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Temporal Changes in Deceased Kidney Donor Characteristics in Australia

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Background. Demand for deceased donor kidneys has exceeded supply in Australia over the past 2 decades. With a desire to use as many donor organs as possible, the health characteristics of accepted donors may have changed over time. **Methods.** All deceased kidney donors actually transplanted in Australia between January 1, 1994, and December 31, 2013, were retrospectively analyzed, using data from the Australian and New Zealand Organ Donor Registry. **Results.** Of 4172 deceased donors, 57% were men. Mean donor age increased from 37.2 ± 16.8 years to 46.1 ± 17.7 years over time, and donor numbers increased from 162 in 1994 to 334 in 2013. As the primary cause of death, motor vehicle accidents decreased from 27% to 12%, whereas cerebral pathology persisted at 50%. There was an increase in the proportion of donors with hypertension (12% to 24%), diabetes (2% to 7%), and an increase in mean body mass index (24.4 ± 4.4 kg/m^2 to 27.5 ± 6.3 kg/m^2) between 1994 and 2013. These changes were reflected by an increase in the median kidney donor risk index from 1.08 (interquartile range, 0.85-1.25) to 1.32 (interquartile range, 0.95-1.53). The proportion of medically higher risk donors increased over time. **Conclusions.** Because deceased kidney donor numbers have increased, the range of donor quality has broadened, with an increase in both the proportion and number of high-risk donors, as well as a decline in donor quality. These data highlight the need for kidney allocation algorithms to evolve to ensure appropriate allocation of deceased donor kidneys.

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Kidney transplantation extends life expectancy and improves quality of life for most individuals with end-stage kidney disease compared to those remaining on dialysis.[1,2] Unfortunately, demand for deceased donor kidneys exceeds supply,[2-4] and has resulted in attempts to increase the pool of potential donors by including more marginal kidneys from so-called expanded criteria donors (ECD) who have characteristics associated with poorer allograft outcomes compared with standard criteria donors (SCD).[3,5,6] An ECD is defined as a donor aged 60 years or older, or a donor aged 50 to 59 years with a history of 2 of the following: hypertension, death due to cerebrovascular event, or serum creatinine concentration greater than 1.5 mg/dL (>133 μmol/L). ECD kidneys are associated with a relative risk of allograft failure of 1.7 compared with SCD kidneys.[3,5-7] However, SCD/ECD status is an imperfect approach to defining donor quality, because it only takes into account a limited number of clinical variables and has relatively poor predictive value for observed allograft survival.[3,6]

In response to the increased utilisation of ECD kidneys, the concept of "longevity matching" has emerged, whereby attempts have been made to allocate higher quality donor kidneys preferentially to recipients who are expected to have the longest posttransplant survival. The application of longevity matching has been limited partly by the lack of a high-quality method for estimating donor quality. Recently, the Kidney Donor Risk Index (KDRI) and Kidney Donor Profile Index

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TABLE 1.

