Patterns of organ donation in children in Australia and New Zealand

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In Australia, the rates of deceased organ donation (OD) have been increasing annually.[1] Paediatric OD represents a small proportion of total donations in Australia and New Zealand, comprising 3% in 2012 and 5% in 2013.[2] This compares similarly with the United States[3] and the United Kingdom.[4] Reasons for this include lower mortality, surgical technical limitations and uncertainty about medical suitability in uncommon or complex diseases. Since the introduction of Australian government reform in 2009, OD rates have increased from 11.4 per million population (pmp) to 18.3 pmp[5] but it is not known how rates have changed for the paediatric population.

Describing paediatric donation as a proportion of intensive care unit deaths may be more reflective of the true potential donor pool compared with pmp. The paediatric population represents a small proportion of the total population, and paediatric ICU mortality in Australia and New Zealand is low. In addition, as the general population ages and OD criteria expand for adult donors, the proportion of paediatric donors is likely to decline. In this context, it is important to describe the contemporary epidemiology and characteristics of paediatric OD.

Both locally and internationally, donation after circulatory death (DCD) has re-emerged over the past decade. Transplant and paediatric societies in Australia,[6] the US[7] and the UK[8] endorse and promote its conduct. Transplant outcomes following DCD suggest equivalence or near equivalence to those following DBD for organs such as the liver and kidney.[9] Whether this applies to the paediatric sphere, where experience is still low, is not yet apparent.

Infants and neonatal donors represent a marginal donor population in paediatrics. Barriers to OD in infants have included the age limits for diagnosing brain death[10] and age criteria for transplantation.[11] There is potential for infants and neonates to contribute to the donor pool,[12,13] and recent reports of successful transplantation outcomes are emerging.[14] Despite having occurred infrequently over many decades, the rates of infant OD compared with the total paediatric population, over time, has not been described.

In light of the increasing OD rates in Australia and New Zealand, it is important to examine paediatric trends. Our aim was to define paediatric OD in a way that meaningfully reflects the potential donor pool and to describe the contemporary patterns of paediatric OD in Australia and

ABSTRACT

Objectives: Paediatric organ donation (OD) represents a small proportion of total OD in Australia and New Zealand. Our aim was to describe the patterns of paediatric OD, specifically, the demographic characteristics and donation outcomes over two time periods.

Design: We performed a retrospective study using national OD and intensive care registry data from intensive care units in Australia and New Zealand from 1 January 2000 to 31 December 2015. Data were analysed between two time periods. Paediatric data were compared with adult data.

Participants: Organ donors aged under 16 years in paediatric and mixed adult and paediatric ICUs.

Results: There were 267 paediatric organ donors, representing 5.4% of all donors. The rate of OD as a percentage of ICU deaths was comparable to adults (6.0% v 4.6%; $P < 0.001$). Over the entire period, donations after brain death totalled 244 (91.4%), and donations after circulatory death (DCDs) totalled 23 (8.6%). DCDs increased from 0.7% to 17% between the time periods ($P < 0.001$). Children aged under 2 years had a lower rate of donation than the general paediatric cohort (1.2% v 6.0%; $P < 0.001$).

Conclusions: Paediatric OD rates have not changed over time but are comparable to adults when expressed as a percentage of ICU deaths. Paediatric DCD has increased significantly over time.

New Zealand. In addition, we aimed to compare OD rates in infants, children and adults.

Methods

A retrospective study was performed between 1 January 2000 to 31 December 2015 on data obtained from two independent registries. OD data were obtained on children from birth to 16 years from the Australian and New Zealand Organ Donation (ANZOD) registry and the Australian and New Zealand Intensive Care Society Centre for Outcomes Research and Evaluation (ANZICS CORE) database. Deaths in children under 16 years were identified from the paediatric and adult patient databases within ANZICS CORE database.

