demographics of LKD for paediatric versus adult KTR.

	LKD for Paediatric KTR (n = 315)	LKD for Adult KTR (n = 3448)	P
LKD age (years)	42 (37–49)	50 (42–58)	<0.001
Categorical LKD age [n (%)]			
<40	120 (38.1)	655 (19.0)	<0.001
40–59	179 (56.8)	2901 (60.6)	
≥60	16 (5.1)	702 (20.4)	
Female gender [n (%)]	163 (51.7)	1991 (57.7)	<0.05
Ethnicity [n (%)]			
White	272 (86.4)	2985 (86.6)	0.41
Asian	16 (5.1)	227 (6.6)	
Australian indigenous	2 (0.6)	13 (0.4)	
Maori or Pacific Islander	10 (3.2)	112 (3.2)	
Other	14 (4.4)	92 (2.7)	
Not reported	1 (0.3)	19 (0.6)	
SBP (mmHg)	120 (110–130)	121 (115–130)	<0.001
≥140 [n (%)]	26 (8.3)	381 (11.0)	0.15
DBP (mmHg)*	72 (69–80)	74 (70–80)	<0.05
≥90 [n (%)]	12 (3.8)	167 (4.8)	0.49
Anti-hypertensive [n (%)]	19 (6.0)	335 (9.7)	<0.05
BMI (kg/m^2)*	26.0 (23.6–28.5)	26.3 (23.8–29.0)	0.32
≥30 [n (%)]	51 (16.2)	619 (18.0)	0.49
Smoking [n (%)]	137 (43.5)	1396 (40.5)	0.35
Current	34 (10.8)	232 (6.7)	<0.05
Former	103 (32.7)	1164 (33.8)	0.76
Diabetes [n (%)]*	2 (0.6)	7 (0.2)	0.17
eGFR (ml/min/1.73 m^2)	98 (88–108)	92 (81–102)	<0.001
<80 [n (%)]	36 (11.4)	737 (21.4)	<0.001
mGFR (ml/min/1.73 m^2)*	118 (102–135)	109 (96–126)	<0.001
<80 [n (%)]	3 (1.2)	75 (2.8)	0.15
uACR (mg/mmol)*	0.5 (0.3–1.0)	0.6 (0.3–1.1)	0.52
(mg/g)	4.4 (2.7–9.1)	5.3 (2.7–9.7)	
Relationship to KTR [n(%)]			
Parent	253 (80.3)	710 (20.6)	<0.001
Grandparent	23 (7.3)	6 (0.2)	
Child	0 (0)	171 (5.0)	
Sibling	2 (0.6)	801 (23.2)	
Spouse	0 (0)	849 (24.6)	
Other – related	15 (4.8)	195 (5.7)	
Other – unrelated	14 (4.4)	560 (16.2)	
KPD	8 (2.5)	156 (4.5)	

BMI, body mass index; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; KPD, kidney paired donation; KTR, kidney transplant recipients; LKD, living kidney donors; mGFR, measured GFR; SBP, systolic blood pressure; uACR, urine albumin:creatinine ratio.

*DBP – paediatric n = 315, adult n = 3447; BMI – paediatric n = 302, adult n = 3338; Diabetes – paediatric n = 314, adult n = 3422; mGFR – paediatric n = 257, adult n = 2721; uACR – paediatric n = 68, adult n = 546.

sensitivity analysis, either 75th percentile or 90th percentile values were imputed for missing uACR and/or BMI (Table S1). LKD of all nonwhite ethnicities (13.4%) in this study were considered as white for the purpose of risk calculation (Table 1).

Statistical analysis

Data analysis was performed using GraphPad Prism 7.02 (GraphPad, San Diego, CA, USA). Continuous variables were presented as median [interquartile range

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(IQR)], and comparisons between two groups were performed by two-tailed Mann–Whitney *U*-test. For HLA mismatches, data were also expressed as mean ± standard deviation (SD) and compared by unpaired t-test with Welch's correction. Categorical variables were presented as number (percentage of group) and compared by Fisher's exact test, or by multiple chi-square tests for those with three or more mutually exclusive categories. A two-sided *p*-value of <0.05 was considered significant. Kernel density plots for comparison of age and ESKD risk distribution in different cohorts were generated using R and the ggplot2 package.