Demographic data summary

	Years of donation					
	1994 to 1997 (n = 681)	**1998 to 2001 (n = 664)**	**2002 to 2005 (n = 755)**	**2006 to 2009 (n = 838)**	**2010 to 2013 (n = 1234)**	***P* (for trend over time)**
Male	408 (60)	387 (58)	448 (59)	470 (56)	685 (56)	0.32
Age, y	37.2 ± 16.8	39.5 ± 18	41.1 ± 17.9	43.7 ± 17.9	46.1 ± 17.7	<0.001
Body mass index, kg/m^2						<0.001
<20	48 (7)	60 (9)	56 (7)	41 (5)	69 (6)	
2 to ≤ 25	399 (59)	383 (58)	367 (46)	385 (46)	539 (44)	
BMI 25 to ≤ 30	184 (27)	182 (27)	268 (32)	268 (32)	376 (30)	
BMI >30	50 (7)	39 (6)	144 (17)	144 (17)	250 (20)	
Ethnicity						<0.001
Whites	640 (94)	615 (93)	705 (93)	770 (92)	1117 (91)	
ATSI	4 (1)	3 (1)	4 (1)	8 (1)	16 (1)	
Other	37 (5)	46 (7)	46 (7)	60 (7)	101 (8)	
Cause of death						<0.001
Trauma	183 (27)	144 (22)	139 (18)	112 (13)	149 (12)	
CVA	338 (50)	341 (51)	387 (51)	436 (52)	592 (48)	
Hypoxia	29 (4)	47 (7)	72 (10)	120 (14)	200 (16)	
Hanging	4 (1)	9 (1)	15 (2)	21 (3)	70 (6)	
Other	127 (19)	123 (18)	142 (19)	149 (18)	223 (18)	
Hypertension	81 (12)	103 (16)	145 (19)	174 (21)	299 (24)	<0.001
Diabetes mellitus	15 (2)	14 (2)	34 (5)	57 (7)	84 (7)	<0.001
Creatinine terminal, μmol/L	91.1 ± 36.7	86.2 ± 42.1	89.8 ± 63.9	91.8 ± 67.9	88.5 ± 66.9	0.68
Hepatitis C antibody	0 (0)	0 (0)	6 (1)	4 (1)	8 (1)	<0.001
DCD	6 (1)	5 (1)	14 (2)	81 (10)	283 (23)	<0.001
KDRI	1.08 (0.88 – 1.33)	1.13 (0.91 – 1.44)	1.14 (0.9 – 1.46)	1.21 (0.93 – 1.60)	1.29 (1.01 – 1.68)	<0.001

N is the denominator for percentage (data not always available for all patients).

NA, not available; NS, not significant; ATSI, Aboriginal and Torres Strait Islander; CVA, cerebrovascular accident; KDRI, kidney disease risk index; BMI, body mass index.

were developed using data from the United States Scientific Registry of Transplant Recipients with the aim of improving deceased donor risk assessment.[6] The KDRI is a continuous numerical score that incorporates 10 donor factors (age, height, weight, ethnicity, history of hypertension, history of diabetes, cause of death, serum creatinine, hepatitis C virus status, and mode of donation [donation after brain death or donation after circulatory death {DCD}]). The relative impact of these variables on allograft survival was evaluated by analysing US data from almost 70 000 recipients of a first deceased donor kidney transplant with adjustment for recipient factors. KDRI provides an estimate of the relative risk of posttransplant kidney graft failure (in an average adult recipient) compared with the median (50th percentile) donor in the United Network for Organ Sharing in the United States.

Kidneys from deceased donors in Australia are allocated based on waiting time and HLA matching, without specific consideration of donor kidney quality or expected long-term renal allograft outcomes. It has been speculated that the spectrum of deceased donor kidney quality in Australia has become broader over time because of expansion of the donor population with respect to age, comorbidity, and mode of donor death (including DCD). Hence, the aim of this article was to describe the temporal changes in Australian donor characteristics during the 20 year period from 1993 to 2014.

MATERIALS AND METHODS

Donor Characteristics

This study included all deceased kidney donors in Australia between January 1, 1994, and December 31, 2013. Potential donors whose organs were not used were excluded. Deidentified donor data were collected from the Australian and New Zealand Organ Donor (ANZOD) Registry, which has recorded information on all organ donations since its inception in 1989 in Australia and 1993 in New Zealand (http://www.anzdata.org.au). Donor characteristics studied included age, height, weight, ethnicity, history of hypertension, history of diabetes, cause of death, serum creatinine, hepatitis C status, and DCD status.

Calculation of KDRI

The calculation of KDRI in this article was based on Rao's KDRI formula[7] which estimates the risk of function loss of a kidney graft transplanted to a "reference" donor. This was defined as a 40-year-old non–African American; brain-dead donor; 170-cm tall; weighing 80 kg; with a creatinine level of 1 mg/dL (88 μmol/L); 2 HLA-B mismatches; 1 HLA-DR mismatch; no prior history of hypertension, diabetes, or hepatitis C; and a cold ischemia time less than 20 hours. Donors were excluded from this analysis if missing data meant that it was not possible to calculate the KDRI. The formula for calculating KDRI[7] was consistent with the approach suggested by the Organ Procurement and Transplantation Network Registry.

