



## Original Article

## Provision of continuous renal replacement therapy in children in intensive care in Australia and New Zealand

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## ABSTRACT

**Objectives:** The objective of this study was to describe current use, clinical practice, and outcomes of continuous renal replacement therapy (CRRT) in children in the intensive care unit (ICU) in Australia and New Zealand.

**Design:** retrospective, binational registry-based cohort study and electronic survey of clinical practice.

**Setting:** ICUs that contribute to the Australian and New Zealand Paediatric Intensive Care Registry and a survey conducted in November 2021 including ICUs accredited for paediatric intensive care training that provide CRRT for children were part of this study.

**Participants:** Patients aged <18 years who received renal replacement therapy (RRT) in the ICU were included. Analysis of Australian and New Zealand Paediatric Intensive Care Registry data encompassed admissions from 1 January 2016 to 31 December 2020.

**Interventions:** None.

**Main outcome measures:** .

**Results:** 1378 of 58,736 (2.4%) ICU admissions received RRT (CRRT or peritoneal dialysis [PD]), of which 592 (1.0%) received CRRT. Patients receiving CRRT were older and had a median age of 43 months (interquartile range: 7–130 months) compared to 0.3 months (interquartile range: 0.1–2.6 months) for PD. CRRT was used more commonly in all patient groups (523/626, 84%), except those with congenital heart disease (CHD). The number of admissions receiving CRRT varied between units from 1 to 160 admissions for the 5-year period. Overall ICU mortality for CRRT was 30% (175/592). ICU mortality was the highest in neonates ([51/108] 47%) and in those with CHD ([40/69] 58%). ICU mortality for CRRT decreased over the 5-year study period (35%–22%,  $p = 0.025$ ). The survey showed consistency in CRRT equipment used between units, but there were differences in choice of dialytic modality and anti-coagulation regimen.

**Conclusion:** CRRT is used less frequently than PD in smaller children and in those with CHD. In all other cohorts, it is the predominant mode of RRT. ICU mortality rates were higher for CRRT than for PD, with a large variation in mortality rates across age and diagnostic groups. The CRRT mortality in ICU decreased over the 5 years of the study.

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## 1. Introduction

Acute kidney injury (AKI) is a significant complication of critical illness in children and infants. An international study found that 12% of children admitted to the intensive care unit (ICU) developed

severe AKI (defined as stage 2 or 3 by Kidney Disease: Improving Global Outcomes criteria) and that 1.5% received renal replacement therapy (RRT).<sup>1,2</sup> Continuous renal replacement therapy (CRRT), using veno-venous modalities, is used to provide life-saving organ support for infants and children with AKI and/or fluid overload in the paediatric intensive care unit (PICU). CRRT is also performed for the removal of circulating toxins, such as ammonia in metabolic disorders, and in the management of certain intoxications.<sup>3</sup> Lack of availability of technology designed to cater for smaller children, particularly neonates, makes the use of CRRT extremely difficult in this cohort of patients, and in many institutions, peritoneal dialysis (PD) remains the preferred option for RRT, particularly for infants, where temporary peritoneal catheters are placed at the time of surgery to aid in management of fluid overload, electrolyte disturbance, or renal failure in the immediate post-operative period. The recent development of CRRT machines designed for smaller infants, allows for smaller calibre vascular access, reduced priming volumes and more reliable filtration rates.<sup>4,5</sup> Whilst these technologies are not yet available in Australia and New Zealand (ANZ), providing safe, effective CRRT for smaller infants remains a difficult undertaking.

No data have been published describing the use and practice of CRRT in children requiring intensive care in ANZ. Therefore, the aim of this study was to comprehensively describe the current use, review the clinical practice of CRRT in ICUs, and to explore factors affecting outcomes, using PD as a comparator.

## 2. Methods

### 2.1. Study design

This study comprises two components: a binational, retrospective cohort study using contemporaneously collected data held in the Australian and New Zealand Paediatric Intensive Care Registry (ANZPICR) and a prospective electronic survey of ICUs accredited for paediatric intensive care training. The study was approved by the Monash Health Human Research Ethics Committee, reference: HREC/79312/MonH-2021-280798, November 19 2021, under the title “Provision of Renal Replacement Therapy In Paediatric and Neonatal Intensive Care in Australia and New Zealand”. All procedures were followed in accordance with ethical standards of the responsible committee on human experimentation and the Helsinki Declaration of 1975.

The Clinical Advisory Committee of ANZPICR authorised data extraction in accordance with the Australian and New Zealand Intensive Care Society Centre for Outcome and Resource Evaluation data access and publication policy.<sup>6</sup>

### 2.2. Retrospective cohort study

The ANZPICR is a binational collaborative data registry with contributions from nine specialist university-affiliated PICUs, over 20 general ICUs (adult units which also have capacity to care for paediatric patients) and one specialist combined neonatal and paediatric ICU, representing approximately 94% of PICU admissions.<sup>7</sup>

Records were included for patients aged less than 18 years admitted to the ICU between 1 January 2016 and 31 December 2020 who received RRT. Variables included demographic data, principal and underlying diagnoses, mode of RRT performed, requirement for mechanical ventilation and inotropic therapy, ICU and hospital length of stay, and mortality. Risk of death was estimated using the Paediatric Index of Mortality 3 (PIM3) score.<sup>8</sup> If admissions were identified having received both CRRT and PD, these cases were allocated to the CRRT category for analysis.