Results

Baseline demographics of LKD for paediatric versus adult KTR

LKD-P (n = 315) compared to LKD-A (n = 3448) were younger (Fig. 1a), more likely to be <40 years of age, less likely to be ≥60 years of age and less likely to be female (Table 1). LKD-P were primarily parents of the KTR (80.3% vs. 20.6%), while 7.3% of the LKD-P were grandparents. LKD-P had less comorbidity, including lower SBP, DBP and anti-hypertensive requirement, higher eGFR and mGFR, but no differences in the proportion of LKD with BP ≥ 140/90 mmHg or mGFR ≤ 80 ml/min/1.73 m^2. They were more likely to be current smokers, but not former smokers. Similar findings were observed from the complete data cohort, except a lack of differences in DBP and current smoking rate, and a lower rate of BMI ≥ 30 kg/m^2 in LKD-P (Table S2).

ESKD risk estimates

LKD-P compared to LKD-A had a significantly lower predonation 15-year but higher lifetime ESKD risk, however, the absolute risk difference was minor (Table 2). The 90, 95 and 98th risk percentile values (LKD with the highest 10%, 5% and 2% ESKD risk, respectively) were similar. There was also no difference in the proportion of LKD exceeding the 1% or 2% lifetime ESKD risk threshold. Density plots of 15-year and lifetime risk estimates for the two groups virtually overlap (Fig. 1b and c), confirming that the differences were unlikely to be clinically relevant. Sensitivity analysis yielded similar findings although the differences in lifetime risk between the two groups were more accentuated (Table S3). In addition, it shows a larger proportion of LKD-P exceeding the 1% lifetime ESKD risk threshold compared with LKD-A.

Subgroup comparisons of age and ESKD risk of LKD for paediatric KTR

Grandparents versus parents and mothers versus fathers as LKD

Paediatric KTR often have multiple LKD candidates. We analysed the ESKD risk and HLA mismatches from grandparents versus parents, and mothers versus fathers as LKD-P (Tables 3 and S4). Grandparents (n = 23), compared to parents (n = 253), donated to younger KTR (3 vs. 12 years), were older (with almost half being ≥60 years of age) and had greater age mismatch (55 vs. 31 years). Grandparents also had marginally higher 15-year but almost half the lifetime ESKD risk, with no grandparent LKD having a lifetime risk >1% (Table 3 and Fig. 1d). They, however, had more comorbidity, including higher SBP, higher anti-hypertensive requirement and lower eGFR and mGFR. Despite this, relatively few grandparent LKD-P had SBP ≥ 140 or required anti-hypertensives, and none had a mGFR < 80 ml/min/1.73 m^2 (Table S4).

Compared with fathers, mothers were of similar age but donated to older KTR with a lower age mismatch. This suggests that a proportion of mothers of childbearing age with younger KTR might have been excluded from donation. Alternatively, this may also reflect younger age of mothers compared to fathers. Mothers had lower 15-year and lower lifetime ESKD risk and were less likely to exceed the 1% lifetime risk threshold (Table 3). They also had lower SBP, DBP and BMI and higher eGFR, reflecting less comorbidity (Table S4). Including grandparents in the comparison, the lifetime ESKD risk was lowest in grandparents followed by mothers, and highest in fathers (Table 3).

With regards to HLA mismatches, grandparents had higher A+B+DR and DR mismatches, and lower likelihood to achieve ≤3 A+B+DR mismatches compared with parents (Table 3). Despite this, over half of the grandparents as LKD had ≤3 A+B+DR mismatches, and there were no significant differences in the rates of zero A+B+DR or zero DR mismatch. As expected, there was no difference in HLA mismatches between mother and father LKD-P.

