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Continuous Kidney Replacement Therapy and Survival in Children and Young Adults: Findings From the Multi-National WE-ROCK Collaborative

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Abstract

Rationale and Objective: There are limited studies describing the epidemiology and outcomes of children and young adults receiving continuous kidney replacement therapy (CKRT). We aimed to describe associations between patient characteristics, CKRT prescription, and survival.

Study Design: Retrospective multicenter cohort study

Setting & Participants: 980 patients aged Birth-25 years old who received CKRT between 2015 and 2021 at 1 of 32 centers in 7 countries participating in the Worldwide Exploration of Renal Replacement Outcomes Collaborative in Kidney Diseases (WE-ROCK).

Exposure: CKRT for acute kidney injury or volume overload

Outcomes: Death prior to ICU discharge

Analytic Approach: Descriptive statistics.

Results: Median age was 8.8 years (IQR 1.6, 15.0) with a median weight of 26.8kg (IQR 11.6, 55.0). CKRT was initiated a median of 2 days (IQR 1, 6) after ICU admission and lasted a median of 6 days (IQR 3, 14). The most common CKRT modality was continuous veno-venous hemodiafiltration. Citrate anticoagulation was used in 62%, and the internal jugular vein was the most common catheter placement location (66%). 629 (64.1%) survived to ICU discharge. The

CKRT dose, filter type, and anticoagulation were similar in those who did and did not survive to ICU discharge. There were apparent practice variations by institutional ICU size.

Limitations: Retrospective design; limited representation from centers outside United States

Conclusions: In this study of children and young adults receiving CKRT approximately two-thirds survived to ICU discharge. While variations in dialysis mode, dose, catheter size and location, and anticoagulation were observed, no survival differences by these parameters were apparent.

Plain Language Summary

Clinical Characteristics and Outcomes of Critically Ill Children and Young Adults Receiving Continuous Dialysis for Acute Kidney Injury

In this large contemporary epidemiological study of children and young adults receiving CKRT in the ICU, we observed that 2 out of 3 patients survived to ICU discharge. However, patients with comorbidities appeared to have worse outcomes. We also observed differences in CKRT practice compared to previously published literature, with greater use of continuous veno-venous hemodiafiltration with regional citrate anticoagulation.

Keywords

continuous kidney replacement therapy; pediatric; WE-ROCK; database; fluid overload; acute kidney injury; technique; intensive care unit

Introduction:

In recent years, our understanding of acute kidney injury (AKI) and the state of pathologic volume overload (VO) in critically ill children and young adults has increased exponentially.¹ AKI and pathologic VO occur commonly among critically ill children and young adults,²⁻⁴ and are associated with increased morbidity and mortality.⁵⁻⁷ As the impact of AKI and VO has become clear, the field has transitioned toward the prevention, mitigation, and optimization of interventions to improve outcomes.

While continuous kidney replacement therapy (CKRT) is a well-established modality for the care of critically ill children and young adults with AKI and VO, studies in pediatric CKRT are hampered by small sample size and single-center evaluation.⁸⁻¹⁰ The largest published multicenter study from the Prospective Pediatric Continuous Renal Replacement Therapy (ppCRRT) Registry was performed almost 20 years ago. The ppCRRT described practice patterns and outcomes of patients treated with CKRT in North America and reported 58% survival to intensive care unit (ICU) discharge.^{11,12} Single center studies from 2005-2015 show survival ranging from 45-80%.^{13,14} Since then, there have been substantial changes in the care of patients with AKI and VO^{8,15} and availability of newer CKRT devices. There are no multicenter reports describing these changes.

The Worldwide Exploration of Renal Replacement Outcomes Collaborative in Kidney Diseases (WE-ROCK) (www.werockstudy.org) is a multi-national investigator driven collaborative formed to better understand the epidemiology, practice differences, and

clinical and patient-centered outcomes of children and young adults receiving CKRT.¹³ The objectives of this report are to (1) describe the patient characteristics in children and young adults receiving CKRT for AKI and VO, (2) characterize differences between those that do and do not survive to ICU discharge, and (3) describe CKRT prescription characteristics at time of therapy initiation.

