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Epidemiology and Outcomes of Children with Kidney Failure Receiving Kidney Replacement Therapy in Australia and New Zealand

Cahyani Gita Ambarsari^{1,2,3,4}, Yeoungjee Cho^{2,5}, Elasma Milanzi^{5,6}, Anna Francis^{3,7}, Lee Jin Koh⁸, Rowena Lalji^{2,3,7,9} and David W. Johnson^{2,5,7,10}

¹Department of Child Health, Faculty of Medicine Universitas Indonesia - Cipto Mangunkusumo Hospital, Jakarta, Indonesia; ²Department of Nephrology, Princess Alexandra Hospital, Brisbane, Queensland, Australia; ³Department of Nephrology, Queensland Children's Hospital, Brisbane, Queensland, Australia; ⁴Medical Technology Cluster, Indonesian Medical Education and Research Institute (IMERI), Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia; ⁵Australasian Kidney Trials Network, The University of Queensland, Queensland, Australia; ⁶Melbourne School of Population and Global Health, University of Melbourne; Melbourne, Victoria, Australia; ⁷Centre for Kidney Disease Research, University of Queensland, Brisbane, Queensland, Australia; ⁸Starship Children's Hospital, Auckland, New Zealand; ⁹Centre for Kidney Research, University of Queensland, St Lucia, Australia; and ¹⁰The Translational Research Institute, Brisbane, Queensland, Australia

Introduction: The incidence and outcomes of kidney replacement therapy (KRT) have been well-studied in adults, but much less so in children. This study aimed to investigate the epidemiology and outcomes of KRT in children in Australia and New Zealand from 2000 to 2020.

Methods: Children aged <18 years initiating KRT in Australia and New Zealand between January 1, 2000 and December 31, 2020 and reported to the Australia and New Zealand Dialysis and Transplant Registry were included. Patient survival, technique-survival, and graft survival were analyzed by Cox regression analyses.

Results: Overall, 1058 children (median [interquartile range (IQR)] age 11 [5–15] years, 41% female, 66% White) were followed-up with for a median period of 12.3 years. First KRT modalities were peritoneal dialysis (PD; 48%), hemodialysis (HD; 34%), and kidney transplantation (KT; 18%). Pre-emptive KT incidence was highest in Caucasian children (80.4%) and lowest in the Indigenous population (3.2%). There was no difference in 5-year patient survival rates between 2011 and 2020 (96.9%, 95% confidence interval [CI] 93.8–98.4) and the preceding decade, 2000–2010 (94.5%, 95% CI 90.4–96.8) (P = 0.79). There was no difference in 5-year death-censored technique survival between 2011 and 2020 (51.2%, 95% CI 39.1–62) and 2000–2010 (48.8%, 95% CI 40.5–56.6) (P = 0.27). However, 5-year derath-censored graft survival was significantly higher in 2011–2020 (88.4%, 95% CI 84.6–91.4) than in 2000–2010 (84.3%, 95% CI 80.4–87.5) (P < 0.001).

Conclusions: PD is the most commonly prescribed KRT modality for children in Australia and New Zealand. Patient-survival, technique-survival, and graft survival rates are excellent and graft survival has improved over the last 2 decades.

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K idney failure is a devastating condition in children, and is associated with a 30-fold increased risk of mortality compared with healthy children.¹ The prevalence of kidney failure requiring KRT among children is

growing across the globe, by 5% per year since 2009 in the United States and by 1.9% per year since 2007 in European countries.^{2,3} Despite ongoing growth in the burden of kidney failure among children, studies of KRT epidemiology and outcomes have predominantly focused on adults, whereas children and adolescents have been less well-studied.

Recent adult studies suggest that improved patient care has led to improved survival rates. Moreover, KRT utilization has increased, particularly for KT.⁴⁻¹¹ However, it remains uncertain whether similar patterns and

Correspondence: Cahyani Gita Ambarsari, Department of Child Health, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo Hospital Diponegoro 71 Jakarta Pusat 10430, Indonesia. E-mail: cahyani.ambarsari@ui.ac.id

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outcomes have been achieved among the pediatric population, given that the etiologies of kidney failure in children are notably different from those in adults.^{5,12-17} Since the 1980s, improved patient care and KRT policies have resulted in the acceptance of more challenging patients into pediatric KRT programs, including very young patients, and prioritization of pediatric patients with kidney failure as KT recipients.^{1,16,18-20} Furthermore, PD has become the primary choice for dialysis for children and adolescents because of its better preservation of residual kidney function, tolerability, and cost-effectiveness.^{10,16,21-25}

The aims of this study were to describe the epidemiology and outcomes of KRT in children and adolescents in Australia and New Zealand between 2000 and 2020 using data obtained from the Australia and New Zealand Dialysis and Transplant (ANZDATA) Registry.

METHODS

The study was approved by the Princess Alexandra Hospital Human Research Ethics Committee (2021-79210) and was conducted and reported in accordance with STROBE guidelines.²⁶

Data Source

Patient data were obtained from the ANZDATA Registry, which used real-time event-based reporting, and an annual survey, which recorded the status of all patients on KRT on December 31 of each year. Regarding consent and privacy provisions of the ANZDATA Registry, there was an opt-out approach for each individual. Registry conduct was in accordance with both the Australian and New Zealand National Privacy Principles.²⁷ Only information with personal identifiers removed was released by the registry with permission granted by the ANZDATA Executive.

Study Population

All children aged <18 years commencing KRT between January 1, 2000 and December 31, 2020 were included in the study. Data collected included age at KRT initiation, sex, ethnicity, primary kidney disease, late referral (defined as referral to a pediatric nephrology unit within 3 months of commencing KRT), socioeconomic status (Australia only), remoteness of residence (Australia only), body weight, body height, and initial and subsequent KRT modalities. Initial treatment modalities were recorded as PD, HD, and KT.

Socioeconomic status was measured only for Australian children according to income, education, and occupation; and assessed based on the index of relative socioeconomic advantage and disadvantage (IRSAD). IRSAD was measured at the level of postcode and was derived from the 2016 census data on 21 census variables related to both advantage (e.g., proportion of people or households with high income, tertiary education, professional occupation, 3 or more cars, and 4 or more bedrooms) and disadvantage (e.g., proportion of people or households with low education level, low income, overcrowding, separated or divorced, unemployed, no internet connection, and 1 parent families, disabilities). Quartiles of IRSAD were used for analyses, with Q1 representing the most disadvantaged group and Q4 the most advantaged group.^{28,29}

Remoteness of residence was evaluated among Australian children by the Accessibility/Remoteness Index of Australia (ARIA), which was developed by the Australian Government's Department of Health and Aged Care.³⁰ The scores were determined based on distance from towns and cities, access to goods and services, and opportunities for social interaction. A low ARIA score indicated high accessibility. ARIAs were defined as major cities (ARIA score 0–0.2), regional (ARIA score 0.2–5.92), and remote (ARIA score 5.92–15).^{30,31} A comparable socioeconomic status data set was collected in New Zealand (New Zealand Index of Multiple Deprivation)³² only from 2018 onward, and thus, was not used in this analysis.