Table 1. Demographic and donation characteristics of organ donations in children in Australia and New Zealand, 2000–2015, by period

Characteristic	Period		Total donations, 2000–2015	
	2000–2007	2008–2015	Paediatric	Adult
Median age, years (IQR)	11.3 (7.5–13.9)	9.8 (4.9–14.1)	10.8 (6.0–14.1)	46.9 (34–59.6)
Males, %	62%	59%	60%	57%
ICU deaths, n	2357	2050	4407	101 354
Donors, n (% of ICU deaths)	135 (5.7%)	132 (6.4%)*	267 (6.0%)	4646 (4.6%)†
DBD, n (% of total donors)	134 (99.3%)	110 (83%)	244 (91.4%)	3994 (86%)
DCD, n (% of total donors)	1 (0.7%)	22 (17%)†	23 (8.6%)	652 (14%)
Organs requested, n (average/donor)	822 (6.1)	856 (6.5)	1706 (6.4)	31 611 (6.8)
Organs retrieved, n (average/donor)	537 (4.0)	533 (4.0)	1071 (4.0)	18 243 (3.9)
Organs transplanted, n (average/donor)	521 (3.9)	519 (3.9)	1040 (3.9)	16 777 (3.6)
Most common causes of death, % of total donors	Trauma 36%, SIH 14%, hypoxia 12%, cerebral‡ 10%, TBI 8%	Trauma 40%, hypoxia 17%, drowning 12%, hanging 11%, cerebral‡ 10%	Trauma 39%, hypoxia 12%, SIH 11%, cerebral‡ 11%, TBI 4%	ICH 47%, trauma 20%, hypoxia 13%, cerebral infarct 6%, cerebral‡ 3%

IQR = interquartile range. ICU = intensive care unit. DBD = donation after brain death. DCD = donation after circulatory death. SIH = spontaneous intracranial haemorrhage. ICH = intracranial haemorrhage. TBI = traumatic brain injury. * $P = 0.34$. † $P < 0.001$. ‡ Infectious, vascular, malignant, oedematous or metabolic origin.

Demographic, clinical and donation characteristics of the population were described. We collected demographic data on age, sex, and cause of death. Donation characteristics included donation modality, and request, retrieval and transplantation rates (defined as number of organs per donor). The maximum potential number of organs per donor was eight. The donation rate per organ was also described.

We analysed the data on an annual basis and compared two time periods, 2000–2007 and 2008–2015. These periods corresponded to the emergence of DCD in Australia and New Zealand. Rates of OD in children, as a percentage of ICU deaths, were compared with adults. An ICU death (for adults and children) is defined by ANZICS CORE as death occurring within 24 hours of ICU discharge. A child was defined as a person aged under 16 years (at the time of death). Donation rates in children aged under 2 years were compared with the overall paediatric rates. In addition, we compared OD rates and modality over time.

Approval to obtain relevant data was sought from both registries. De-identified data were obtained and not re-identified at any stage during the study. Databases were not linked and therefore individual patient characteristics and outcomes were not analysed. Ethics approval was granted through the Human Research Ethics Committee at the Royal Children's Hospital, Melbourne (HREC 35234A).

Statistical analysis

We used Stata, version 14 (StataCorp) to analyse the data. Means and standard deviations (SDs) are used to describe normally distributed data, and medians and interquartile ranges (IQRs) are used to describe non-normally distributed data. A two-sided Fisher exact test was used to compare proportions between groups. Statistical significance was deemed as $P < 0.05$.

Results

There were 4407 paediatric deaths in ICUs between 1 January 2000 and 31 December 2015, of which 4084 (92%) occurred in specialist paediatric ICUs (PICUs). The total number of organ donors was 267, yielding an overall donation rate of 6.0% of ICU deaths (Table 1). The median age and donation rates were not different between time periods, but DCDs increased from 0.7% to 17% of ICU deaths ($P < 0.001$). The paediatric OD rate was comparable to that in adults (6.0% v 4.6%; $P < 0.001$) (Table 1) Over the entire study period, the contribution of paediatric ODs to the donor pool was 267/4913 (5.4%). Figure 1 shows the annual donation rate per modality over the study period.

Over the entire period, the median age of ICU death was 4.6 years (IQR, 0.3–9.1 years) and the median age of OD was 10.8 years (IQR, 6.0–14.1 years). Figure 2 shows the number of deaths and organ donors by age.