### 2.3. Survey of CRRT practice

We conducted a prospective electronic survey of ICUs providing CRRT. Fifteen paediatric and mixed ICUs accredited for paediatric intensive care training were identified from the College of Intensive Care Medicine.<sup>9</sup> This included nine PICUs, one combined neonatal and paediatric ICU, and five general ICUs. ICUs were eligible to participate if they provided CRRT for paediatric patients. Prior to distribution of the survey, each unit was contacted to determine eligibility and ascertain their willingness to participate in the project. An electronic questionnaire developed on SurveyMonkey™ (Momentive Inc., San Mateo, California, USA) was sent to the unit representative to complete details of the clinical practice of CRRT within the unit. The questionnaire was modified from the survey of CRRT practice performed in ICUs in 2015 and included questions about unit size, frequency of use of CRRT, equipment used, preferred mode of CRRT, and anticoagulation strategy used.<sup>10</sup> A copy of the questionnaire is available in [Appendix 1](#).

### 2.4. Statistical analysis

Admissions were allocated a diagnostic group based on principal diagnosis and, if more specific, underlying diagnosis. Sepsis included patients with septic shock or sepsis as principal diagnosis and includes an assortment of aetiologies such as pneumonia, toxic shock, and peritonitis.

Descriptive statistics were used to describe demographic and clinical data, as well as survey responses. Continuous variables are presented as median with interquartile range (IQR) and are analysed by the Mann–Whitney *U* test. Categorical variables are presented as counts and percentages and analysed by chi-square test. The linear trend over time was assessed using chi-square test for linear trend (extended Mantel–Haenszel). Bivariate logistic regression was performed to explore the association between age, diagnosis, and the year of admission with ICU mortality. Odds ratios are presented alongside 95% confidence intervals (CIs). All analysis was performed using IBM SPSS statistics 29.0 (SPSS Inc., Chicago, IL). Standardised mortality ratios (SMRs) for ICU mortality were calculated to compare individual units that performed CRRT on at least two admissions per year, and yearly mortality, by dividing the observed ICU mortality by the expected number using the PIM3 score to estimate risk of death.<sup>8</sup> Funnel plots were constructed to describe the adjusted mortality across ICUs, as described in the [Appendix](#).<sup>11,12</sup> Given the descriptive nature of the study, an a priori sample size calculation was not undertaken. The level of significance was set at 0.05, with no adjustment for multiple comparisons, and results are interpreted with an exploratory lens.

## 3. Results

### 3.1. Retrospective cohort study

In the study period, there were 58,736 admissions extracted from ANZPICR. RRT was performed during 1378 (2.4%) admissions, 592 (1.0%) admissions received CRRT, and 857 (1.5%) received PD. 71 admissions received both CRRT and PD. RRT was supplied by 18 units: eight designated PICUs and 10 non-PICUs.

The median age of patients receiving RRT was 2.16 months (IQR: 0.2–36.7), median weight: 4.3 kg (IQR: 3.2–14.3), and 58% of patients were male ([Table 1](#)). Congenital heart disease (CHD) was the largest diagnostic group requiring RRT (752/1378, 55%) followed by sepsis ( $n = 171/1378$ , 12%) and renal disease (136/1378, 10%). A total of 756 (55%) admissions were associated with procedures requiring cardiopulmonary bypass.

### 3.1.1. Mode of renal replacement therapy

CRRT was used for 43% and PD only for 57% of admissions requiring RRT. There was no change in the number of admissions requiring RRT or in the pattern of RRT modality over the 5-year period studied (Fig. 1a). PD was used more frequently in admissions with CHD (PD: 91% vs CRRT: 9%), and CRRT was used more commonly in all other diagnostic groups. CRRT was used exclusively in metabolic disease and ingestions requiring rapid clearance of solutes (Table 1). In neonates and infants (<1 year of age), PD was more commonly used than CRRT (711 admissions: [80%] vs 178 [20%]) compared with children >1 year of age (75 admissions [15%] v 414 [85%]). Five of the eight PICUs used CRRT more than PD. Six units perform cardiac surgery; three of these used PD more commonly than CRRT overall (Fig. 1b). Thirty percent of patients treated with CRRT received non-congenital heart disease support at some time during their ICU admission (Appendix Table 1). The number of admissions treated with CRRT varied between PICUs (18–160 admissions over 5 years), and between the non-PICU sites (1–11 admissions over 5 years).

Thirty-seven percent of admissions receiving RRT were neonates (<28 days old) undergoing cardiopulmonary bypass procedures. In this population, PD was used in 95%. Nineteen infants weighing less than 2 kg were treated with RRT, with 18 of these receiving PD.