Study Outcomes

The primary outcome was patient survival. Follow-up period was defined as time from dialysis initiation to death, censored at kidney function recovery lasting over 30 days, KRT modality switch, loss to follow-up, or end of study period (December 31, 2020), whichever occurred first. Death occurring within 30 days of transfer between modalities was assigned to the initial KRT modality. The secondary outcomes were mortality incidence and prevalence, KRT modality change, technique failure (censored for kidney function recovery, loss to follow-up, and end of study), graft failure, and association of KRT commencement decade with patient survival, technique failure, and graft failure. Technique failure was defined as transfer to a different dialysis modality for \geq 30 days.³³ Graft failure was defined as return to dialysis after receiving KT. Technique survival was defined as staying on the same initial KRT modality and was analyzed in the subpopulation of patients with dialysis and KT as initial KRT.

A sensitivity analysis of death as a competing event to technique failure and graft failure was performed. Furthermore, we performed a sensitivity analysis excluding children who received pre-emptive KT and children who started dialysis at age <5 years. We compared the results of these sensitivity analyses with the result of the main analysis.

Statistical Analysis

Patient characteristics were expressed as frequency and percentages for categorical variables, mean \pm standard deviation for normally distributed continuous variables, and median (IQR) for nonnormally distributed continuous variables. Differences between categorical variables were assessed with the χ^2 test, parametric continuous variables with Student's t-test, and nonparametric continuous variables with Mann-Whitney U test. Kaplan-Meier plots were used to visualize survival probabilities and multivariable Cox proportional hazards regression models were used to evaluate association between survival outcomes and risk factors of interest. Adjustments were made for initial KRT modalities, age categories, sex, ethnicities, primary kidney diseases, late referral, and decade of KRT initiation, with IRSAD and ARIA specifically for Australian children. The proportionality assumption was examined visually with log-log survival plots. There were no significant first-order interactions identified. Analyses were performed using STATA statistical software package (version 17; StataCorp LP, College Station, TX). Z-score for anthropometric status were calculated with zanthro³⁴ and zscore06 STATA package.³⁵ P-values less than 0.05 were considered statistically significant.

RESULTS

Overall, 1058 children (58.9% male) with a median age of 11 years (IQR, 5–15) started KRT for kidney failure in Australia and New Zealand. The median follow-up time was 12.3 years (IQR, 7.1–17.1). A large proportion started KRT on PD (48.1%), followed by HD (34%), and the rest were pre-emptive KT (17.9%) (Table 1 and Supplementary Figure S1). When examined by age, the most common initial KRT mode was PD for children aged 14 years and younger and HD for patients aged 15 years and older. Compared to 2000–2010, a greater proportion of younger children (0–4 years old) were admitted to the HD program in 2011–2020, from 8% to 21% (P < 0.05, Table 1).^{36,37}

Across the decades, the proportions of pre-emptive KT incidences were similar across different Australian IRSAD quartiles. However, pre-emptive KT incidence remained the highest in Caucasian children (70%–80%), aged 5–14 years old (60%), children with congenital anomalies of the kidney and urinary tract as the primary cause of kidney failure (60%), and Australian children who lived in major cities (50%–80%, P < 0.05). No Australian patients who lived in remote areas ever received pre-emptive KT. Compared with 2000–2010, the proportion of children with a non-congenital anomalies of the kidney and urinary tract because of

kidney failure receiving pre-emptive KT in 2011–2020, increased from 30% to 45% (P = 0.01, Table 1). All preemptive KT patients received transplantation from living donors.

Patient Survival on the First KRT Modalities

Mortality during the study was 8.7% (92/1058), with a median follow-up of 8.1 years (IQR, 3.5-13.2). Of these, 35% (32/92) of deaths occurred at the first KRT modality (18 on PD, 11 on HD, and 3 with KT, Supplementary Table S1). The overall mortality rate on the first KRT modality in this study was 1.2 (95% CI, 0.8-1.6) per 100 patient years. Across the decades, patients who received pre-emptive KT had consistently lower mortality rate compared with patients started on dialysis, 0.3 (95% CI, 0.1-0.9) versus 2.4 (95% CI, 1.5–3.8) in 2000–2010 and 0 versus 2.2 (95% CI, 1.2–3.9) in 2011–2020 (P < 0.05, Supplementary Table S2, Supplementary Figures S2 and S3). The most common causes of death on the first KRT modality within the 2 decades were cardiovascular disease (46.88%) and infections (21.88%) (P < 0.05, Supplementary Table S3).

Based on age at KRT initiation, infants had lower survival rates than other age groups, particularly 6 months and 1 year after KRT initiation. The highest survival was seen in children aged 10–14 years (Supplementary Table S4). Patients whose KRT was initiated at age <1 year had the shortest time to death at a median of 1 year (IQR, 0–1), whereas those who had the KRT initiation at age 10–14 years had the longest time to death at 9 years (3–11) (P < 0.05, Supplementary Table S5, Supplementary Figures S4–S9). Infectionrelated deaths were primarily noted in patients started on PD and aged <5 years (Supplementary Tables S3 and S5).

Among patients who died on PD as the last KRT modality, infections were the most common cause (40.63%), whereas cardiovascular problems were the most common cause (59.1%) for those who died on HD. Most patients who died on KT was because of other causes, namely severe metabolic acidosis, chronic respiratory failure, and vehicle accident. Approximately 56% of reported deaths on PD were in patients aged <5 years, whereas 61% of reported deaths on HD were aged >18 years (P < 0.05), with the most common cause of death being cardiovascular diseases in both groups (Supplementary Table S6).