Cause of death

The most common cause of death was trauma (43%), followed by hypoxic brain injury (12%), spontaneous intracranial haemorrhage (11.8%) and cerebral insults (11.3%) including meningoencephalitis, diabetic keto-acidosis and malignancy (Table 1).

Organ donation in children aged under 2 years

There were 28 donations in children aged under 2 years over the entire period. In this age group there was a significantly lower donation rate compared with the total paediatric population (1.2% v 6.0%; $P < 0.001$) (Table 2).

Transplant outcomes

There were no differences in organ request, retrieval or transplantation rates between the two periods. The median number of organs requested, retrieved and transplanted were 6.4, 4.0 and 3.9 respectively (Table 1). The numbers of specific organs retrieved per year are shown in Figure 3.

The reasons some organs were not requested from donors included low age limitation (32%), declined consent (11%) and no suitable recipient (9%).

Discussion

Our key findings are that paediatric OD rates are comparable to the adult rate but have not changed between the two periods of our study. DCD has emerged since 2007. The median age of donation has remained constant over time and is higher than the median age of death. The donation rate in children aged under 2 years is significantly lower than the overall paediatric rate. Describing OD rates as a percentage of ICU deaths provides an appropriate metric for comparison.

Donation rates in children

In Australia, since the inception of the Federal Government's National Reform Agenda in 2009, annual donation rates have increased from 11.4 pmp to 18.3 pmp.[5] However, paediatric donation rates have remained static; we found no difference in donation rate, expressed as a percentage of ICU deaths, between the periods studied. We have, however, shown that these rates are similar to the adult rates. There are no prior reports of paediatric OD as a proportion of paediatric deaths in ICUs.

Internationally, the reported proportion of organ donors who are children is generally comparable to that seen in Australia and New Zealand.[4] In the UK, from 2003 to 2012, paediatric OD as a proportion of the total donor pool

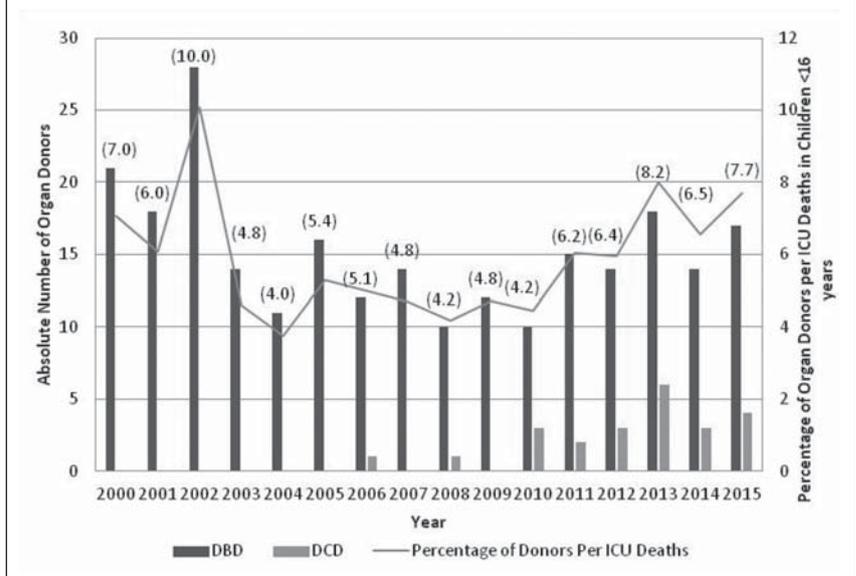**Figure 1. Total annual number of organ donors, by mode and annual donation rate, as a percentage of ICU deaths**