Age of paediatric KTR

Table S5 shows the LKD age, age mismatch between LKD and KTR, and ESKD risk stratified by the median paediatric KTR age (≤10 vs. ≥ 11), for all LKD-P and for parent LKD-P only. Parent LKD for younger paediatric KTR were also younger, with 61.3% being <40 years of age. The age mismatch was however

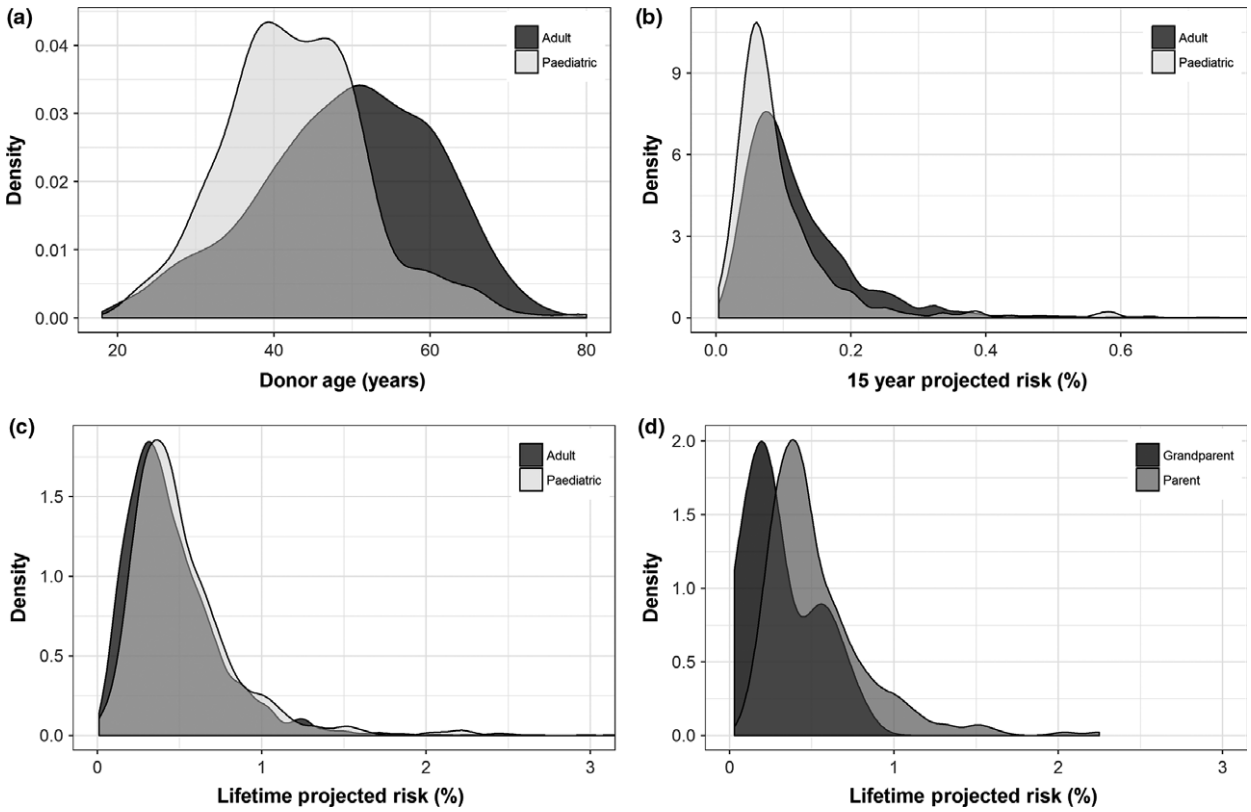

Figure 1 Age and predonation ESKD risk in LKD. (a–d) Density plots of age (a), 15-year (b) and lifetime (c) ESKD risk of LKD for paediatric versus adult KTR, and lifetime ESKD risk of parents versus grandparents as LKD for paediatric KTR (d). Outliers with 15-year risk >0.75% (n = 19) in b and with lifetime risk >3% (n = 7) in c are not displayed.

Table 2. Predonation ESKD risk estimates in LKD for paediatric versus adult KTR.