The overall patient survival rates among those who stayed on the first KRT modality at 1-year and 5years were 98.3% (95% CI, 97–99) and 95.5% (95% CI, 93–97.1), respectively (Figure 1, Supplementary Table S7). Patient survival rates on the first KRT modality did not differ significantly across decades

Table 1. Demographics of children (0–18 years of age) with kidney failure by the first KRT modality in Australia and New Zealand, 2000–2020

		First KRT modalities/Decade					
Characteristics	All (<i>n</i> = 1058)	2000-2010 2011-2020					
		PD (<i>n</i> = 249)	HD (<i>n</i> = 19 7)	KT (<i>n</i> = 90)	PD (<i>n</i> = 260)	HD (<i>n</i> = 163)	KT (<i>n</i> = 99
Age (yrs), median (IQR)	11 (5–†15)	7 (2–13)	15 (11–16)	10 (6–15)	9 (2–13)	12 (7–16)	12 (6–14)
0-4 yrs old, n (%)	252 (23.8)	84 (33.7)	15 (7.6)	15 (16.7)	86 (33.1)	34 (20.9)	18 (18.2)
5–9 yrs old, n (%)	218 (20.6)	66 (26.5)	25 (12.7)	26 (28.9)	51 (19.6)	27 (16.6)	23 (23.2)
10-14 yrs old, n (%)	287 (27.1)	51 (20.5)	51(25.9)	25 (27.8)	80 (30.7)	46 (28.2)	34 (34.3)
15–18 yrs old, n (%)	301 (28.5)	48 (19.3)	106 (53.8)	24 (26.7)	43 (16.5)	56 (34.4)	24 (24.2)
Sex (male), n (%)	623 (58.9)	141 (56.6)	99 (50.3)	61 (67.8)	159 (61.2)	90 (55.2)	73 (73.7)
Weight-for-length (z score) ^a							
Overweight or obese (> 1 SD)	39 (26.9)	16 (29.6)	1 (20)	0 (0)	16 (25.8)	4 (23.5)	2 (40)
Normal (> -2 SD and <1)	85 (58.6)	28 (51.9)	3 (60)	2 (100)	39 (62.9)	10 (58.8)	3 (60)
Wasted (< -2 SD)	15 (10.3)	7 (12.9)	1 (20)	0 (0)	6 (9.7)	1 (5.9)	0 (0)
Severely wasted (< -3 SD)	6 (2.2)	3 (5.6)	0 (0)	0 (0)	1 (1.6)	2 (11.8)	0 (0)
Body mass index (z score) ^b							
Overweight or obese (> 1 SD)	222 (24.5)	41 (23.3)	48 (27.6)	21 (26.9)	45 (21.1)	46 (28.6)	21 (20.4)
Normal (> -2 SD and <1)	636 (70.3)	123 (69.9)	113 (64.9)	55 (70.5)	161 (75.6)	108 (67.1)	76 (73.8)
Wasted (< -2 SD)	24 (2.7)	7 (4)	5 (2.9)	1 (1.3)	4 (1.9)	4 (2.5)	3 (2.9)
Severely wasted (<-3 SD)	23 (2.5)	5 (2.8)	8 (4.6)	1 (1.3)	3 (1.4)	3 (1.8)	3 (2.9)
Ethnicity, n (%)							
Caucasian	701 (66.3)	175 (70.3)	117 (59.4)	79 (87.8)	163 (62.7)	94 (57.7)	73 (73.7)
Asian	101 (9.6)	25 (10.0)	19 (9.6)	2 (2.2)	30 (11.5)	21 (12.9)	4 (4.0)
ATSI	45 (4.3)	10 (4.0)	9 (4.6)	0	14 (5.4)	11 (6.8)	1 (1.0)
Māori	60 (5.7)	19 (7.6)	16 (8.1)	1 (1.1)	16 (6.2)	7 (4.3)	1 (1.0)
Pacific Islander	49 (4.6)	10 (4.0)	17 (8.6)	1 (1.1)	11 (4.2)	8 (4.9)	2 (2.0)
Other	102 (9.4)	10 (4.0)	19 (9.6)	7 (7.8)	26 (10.0)	22 (13.5)	18 (18.2)
Primary kidney diseases							
CAKUT	409 (38.7)	98 (39.4)	48 (24.4)	64 (71.1)	102 (39.2)	43 (26.4)	54 (54.6)
Cystic renal diseases	100 (9.5)	25 (10.0)	11 (5.6)	6 (6.7)	31 (11.9)	11 (6.8)	16 (16.2)
Glomerulonephritis	293 (27.7)	74 (29.7)	95 (48.2)	6 (6.7)	61 (23.5)	55 (33.7)	2 (2.0)
Other	256 (24.2)	52 (20.9)	43 (21.8)	14 (15.5)	66 (25.4)	54 (33.1)	27 (27.3)
Late referral, n (%)	242 (22.9)	62 (24.9)	67 (34.0)	1 (1.1)	59 (23.0)	51 (32.1)	2 (2.1)
Initial parent center state							
Australia, n (%)	850 (80.3)	183 (73.5)	164 (83.3)	75 (83.3)	201 (77.3)	143 (87.7)	84 (84.9)
New Zealand, n (%)	208 (19.7)	66 (26.5)	33 (16.8)	15 (16.7)	59 (22.7)	20 (12.3)	15 (15.2)
Socio economic indexes for area (IRSAD), $n = 847$ IRSAD quartiles [°]							
1, n (%)	213 (25.2)	46 (25.1)	44 (26.8)	19 (25.3)	50 (24.9)	43 (30.3)	11 (13.4)
2, n (%)	212 (25)	46 (25.1)	35 (21.3)	17 (22.7)	60 (29.9)	35 (24.7)	19 (23.2)
3, n (%)	211 (24.9)	47 (25.7)	45 (27.4)	18 (24.0)	42 (20.9)	43 (30.3)	16 (19.5)
4, n (%)	211 (24.9)	44 (24.0)	40 (24.4)	21 (28.0)	49 (24.4)	21 (14.8)	36 (43.9)
Accessibility/Remoteness Index of Australia (ARIA), $n = 847^{\circ}$							
Major, n (%)	615 (72.6)	133 (72.7)	124 (75.6)	44 (58.7)	141 (70.2)	105 (73.9)	68 (82.9)
Regional, n (%)	214 (25.3)	46 (25.1)	33 (20.1)	31 (41.3)	56 (27.9)	34 (23.9)	14 (17.1)
Remote, n (%)	18 (2.1)	4 (2.2)	7 (4.3)	0	4 (2.0)	3 (2.1)	0

ATSI, Aboriginal and Torres Strait Islander; CAKUT, congenital anomalies of the kidneys and urinary tract; HD, hemodialysis; IRSAD, Index of Relative Socioeconomic Advantage and Disadvantage; IQR, interquartile range; KRT, kidney replacement therapy; KT, kidney transplantation; N/A, not available; PD, peritoneal dialysis.

