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WHY DON'T ALL LIVING KIDNEY DONOR CANDIDATES PROCEED TO DONATION?

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Key words: living kidney donor, transplant, risk factors, outcomes.

Background:

The first successful living donor kidney transplant occurred in 1954 between identical twins. Although 23 years old at the time, the donor went on to develop end-stage kidney disease (ESKD) requiring haemodialysis 56 years later[1]. The success of this initial living donor

transplant led to transplant programs adopting this as the preferred method of kidney transplantation with tremendous benefits for the recipient. The very long-term outcomes of living kidney donors are still being debated and may be one reason for the lack of increase in the number of living donors in Australia over many years[2]. It is not clear whether the number of people offering to be LKDC is decreasing, or if candidates themselves fail to pass the acceptance criteria.

The shared decision to proceed with kidney donation from a living person is based on sufficient knowledge of the risks and benefits following a living donor education program and extensive interviewing, examination and testing of the potential donor[3]. Acceptance criteria and guidelines have been published, yet there is not stringent adherence to these guidelines in Australia, possibly because of the relationship that donors have with the recipients[4, 5]. Some donors may be willing to accept some increased risk due to the influence of their relationship to the recipient [6].

Recently there have been several large studies examining the long-term outcomes of kidney donors, which allow estimation of the risk of end-stage kidney disease (ESKD) for the donors themselves[7-10]. Together, these studies suggest a small increase in risk, that can now be estimated using online calculators[11].

We examined the risk factor profile of all LKDC presenting to our unit to compare those accepted versus those not against the current clinical guidelines, to better understand reasons for and implications of non-acceptance.

Methods:

We performed a retrospective review of all LKDC referred between 1st January 2006 to 1st January 2017 at the Royal Hobart Hospital (RHH), Tasmania, Australia. Kidney transplantation for Tasmanians with ESKD is performed by Melbourne Health at the Royal Melbourne Hospital (RMH). LKDC and their recipients are assessed locally by the RHH Renal Unit clinicians and subsequently by the RMH Transplant Team prior to acceptance.

Individuals were considered LKDC upon referral to the Renal Unit at the RHH from their General Practitioner and were categorised as potential (currently under assessment or accepted, but not yet donated), not accepted (a decision has been made and communicated that donation will not proceed) and donated (kidney donation has already occurred following acceptance).

Comparison of pre-donation risk factor profile was made against Caring for Australasians with Renal Impairment (CARI) living kidney donor guidelines and Kidney Disease: Improving Global Outcomes (KDIGO) clinical practice guidelines on the evaluation and care of living kidney donors[4, 12, 13]. The risk factors of interest included: estimated glomerular filtration rate (eGFR) < 80mls/min/1.73m^2, proteinuria >300mg/24 hours, blood pressure >140/80 (or use of antihypertensive medications), body mass index (BMI) > 30kg/m^2, or glucose intolerance or diabetes.

Risk calculators were used as per the CKD-Prognosis Consortium risk calculators (*transplantmodels.com*) of ESKD[11]. ESKD was defined as initiation of renal replacement

therapy, placement on the waiting list for transplantation, or receipt of a living or deceased donor kidney transplant[9].For LKDC considering donation, their estimated 15-year and lifetime risk of ESKD was calculated using the *ESRD risk tool for kidney donor candidates* [14]. To inform LKDC of their 5, 10, 15 or 20-year risk of ESKD having already donated a kidney, we used the *Kidney Donor risk of ESRD calculator* [15].

Data was extracted from the Digital Medical Record at the Royal Hobart Hospital and AUDIT4 database (Software for Specialists, Australia) into Microsoft Excel. All data analysis was performed using STATA15 (StataCorp, USA). Continuous parametric data were analysed using Student's t-test and categorical values using the Pearson's chi-squared test. A $p < 0.05$ was considered to represent a statistically significant difference.

Approval for this living kidney donor study was granted after review by the Tasmanian Health and Medical Research Ethics Committee (approval number H0012959).