Methods:

Study Population:

This study from the WE-ROCK group included patients from 32 institutions in 7 countries (USA, Canada, United Kingdom, Italy, Spain, Austria, and Australia) receiving CKRT for AKI or VO in the pediatric, neonatal, or cardiac ICU from January 2015 to December 2021. The study design has been previously reported in detail.¹³ Briefly, the inclusion criteria were all children and young adults (<25 years old) receiving CKRT for AKI or VO. As young adults with various chronic diseases or comorbidities starting in early childhood are often cared for in pediatric institutions into adulthood, we included those up to age 25 to capture the full spectrum of CKRT in children and young adults managed in pediatric hospitals.^{5,16} All patients were managed by pediatric subspecialists (intensivists and nephrologists). Patients were identified from institutional CKRT databases, and consecutive patients who met the inclusion criteria were included. Exclusion criteria were: (1) end stage kidney disease (ESKD) defined as dialysis dependence prior to CKRT initiation; (2) infants with severe congenital anomalies of the kidney and urinary tract likely to result in ESKD who were initiated on CKRT while awaiting peritoneal dialysis (PD) catheter placement or initiation of PD as their chronic dialysis modality; (3) patients receiving CKRT for a non-AKI/VO indication (i.e., toxic ingestion, inborn errors of metabolism [IEM]); (4) patients on extracorporeal membrane oxygenation (ECMO), (5) patients receiving PD after cardiac surgery in the same admission prior to CKRT initiation; and (6) patients receiving CKRT with CARPEDIEM™ due to the presence of an existing registry focusing on the device. During the study period, CARPEDIEM™ was used in 4 centers, and 14 patients who received CKRT with it for a primary indication of AKI and/or VO were excluded from this study. The Institutional Review Board (IRB) at Cincinnati Children's Hospital Medical Center approved this collaborative study, and each center received approval from their IRB or Human Research Ethics Committee with waiver of informed consent due to the retrospective nature of the study.

Demographic and CKRT technique data

Demographic data were collected including sex, age and time to CKRT initiation after ICU admission. Data collected at the time of CKRT initiation included serum creatinine, presence of sepsis (defined as the presence of an infection and systemic inflammatory response syndrome within 24 hours of ICU admission)¹⁷, vasoactive-inotrope score (VIS)¹⁸, Pediatric Logistic Organ Dysfunction 2 (PELOD-2) score¹⁹ in the 24 hours prior to CKRT initiation, volume overload, and loop diuretic use. Detailed descriptions of admission criteria and comorbidities were made available to the sites in a manual of procedures. These descriptions were kept consistent with previously published pediatric AKI studies.⁵

We used fluid intake/output to calculate VO.^{20–22} While daily weights were collected when available, cumulative fluid balance was available in most patients whereas daily weights were infrequently obtained. Percent VO was calculated from ICU admission to CKRT initiation using the following equation.²³

$$\text{Percent Volume Overload} = \frac{(\text{Fluid Intake} - \text{Fluid Output})[\text{L}]}{\text{ICU Admission weight (kg)}} * 100$$

Education on data collection was provided during monthly collaboration calls to ensure consistent coding, and members of the WE-ROCK steering committee and data analysts at the data coordinating center were available *ad hoc* for additional queries. Details of CKRT prescription including device, modality, filter, dose, fluid type and anticoagulation were also collected. Centers were classified based on the number of pediatric and cardiac ICU beds into small (< 30 ICU beds), medium (>30-60 ICU beds) and large (>60 ICU beds). Because of the heterogeneity in degree of critical illness among children cared for in the Neonatal ICU (NICU) (from severely ill to “feeding and growing” premature infants), we did not include the NICU bed number in the total center ICU bed count. In addition, many participating centers do not perform CKRT in the NICU and transfer patients to the PICU for CKRT²⁴.