### 3.2. Clinical outcomes

The overall ICU mortality for children receiving all forms of RRT was 17% (232/1378). ICU mortality was higher for patients who received CRRT than for those receiving PD (30% v 7.3%; odds ratio:

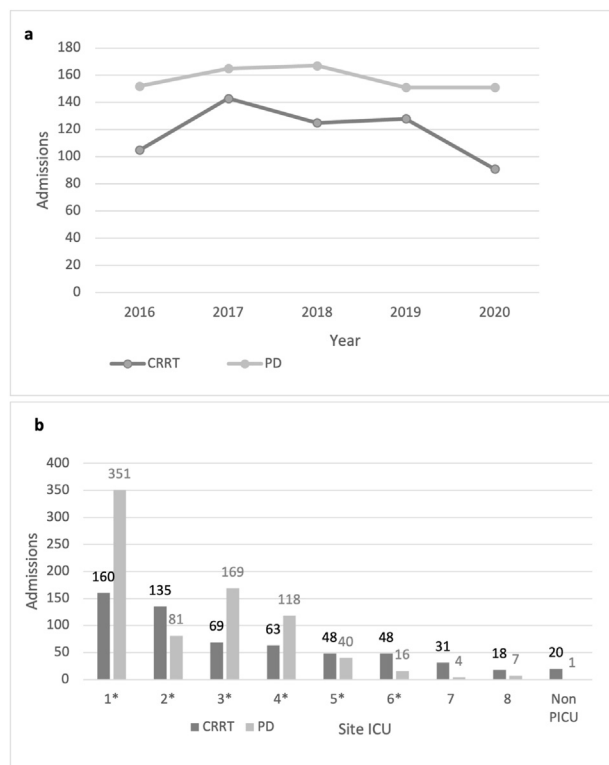
0.18; 95% CI: 0.13–0.26,  $p < 0.001$ ), these admissions had a higher PIM3 risk of death (median: 4.9% [IQR: 1.5–11.7] vs 1.9% [1.2–5.0]). SMR for CRRT was 2.76 (95% CI: 2.35–3.17) and that for PD was 1.60 (95% CI: 1.18–2.01).

There was a decline in crude mortality in patients treated with CRRT over the 5-year period from 35% to 22%,  $p = 0.025$ , with a fall in SMR from 3.2 to 2.4 (Fig. 2a). A funnel plot of SMR showed no relationship between the volume of CRRT performed in individual units and ICU mortality (Fig. 2b and appendix). Mortality was highest in the neonatal admissions receiving CRRT (47% [51/108]) and decreased with age group to 31% (22/70) in infants and 25% (102/414) in children over 1 year of age. This trend is also reflected with a decrease in mortality with a weight of up to 20 kg. Outcome varied with diagnostic group, being the highest for children with CHD (40/69, 58%) and the lowest for children with primary renal disease (2/91, 2%) and ingestions (0/8, 0%) (Table 2).

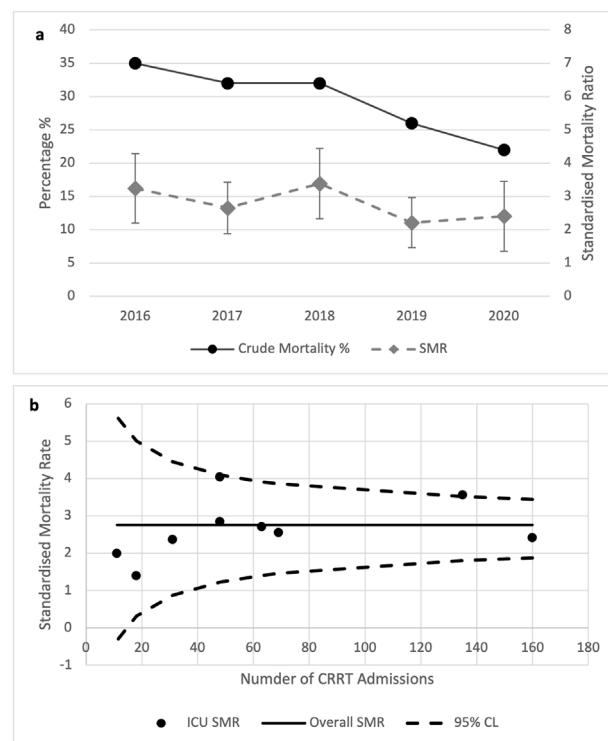
### 3.3. Survey of practice

Thirteen units were deemed eligible (i.e., administered CRRT), and complete survey responses were received from 11 units, including eight PICUs, two general ICUs, and one mixed neonatal and paediatric ICU. Six units reported <10 admissions receiving CRRT per year, and two units reported >30 admissions per year (Appendix Table 2).

The Prismaflex/PrismaMax (Gambro Lundia AB, USA) was used in 10 units. The HF440 (Infomed, Geneva, Switzerland) was used in one unit (Appendix Table 3). The internal jugular vein (IJV) was the preferred site for vascath insertion in all age groups.