Results:

116 people were referred (51% female, mean 53.7 years) as LKDC. Of these, 65 (56%) progressed to donation, 33 (28%) were not accepted for donation and 18 (16%) remained under assessment.

Those accepted were more likely to be younger (50.5 v 58.7 years if not accepted, p=0.001), have no contraindications (78% v 42%, p=0.004) and have never smoked (91% v 42%, p<0.001). At least 1 relative contraindication was identified in 22% of accepted donors and 57% of donors not accepted. The most common relative contraindication in accepted donors was eGFR <80mls/min/1.73m^2 (15% of accepted donors). Both genders were equally accepted (table 1).

There were thirty-three LKDC not accepted for donation due to an identified current health issue (60%), the presence of risk factors for long-term ESKD (17%), social reasons (13%) or positive cross-match (7%). Social reasons consisted of withdrawal after education and assessment.

Those accepted for donation had a lower projected 15-year (0.08% v 0.19%, p<0.05) and lifetime (0.21% v 0.40%, p<0.05) incidence of ESKD. However, the estimated risk of developing ESKD at 20 years post-donation was not different between those accepted or not (0.44% v 0.46%, p=NS).

Discussion

Clinical practice variation in donor acceptance exists in Australia despite published national and international guidelines[5, 13, 16]. Our results demonstrate that the majority of LKDC can be accepted in accordance with current local clinical guidelines and yet still maintain a high rate of transplantation.

The long-term outcome of living kidney donors is likely favourable with respect to progression to ESKD. However, the majority of international evidence is based on Caucasian populations from western countries, and not all LKDC will fit this demographic and clearly need special consideration, including Aboriginal Australian kidney donors [17]. Acceptance or rejection is often based on one or more contraindications, yet the measures themselves are not categorical, nor fixed. For many LKDC, the donor assessment may provide a motivation to long-term self-management of these modifiable risk factors that may be present at donation. Our data show a high rate of smoking and elevated blood pressure in those not accepted, with communication back to the referring General Practitioner recommending ongoing management of these disease risk factors. However, in those accepted, we also found an eGFR <80mls/min/1.73m^2 in 15%, elevated blood pressure in 5% and ongoing smoking in 5%, all of which are risk factors for chronic kidney disease. This data again highlights the need for long-term donor surveillance for individual management.

The use of calculators and risk prediction models is helpful to both clinicians and LKDC, by allowing numerical prediction of future ESKD risk However, the calculators are unable to predict risk of other possible complications. The risk of ESKD is small and the acceptable risk threshold varies by LKDC and transplanting centre. The right to autonomy of a LKDC and transplanting centre is likely to drive the clinical practice variation seen in Australia and internationally. Clinical experience is continually improving, but clinicians are required to advise on a fifty-year horizon for which evidence is lacking.

This work has several limitations that may limit its applicability to other units. Firstly, it is a single-unit, retrospective audit of clinical assessment and decision-making. Secondly, the time period of inclusion commenced prior to the publication of the current guidelines. Finally, the LKDC assessed in this study are nearly all Caucasian.

Rates of LKD in Australia are not increasing – our data would suggest assessment is rigorous and according to guidelines, thus more needs to be done to increase the number of accepted donors. This could be achieved by lowering acceptance thresholds (accepting a greater long-term risk) or recruiting more potential LKDC for assessment via community or family education programs. The former option may be less safe for the LKDC, although evidence for this is lacking.

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Table 1 Baseline demographics and clinical assessment of living kidney donor candidates not accepted (No) and those who were accepted and donated (Yes).