Statistical analysis

Patient and CKRT technical characteristics were described using medians (interquartile ranges [IQR]) for continuous variables and frequencies (percentages) for categorical variables. Wilcoxon rank sum tests, Kruskal-Wallis test, and chi-square tests were used to test for differences in continuous and categorical variables as appropriate.

In all analyses, a p-value <0.05 was considered statistically significant. All statistical analyses were performed using R (V3.6.1).

Results

Patient Characteristics

The WE-ROCK Registry includes data from 980 children from January 1, 2015 to December 31, 2021 (Supplemental Figure 1). Enrollment was initially planned from 2018-2021¹³. However, 64 patients were entered in the registry from 2015 to 2018 and were included in the analysis, as CKRT practices have not changed significantly over this period. Selected patient characteristics for the 980 patients at the 32 participating centers are displayed in Table 1. Of the patients, 55% were male. Patient median weight was 26.8kg (IQR 11.6–55.0), 228 (23%) weighed <10kg, with 150 (15%) weighing 5-10 kg, and 78 (8%) <5kg. Ages ranged from newborn to 25 years; 803 (82%) were older than 1 year at the time of CKRT initiation and 50 (5%) were younger than 1 month. The most common reason for admission was shock, infection, or trauma (37%), followed by respiratory failure (20%), and 46% had sepsis at ICU admission. Co-morbidities were seen in 81%, with oncologic (23%), cardiac (20%), and gastrointestinal (19%) being most common.

CKRT Initiation

CKRT was initiated a median of 2 days (IQR 1, 6) after ICU admission and lasted a median of 6 days (IQR 3, 14). At the time of CKRT initiation, the median PELOD-2 score was 7 (IQR 4, 9) and vasoactive-inotrope score was 5 (IQR 0, 20). A diuretic challenge was performed before CKRT initiation in 322 (33%) patients, with the vast majority (96%) receiving furosemide. At the time of CKRT initiation, the median VO for the group was 7.4% (IQR 2.4, 18.1) with 404 (41%) patients having >10% VO, and 224 (23%) > 20% VO. Selected patient characteristics at the time of CKRT initiation across the different countries are shown in Supplemental Table 1.

CKRT Technical Characteristics

Table 2 displays CKRT technical characteristics. The most common modality prescribed at initiation was continuous veno-venous hemodiafiltration (CVVHDF) in 747 (76%) patients, followed by continuous veno-venous hemofiltration (CVVH) (11%) and continuous veno-venous hemodialysis (CVVHD) (10%). Polysulfone filters were most used (80%). Anticoagulation was with citrate in 62%, heparin in 24%, and no anticoagulation was used in 7.2%. Other anticoagulation was used in 59 (6.0%) and included eprostenol and bivalirudin. The internal jugular vein was the most common catheter placement location (66%) with catheter size ranging from 6Fr to 14Fr.

Median blood flow per body weight was 3.9 ml/kg/min (IQR 2.7, 5.5). Median hourly prescribed CKRT dose was 2060 ml/1.73m² (IQR 1745, 2659) or 41.9 ml/kg (IQR 30.9, 59.9), with most patients (55%) prescribed a CKRT dose of >40ml/kg/hr.

Table 3 displays CKRT technical characteristics by center ICU size. The modality prescribed at initiation varied, with large centers (>60 ICU beds) more likely to use CVVHDF initially (95% vs 62%) compared to small centers (< 30 ICU beds). Centers with small ICUs had a higher relative percentage of CVVH as their initial modality (21% vs 2.6%) and were more likely to use non-polysulfone membranes compared with large centers (32% vs 13%, $p<0.001$). Large ICUs were more likely to use citrate anticoagulation (82% vs 46%, $p<0.001$) and were more likely to use lower CKRT doses ($p<0.001$).