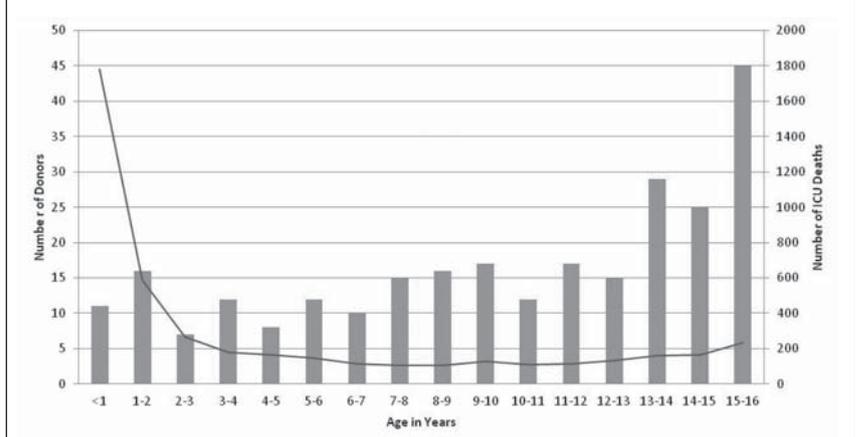**Figure 2. Distribution of organ donors and ICU deaths in children < 16 years, by age, over the study period**

Table 2. Donation outcomes for children < 2 years, compared with total paediatric outcomes over total period

Demographic variable	Age 0–2 years	Age 0–16 years
ICU deaths, n	2285	4407
Males, %	53%	60%
Number of donors, n (% of ICU deaths)	28 (1.2%)*	267 (6.0%)
DBD, n (% of total donors)	26 (92.9%)	244 (91.4%)
DCD, n (% of total donors)	2 (7.1%)	23 (8.6%)
Most common cause of death, (% of total donors)	Hypoxia (24%), drowning (24%), trauma (16%), cerebral (16%)	Trauma (39%), hypoxia (12%), SIH (11%), cerebral (11%)

DBD = donation after brain death. DCD = donation after circulatory death. SIH = spontaneous intracranial haemorrhage. * $P < 0.001$.

Figure 3. Annual number of organs retrieved per year*
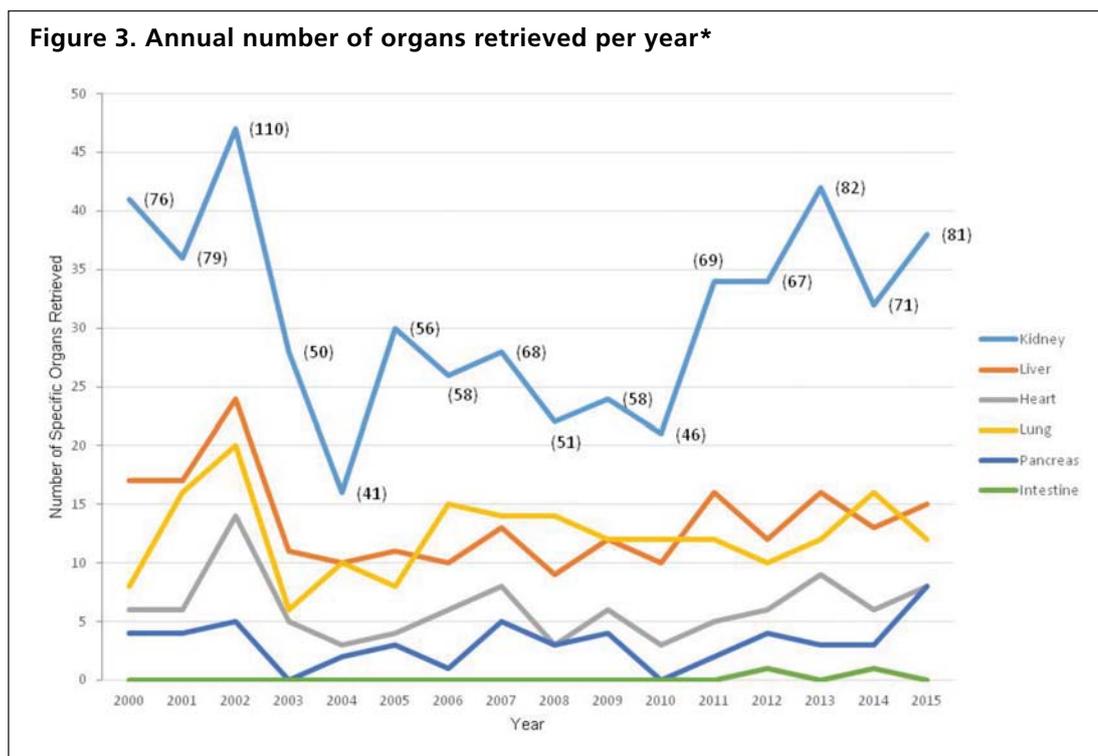
declined from 8% to 3%, but absolute numbers did not change. This appears to have resulted from an increase in the number of adult donors aged over 60 years. Similarly in Spain, a country that has high overall donation rates, paediatric donation as a proportion of the total pool remains low, ranging from 1.5 to 4.8% over the same period as our study).[15] The fundamental question is whether the metric by which paediatric OD rates are compared requires re-evaluation.