Statistical Analyses

Results were expressed as frequencies (percentages) for categorical variables, mean ± SD for continuous normally distributed variables, and median (interquartile range [IQR]) for continuous non-normally distributed variables. Differences between variables were analyzed by the χ^2 test for categorical data, *t* test for continuous normally distributed data and Mann-Whitney *U* test for continuous non-normally distributed data. Analysis of trend over time in KDRI was performed after conversion of KDRI to a categorical variable (quartiles determined by data in 1994 because KDRI did not adequately normalize with standard transformation procedures), and a nonparametric test of trend for the ranks across ordered groups was performed (using nptrend Stata command); this method was used for examining trends in all ordinal categorical variables. Analysis of trends over time for normally distributed variables was assessed using linear regression technique. Statistical analysis was performed using standard statistical software (Stata 14 SE, College Station, TX).

RESULTS

Overall, 4240 deceased kidney donors were recorded with the ANZOD registry during the 20-year study period. Data were missing for 68 donors and hence KDRI could only be calculated for 4172 deceased kidney donors in this study. Annual donor numbers increased from 162 in 1994 to 334 in 2013. Mean donor age progressively increased over 10 years from 37.2 ± 16.8 years in 1994 to 46.1 ± 17.7 years in 2013 (Table 1). Similarly, mean body mass index increased by 3 kg/m^2 and the proportion of donors who were overweight or obese increased from 38.5% in 1994 to 58.4% in 2013 ($P < 0.001$) (Table 1, Figure 1). In terms of ethnicity, the majority of donors were white, but there were a modest increase in the proportion of Aboriginal and Torres Strait Islander donors over time. Significant increases were also observed in the proportions of donors with hypertension (approximately 4-fold increase) and diabetes mellitus (approximately 2-fold

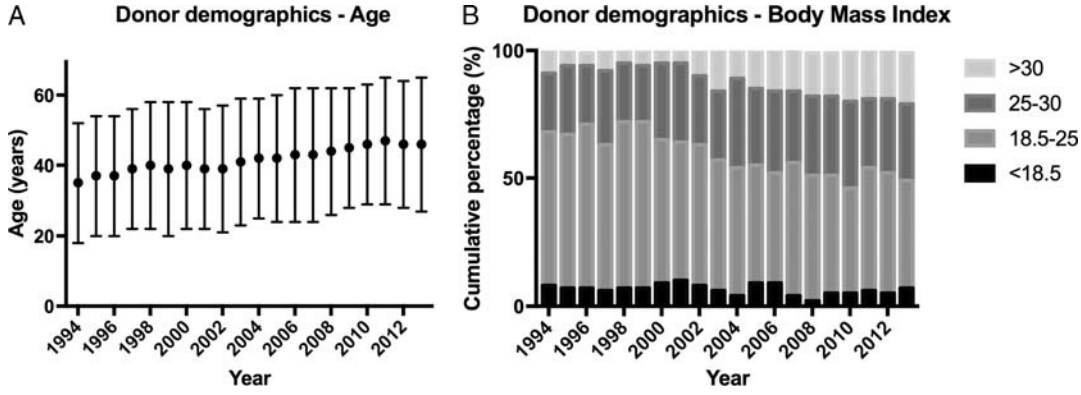

FIGURE 1. Distribution of (A) age and (B) body mass index, in all Australian kidney donors over a 20-year period.