Survival to ICU Discharge

Overall, 629 (64.1%) survived to ICU discharge. Those who survived to ICU discharge had higher weights (27.6kg vs 24.8kg, $p=0.018$). Infants and smaller children were less likely to survive to ICU discharge (44% survival in those <5kg compared to 73% survival in those >70kg, $p<0.001$). Those with sepsis at ICU admission, and those with cardiac, immunologic (including patients with hematopoietic stem cell transplants), or oncologic co-morbidities were also less likely to survive to ICU discharge (Table 1).

Patients who died prior to ICU discharge had more VO (8.8% vs 6.8%, $p=0.002$) at CKRT initiation, and later initiation of CKRT (3d vs 2d, $p<0.001$). Patients who died prior to ICU discharge also had lower serum creatinine at CKRT initiation (1.39mg/dl vs 2.10mg/dL, $p<0.001$). They had higher vasoactive-inotrope scores (10 vs 2, $p<0.001$) and

higher PELOD-2 scores (8 vs 6, $p<0.001$). Those who died prior to ICU discharge had longer duration of CKRT (8d vs 6d, $p=0.042$).

There were no differences between ICU survivors and non-survivors with regards to CKRT dose, filter, anticoagulation, or institutional ICU size. Blood flow was higher in those that did not survive to ICU discharge (4.1ml/min/kg vs 3.9ml/kg/min, $p=0.029$) and internal jugular catheter position was more common in survivors (67% vs 63%, $p=0.035$).

Over 100 patients received CKRT for > 28 days, and of those 44 (41%) survived to ICU discharge.

Discussion

The WE-ROCK Registry represents a large and varied CKRT experience in children and young adults and provides an update of the current state of pediatric CKRT prescription practices, with notable changes in technical approaches and patient outcomes from previous studies.^{8,12} We report on 980 patients distributed across all age and weight groups. While most patients were older children and young adults, 41% of those included in the registry were younger than 5 years, including 18% infants and neonates.

The overall survival to ICU discharge of 62% is modestly higher than previous reports which have typically included patients with IEM and intoxications, groups with traditionally better CKRT outcomes.^{8,12} While the study design and patient populations differed across these reports, we are unable to ascertain the reasons in our population. A previous single center study suggested such differences in outcomes may be partly reflective of improved overall care of critically ill pediatric patients and CKRT technology, including smaller filters and pediatric specific practices.⁸ We noted lower survival to ICU discharge in those with co-morbidities (especially oncologic, immunologic, and cardiac) which has also been reported previously, and suggests that patients with isolated kidney dysfunction and those without comorbidities have higher likelihood of CKRT survival.¹² Separate evaluation of these subpopulations are needed to delineate modifiable factors that offer opportunities for improving survival.

Over 10% of patients stayed on CKRT for >28 days, whose survival to ICU discharge was 41%. This suggests that even in the group with protracted kidney and multi-organ dysfunction requiring prolonged CKRT, nearly half survive to ICU discharge. This finding highlights the importance of evaluating longer term survival outcomes in this patient population.

We note that patients who did not survive to ICU discharge had lower SCr at CKRT initiation. This may be a reflection of their volume balance as VO dilutes SCr values, which is further supported by the observation that those who died prior to ICU discharge had higher VO at CKRT initiation. We note that the median VO in our study (7.4%) is lower than what has been previously reported by Sutherland et al (9.6%) and Riley et al (14%).^{8,25} This suggests likely improvement in the recognition and management of pathologic VO in recent years.²⁶