Metrics for measuring organ donation rates in children

Donation rates are commonly presented as pmp.[16,17] This takes into account population size and enables benchmarking internationally. In Australia and New Zealand, OD rates have been described as a proportion of intubated ICU deaths but rates are rarely presented in this way. Pilcher and colleagues showed that if deaths of intubated patients were used as a denominator, OD occurred in 8.1%.[18] In paediatrics, eligibility rates have been reported per 100 ICU beds,[19] but there are few reports on OD rates described as a percentage of ICU deaths. Godown and colleagues reported donation rates in the US using population mortality by age group, but not ICU mortality.[20] Donation rates as a percentage of ICU deaths compared with population-based mortality or pmp, although imperfect, more accurately reflect the potential donor pool in paediatrics. The ANZICS CORE adult and paediatric registries record deaths within 24 hours of ICU discharge. It is reasonable to assume that, in both adults

and paediatric patients, a proportion of these are unlikely to be eligible for OD, so using a denominator of intubated ICU deaths may be an even more accurate denominator.

PICU admission and mortality rates in Australia and New Zealand have changed substantially over several decades. PICU admissions in Australia and New Zealand reported to the Australian and New Zealand Paediatric Intensive Care (ANZPIC) registry have almost doubled over two decades, from 6366 in 2000 to 11 471 in 2015, but the mortality rate has decreased from 4.25% in 2000 to 2.21% in 2014.[21,22] In absolute terms, the annual number of paediatric ICU deaths in Australia and New Zealand has remained relatively static, ranging from 249 to 297 per year over the duration of our study.

Donation after circulatory death in children

Our study showed that DCD significantly increased in the second period of our study, although absolute numbers were small. DCD in children is ethically and procedurally challenging,[23] but is regarded as a feasible and acceptable practice.[7] The opportunity for DCD is high, given the proportion of children who die after withdrawal of life-sustaining therapies, compared with brain death.[24] Historically, the potential for DCD has been described as low — 5.5% of ICU deaths in a US study from 2003.[25] A more recent US single-centre study showed that 10% of PICU deaths met neurological criteria for brain death, but 69% died after withdrawal of life-sustaining therapies.[24] The OD

rates in each group were 78% and 10%, respectively. A UK study in 2011 showed that about one-third of PICU deaths could have been eligible for DCD, but a large proportion had contraindications to DCD (69%).[26]

Discrepancies between these findings show practice variability and lack of internationally accepted guidelines or recommendations. The Society of Critical Care Medicine in the US endorses the development of standardised protocols for paediatric donation,[27] but practice is likely to have subtle differences between jurisdictions, internationally. Parental experiences of DCD are positive if empathy and due attendance to end-of-life care is preserved.[28] Paediatric critical care staff recognise DCD as an acceptable component of end-of-life care,[29] but also recognise the need to improve and standardise processes.[30]

Younger children and neonatal donors

In our study, the rate of OD in children aged under 2 years was significantly lower than that for the entire cohort. Age and size appear to be common reasons for organs not to be requested for OD. Several studies describe the potential for infant and neonatal donors and show that fewer than half of infant deaths may be eligible.[12,13,31,32] One of these studies reported a DCD rate of all neonatal deaths of 2.9%, but 7% of eligible deaths.[13] In Australia and New Zealand PICUs, 42% of deaths occur in children aged under 1 year,[22] suggesting that there is a considerable potential donor population. The profile of neonatal OD has recently been raised in the UK[33,34] in the context of recent successful cases.[35] The definition of brain death has also recently been revised in the UK to encompass neonates and infants aged under 2 months, in line with North America and Australia.[27,36] OD has occurred in children weighing less than 3 kg, showing donation feasibility even at size extremes.[37] The Transplantation Society of Australia and New Zealand prescribe the current lower age criteria for OD (Table 3).[11] There is possibly scope to reconsider these. Transplantation outcomes from infant kidney donors are increasingly recognised as equivalent to older children. In infant donors weighing less than 8 kg, one-year graft survival (88%–90%) is equivalent to that of 20 kg donors in large volume centres, whether single or "en bloc".[38] The utilisation rates of kidneys donated by infants aged under 2 years are lower than rates for older children (65% compared with 88%), despite excellent outcomes.[39]