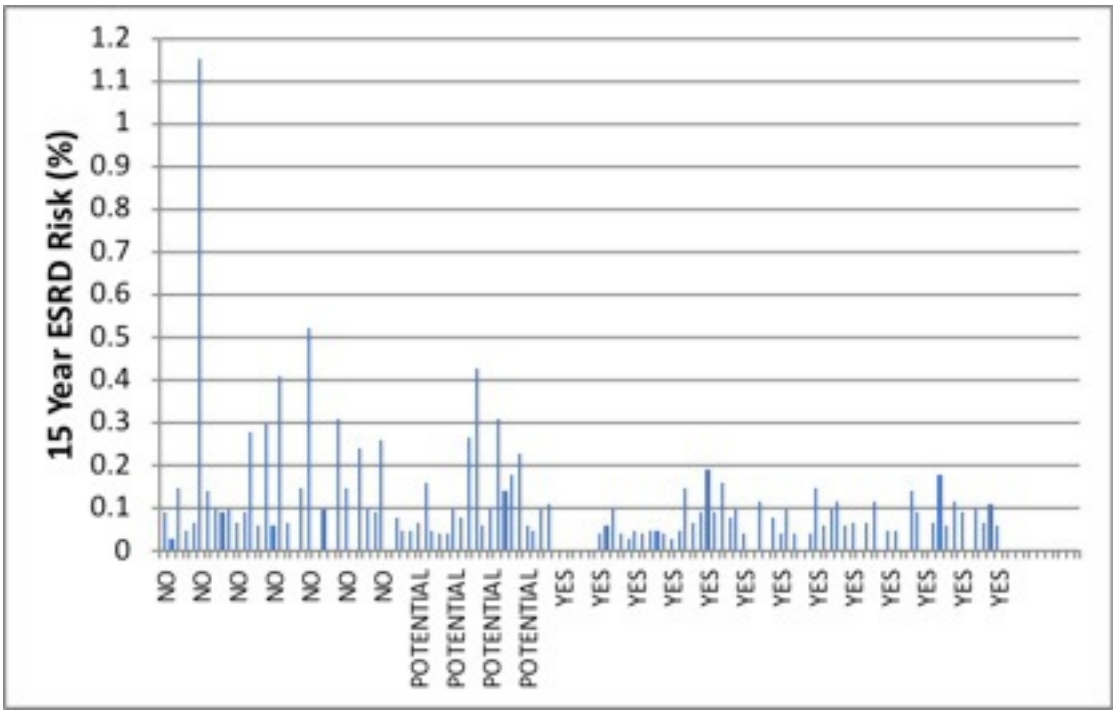
Factor	Level	No	Yes	p-value
N		33	65	
Age, mean (SD)		58.727272 (12.05527)	50.53846 (9.8553238)	<0.001
Gender	Female	17 (52%)	35 (54%)	0.83
	Male	16 (48%)	30 (46%)	
Racial Origin	Asian	0 (0%)	1 (2%)	0.47
	Caucasian	33 (100%)	64 (98%)	
Smoking history	Never smoked	13 (39%)	59 (91%)	<0.001
	Ex smoker	10 (30%)	3 (5%)	
	Current smoker	10 (30%)	3 (5%)	
Total contraindications	0	14 (42%)	51 (78%)	<0.001
	1	14 (42%)	13 (20%)	
	2	5 (15%)	1 (2%)	
eGFR<80mls/min/1.73m2	>80	30 (91%)	55 (85%)	0.39
	<80	3 (9%)	10 (15%)	
Urine protein >300mg	No	32 (97%)	65 (100%)	0.16
	Yes	1 (3%)	0 (0%)	
Blood pressure >140/80	No	17 (52%)	62 (95%)	<0.001
	Yes	16 (48%)	3 (5%)	
BMI >30kg/m2	No	31 (94%)	63 (97%)	0.48
	Yes	2 (6%)	2 (3%)	
Impaired glucose tolerance	No	31 (94%)	65 (100%)	0.045
	Yes	2 (6%)	0 (0%)	

Figure 1 Pre-donation estimated 15-year risk of end-stage kidney disease [14]

Abstract word count: 78

Abstract

There are national and international guidelines for donor workup and acceptance criteria of potential living kidney donor candidates (LKDC), but there is significant variation in clinical practice. We examined our local practice in assessing potential LKDC against current guidelines; nearly all of our accepted donors met these guidelines. LKDC who did not proceed to donation had an identified health issue (60%), the presence of risk factors for long-term end-stage kidney disease (17%), social (13%) or immunological reasons (7%).



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