**Fig. 1.** Factors influencing choice of RRT modality. (a) Mode of RRT provided in years reviewed did not change ( $p = 0.48$ , chi-square analysis for linear trend); (b) Mode of RRT varied by unit (non-PICU sites are combined). CRRT = continuous renal replacement therapy, PD = peritoneal dialysis, PICU = paediatric intensive care unit, RRT = renal replacement therapy. \* Units that perform cardiac surgery.



**Fig. 2.** Mortality in admissions receiving CRRT: (a) Mortality decreased over the years studied ( $p = 0.025$ ; chi-square analysis for linear trend); (b) funnel plot of standardised ICU mortality. The horizontal line represents the average SMR for children receiving CRRT, and each dot represents one unit (only units with more than 10 admissions included). CRRT = continuous renal replacement therapy; ICU = intensive care unit; SMR = standardised mortality ratio.

**Table 1**  
Demographic characteristics of patients who received renal replacement therapy.

Characteristics	All renal replacement therapy <i>n</i> = 1378	Continuous renal replacement therapy <i>n</i> = 592	Peritoneal dialysis only <i>n</i> = 786	<i>P</i> value
Age, mo, median (IQR)	2.2 (0.2–36.7)	43 (7.0–130)	0.3 (0.1–2.6)	<0.001
Weight, kg, median (IQR)	4.3 (3.2–14.3)	15.9 (6.6–35.1)	3.5 (3.0–4.4)	<0.001
Sex, <i>n</i> (%)				0.016
Female	580 (42)	271 (46)	309 (39)	
Male	798 (58)	321 (54)	477 (61)	
Weight, <i>n</i> (%)				<0.001
<5 kg	746 (54)	130 (22)	616 (78)	
5–10 kg	175 (13)	64 (11)	111 (14)	
10–20 kg	191 (14)	146 (25)	45 (5.7)	
20–30 kg	74 (5.4)	69 (12)	5 (0.6)	
30–40 kg	55 (4.0)	51 (8.6)	4 (0.5)	
40–50 kg	34 (2.5)	31 (5.2)	3 (0.4)	
> 50 kg	103 (7.5)	101 (17)	2 (0.3)	
Diagnostic group, <i>n</i> (%)				<0.001
CHD	752 (55)	69 (12)	683 (87)	
Sepsis	171 (12)	153 (26)	18 (2.3)	
Renal	136 (10)	91 (15)	45 (5.7)	
Cardiac—non-CHD	64 (4.6)	45 (7.6)	19 (2.4)	
Miscellaneous	58 (4.2)	47 (7.9)	11 (1.4)	
Metabolic	53 (3.8)	53 (9.0)	0	
Oncology	48 (3.5)	48 (8.1)	0	
Respiratory	45 (3.3)	36 (6.1)	9 (1.1)	
Liver disease	43 (3.1)	42 (7.1)	1 (0.1)	
Ingestion	8 (0.6)	8 (1.4)	0	
Other therapies, <i>n</i> (%)				
Invasive ventilation	1271 (92)	529 (89)	742 (94)	<0.001
Inotropes	1165 (85)	439 (74)	726 (92)	<0.001
Post CPB	756 (55)	74 (13)	682 (87)	<0.001
ECMO	278 (20)	176 (30)	102 (13)	<0.001
Plasma filtration	25 (1.8)	23 (3.9)	2 (0.3)	<0.001
PIM3 risk of death %, median (IQR)	2.6 (1.3–7.1)	4.9 (1.5–11.7)	1.9 (1.2–5.0)	<0.001
Outcomes				
ICU LOS, d, median (IQR)	8.8 (4.8–18.1)	9.8 (4.3–21.5)	8.0 (4.9–15.9)	0.054
Hospital LOS, d, median (IQR)	27 (14.6–55.0)	27 (12.2–61.0)	27.3 (15.2–52.0)	0.551
ICU mortality, <i>n</i> (%)	232 (17)	175 (30)	57 (7.3)	<0.001
Hospital mortality, <i>n</i> (%)	271 (20)	197 (33)	74 (9.4)	<0.001

CPB = cardiopulmonary bypass procedure; CHD = congenital heart disease; ECMO = extracorporeal membrane oxygenation; ICU = intensive Care Unit; IQR = interquartile range; LOS = length of stay; PIM3 = Paediatric Index of Mortality 3.

Cardiac—non-CHD includes non-congenital heart diseases such as cardiomyopathies and arrhythmias. 'Miscellaneous' includes a range of neurological disorders, burns, trauma, gastro-intestinal and endocrine diagnoses.

Subclavian veins were avoided in all centres. The smallest dual lumen vascath used was 6.5 French gauge (fg). Other sizes used were 8 fg and 11 fg.

Continuous venovenous haemodiafiltration was the preferred modality (seven units) followed by continuous venovenous haemofiltration (four units). Eight units also provided PD, and intermittent haemodialysis was performed in five units. No units provided sustained low-efficiency dialysis, a modality used in some adult ICUs as an alternative to CRRT.