The alignment of guidelines and cooperation between paediatric critical care, organ donation and transplant sectors could facilitate expansion of donation capability in this age group, which could have a major impact on transplantation rates and outcomes. International collaboration in understanding paediatric OD practice is warranted and is currently being undertaken (Professor Sam Shemie, Professor of Pediatrics, McGill University, personal communication, October 2015).

Limitations

The strength of our study is that it is the first to describe contemporary patterns of OD in children in Australia and New Zealand and compare OD rates between children and adults. It provides a baseline for assessing future interventions to enhance paediatric OD.

Our study has several limitations. The denominator for ICU deaths has some limitations as it does not reflect the true potential donor pool. Some paediatric and adult patients who die in the ICU are likely not to be potential donors. The definition of an ICU death is equivalent in adults and children in Australia and New Zealand, although it is likely that differences in donor potential between adults and children exist. As OD criteria expand, so too may the potential donor pool, so using this denominator is perhaps the optimal method for the purpose of comparison. We did not compare donation outcomes between PICUs and mixed ICUs or by donation modality.

Conclusions

OD is an increasingly dynamic field and recognised as an integral component of end-of-life care. Efforts to improve OD rates focus on improving donor identification, developing DCD as a modality, enhancing donation conversations,[40] and technological improvements for organ procurement.[41] ICU mortality is low in children[42,43] and therefore OD is an infrequent possibility relative to that in adults. We have shown that, although small in proportion to the entire donor pool, paediatric OD rates per ICU deaths are similar to adults. Describing ODs as a percentage of ICU deaths is a more meaningful metric for defining paediatric OD rates. Opportunities exist to increase donation opportunities in children but require broad organisational strategies encompassing the transplantation community, organ

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Table 3. Transplantation Society of Australia and New Zealand lower limit of age and weight criteria for organ donors[11]

Organ	Lower age* or weight limit
Heart	Not defined
Lungs	5 years
Liver	Not defined
Pancreas	3 years
Kidneys	2 years
Stomach, intestines	Not defined

* No difference between DCD and DBD for paediatric donor lower age limits.

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procurement agencies and paediatric critical care societies on an international scale.

Competing interests

Ben Gelbart and Elena Cavazzoni are employed as Medical Donation Specialist and State Medical Director, respectively, by the Australian Government Organ and Tissue Authority.

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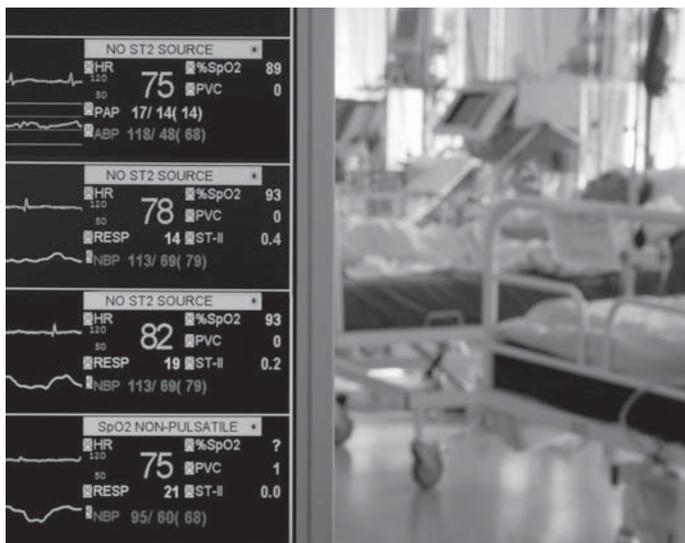
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