	LKD for Paediatric KTR (n = 315)	LKD for Adult KTR (n = 3448)	P
15-year ESKD risk			
Median (IQR) (%)	0.07 (0.05–0.11)	0.10 (0.07–0.16)	<0.001
Risk percentile (%)			
90th (highest 10% risk percentile)	0.17	0.23	
95th (highest 5% risk percentile)	0.23	0.30	
98th (highest 2% risk percentile)	0.38	0.42	
Lifetime ESKD risk			
Median (IQR) (%)	0.44 (0.31–0.63)	0.40 (0.26–0.59)	<0.01
Risk percentile (%)			
90th (highest 10% risk percentile)	0.88	0.84	
95th (highest 5% risk percentile)	1.08	1.03	
98th (highest 2% risk percentile)	1.49	1.30	
Proportion of LKD exceeding threshold [(n (%)]			
1% ESKD risk	17 (5.4)	193 (5.6)	>0.99
2% ESKD risk	2 (0.6)	23 (0.7)	>0.99

ESKD, end-stage kidney disease; KTR, kidney transplant recipients; IQR, interquartile range; LKD, living kidney donors.

marginally greater, suggesting that some younger parents were declined as LKD. There was a significantly lower 15-year but higher lifetime ESKD risk in parent LKD for younger paediatric KTR. The proportion of LKD exceeding the 1% or 2% lifetime ESKD risk threshold was similar.

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Table 3. Demographics, predonation ESKD estimates and HLA mismatches of grandparent versus parent and mother versus father LKD for paediatric KTR.

	Grandparents (n = 23)	Parents (n = 253)	P	Mothers (n = 124)	Fathers (n = 129)	P
KTR age (years)	3 (2–7)	12 (6–15)	<0.001	12 (7–16)	10 (4–14)	<0.05
LKD age (years)	59 (55–65)	41 (37–47)	<0.001	41 (37–46)	42 (37–49)	0.07
Categorical LKD age [n (%)]						
<40	0 (0)	102 (40.3)	<0.001	53 (42.7)	49 (38.0)	0.38
40–59	12 (52.2)	150 (59.3)		71 (57.3)	79 (61.2)	
≥60	11 (47.8)	1 (0.4)		0	1 (0.8)	
Age mismatch (years)	55 (49–57)	31 (27–36)	<0.001	29 (25–34)	34 (29–37)	<0.001
15-year ESKD risk						
Median (IQR) (%)	0.11 (0.07–0.17)	0.07 (0.05–0.11)	<0.001	0.06 (0.04–0.07)	0.09 (0.06–0.13)	<0.001
Lifetime ESKD risk						
Median (IQR) (%)	0.25 (0.16–0.50)	0.44 (0.33–0.63)	<0.001	0.36 (0.28–0.47)	0.56 (0.41–0.78)	<0.001
Proportion of LKD exceeding threshold [n (%)]						
1% ESKD risk	0 (0)	20 (7.9)	0.39	4 (3.2)	16 (12.4)	<0.01
2% ESKD risk	0 (0)	2 (0.8)	>0.99	1 (0.8)	1 (0.8)	>0.99
HLA mismatches*						
HLA A+B+DR mismatches						
Median (IQR)	3 (2–4)	2 (2–3)	<0.001	2 (2–3)	2 (2–3)	0.48
Mean ± SD	3.0 ± 1.3	2.2 ± 0.8	<0.05	2.2 ± 0.8	2.3 ± 0.8	0.53
0 mismatch [n(%)]	1 (5.0)	7 (3.1)	0.50	4 (3.7)	3 (2.1)	0.16
≤3 mismatches [n (%)]	11 (55.0)	223 (100)	<0.001	108 (100)	115 (100)	>0.99
HLA DR mismatches						
Median (IQR)	1 (1–2)	1 (0–1)	<0.01	1 (0–1)	1 (0–1)	0.14
Mean ± SD	1.1 ± 0.7	0.7 ± 0.5	<0.05	0.6 ± 0.5	0.7 ± 0.5	0.14
0 mismatch [n (%)]	4 (20.0)	74 (33.2)	0.32	41 (38.0)	33 (28.7)	0.16

ESKD, end-stage kidney disease; IQR, interquartile range; KTR, kidney transplant recipients; LKD, living kidney donors; SD, standard deviation.