The technical characteristics of CKRT in the WE ROCK registry reveal significant changes in practice from previously published literature.¹¹ The use of CVVHDF as an initial dialytic modality increased from 30% (ppCRRT) to 78% in the current study.¹² Two recent surveys of CKRT practices across ICUs in Europe and North America showed that CVVHDF was the most commonly used modality.^{27,28} Studies have shown no difference in survival between convective and dialytic CKRT modalities and these differences likely reflect center preference. This was also suggested by a survey of pediatric ICUs in Japan where CVVHD was the most common modality.²⁹ While citrate-based anticoagulation remains the most prevalent, use of heparin decreased from 37% in ppCRRT to 24% in the current study. It is possible that this reduction in the use of heparin reflects availability and use of other agents, including bivalirudin and epoprostenol. Most vascular access for CKRT is by internal jugular vein in accordance with the current recommendations, and denoting a shift from the femoral vein as had been the previous practice.¹² Our findings are in line with a recent survey of European pediatric ICUs which reported that the internal jugular vein was the preferred vessel across all age groups.^{27,28} This study did not capture reason for line position. Similar to previous reports, we describe wide ranges of blood flow rates and prescribed dialytic doses, which likely reflect variations in patient size and vascular access as well as availability of newer devices and filters that allow for lower blood flows,¹² highlighting the advancements in technology.

We describe substantial variation in practice by center size, with larger centers more likely to use CVVHDF as an initial modality, citrate anticoagulation and polysulfone filters. It remains unclear if the preference for a certain modality is guided by regional practices, product availability or center size. Indeed, there were no apparent differences among these factors between ICU survivors and non-survivors. Our report extends the previous findings of practice heterogeneity among centers performing CKRT in pediatric patients,²⁷ consistent with findings from Europe²⁸ and Japan.²⁹ Understanding how these variations in practice associate with outcomes in critically ill children is essential for advancing our knowledge, determining best practice, and improving outcomes of children through prospective multicenter, multinational, and multi-disciplinary quality improvement based collaborative work.³⁰

The strength of this study is its multi-national approach with diversity in center size providing a broader understanding of CKRT practices and patient outcomes. However, we also acknowledge several limitations. All sites included are tertiary or quaternary care centers from high income countries in North America, Western Europe, United Kingdom, and Australia; therefore, the findings may only be applicable to centers with similar practice models and resources. The collaborative is actively attempting to increase participation from centers in Asia, Central/South America and Africa to improve generalizability. Secondly, we only included patients receiving CKRT which limits our ability to identify risk factors for starting CKRT. Third, the retrospective study design results in missing data points, particularly around details of hourly urine output quantification and response to diuretic challenges, and limits our conclusions to only associations, not causality. Additionally, details of individual CKRT treatments, notably delivered dose was not collected. Adjudication of differences in the prescribed and delivered dose will be important for quality improvement initiatives to improve patient centered outcomes. Finally, we

acknowledge that peritoneal dialysis is the most used dialytic modality in many countries³¹ for AKI and VO, particularly in children, but WE-ROCK was designed to look at practice patterns and outcomes of extracorporeal CKRT, and only focuses on that modality.

In summary, we describe a large contemporary epidemiological study of children and young adults receiving CKRT in the ICU. While we noted differences in dialysis mode, dose, catheter size and location, and anticoagulation in this study, as well as variations by center size, there were no differences in survival by these characteristics. Practice variation across centers might present opportunities to define best practices and develop future prospective studies to evaluate the timing, dose, and strategies for performing CKRT in critically ill children and young adults.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data Sharing:

De-identified summary data are available through the WE-ROCK collaborative. Data dictionaries, in addition to study protocol, the statistical analysis plan will be made available upon request. More information about the process and available data can be obtained by contacting the corresponding author (SM). The data from the WE-ROCK collaborative will be made available to researchers who provide a methodologically sound proposal for use in achieving the goals of the approved proposal following an application process and execution of a data-use agreement as required by the Institutional Review Board at the Cincinnati Children's Hospital Medical as part of the approval of this collaborative study.

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Table 1.