^aWeight-for-length was used for patients aged < 2 years old.

^bBody mass index was used for patients aged ≥2 years old; There were 8 missing data in this age group Z-scores were calculated according to the World Health Organization 2006 growth chart³⁶ and the Center for Disease Control 2000 reference values.³⁷

^cApplicable only to Australia.

(Supplementary Table S8). However, patients who received pre-emptive KT consistently had significantly higher survival rates at 5, 10, and 15 years after KRT initiation than patients who were started on dialysis (P < 0.05). Among patients who started on dialysis, the association of better survival with PD compared with HD as the initial KRT modality was

most pronounced within 6 months after KRT commencement (P < 0.05, Figure 1, Supplementary Table S7). Moreover, younger patients (aged <5 years) who started KRT with dialysis had consistently lower survival rates compared to older patients, 95.4% (95% CI, 91.0–97.7) versus 98.8% (95% CI, 96.8–99.6) at 1 year and 89.4% (95% CI,



Figure 1. Patient survival on the first KRT modality: Australia and New Zealand Registry 2000–2020, log rank *P* < 0.001. HD, hemodialysis; KRT, kidney replacement therapy; KT, kidney transplantation; PD, peritoneal dialysis.

81.6–94.0) versus 94.4% (95% CI, 86.8–97.7) at 5 years after initial KRT commencement, P < 0.05 (Supplementary Table S9). No improvements were observed in the survival of younger patients on dialysis over time (Supplementary Table S10).

Compared with pre-emptive KT, having PD or HD as the initial KRT modality was associated with 2.4-fold (adjusted hazard ratio [aHR] 2.4, 95% CI 1.1– 5.7) and 3.6-fold (aHR 3.6, 95% CI 1.5–8.8) increases in mortality hazard, respectively (Table 2, Supplementary Figure S10). Age under 4 years at KRT initiation was associated with higher mortality, as was Māori ethnicity among Australian children (Table 2).³⁸⁻⁴⁰ Restricting the analysis model to include only

 Table 2.
 Multivariable Cox proportional hazards analysis of mortality among children staying on the first KRT modality: Australia and New Zealand Registry 2000–2020

ultivariable-adjusted	Multivariable-adjusted hazard
izard ratio (95% CI) for Australia only	ratio (95% CI) for Australia and New Zealand
27.8 (4.6–168.3) ^a	2.4 (1.1–5.7) [°]
21.2 (3.2–142.5) ^a	3.6 (1.5–8.8) ^a
1.2 (0.4–3.2)	0.9 (0.4–1.9)
0.2 (0.1–1.1)	0.5 (0.2–0.8) ^a
0.2 (0.1–0.8)ª	0.4 (0.2–0.7) ^a
0.4 (0.1–1.6)	0.5 (0.3–0.9) ^a
	27.8 (4.6–168.3) ^a 21.2 (3.2–142.5) ^a 1.2 (0.4–3.2) 0.2 (0.1–1.1) 0.2 (0.1–0.8) ^a

ATSI, Aboriginal and Torres Strait Islander; CAKUT, congenital anomalies of the kidneys and urinary tract; HD, hemodialysis; KRT, kidney replacement therapy; KT, kidney transplantation; PD, peritoneal dialysis

^aStatistically significant.

Data from New Zealand alone was too limited to be shown separately. Variables included in the model were selected based on background knowledge; these variables have been proven to be related to mortality in children receiving KRT.³⁸⁻⁴⁰

patients started on dialysis produced similar results. However, dialysis modality (HD vs. PD) was not associated with increased mortality (aHR 1.2, 95% CI 0.4–3.4, P = 0.76; Supplementary Table S11). Compared with pre-emptive KT, having dialysis for more than 2 years before KT was associated with a 4.7-fold (aHR 4.7, 95% CI 1.6–13.5) increase in graft failure (Table 3).

KRT Modality Changes/Sequential KRT Modality Utilization

Among 869 children commencing dialysis as the first KRT modality, 59.7% (519/869) received KT as their first change of treatment modality. Overall, 83.5% (726/869) of patients with dialysis at KRT commencement received KT after a median period of 1.3 years (IQR 0.7–2.7) (Supplementary Table S1). Among these, 28.5% (207/726) of patients switched between dialysis modalities (PD and HD) with a total of 281 changes before receiving KT (range of modality changes per patient, 1–6).

The prospect of receiving KT was similar among children started on PD and HD (aHR 0.9, 95% CI 0.8–1.1). However, lower KT probability was observed in children who started dialysis at age <5 years (aHR 0.7, 95% CI 0.6–0.9), age >14 years (aHR 0.7, 95% CI 0.5–0.8), and non-Caucasian ethnicities (aHR 0.6, 95% CI 0.5–0.7). Among those from non-Caucasian ethnicities, Māori children had the lowest chance of receiving KT (aHR 0.3, 95% CI 0.2–0.5). Overall, there were 1040 KTs in 915 patients, with 27.3% (250/915) of children returning to dialysis after their first KT. Furthermore, approximately 16.4% (41/250) of these graft failure episodes were

Table 3. Crude and multivariable Cox proportional hazards analysis of graft failure and mortality comparing pre-emptive transplantation with effect of dialysis by vintage (time to transplant since dialysis initiation in months): Australia and New Zealand Registry 2000–2020