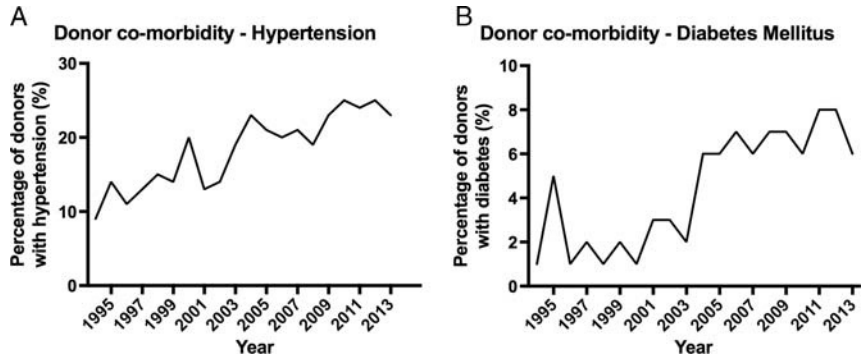

FIGURE 2. Distribution of (A) hypertension and (B) diabetes mellitus in all Australian kidney donors over a 20-year period.

increase) ($P < 0.001$) (Table 1, Figure 2). With respect to primary cause of death, cerebral anoxia increased in frequency over time, whereas an appreciable decrease was observed in road trauma (Table 1, Figure 3). No appreciable temporal trends were observed for serum creatinine or hepatitis C status (Table 1). The proportion of DCD donors also increased substantially over time, more significantly in final 6 years of the study period, reaching 23% of total donors in 2013 ($P < 0.001$). These temporal changes in donor characteristics between 1993 and 2013 were reflected by a rise in the median KDRI from 1.02 (IQR, 0.85-1.25) to 1.32 (IQR, 0.95-1.53) (95% confidence interval, 0.007-0.010; $P < 0.001$) (Figure 4A). When divided into 5 sections, the proportion of higher-risk donors (KDRI >1.5) increased over time rising from 10% in 1994 to 29.5% in 2013 (Figure 4B).

DISCUSSION

Because transplantation evolved from an experimental technique to an accepted and optimal therapy for end-stage kidney disease, there has been an imbalance between supply and demand for deceased donor kidneys. This has resulted in pressure for the transplant community to accept a broader range of donors, albeit with concerns about the longevity of kidneys from more "marginal" donors. Earlier studies identified significant interactions between deceased kidney donor characteristics and allograft survival. Port et al[5] identified increased donor age, hypertension, diabetes, and acute kidney injury as important predictors of lower allograft survival, leading to the dichotomous definition of SCD or ECD.

Besides scores based on clinical donor variables, other groups have advocated histological assessment of deceased donor kidneys to assess organ quality.[8] In recent years, KDRI has emerged as a metric that allows estimation of deceased donor kidney risk and has been validated in the United States donor population with good predictive value for allograft survival. This is the first study to evaluate temporal changes in the characteristics of deceased kidney donors in Australia. The key finding was that the range of donor quality, as estimated by KDRI, has increased over the last 20 years, with a progressive reduction in median donor quality.

The growth in donor numbers during this time has occurred primarily in higher risk donors with a KDRI greater than 1.5, driven by increases in donor age, obesity, hypertension, and diabetes, as well as more frequent donation after circulatory death and cerebrovascular disease as a cause of death. There are several potential reasons why donor characteristics may have changed over time. First, the changes may be a consequence of a broader shift in the age and health of the general population. In support of this, the increases in donor age and in the prevalence of hypertension, obesity and diabetes mirrors commensurate changes in the general population, as evidenced by data published from the Australian Institute of Health and Welfare.[9] In terms of donor cause of death, over the 20-year period, there was a reduction in head trauma associated with motor vehicle accidents which likely reflects improvements in road safety over the same period.[10,11] Indeed, across the 10 variables in this study, age, hypertension, DCD followed by the height and the weight of the donors in this order accounted for the largest contributions to the KDRI over the 20-year period. Changes in age, body mass index, hypertension, diabetes and DCD were statistically significant over the 20-year period. A second explanation for