Regional citrate anticoagulation (RCA) was the default mode of anticoagulation in six units. Systemic unfractionated heparin was the anticoagulant of choice in four units, and one unit routinely used regional anticoagulation with heparin and protamine. Two units used prostacyclin as an alternative agent for anticoagulation. No units used low-molecular-weight heparin.

The minimum patient weight considered suitable for provision of CRRT varied between units from 1.8 kg to 4 kg.

#### 4. Discussion

This analysis of data from the ANZPIC registry and information from an online survey provides the first comprehensive description of RRT in children in the ICU in ANZ. RRT is an uncommon treatment in the PICU. Over one-third of admissions were neonates and infants admitted for cardiac surgery. Overall, PD was the more commonly used technique for RRT in ANZ; however, if we exclude

children with CHD, CRRT is the more frequently used modality. Mortality rates were higher for children receiving CRRT than for those receiving PD but varied greatly with diagnosis and age.

Data published from the United Kingdom (UK) Paediatric Intensive Care Audit Network showed a similar pattern of use for CRRT and PD to this study.<sup>13</sup> In the United States (US), CRRT use now exceeds that of PD overall possibly due to increased physician experience and confidence in the technique; however, in common with this study and the UK study, for the infant population, PD remains the most widely used modality.<sup>14</sup> The relative ease and safety of PD, especially in small infants undergoing surgery for CHD, when dialysis catheter access can be inserted in the perioperative period, allows easy and early initiation of therapy for fluid overload or electrolyte correction even when criteria for established AKI are not met.

CRRT was used more frequently in children with a non-cardiac surgical diagnosis. CRRT provides more precise delivery of solute clearance and controlled rates of ultrafiltration in critically ill patients and rapid clearance of toxins and metabolites in patients with liver and metabolic disease with hyperammonaemia at risk of cerebral oedema. However, the limited availability of technology available in ANZ to provide CRRT for small infants may also influence the decision to proceed with PD as an initial therapy. PD was rarely used in children admitted to general ICUs, which may reflect lack of experience with this technique, or the older cohort of patients admitted to these units.

**Table 2**

Bivariate analysis of risk factors for ICU mortality risk for those receiving continuous renal replacement therapy (N = 592).

Risk Factors	N	ICU Mortality n (%)	Odds ratio	95% Confidence limit	P value
Age					
Neonate aged <28 days	108	51 (47)	1	Reference	
Infant aged 28 days–1 year	70	22 (31)	0.51	0.27–0.96	0.038
Older child aged >1 year	414	102 (25)	0.37	0.24–0.57	<0.001
Weight					
<10 kg	194	80 (41)	1	Reference	
10–20 kg	146	36 (25)	0.47	0.29–0.75	0.0016
20–30 kg	69	13 (19)	0.33	0.16–0.65	0.0012
30–40 kg	51	16 (31)	0.51	0.27–0.96	0.039
40–50 kg	31	5 (16)	0.27	0.10–0.74	0.011
>50 kg	101	25 (25)	0.47	0.27–0.80	0.006
Diagnostic group <sup>a</sup>					
Sepsis	153	46 (30)	1	Reference	
Renal	91	2 (2)	0.05	0.12–0.22	<0.001
CHD	69	40 (58)	3.21	1.38–5.79	<0.001
Metabolic	53	11 (21)	0.61	0.29–1.29	0.194
Oncology	48	9 (19)	0.54	0.24–1.20	0.129
Miscellaneous	47	21 (45)	1.88	0.96–3.68	0.065
Cardiac, non-CHD	45	17 (38)	1.41	0.71–2.82	0.330
Liver	42	13 (31)	1.04	0.50–2.18	0.911
Respiratory	36	16 (44)	1.86	0.89–3.91	0.101
Ingestion	8	0	0.13	0.01–2.41	0.170
Year					
2016	105	37 (35)	1	Reference	
2017	143	45 (31)	0.84	0.45–1.44	0.533
2018	125	40 (32)	0.87	0.50–1.50	0.604
2019	128	33 (26)	0.64	0.36–1.12	0.118
2020	91	20 (22)	0.52	0.27–0.98	0.043

CHD = congenital heart disease; ICU = intensive care unit. Cardiac—non-CHD = cardiac disease not related to congenital conditions, e.g., cardiomyopathies and arrhythmias.

<sup>a</sup> Sepsis was chosen as the reference category as it contained the largest number of admissions.