Parameter	Crude hazard ratio (95% CI)	Multivariate-adjusted hazard ratio (95% CI)
Graft failure-death censored		
Non pre-emptive vs. pre-emptive		
0-6 months vs. pre-emptive	1.3 (0.8–2)	1.1 (0.7–1.7)
6-12 months vs. pre-emptive	1.4 (0.9–2.1)	1.2 (0.8–1.9)
12-24 months vs. pre-emptive	1.6 (1.1–2.4) ^a	1.5 (0.9–2.2)
>24 months vs. pre-emptive	2 (1.3–3) ^a	1.7 (1.1–2.7) ^a
PD as first KRT vs. pre-emptive		
0-6 months vs. pre-emptive	1.4 (0.8–2.2)	1.3 (0.8–2.2)
6-12 months vs. pre-emptive	1.2 (0.7–2.1)	1.1 (0.7–1.9)
12-24 months vs. pre-emptive	1.4 (0.9–2.2)	1.5 (0.9–2.5)
>24 months vs. pre-emptive	1.9 (1.2–3) ^a	2.1 (1.2–3.6) ^d
HD as first KRT vs. pre-emptive		
0-6 months vs. pre-emptive	1.1 (0.6–2)	0.8 (0.5–1.5)
6-12 months vs. pre-emptive	1.6 (0.9–2.7)	1.2 (0.7–2.2)
12-24 months vs. pre-emptive	2 (1.3–3.2) ^a	1.4 (0.8–2.4)
>24 months vs. pre-emptive	2.1 (1.3–3.5) [°]	1.2 (0.6–2.4)
Mortality		
Non-pre-emptive vs. pre-emptive		
0-6 months vs. pre-emptive	1.2 (0.4–4.1)	1.1 (0.3–3.8)
6-12 months vs. pre-emptive	1.6 (0.5–5.1)	1.5 (0.5–5)
12-24 months vs. pre-emptive	1.3 (0.4–4)	1.5 (0.5–4.6)
>24 months vs. pre-emptive	3.6 (1.3–9.7) ^a	4.7 (1.6–13.5) ^a
PD as first KRT vs. pre-emptive		
0-6 months vs. pre-emptive	1.8 (0.5–6.4)	2.4 (0.6–9.2)
6-12 months vs. pre-emptive	1.4 (0.3–5.6)	1.5 (0.3–6.4)
12-24 months vs. pre-emptive	1.2 (0.3–4.5)	1.7 (0.5–6.6)
>24 months vs. pre-emptive	2.9 (0.9–9.4)	4.5 (1.2–16.5) ^a
HD as first KRT vs. pre-emptive		
0-6 months vs. pre-emptive	0.5 (0.1–4.4)	0.3 (0.1–2.8)
6-12 months vs. pre-emptive	1.9 (0.5–7.6)	1 (0.2–4.7)
12-24 months vs. pre-emptive	1.4 (0.3–5.5)	0.8 (0.2–3.7)
>24 months vs. pre-emptive	3.9 (1.3–11.7) ^a	3.6 (0.9–14.6)

CI, confidence interval; HD, hemodialysis; KRT, kidney replacement therapy; PD, peritoneal dialysis. ^aStatistically significant.

observed in children who received KT pre-emptively (Supplementary Table S1).

Technique Failure

Among children who started on dialysis as the first KRT modality, 27.2% (237/869) experienced technique failure, with a median number of technique failure episodes of 1 (IQR, 1-2) per patient. The most common cause of technique failure in children who started on PD was infection (44.7% [46/102]), whereas for HD it was planned conversion to PD after acute HD (34.1% [46/135]) (Supplementary Table S12). The overall technique survival rates at 1, 2, and 5 years were 74.9% (95% CI, 71.6-77.9), 65.1% (95% CI, 60.8-69), and 49.9% (95% CI, 43.1–56.3), respectively (Supplementary Figure S10). Compared with patients who started on HD, patients who started on PD had significantly higher technique survival in the first 3 years (P < 0.05, Supplementary Table S13, Figure 2, Supplementary Figures S11 and S12). Furthermore, technique

survival after initial KRT commencement did not significantly change across decades (Supplementary Table S14, Supplementary Figures S13–S20).

Poorer technique survival was associated with commencing HD as the first KRT (aHR 2.3, 95% CI, 1.7–3.1), having glomerulonephritis as the cause of kidney failure (aHR 1.6, 95% CI, 1.2–2.3), and being referred late to a pediatric nephrology unit (aHR 1.7, 95% CI, 1.3–2.2) (Table 4). Treating death as a competing risk yielded similar technique survival estimates and risk factors (Supplementary Tables S15–17).

Graft Failure

The overall 1-year, 5-year, 10-year, and 15-year graft survival rates on first KT were 97% (95% CI, 95.3–98), 86.5% (95% CI 83.9–88.7), 70.7% (95% CI 66.8–74.2), and 53.2% (95% CI 47.8–58.2), respectively. Patients with pre-emptive KT had the highest graft survival rates at 5 years and 10 years (92% [95% CI, 86.5–95.1] and 79.4% [95% CI, 71.2–85.6], respectively), followed by patients who had PD or HD at KRT initiation



Figure 2. Death-censored dialysis technique survival and graft survival stratified by the first KRT modality: Australia and New Zealand Registry 2000–2020, log rank P < 0.001.

HD, hemodialysis; KRT, kidney replacement therapy; KT, kidney transplantation; PD, peritoneal dialysis.

(P < 0.05, Supplementary Table S18, Figure 3).Compared with pre-emptive KT, having dialysis for more than 2 years before receiving KT was associated with a 1.7-fold (aHR 1.7, 95% CI 1.1-2.7) increase in graft failure (Table 3). Graft survival probability at 2 to 5 years after pre-emptive KT improved significantly across decades (P < 0.05, Supplementary Table S19, Supplementary Figures S21-S32). However, dialysis exposure before KT, age between 10 and 18 years at KT, and Aboriginal and Torres Strait Islander ethnicity (hereafter respectfully termed Indigenous Australians) were associated with an increased risk for graft failure. Compared with Caucasians, Asian ethnicity was associated with a decreased risk of graft failure, whereas Pacific Islander and Māori ethnicities were not associated with altered risks of graft failure (Table 5).

DISCUSSION

This study, comprising a large binational sample of pediatric patients with kidney failure, showed that overall 1-year and 5-year survival rates on KRT were excellent at 98.3% and 95.5%, respectively. These rates had not significantly changed over the last 2 decades and better survival was significantly associated with age >4 years and pre-emptive KT. Similarly, technique survival rates were excellent and stable over the last 2 decades. For KT, graft survival rates significantly improved over the last 2 decades and poorer graft survival rates were associated with dialysis exposure prior to KT, age between 10 and 18 years at the time of

transplant, and Indigenous status. Better early transplant outcomes and a reduction in risk of early graft loss have improved graft survival in the last decade.^{18,19} The use of a tacrolimus/mycophenolate/prednisone regimen in the last decade, which was changed from a regimen of cyclosporine/mycophenolate/prednisone in the earlier decade, might have contributed to this early allograft loss risk reduction.⁴¹

The survival rates observed on KRT in Australia and New Zealand in this study were similar to those reported in other high-income countries, ranging from 97.6% to 99.2% for 1-year survival and 93% to survival.^{2,42-44} for 5-year Furthermore, 96.7% although a previous ANZDATA Registry study reported a significant improvement in pediatric KRT survival in Australia and New Zealand between 1963 and 2002,¹ no further significant improvements in survival were observed over the last 20 years in the present study. Although overall survival rates of pediatric patients with kidney failure on KRT were excellent, their overall mortality rate remains at least 20-fold higher than that of the general pediatric populations.45