Patient Characteristics and Association with Death Prior to ICU Discharge

Variable	Overall N = 980	ICU survival		p-value ²
		Survivor to ICU discharge N = 629 ¹	Death prior to ICU discharge N = 351 ¹	
Patient Characteristics ¹				
Female	445 (45)	294 (47)	151 (43)	0.3
Admission Weight (kg)	26.8 (11.6, 55.0)	27.6 (12.6, 58.1)	24.8 (9.8, 51.9)	0.02
Weight categories (kg) *				<0.001
<5	78 (8.0)	34 (5.4)	44 (13)	
5- 10	150 (15)	96 (15)	54 (15)	
11- 20	204 (21)	140 (22)	64 (18)	
21- 50	268 (27)	171 (27)	97 (28)	
51- 70	149 (15)	93 (15)	56 (16)	
>70	126 (13)	92 (15)	34 (9.7)	
Age, years	8.8 (1.6, 15.0)	9.0 (2.0, 14.9)	8.3 (1.1, 15.2)	0.3
Age categories				0.03
< 1 month	50 (5.1)	24 (3.8)	26 (7.4)	
1 month-<1 year	127 (13)	73 (12)	54 (15)	
1-<5 year	223 (23)	154 (24)	69 (20)	
5-<15 year	333 (34)	224 (36)	109 (31)	
15-<21 year	213 (22)	132 (21)	81 (23)	
21 year	34 (3.5)	22 (3.5)	12 (3.4)	
Admission Category				<0.001
Shock/Infection/Major Trauma	364 (37)	242 (38)	122 (35)	
Respiratory Failure	195 (20)	87 (14)	108 (31)	
Post-surgical/Minor trauma	49 (5.0)	35 (5.6)	14 (4.0)	
Neurological Dysfunction	39 (4.0)	22 (3.5)	17 (4.8)	
Pain/Sedation Management	8 (0.8)	6 (1.0)	2 (0.6)	
Congenital Heart disease	31 (3.2)	14 (2.2)	17 (4.8)	
Post-surgical cardiac	49 (5.0)	40 (6.4)	9 (2.6)	
Heart failure/cardiomyopathy	39 (4.0)	23 (3.7)	16 (4.6)	
Other	206 (21)	160 (25)	46 (13)	
Sepsis at ICU admission	446 (46)	265 (42)	181 (52)	0.005
Comorbidities				
None	193 (20)	153 (24)	40 (11)	<0.001
Any	787 (80)	476 (76)	311 (89)	
Type of Comorbidity				
Respiratory	133 (14)	79 (13)	54 (15)	0.3

Variable	Overall N = 980	ICU survival		p-value ²
		Survivor to ICU discharge N = 629 ¹	Death prior to ICU discharge N = 351 ¹	
Cardiac	192 (20)	109 (17)	83 (24)	0.02
Neurologic/Neuromuscular	132 (13)	83 (13)	49 (14)	0.8
Kidney/Urologic	91 (9.3)	66 (10)	25 (7.1)	0.1
Hematologic	132 (13)	79 (13)	53 (15)	0.3
Oncologic	222 (23)	121 (19)	101 (29)	<0.001
Immunologic	153 (16)	71 (11)	82 (23)	<0.001
Gastrointestinal	185 (19)	126 (20)	59 (17)	0.2
Endocrinologic	62 (6.3)	43 (6.8)	19 (5.4)	0.5
PRISM-III Score at ICU Admission	14 (10, 18)	14 (9, 18)	15 (11, 19)	0.08
PELOD-2 Score at CKRT initiation	7 (4, 9)	6 (4, 8)	8 (6, 10.5)	<0.001
Volume overload (% over baseline from ICU admit to CKRT initiation)	7.4 (2.4, 18.1)	6.8 (1.9, 16.6)	8.8 (3.5, 21.55)	0.002
Vasoactive-Inotrope Score	5 (0, 20)	2 (0, 13)	10 (0, 28)	<0.001
% Volume Overload				
<10%	571 (59)	380 (61)	191 (54)	0.13
10-20%	180 (18)	114 (18)	66 (19)	
>20%	224 (23)	132 (21)	92 (26)	
Time from ICU Admission to CKRT initiation (days)	2 (1, 6)	2 (1, 5)	3 (1, 10)	<0.001
Use of diuretic bolus or continuous infusion before CKRT	560 (57.1)	358 (56.9)	202 (57.5)	0.12
Urine output (24 h prior to CKRT initiation) (ml/kg/h)	0.46 (0.13, 1.22)	0.42 (0.13, 1.21)	0.53 (0.14, 1.23)	0.7
Serum Creatinine (mg/dL)	1.71 (0.89, 3.24)	2.10 (0.98, 3.69)	1.39 (0.80, 2.48)	<0.001
eGFR (ml/min/1.73 m ²)	26.5 (15.8, 46.7)	23.8 (13.7, 44.8)	30.9 (19.1, 48.1)	<0.001