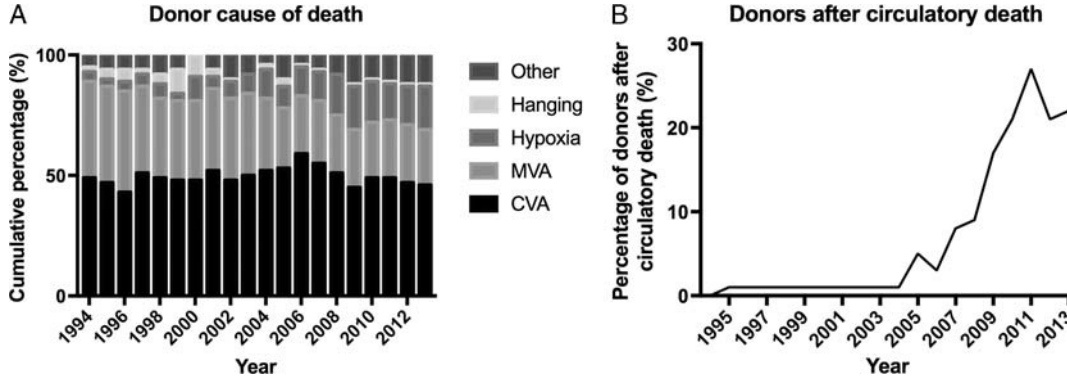

FIGURE 3. Distribution of (A) causes of death and (C) DCD in all Australian kidney donors over a 20-year period.

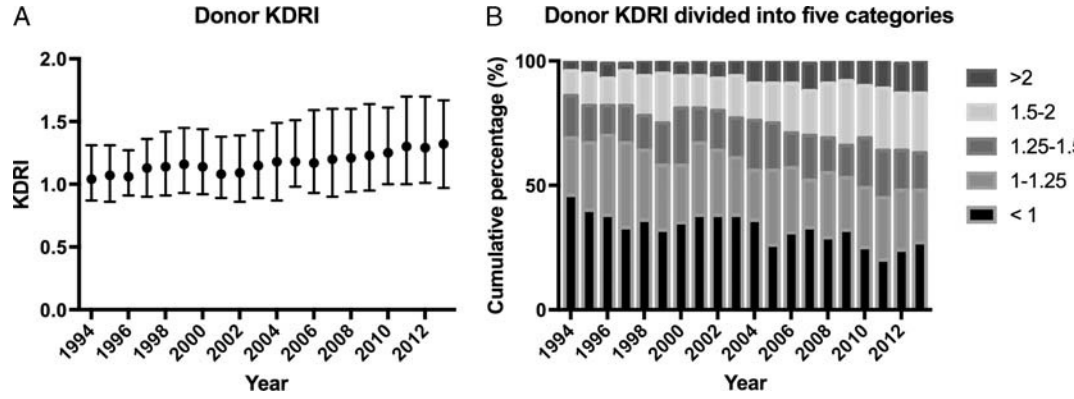

FIGURE 4. Distribution of KDRI as a (A) continuous variable or (B) 5 category variables in all Australian kidney donors over a 20-year period.

the variation in donor characteristics is that changes in critical care management in Australia over the last 20 years have potentially resulted both in acceptance of a broader range of patients for intensive care support, as well as subsequent referral for consideration of donation. One major change affecting the selection and quality of deceased kidney donors has been the recent increase in utilisation of kidneys donated after circulatory death. Finally, the criteria used by the transplant community in Australia to accept or reject donors may have been modified over time. It was not possible for us to investigate this possibility further as the characteristics of potential donors who were subsequently rejected as medically unsuitable were not available.

The observation that the range of donor quality is increasing over time has important implications for the design of kidney allocation algorithms. Currently in Australia, deceased donor kidneys are allocated primarily by waiting time and degree of HLA matching, without formal consideration of donor or recipient longevity matching. However, as the variation in donor quality increases, there is an escalating risk of suboptimal kidney allocation in terms of estimated allograft longevity. From a utilitarian and health economic perspective, it is undesirable to allocate a kidney with relatively short predicted survival to a young and otherwise healthy recipient, because they are likely to return to dialysis and require re-transplantation much earlier than if they received a higher quality organ. Similarly, allocating a kidney from an optimal donor to a recipient with an estimated post-transplant life expectancy that is substantially shorter than the potential graft survival makes poor use of the limited supply of donor organs.