Similar to what has been previously reported in United States, United Kingdom, and European studies,^{44,46,47} we found that patients who started on dialysis had a higher risk of death than patients who received pre-emptive KT, even following adjustment for demographic and clinical factors. These findings may be related to dialysis-associated cardiovascular damage, access complications, infections, retarded linear growth, and poor cognitive development in **Table 4.** Multivariable Cox proportional hazards analysis of death-
censored technique failure among children receiving dialysis mo-
dalities (PD and HD) as the first KRT modality: Australia and New
Zealand Registry 2000–2020

Parameter	Multivariable-adjusted hazard ratio (95% CI) for Australia only	Multivariable-adjusted hazard ratio (95% CI) for Australia and New Zealand
First KRT modality		
Hemodialysis vs. PD	2.7 (1.9–3.7) ^a	2.3 (1.7–3.1) ^a
Period		
2011-2020 vs. 2000-2010	0.9 (0.7-1.2)	1 (0.8–1.3)
Age at KRT		
5–9 vs. 0–4 years old	1.1 (0.8–1.9)	1.4 (0.9–2)
10-14 vs. 0-4 years old	0.7 (0.4–1)	0.7 (0.5–1.1)
15–18 vs. 0–4 years old	0.6 (0.4–0.9)ª	0.6 (0.4–0.9) ^a
Gender		
Female vs. male	1.1 (0.8–1.4)	1.1 (0.9–1.5)
Ethnicity		
Asian vs. Caucasian	0.8 (0.5–1.3)	0.8 (0.5–1.3)
ATSI ^a vs. Caucasian	0.9 (0.5–1.6)	1 (0.6–1.7)
Māori vs. Caucasian	1 (0.2–4.2)	1.2 (0.7–2)
Pacific Islander vs. Caucasian	1 (0.5–2)	1.1 (0.7–1.9)
Other vs. Caucasian	1 (0.6–1.6)	1 (0.6–1.7)
Primary kidney diseases		
Cystic diseases vs. CAKUT	0.8 (0.4–1.4)	0.7 (0.4–1.3)
Glomerulonephritis vs. CAKUT	1.7 (1.2–2.5) ^a	1.6 (1.2–2.3) ^a
Others vs. CAKUT	1.1 (0.7–1.6)	1 (0.7–1.5)
Late referral	1.9 (1.4–2.6) ^a	1.7 (1.3–2.2) ^a
Parent center state		
New Zealand vs. Australia		0.8 (0.6–1.2)
Socio economic indexes for Area (IRSAD)		
Quartile 2 vs. quartile 1	1 (0.7–1.4)	N/A
Quartile 3 vs. quartile 1	0.9 (0.6–1.4)	N/A
Quartile 4 vs. quartile 1	0.9 (0.6–1.4)	N/A
Accessibility/Remoteness Index of Australia (ARIA),		
Regional vs. major	1 (0.7–1.5)	N/A
Remote vs. major	1.4 (0.6–3.2)	N/A

ATSI, Aboriginal and Torres Strait Islander; CAKUT, congenital anomalies of the kidneys and urinary tract; HD, hemodialysis; KRT, kidney replacement therapy; KT, kidney transplantation; N/A, not available; PD, peritoneal dialysis. "Statistically significant.

Data from New Zealand alone was too limited to be shown separately.

children.⁴⁸⁻⁵⁰ A previous study from the United States involving over 7500 patients aged <18 years receiving KT demonstrated that children who received any dialysis modalities had a 2-fold higher risk for death (aHR 1.7, 95% CI 1.2–2.3) compared with children who received pre-emptive KT, regardless of the type of donor sources and transplant factors.⁵¹

Pre-emptive KT is a superior KRT option for children with kidney failure because it potentially avoids patient exposure to the adverse outcomes associated with dialysis.⁵² Its only caveat was that pre-emptive KT was not always possible, because it was generally delayed until the patients' weight was 10 kg or higher.⁵³ In our study, the minimum weight of a child having pre-emptive KT was 9.4 kg. Medical conditions, such as active
 Table 5. Multivariable Cox proportional hazards analysis of deathcensored graft failure among children by the first KRT modality:

 Australia and New Zealand Registry 2000–2020

Parameter	Multivariable-adjusted hazard ratio (95% CI) for Australia only	Multivariable-adjusted hazard ratio (95% CI) for Australia and New Zealand
First KRT modality		
PD vs. KT	1.1 (0.7–1.7)	1.4 (0.9–2.1)
HD vs. KT	1 (0.6–1.6)	1.3 (0.9–2)
Period		
2011-2020 vs. 2000-2010	0.6 (0.4–0.9) ^a	0.6 (0.4–0.9) ^a
Age at KRT		
5-9 vs. 0-4 years old	0.9 (0.5–1.6)	1.2 (0.7–1.9)
10-14 vs. 0-4 years old	1.8 (1.1–2.9) ^a	2 (1.2–3.1) ^a
15–18 vs. 0–4 years old	2 (1.2–3.2)	2.2 (1.4–3.5) ^a
Gender		
Female vs. male	1.1 (0.8–1.5)	1.3 (0.9–1.7)
Ethnicity		
Asian vs. Caucasian	0.6 (0.3–1.2)	0.5 (0.3–0.9) ^a
ATSI ^a vs. Caucasian	2.7 (1.3-5.4) ^a	2.6 (1.3-5.1) ^a
Māori vs. Caucasian	N/A	0.7 (0.3–1.6)
Pacific Islander vs. Caucasian	0.8 (0.2–2.5)	1.4 (0.7–2.9)
Other vs. Caucasian	1.2 (0.7–2)	1.4 (0.8–2.2)
Primary kidney diseases		
Cystic diseases vs. CAKUT	1.5 (0.9–2.5)	1.3 (0.8–2.1)
Glomerulonephritis vs. CAKUT	1.3 (0.9–1.9)	1.2 (0.8–1.7)
Others vs. CAKUT	0.8 (0.5–1.3)	0.8 (0.5–1.1)
Late referral	0.8 (0.5-1.2)	0.8 (0.5-1.1)
Parent center state		
New Zealand vs. Australia		1.3 (0.9–1.9)
Socio economic indexes for Area (IRSAD)		
Quartile 2 vs. quartile 1	0.9 (0.6–1.4)	N/A
Quartile 3 vs. quartile 1	0.9 (0.6–1.3)	N/A
Quartile 4 vs. quartile 1	0.7 (0.4–1.1)	N/A
Accessibility/Remoteness Index of Australia (ARIA),		
Regional vs. major	0.9 (0.6–1.3)	N/A
Remote vs. major	1.6 (0.6–4.3)	N/A

HD, hemodialysis; KRT, kidney replacement therapy; KT, kidney transplantation; N/A, not available; PD, peritoneal dialysis. ^aStatistically significant.