*HLA mismatches – grandparents n = 20, parents n = 223, mothers n = 108, fathers n = 115.

Discussion

This study demonstrates that LKD-P had significantly lower 15-year but paradoxically higher lifetime predonation risk of ESKD compared to LKD-A. The lower 15-year risk likely reflects the LKD-P being primarily younger parents with fewer comorbidities, while the longer anticipated life expectancy would explain the consequent higher lifetime ESKD risk [11,12]. Although the differences were statistically significant, the absolute risk differences were minor. Therefore, any marginal increase in lifetime ESKD risk may be arguably outweighed by the benefits to the paediatric KTR and their parent LKD. There was no difference in the proportion of LKD-P exceeding the 1% or 2% lifetime predonation ESKD risk threshold, suggesting that similar acceptance criteria were used for LKD-P and LKD-A.

There are, however, limitations with the use of prediction tools for younger LKD. The modelling of these tools employed relatively short-term follow-up [10], while the incidence of ESKD only starts to rise exponentially from 10 years postdonation [18]. Although KDIGO has proposed extrapolation of the postdonation ESKD risk by multiplying the predonation risk estimates by 3.5–5.3-fold [10], other studies have reported donation-attributable risk to be 8–11-fold [7,8]. Uncaptured risk factors such as family history and prediabetes likely further underestimate the postdonation ESKD risk. The imprecise risk prediction in younger LKD-P highlights the importance of long-term postdonation follow-up for early identification and optimization of risk factors, as young motivated parents will likely continue to be the majority of LKD-P for their children.

Children with ESKD not uncommonly have multiple LKD candidates. The selection of the LKD should balance the risk to the LKD against that to the paediatric KTR. Since younger paediatric KTR had younger parents as LKD with attendant higher lifetime ESKD risk, grandparents would seem a reasonable alternative; however, this group consisted of only 7.3% of all LKD-P, similar to the International Collaborative Transplant Study [19]. As grandparents tended to donate to younger paediatric KTR compared with parents, this would suggest that grandparents have already been used to mitigate risk to younger parents as LKD-P in Australia and New Zealand. Furthermore, as paediatric KTR likely require multiple transplants during their ESKD journey, one could argue for grandparents to be the first choice. This would allow younger parents to donate for subsequent transplants when their ESKD risk prediction improves in precision with advancing age. In small studies, grandparents (age 50–67) [16] and older LKD (age $\geq$ 50) [17] offered similar graft outcomes compared with parents and younger LKD, respectively. However, caution should be exercised as grandparent LKD in these studies were likely a highly selected group with acceptable comorbidity profiles and HLA matching, as observed in our study. In addition, our cohort of grandparent LKD-P was relatively small.

Better HLA matching in paediatric KTR is associated with superior graft outcome, even in the contemporary era [17,19]. Recently, the combination of higher HLA eplet mismatch and poor adherence was found to synergistically worsen graft outcomes [20], a pertinent issue for paediatric KTR growing into adolescence and young adulthood. Furthermore, poor HLA matching for the first transplant is associated with broad HLA sensitization, lower re-transplant rate and reduced re-graft survival [13], highly relevant for paediatric KTR requiring multiple transplants. There is also a risk of repeat HLA mismatches from grandparent LKD for the first transplant, and the development of specific alloimmunity may limit the prospect of one of the parents to become LKD for the second transplant. In this analysis, grandparents were more likely to have a higher HLA A+B+DR and DR mismatches compared with parents, but there were no significant differences in the rates of zero A+B+DR or DR mismatch. While all parent LKD-P would offer $\leq$3 A+B+DR mismatches (associated with superior graft survival compared with $\geq$4 A+B+DR mismatches [19]), over half of grandparent LKD-P also achieved this.