¹ Statistics presented: n (%); median (IQR)

² Statistical tests performed: chi-square test of independence; Wilcoxon rank-sum test

ICU, intensive care unit; CKRT, continuous kidney replacement therapy; PRISM-III, Pediatric Risk of Mortality-III; PELOD-2, Pediatric Organ Logistic Dysfunction-2 score ; eGFR, estimated glomerular filtration rate **determined using the bedside Schwartz equation.**

* 5 patients were missing weight

Table 2.

CKRT technical characteristics and association with death prior to ICU discharge

	Overall N = 980	ICU survival		p-value ²
		Survivor to ICU discharge N = 629 ¹	Death prior to ICU discharge N = 351 ¹	
Initial Modality				0.3
SCUF	12 (1.2)	7 (1.1)	5 (1.4)	
CVVH	112 (11)	82 (13)	30 (8.6)	
CVVHD	98 (10)	62 (9.9)	36 (10)	
CVVHDF	747 (76)	472 (75)	275 (79)	
mCVVH	8 (0.8)	4 (0.6)	4 (1.1)	
Filter				0.8
Polysulfone	777 (80)	501 (80)	276 (79)	
Non-Polysulfone	200 (20)	126 (20)	74 (21)	
Anticoagulation				0.08
No anticoagulation	70 (7.2)	35 (5.6)	35 (10)	
Citrate	610 (62)	395 (63)	215 (61)	
Heparin	238 (24)	158 (25)	80 (23)	
Other	59 (6.0)	39 (6.2)	20 (5.7)	
CKRT Dose ml/hour per 1.73m ²	2060 (1745, 2659)	2043 (1721, 2564)	2086 (1788, 2764)	0.3
CKRT Dose per kg/hour	41.9 (30.9, 59.9)	41.2 (30.0, 59.6)	45.5 (32.2, 60.5)	0.07
CKRT Dose per kg/hour				0.2
<25ml/kg/hr	131 (13)	91 (15)	40 (11)	
25-40 ml/kg/hr	306 (32)	200 (32)	106 (30)	
>40ml/kg/hr	534 (55)	331 (53)	203 (58)	
Blood flow rate scaled to body weight (ml/min per kg)	3.9 (2.7, 5.5)	3.9 (2.6, 5.2)	4.1 (2.7, 6.6)	0.03
Initial catheter position				0.03
Internal Jugular	638 (66)	420 (67)	218 (63)	
Subclavian	19 (2.0)	13 (2.1)	6 (1.7)	
Femoral	297 (30)	186 (30)	111 (32)	
Other	20 (2.1)	7 (1.1)	13 (3.7)	
Line size, French				0.3
6	64 (6.7)	36 (5.8)	28 (8.2)	
7	94 (9.8)	54 (8.7)	40 (12)	
8	205 (21)	130 (21)	75 (22)	
9	97 (10)	65 (10)	32 (9.4)	
10	70 (7.3)	44 (7.1)	26 (7.6)	
>10	432 (45)	292 (47)	140 (41)	
CKRT duration (days)	6 (3, 14)	6 (3, 12)	8 (3, 19)	0.04

¹Statistics presented: n (%); median (IQR),

²Statistical tests performed: chi-square test of independence; Wilcoxon rank-sum test.