Data from New Zealand alone was too limited to be shown separately.

glomerulonephritis, severe cardiac dysfunction, or malignancy may also preclude pre-emptive KT.^{54,55} Children who lived in regional or remote areas also had a 35% lower likelihood of receiving pre-emptive KT compared with children who lived in major cities where transplant centers were located.⁵⁶ Furthermore, Australia's current practice of performing pediatric preemptive KT exclusively with living donor kidneys may have limited patients' chances of accessing preemptive KT. Patients who did not have a living kidney donor at planned pre-emptive KT were left with dialysis modality as the sole life-saving alternative.

In the adult literature, PD was seen as an ideal bridge to KT due to its favorable profile in relation to patient survival, hemodynamic stability, infection risk,



Figure 3. Death-censored graft survival among children receiving the first KT, stratified by the first KRT modality (PD, HD, and KT): Australia and New Zealand Registry 2000–2020, log rank P = 0.01. HD, hemodialysis; KRT, kidney replacement therapy; KT, kidney transplantation; PD, peritoneal dialysis.

and preservation of residual kidney function and vascular access.^{54,55} In children, PD is particularly advantageous in facilitating regular school attendance and maintaining functional and complication-free vascular access in very small patients.⁵⁷ However, we did not find any significant survival benefit associated with starting patients on PD compared with HD. This result agreed with those reported in previous similarsized studies (<1000 patients) from Taiwanese, Korean, and Italian registries.⁵⁸⁻⁶⁰ In contrast, a propensity score-matched study of 3784 European children aged <19 years on dialysis showed that children who initially started on HD had a higher mortality risk compared with those on PD (propensity score 1.39, 95% CI 1.1-1.8), especially during the first year of dialysis (propensity score 1.8, 95% CI 1.0-2.4).42 Conversely, data from the United States, with >11,000 dialysis patients aged <21 years old, showed that PD was associated with a higher risk of death compared to HD, especially in patients starting at age >12 years (aHR 1.73, 95%CI 1.3–2.2, P < 0.001). Aside from having a larger cohort, study design and case-mix differences might explain the conflicting results between our study and the previous European and United States studies. First, the majority of patients in our study and the European cohort initiated HD using a central venous catheter, whereas the majority of patients aged >12 years in the United States study used arteriovenous fistulas or grafts.^{42,61,62} Second, the previous European study defined initial dialysis modality as treatment at day 30. Therefore, deaths occurring before day 30 were not counted. They also had a higher proportion of patients aged <5 years started on HD than in our study; 50% (278/555) versus

22% (49/219), respectively; and spent longer time on HD (1.76 years [95% CI 1.64–1.87] than those in our study, 1.1 years (95% CI 1.1–1.5).⁴²

HD access type has been recognized as an essential modifier of dialysis modality and survival association. A previous study in adult patients reported that a survival advantage in patients with PD was only significant when comparing patients with HD who initiated with central venous catheter.63 Younger age at KRT initiation has also been reported to be associated with poorer patient survival and post KT graft survival.^{18,53,60} Furthermore, a Scottish study with 477 patients aged <18 years reported that patients staying on either PD or HD conferred a 20-fold increased risk of all-cause mortality compared with patients who received KT on follow-up, P < 0.05.⁶⁴ Similarly, previous work by Amaral et al.⁵¹ demonstrated that in the United States, patients <18 years old who stayed <12 and >18 months on dialysis experienced 60% (aHR 1.6, 95% CI 1.1-2.3) and 90% (aHR 1.9, 95% CI 1.3-2.7) increased risks of death, respectively, compared to patients who received pre-emptive KT. Nevertheless, most decision-making processes for choosing the initial KRT modality for children with kidney failure in clinical practice are multifactorial.^{25,65-68} The clinicians will assess not only medical but also social factors, quality of life, patient and family preferences, and even contextual factors such as the location of residence.⁶⁹ Therefore, strategies to increase patient survival on KRT should include choosing a particular dialysis modality and expediting KT for patients on dialysis. These strategies are particularly needed for non-Caucasians and patients commencing KRT under 5 years of age, because these patients were less likely to

receive KT and had a higher mortality risk than the general cohort.^{18,47,70-73}

We observed a higher technique survival rate in patients who started on PD compared with HD. This result should be interpreted with caution, because 41% of HD technique failure causes were unknown, and 36% resulted from an initial plan to convert to PD after an acute HD (Supplementary Table S6).

Interestingly, only 3.2% (6/189) of children receiving pre-emptive KT were from Aboriginal and Torres Strait Islander, Māori, and Pacific Islander ethnicities. Although Indigenous peoples have a higher incidence of kidney failure and earlier age at CKD onset, their use of KRT was less than that of non-Indigenous peoples.^{56,70,74,75} The Indigenous population had a longer duration of dialysis before KT, lower frequency of receiving a live kidney donor transplant, a lower rate of pre-emptive KT, and a higher frequency of not receiving KT for their kidney failure treatment. Language barriers, remoteness, poor access to dialysis and transplant services, and health care professionals' attitudes have contributed to the long waiting times and worse transplant outcomes in Indigenous populations. The disparities in KRT access among Indigenous peoples in Australia and New Zealand need to be addressed, because these also affect their survival.⁷⁰

A key strength of our study is the large sample size and inclusion of all children with treated kidney failure from all units in Australia and New Zealand. Other strengths include prospective data collection, long follow-up duration with minimal loss to follow-up, and the use of robust statistical methodologies. These enabled us to provide valid and reasonably precise long-term survival estimates and identify modifiable and unmodifiable risk factors for death. However, the current study has limitations. The ANZDATA Registry does not record details of patients with kidney failure who are not treated with KRT. Attitudes among nephrologists toward offering KRT to very young children may vary considerably. Other information regarding details of treatment in the registry is limited. Data on parameters and interventions associated with morbidity and mortality, such as hemoglobin concentration, erythropoiesis-stimulating agents, lipid levels, blood pressure, growth hormone, cardiac function, mineral bone disorders, and vascular access peritoneal membrane characteristics, were not collected. The possibility of coding bias cannot be excluded.