PICU mortality for all admissions recorded in the ANZPICR for 2018 was 2.2%.<sup>15</sup> This year represents the midpoint of our study and is the most recently reported figure. Admissions requiring any form of RRT have a higher crude mortality of 17%, and those that require CRRT had a crude mortality of 30%, reflecting higher severity of illness, as shown by PIM3 admission scores. Similar studies in the UK and US reported a mortality of 32% and 39% for CRRT, respectively.<sup>13,14</sup> A recent study from China showed an increase in survival of children receiving CRRT over a 10-year period (2010–2020) from 36% to 58%.<sup>16</sup> Factors leading to increased survival were identified as practice changes including the use of RCA, a lower degree of fluid overload and earlier initiation of CRRT. Our study reflects that trend with mortality falling from 35% to 22% over the 5-year period; however, our data did not allow for analysis of factors associated with this change. The number of admissions receiving CRRT varied greatly between units; however, the volume of practice within each unit did not correlate with mortality. The main factors associated with mortality rate were diagnostic group and age, with neonates with CHD receiving CRRT having the highest mortality. This may partially reflect the high rate of use of PD in the less severely unwell neonates and the use of CRRT more commonly in patients supported with extracorporeal circuits.

Only two models of dialysis machine were used to provide paediatric CRRT in ANZ. The Prismaflex has a priming volume of 58 ml for the paediatric HF20 filter set, and the HF440 PECOPEN DF-030 filter set requires 55 ml. In infants weighing less than 5 kg, this exceeds 15% of the blood volume, necessitating a blood prime with each filter commencement, and increasing the risk of complications such as acidosis, hyperkalaemia, hypocalcaemia, and coagulopathy, and risking sensitisation of the immune system to blood antigens, a concern for patients who may require renal transplantation. Newer machines have been developed specifically for paediatrics. The CARPEDIEM (Medtronic, Mirandola, Italy) is now approved in several countries for use in patients weighing 2–10 kg and has been shown to improve survival compared to machines not specifically

designed for the infant population using historical controls.<sup>17</sup> The NIDUS machine (Allmed, London, UK) was assessed in children weighing <8 kg and was shown to deliver appropriate blood clearances and accurate, controllable fluid removal with a good safety profile.<sup>18</sup> There have been no large-scale studies reported as yet. Whilst ANZ units indicated a willingness to consider infants as small as those weighing 1.8 kg for CRRT, the availability of technology for this purpose in ANZ is limited, and from our data, only a single infant weighing <2 kg received CRRT.

Successful delivery of CRRT depends on circuit survival. Larger bore catheters have been shown to improve circuit survival.<sup>19</sup> This leads to significant access problems in smaller infants. The smallest dual-lumen catheter available in ANZ is 6.5 fg; however, smaller catheters have been used successfully in Europe.<sup>20</sup> The site for vascular access is important for circuit-life duration. The optimal site for catheter placement depends on factors including procedural risk, risk of thrombosis or stenosis of vessels, infection risk, and expertise. In this study, the IJV was preferred. The right IJV provides the most direct route through the superior vena cava to the right atrium.<sup>2</sup> Positioning the tip in the right atrium provides best flow dynamics and lower recirculation rate. The routine use of bedside ultrasound has made IJV insertion easier and safer, and IJV lines are associated with a significantly higher circuit survival than are femoral lines.<sup>19</sup> The use of lower blood flows in paediatric patients increases the risk of clotting, and filter clotting reduces efficiency of filtration and leads to multiple blood transfusions in small infants as each new filter requires priming. Optimum circuit anticoagulation of the extracorporeal circuit is vital to the successful use of CRRT. Until recently, heparin was used predominantly, and there is wide experience with its use. Recent research suggests that RCA offers a safer option and increases the life span of circuits.<sup>20,21</sup> RCA is now the preferred mode of anticoagulation in the PICU in ANZ and in the US.<sup>22</sup>

Continuous venovenous haemodiafiltration with pre-filter and post-filter replacement was the most frequently used mode of CRRT



in ANZ PICUs, similar to the study of adult ICUs in ANZ.<sup>10</sup> Despite theoretical differences in solute clearance with diffusive and convective modes, no research data have demonstrated a difference in benefit between modes.<sup>23</sup> No information on dosage of filtration and dialysis was collected for this study.

A strength of this study is the use of a large database providing a comprehensive representation of paediatric ICU practice across ANZ. The addition of a survey provides more detailed information on practical aspects of the application of CRRT.

A major limitation of this study is the general nature of the dataset, which is not designed to capture data specific to the use of RRT, such as details on precipitant for initiation of RRT, acid–base status, urine output, plasma creatinine, or details of the clinical practice of RRT. CRRT remains an infrequently used treatment in children in the ICU, and the diverse range of diagnoses makes examination of modifiable factors that could influence outcomes complex.

5. Conclusion

The use of CRRT remained stable over the 5-year period. Whilst it is used less frequently than PD in smaller children and those with CHD, in all other cohorts, it is the predominant mode of RRT. ICU mortality rates were for CRRT showed large variation across age and diagnostic groups. Mortality rate fell over the 5 years of the study. The practical technique of CRRT showed consistency across units with variation in dialytic modality and anticoagulation preference.

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Conflict of interest

None of the authors have conflicts of interest to declare.

CRediT authorship contribution statement

Conceptualisation: C.K. and F.O.; Methodology: C.K. and F.O.; Investigation: C.K.; Formal Analysis: C.K. and K.G.; Writing - original draft: C.K., F.O. and K.G.; Writing - review & editing: C.K., F.O., K.G. and S.G.