When challenged to balance the lifetime ESKD risk in a very young parent LKD candidate against the unfavourable HLA mismatch profile from a grandparent, a feasible option in some jurisdictions is for the grandparent LKD and paediatric KTR to participate in a KPD program as a quasi-compatible pair [21]. This does not only offer the opportunity to improve the HLA mismatches but also increase the match rate for incompatible pairs in the program [22], a feasible option for paediatric KTR [23]. It is, however, somewhat contentious to utilize KPD for reducing the donor/recipient age mismatch, and this is not presently permitted in some KPD programs.

Father LKD-P had both higher 15-year and lifetime ESKD risk compared to mother LKD-P. This was also observed in fathers and males in the LKD-A cohort compared with mothers and females, respectively (data not shown). It is thought that this reflects male gender as an independent risk factor for ESKD in both the nondonor [24] and LKD [25] populations, in addition

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to having more comorbidity. The lower ESKD risk in mothers as LKD-P needs to be balanced against the increased obstetric risk of pre-eclampsia and gestational hypertension for those of childbearing age yet to complete their family [26].

Our study has several important limitations. Despite the ANZDATA registry capturing all LKD in Australia and New Zealand over the 12 years studied, the sample size for LKD-P was modest, particularly when stratified for the subgroup analysis of grandparents. Due to missing data (primarily uACR), 85% of the included LKD required imputed values to generate ESKD risk estimates. However, the baseline characteristics and ESKD risk estimates of the imputed data and complete data cohorts were comparable (Table S2), and such an approach has been adopted in other studies [10,27] to minimize selection bias and Type II errors. Furthermore, sensitivity analysis generated the consistent conclusion that LKD-P had a lower 15-year but higher lifetime ESKD risk, although the differences were accentuated. The lifetime ESKD risk estimates using the imputed median values (Table 2) rather than the 75 and 90th percentile values (Table S3) would more likely reflect the actual risk, supported by Grams *et al.* [10] reporting that 6% of previous donors in the United States exceeded the 1% risk threshold. We acknowledge that a small proportion of LKD-P with missing uACR might have increased albuminuria and their consequent ESKD risk underestimated. However, any such potential underestimation should affect both LKD-P and LKD-A, as evidenced by the similar reported uACR values (Table 1). Finally, our study cohort was predominantly Caucasians and might not apply to other nonwhite ethnic groups at increased risk. For instance, African Americans have an approximate fourfold increase in ESKD risk compared with white LKD [8]. Despite these limitations, to our knowledge, this is the first novel study using national registry data to compare the predonation ESKD risk estimates to risk stratify the LKD-P subpopulations and highlight the influence of LKD age on lifetime ESKD.

In summary, LKD-P, primarily young parents, have a lower 15-year but higher lifetime ESKD risk. Although donor well-being remains a major clinical consideration, our study provides cautious reassurance that the absolute risk difference is minor. Furthermore, in the context of significant benefits to the paediatric KTR and emotional considerations, this small increased risk is likely outweighed by the unique relationship between the KTR and the parent LKD. To avoid the lifetime risk of ESKD in the very young parents as LKD, carefully selected grandparents should be considered as an alternative, and KPD might be a strategy to mitigate the immunologic risk to the paediatric KTR.

Authorship

DL, JBW, NC, AMW, FLI, MAR and JYK: designed study. DL and NC: collected data. DL and JBW: analysed data. DL: wrote the manuscript. JBW, NC, AMW, FLI, MAR and JYK: manuscript review and revision.

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Conflict of interest

The authors have declared no conflicts of interest.

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SUPPORTING INFORMATION

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

Figure S1. Schematic flow chart of the study cohorts.

Table S1. Imputed values of missing uACR and BMI using median, 75 and 90th percentile values for the imputed data cohort.

Table S2. Demographics and predonation risk estimates of LKD for paediatric versus adult KTR in compete data and imputed data cohorts.

Table S3. Sensitivity analysis of predonation ESKD risk estimates in LKD for paediatric versus adult KTR.

Table S4. ESKD risk profile of grandparent versus parent and mother versus father LKD for paediatric KTR.

Table S5. Demographics and predonation ESKD risk estimates of LKD for paediatric KTR stratified by median KTR age.

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