CONCLUSION

Compared with previously published ANZDATA Registry data, KRT utilization increased in all age categories, with PD being the most commonly prescribed modality for Australasian children. Patient survival rates on KRT were excellent and remained stable over the last 20 years. Given that mortality rates in children with kidney failure on KRT remain 20-fold higher than in the general pediatric population, there is an exigent need to try to further improve outcomes in this vulnerable group.

DISCLOSURE

CGA, EM, AF, LJK, and RL have declared no conflicting interests. DWJ has received consultancy fees, research grants, and speaker's honoraria from Baxter Healthcare and Fresenius Medical Care, consultancy fees from AstraZeneca, Bayer and AWAK, speaker's honoraria from ONO and BI & Lilly, and travel sponsorships from ONO and Amgen. He is a current recipient of an Australian National Health and Medical Research Council Leadership Investigator Grant. YC has received research grants and speaker's honoraria from Baxter Healthcare and Fresenius Medical Care. She is a current recipient of an Australian National Health and Medical Research Council Emerging Leadership Investigator Grant, and the Advancing Queensland Clinical Research Fellowship.

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SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Figure S1. Proportion of the first KRT modalities in children (0–18 years old) in Australia and New Zealand, 2000–2020, by year.

Figure S2. Overall patient survival in children receiving the first KRT modality.

Figure S3. Patient survival in children based on first KRT modality.

Figure S4. Patient survival in children receiving KRT based on age at KRT initiation.

Figure S5. Patient survival in children started on KRT at < 1 year old.

Figure S6. Patient survival in children started on KRT at 1–4 years old.

Figure S7. Patient survival in children started on KRT at 5–9 years old.

Figure S8. Patient survival in children started on KRT at 10–14 years old.

Figure S9. Patient survival in children started on KRT at 15– 18 years old.

Figure S10. Dialysis patient survival related with history of technique failure (among all patients receiving PD and HD as the first KRT modality).

Figure S11. Overall technique survival in children receiving the first KRT modality.

Figure S12. Non-censored for death technique survival stratified by the first KRT modality.

Figure S13. Death-censored PD technique survival as the first KRT modality by decade.

Figure S14. Death-censored HD technique survival as the first KRT modality by decade.

Figure S15. Non-censored for death PD technique survival by decade.

Figure S16. Non-censored for death HD technique survival by decade.

Figure S17. Death-censored PD technique survival as the first KRT modality by age categories.

Figure S18. Death-censored HD technique survival as the first KRT modality by age categories.

Figure S19. Non-censored for death PD technique survival for PD as the first KRT modality by age categories.

Figure S20. Non-censored for death HD technique survival for HD as the first KRT modality.

Figure S21. Death-censored graft survival by age categories at time of transplantation.

Figure S22. Non-censored for death graft survival after preemptive KT by decade by age categories.

Figure S23. Death-censored graft survival after preemptive KT by decade.

Figure S24. Non-censored for death graft survival after preemptive KT by age categories at time of transplantation.

Figure S25. Death-censored dialysis technique survival and graft survival stratified by first KRT modality in children aged 0–4 years old.

Figure S26. Death-censored dialysis technique survival and graft survival stratified by first KRT modality in children aged 5–9 years old.

Figure S27. Death-censored dialysis technique survival and graft survival stratified by first KRT modality in children aged 10–14 years old.

Figure S28. Death-censored dialysis technique survival and graft survival stratified by first KRT modality in children aged 15–18 years old.

Figure S29. Non-censored for death dialysis technique survival and graft survival stratified by first KRT modality in children aged 0–4 years old.

Figure S30. Non-censored for death dialysis technique survival and graft survival stratified by first KRT modality in children aged 5–9 years old.

Figure S31. Non-censored for death dialysis technique survival and graft survival stratified by first KRT modality in children aged 10–14 years old.

Figure S32. Non-censored for death dialysis technique survival and graft survival stratified by first KRT modality in children aged 15–18 years old.

Table S1. Failures, death, and dialysis modality changes atthe first KRT modality: Australia and New Zealand Registry2000–2020.

 Table S2. Death rates on the first KRT modality.

Table S3. Cause of death on the first KRT modality amongpediatric KRT patients: Australia and New Zealand Registry2000–2020.

Table S4. Comparison of patient survival among childrenreceiving KRT, stratified by the age at KRT initiation:Australia and New Zealand Registry 2000–2020.

Table S5. Time to death, cause of death, and number ofKRT sequences, by age at KRT initiation.

Table S6. Overall cause of death based on the last KRT modality among pediatric KRT patients: Australia and New Zealand Registry 2000–2020.

Table S7. Comparison of patient survival among childrenreceiving PD, HD, and KT on the first KRT modality:Australia and New Zealand Registry 2000–2020.

Table S8. Patient survival among children staying on thefirst KRT modality, by decade.

Table S9. Comparison of patient survival among childrenwho commenced dialysis at age < 5 years old and > 5years old: Australia and New Zealand Registry 2000–2020.**Table S10.** Patient survival among children aged < 5 years</td>old staying on the first dialysis modality, by decade.

Table S11. Multivariable Cox proportional hazards analysis of mortality among children receiving dialysis modalities (PD and HD) as the first KRT: Australia and New Zealand Registry 2000–2020.

Table S12. Causes of technique failure in children withdialysis as the first KRT modality: Australia and NewZealand Registry 2000–2020.

Table S13. Death-censored technique survival among children receiving dialysis (PD and HD) as the first KRT modality: Australia and New Zealand Registry 2000–2020. Table S14. Death-censored technique survival among children receiving dialysis (PD and HD) as the first KRT modality, by decade.

Table S15. Non-censored for death technique survival amongchildren receiving dialysis (PD and HD) as the first KRT mo-dality: Australia and New Zealand Registry 2000–2020.

Table S16. Non-censored for death technique survival among children receiving dialysis (PD and HD) as the first KRT modality, by decade.

Table S17. Multivariable Cox proportional hazards analysis of non-censored for death technique failure among children receiving dialysis modalities (PD and HD) as the first KRT: Australia and New Zealand Registry 2000–2020.

Table S18. Comparison of death-censored graft survivalamong children receiving first KT, stratified by the first KRTmodality: Australia and New Zealand Registry 2000–2020.Table S19. Death-censored graft survival among childrenreceiving pre-emptive kidney transplantation, by decade.

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