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Survey respondents

Sidharth Agarwal, Royal Darwin Hospital, NT; Roberto Chiletto, Royal Children's Hospital, Melbourne, VIC; Simon Erickson, Perth Children's Hospital, WA; Hamish Jackson, Royal Hobart Hospital, Tas; Andrew Numa, Sydney Children's Hospital, Sydney, NSW; Kevin Plumpton, Queensland Children's Hospital, Brisbane, QLD; Greg Wiseman, Townsville University Hospital, QLD; Kiraka Nakazawa, Monash Children's Hospital, Clayton, VIC; Subodh Ganu, Women's and Children's Hospital, Adelaide, SA; The Children's Hospital Westmead, Sydney, NSW; John Hunter Children's Hospital, Newcastle, NSW.

Appendix

- Copy of survey questionnaire.
- Construction of funnel plot.
- Funnel plot for crude mortality.
- Table 1. Profile of units participating in survey.
- Table 2. Summary of survey responses.
- Table 3. Age and diagnostic group ICU mortality for CRRT.
- Table 4. ICU mortality for CRRT in age and diagnostic groups.

Copy of survey questionnaire

Continuous renal replacement therapy survey.

Location of Hospital

State

AustraliaChoose an item.

or

New ZealandChoose an item.

Name of Hospital (requested to ensure that data is not duplicated)

Click here to enter text.

Type of Intensive Care Unit

Choose an item.

What is the size of your ICU? (bed numbers)

Choose an item.

Approximate number of patients treated with CRRT per year?

Choose an item.

CRRT Practice

Which is the most frequently used modality of CRRT in your unit?

Choose an item.

Other modalities used

tick all that apply

predilution

postdilution

pre&postdilution

CVVH☐

CVVHDF☐

CVVHD☐

SLED☐

Peritoneal Dialysis☐

Intermittent Haemodialysis☐

CRRT Machine

Which CRRT machine(s) do you use to perform CRRT?

Prismaflex/Prismax☐

Aquarius☐

Tick all that apply

Infomed HF440☐

Fresenius☐

OtherClick here to enter text.

Vascular Access

Which brand(s) of vascath do you use?

Choose an item.

If two brands used please select

Choose an item.

Which sizes of vascath do you use?

6F☐6.5☐7F☐7.5☐8F☐8.5☐9F☐9.5☐10F☐10.5☐11F☐11.5☐12F☐12.5☐13F☐13+☐

Please tick all that apply

Do you use catheters <6F, or another brand?  
Please enter details

Click here to enter text.

#### Site of Access

Preferred Site of access

Choose an item.

Other access points used

Lt IJV ☐

Rt IJV ☐

Lt SCV ☐

Tick all that apply

Rt SCV ☐

Femoral ☐

ECMO ☐

Do you routinely use tunnelled lines?

Choose an item.

#### Anticoagulation

Default method used in your unit

Choose an item.

Other methods of anticoagulation used

Citrate-Ca ☐

Heparin only ☐

Please tick all that apply

Heparin-Protamine ☐

LMW heparin ☐

Prostacyclin ☐

No A/C ☐

Other techniques for anticoagulation used

Click here to enter text.

#### Patient Weight Limitation

Is there a minimum patient weight you would consider for

Click here to enter text.

CRRT **without** ECMO support?

Is there a minimum patient weight you would consider for

Click here to enter text.

CRRT **with** ECMO support?

Survey developed on SurveyMonkey ([www.surveymonkey.com](http://www.surveymonkey.com)).

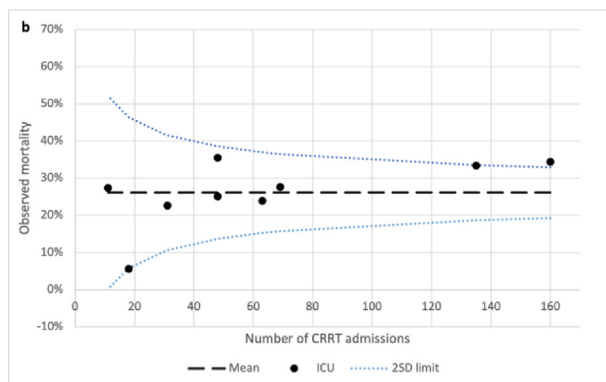
### Construction of funnel plot

A funnel plot was constructed for crude mortality plotting intensive care unit (ICU) mortality for individual units with >10 continuous renal replacement therapy (CRRT) admissions against overall cohort mortality (p) and 95% control limits (CL) where

$$CL = p \pm Z_{crit} \times \sqrt{\frac{p(1-p)}{n}}$$

and  $Z_{crit} = 1.96$ .