CKRT, Continuous kidney replacement therapy; SCUF, slow continuous ultrafiltration; CVVHDF, continuous venovenous hemodiafiltration; CVVH, continuous venovenous hemofiltration; CVVHD, continuous venovenous hemodialysis; mCVVH, modified CVVH, performed using Aquadex

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Table 3.

CKRT technical characteristics by center ICU size

Variable	Overall, N = 980	Center ICU Size			p-value ²
		Small, 12 hospitals N = 252 ¹	Medium, 11 hospitals N = 377 ¹	Large, 9 hospitals N = 351 ¹	
Initial Modality					<0.001
SCUF	12 (1.2)	1 (0.4)	11 (2.9)	0 (0)	
CVVH	112 (11)	52 (21)	51 (14)	9 (2.6)	
CVVHD	98 (10)	43 (17)	47 (12)	8 (2.3)	
CVVHDF	747 (76)	156 (62)	260 (69)	331 (95)	
mCVVH	8 (0.8)	0 (0%)	8 (2.1)	0 (0)	
Filter					<0.001
Polysulfone	777 (80)	171 (68)	302 (80)	304 (87)	
Non-Polysulfone	200 (20)	81 (32)	75 (20)	44 (13)	
Anticoagulation					<0.001
None	70 (7.2)	31 (12)	31 (8.2)	8 (2.3)	
Citrate	610 (62)	116 (46)	207 (55)	287 (82)	
Heparin	238 (24)	64 (25)	132 (35)	42 (12)	
Other	59 (6.0)	41 (16)	7 (1.9)	11 (3.2)	
CKRT Dose ml/hour per 1.73m ²	2060 (1745, 2659)	2132 (1674, 2800)	2125 (1700, 2871)	2016 (1805, 2238)	0.01
CKRT Dose per kg/hour	41.9 (30.9, 59.9)	50.0 (32.2, 64.1)	40.0 (30.9, 60.1)	40.6 (30.1, 53.7)	<0.001
<25ml/kg/hr	131 (13)	28 (11)	55 (15)	48 (14)	0.006
25-40 ml/kg/hr	306 (32)	60 (24)	127 (34)	119 (34)	
>40ml/kg/hr	534 (55)	164 (65)	189 (51)	181 (52)	
Blood flow rate scaled to weight (ml/min/kg)	3.9 (2.7, 5.5)	3.9 (2.7, 6.1)	4.0 (2.5, 5.6)	3.9 (2.8, 5.3)	0.8
Initial catheter position					<0.001
Internal Jugular	638 (66)	155 (62)	271 (72)	212 (61)	
Subclavian	19 (2.0)	9 (3.6)	6 (1.6)	4 (1.1)	
Femoral	297 (30)	85 (34)	88 (23)	124 (36)	
Other	20 (2.1)	1 (0.4)	11 (2.9)	8 (2.3)	
Line size, French					<0.001
6	64 (6.7)	26 (10)	33 (9.0)	5 (1.4)	
7	94 (9.8)	22 (8.9)	30 (8.2)	42 (12)	
8	205 (21)	52 (21)	86 (23)	67 (19)	
9	97 (10)	26 (10)	16 (4.4)	55 (16)	
10	70 (7.3)	14 (5.6)	35 (9.6)	21 (6.0)	
>10	432 (45)	108 (44)	166 (45)	158 (45)	
Survival to ICU Discharge	629 (64%)	174 (69%)	377 (64%)	213 (61%)	0.1

¹Statistics presented: n (%); median (IQR)

²Statistical tests performed: chi-square test of independence; Kruskal-Wallis test

SCUF, slow continuous ultrafiltration; CVVHDF, continuous venovenous hemodiafiltration; CVVH, continuous venovenous hemofiltration; CVVHD, continuous venovenous hemodialysis; mCVVH, modified CVVH, performed using Aquadex

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