"Longevity matching," using the KDRI, as has recently been introduced in the United States, offers a qualitative evaluation of deceased donor quality, as well as an estimate of recipient survival posttransplant. Kidneys from the donors with the highest estimated graft survival (top 20% of Kidney Donor Profile Index) are allocated preferentially to recipients with the longest predicted posttransplant survival. Such a system has the potential to match donors and recipients more closely and maximize the utility of donor organs. The KDRI score in the United Statesin 2013 was approximately 1.2 which is similar to the Australian KDRI score in 2013 of 1.22. KDRI has been validated in the transplant recipients in the United States; therefore, the median donor risk, as assessed by KDRI, is similar in contemporary United States and Australian donor populations.

In other countries, both Norway and Catalonia have incorporated age matching in allocation policies mainly because of the rapid aging population. Compared with the Australian deceased donor pool, the mean age of deceased donors in Norway and Catalonia was higher, the mean age of donors in the United States was significantly lower, and the mean age of donors in the United Kingdom was similar.[12-15] Eurotransplant has addressed the issue of population ageing in its kidney allocation policies through the introduction of the Eurotransplant Seniors Program (ESP) in 1999,[16] which allocates kidneys from deceased donors aged over 65 years to antibody incompatible recipients older than 65 years without the use of HLA typing. Kidneys are allocated locally to minimise cold ischemia time. The intention of the ESP is to match kidneys to recipients based on their expected lifespan. The ESP has reduced waiting times for older candidates and improved access to younger donor kidneys for younger candidates.[17] Recipients of "old-for-old" kidneys through the ESP experience a lower risk of delayed graft function (as a consequence of local allocation and shorter cold ischemia times), but higher rates of biopsy-proven acute rejection and late rejection compared with "old-to-any" or "any-to-old allocation."[18] These ideas are currently not a prime focus in the Australian kidney allocation algorithm, but should be strongly considered given the donor characteristics in Australia are similar to other countries.

The present study has some limitations. As a descriptive study, there is limited depth of data collection. ANZOD does not collect information on the severity of co-morbidities and only provides a limited range of comorbidities recorded but lacks donor details such as proteinuria, smoking status, and preimplantation or postimplantation biopsy results. Second, there is no external audit of the accuracy of the data provided to ANZOD, and so there is no way of ensuring the validity of these data. In this study, no attempt was made to link KDRI scores with clinical outcomes, because this forms the focus of an ongoing research project. Nevertheless, it is interesting to note that published data from the Australian and New Zealand Dialysis Transplantation registry indicate progressive improvements in deceased donor graft survival over the 20-year study period, despite the increasing KDRI scores.[19] A further limitation is that ANZOD does not collect data on potential donors whose kidneys were not subsequently transplanted, for example, donors whose kidney were discarded due to poor quality after retrieval, or where an incidental finding of unsuspected infection or cancer was found in the donor at

retrieval. However, despite these limitations, a key strength of the present study is its completeness, with inclusion of donor data from all kidney transplants in Australia over a 20-year period.

In conclusion, this study has shown that as kidney donation rates have increased in Australia over the past 2 decades, the range of donor quality has increased and average donor quality has decreased. This highlights the importance of strategies to ensure appropriate allocation of both better quality and more marginal kidneys to the most appropriate recipients. Reporting KDRI for potential deceased donors may provide transplant candidates and their physicians with important information about the risk associated with accepting a particular donor kidney offer, which can be balanced against the risk of remaining on the waiting list. Furthermore, KDRI or a similar donor risk score could be introduced as part of the Australian kidney allocation algorithm, with the aim of enhancing organ and recipient longevity matching. An important step in this process would be to validate the predictive value of KDRI on allograft survival in the Australian transplant population, which should form the basis for a further study.

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