Funnel plot for crude mortality.FLA



Funnel plot for standardised mortality ratio (SMR) was constructed plotting SMR for individual units with >10 CRRT admissions against overall SMR and 95% CL where

$$CL = SMRo \pm Z_{crit} \times \frac{\sqrt{O}}{E}$$

where  $SMRo$  is overall SMR,  $O$  = observed deaths for all units scaled for number of admissions,  $E$  = expected deaths for all units scaled for number of admissions,  $O$  = total observed deaths x admissions/total admissions,  $E$  = total expected deaths x admissions/total admissions.

From: An Introduction to Medical Statistics, 4th Edition, 2015, M Bland, Oxford University Press. p527.

**Table 1**

Demographics for patients receiving ECMO and RRT during the same admission.

Characteristics	Continuous renal replacement therapy $n = 176$	Peritoneal dialysis only $n = 102$
Age, mo, median (IQR)	13 (0.2–80)	0.2 (0–0.1)
Weight, kg, median (IQR)	9.2 (3.4–21)	3.4 (2.8–4.0)
Sex, $n$ (%)		
Female	89 (50)	38 (37)
Male	87 (50)	64 (63)
Diagnostic Group, $n$ (%)		
CHD	53 (30)	88 (86)
Sepsis	48 (27)	2 (2)
Renal	1 (0.5)	0
Cardiac—non-CHD	35 (20)	11 (11)
Miscellaneous	6 (3)	1 (1)
Metabolic	2 (1)	0
Oncology	3 (1)	0
Respiratory	27 (15)	0
Liver disease	1 (0.5)	0
PIM3 risk of death %, median (IQR)	8.4 (4–22)	5.1 (2–11)
Outcomes		
ICU LOS, d, median (IQR)	18 (7.4–33)	24 (12–41)
ICU mortality, $n$ (%)	87 (49)	35 (34)

ICU = intensive care unit; LOS = length of stay; PIM3 = Paediatric Index of Mortality 3; CHD = congenital heart disease; IQR = interquartile range; ECMO = extracorporeal membrane oxygenation; RRT = renal replacement therapy.

**Table 2**

Profile of units participating in survey.

Units providing continuous renal replacement therapy	Number of units $n = 11$
Unit type	
PICU	8
General ICU	2
Mixed NICU/PICU	1
Number of ICU beds	
1–5 beds	3
6–10 beds	1
11–20 beds	4
>20 beds	3
Number of patients treated with CRRT/year	
1–10 patients	6
11–30 patients	3
31–50 patients	2

CRRT = continuous renal replacement therapy; PICU = paediatric intensive care unit; NICU = neonatal intensive care unit.

**Table 3**  
Summary of survey responses.

Continuous renal replacement therapy practice	Number of units n = 11		
Haemofilter machine			
Prismaflex/prismax (Gambro)	10		
HF 440 (Infomed)	1		
Vascath			
Gamcath, Baxter, USA	8		
Arrow™, Teleflex, Ireland	2		
Cook, Cook medical	1		
Site of insertion preferred	<5 kg	5–10 kg	>10 kg
IJV	6	7	6
Femoral	4	3	4
Mode of CRRT preferred	Pre dilution	Post dilution	Pre/post dilution
CVVHDF	2	0	5
CVVH	1	1	2
CVVHD	0		
Mode of anticoagulation			
Citrate-calcium	6		
Unfractionated heparin	4		
Regional heparin-protamine	1		
Alternative mode of RRT			
Peritoneal Dialysis	8		
Intermittent haemodialysis	5		

CRRT = continuous renal replacement therapy; IJV = internal jugular vein; CVVHDF = continuous veno-venous haemodiafiltration; CVVH = continuous venovenous haemofiltration; CVVHD = continuous veno-venous haemodialysis; RRT = renal replacement therapy.

**Table 4**  
ICU mortality for CRRT in age and diagnostic groups

Variables	All admissions		Neonate: Aged <28 days		Infant: Aged 28 days–1 year		Older child: Aged >1 year	
	n	Mortality n (%)	n	Mortality n (%)	n	Mortality n (%)	n	Mortality n (%)
Diagnostic group								
All	592	175 (30)	108	51 (47)	70	22 (31)	414	102 (25)
Sepsis	153	46 (30)	10	4 (40)	13	4 (31)	130	38 (29)
Renal	91	2 (2)	1	0 (0)	12	0 (0)	78	2 (2.6)
CHD	69	40 (58)	31	23 (74)	11	7 (63)	27	10 (37)
Metabolic	53	11 (21)	29	7 (24)	10	1 (10)	14	3 (21)
Oncology	48	9 (19)	1	0 (0)	3	0 (0)	44	9 (21)
Miscellaneous	47	21 (45)	2	1 (50)	8	3 (38)	37	17 (46)
Cardiac	45	17 (38)	7	4 (57)	7	3 (43)	31	10 (32)
Liver	42	13 (31)	6	5 (83)	5	3 (60)	31	5 (16)
Respiratory	36	16 (44)	21	7 (33)	1	1 (100)	14	8 (57)
Ingestion	8	0 (0)	0	–	0	–	8	0 (0)

ICU = intensive care unit; CRRT = continuous renal replacement therapy.

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