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Association of hospital-level continuous kidney replacement therapy use and mortality in critically ill patients with acute kidney injury

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Abstract

Purpose: In numerous high-risk medical and surgical conditions, an increased volume of patients and procedures is associated with improved processes and survival. This study examined the association of hospital-level continuous kidney replacement therapy (CKRT) utilization rates with all-cause hospital mortality in critically ill patients with acute kidney injury (AKI).

Methods: This multicenter cohort study used data from patients admitted to the intensive care unit (ICU) within the Premier Incorporated AI (PINC-AI) database. Patients were critically ill adults with AKI receiving kidney replacement therapy (KRT) in U.S. hospitals that offered both CKRT and intermittent hemodialysis. Hospitals were characterized according to their CKRT utilization in the ICU, and risk-adjusted association with all-cause hospital mortality by day 90 was estimated.

Results: Among 49,685 patients with AKI admitted to 426 acute care U.S. hospitals and treated with KRT in the ICU, a higher hospital-level CKRT utilization rate was associated with lower patient-level risk-adjusted hospital mortality. Hospitals with higher CKRT utilization rates (CKRT use in ≥ 31.5% of KRT patients per year) had a 15% lower adjusted probability of death compared with hospitals with lower CKRT utilization rates (CKRT use in < 8% of KRT patients per year). When compared with the first quartile of hospital-level CKRT use, the third (adjusted hazard ratio [aHR], 0.93, 95%CI: 0.89–0.98) and fourth (aHR, 0.85, 95%CI: 0.81–0.89) quartiles were associated with lower risk-adjusted hospital mortality. Findings were consistent in several sensitivity analyses.

Conclusions: Among critically ill adults with AKI requiring KRT, treatment in hospitals with higher CKRT utilization rates was associated with reduced hospital mortality.

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Introduction

Acute kidney injury (AKI) affects 50%-60% of critically ill patients admitted to the intensive care unit (ICU), with 5–15% requiring kidney replacement therapy (KRT), and among these, > 40% die despite KRT [1–3]. Two widely used KRT modalities in the ICU are intermittent hemodialysis (IHD) and continuous kidney replacement therapy (CKRT), and the choice of KRT modality is primarily determined by the patient's clinical condition and the institution's KRT capabilities. Guidelines recommend CKRT in hemodynamically unstable patients and IHD in hemodynamically stable patients [4]. Observational studies suggest that CKRT is used in two-thirds of critically ill patients [1, 5]. Whether higher utilization of CKRT is associated with improved patient outcomes is unclear.

Volume-outcome relationships, whereby increased procedural volume is associated with improved patient outcomes due to the development of procedural skills, have been well-documented in numerous surgical contexts [6]. This phenomenon has also been observed in critically ill patients treated with mechanical ventilation [7] and among patients with end-stage kidney disease treated with in-center hemodialysis [8, 9]. Several factors, such as adherence to best practices, nurse-patient ratios, experience levels, multidisciplinary care, and organizational efficiency, may contribute to these positive effects. However, to our knowledge, no study has evaluated the impact of hospital-level CKRT utilization rate on patient-level clinical outcomes. We hypothesized that hospitals with higher CKRT utilization rates would have higher risk-adjusted patient survival than those with lower CKRT utilization rates.

Take Home Message

In this multicenter analysis involving 49,685 patients across 426 U.S. hospitals, treatment with KRT in hospitals with high utilization of CKRT was independently associated with lower hospital mortality when compared with hospitals with lower CKRT utilization. These findings suggest that among critically ill adults with AKI requiring KRT, processes of care related to CKRT utilization are associated with patient outcomes.

Methods

Study design

We conducted a multicenter retrospective cohort study using the Premier Incorporated Healthcare (PINC-AI) database of critically ill patients with AKI treated with KRT in acute care U.S. hospitals and discharged between January 1, 2018, and June 30, 2021. This analysis was conducted between February 26 and October 18, 2024. The PINC AI database comprises inpatient and outpatient discharge data from more than 1000 U.S. healthcare providers, capturing about 20%–25% of U.S. hospital discharges (electronic supplementary material 1, eMethods 1) [10]. The PINC-AI database is a limited dataset compliant with the Health Insurance Portability and Accountability Act; therefore, it is not subject to institutional review board approval. All analytical methods and reporting were performed according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) [11].

Patient selection

Detailed demographic and physiological variables were available for 434,887 patients admitted to 708 acute care hospitals who received KRT in the ICU and were discharged between January 1, 2018, and June 30, 2021. We included critically ill adults (≥ 18 years of age) who had AKI and received initial KRT in the ICU of a hospital that offered both CKRT and IHD as KRT modalities. Only the first ICU encounter with KRT use for each patient was considered to avoid counting multiple hospital encounters for a single patient. We used the International Statistical Classification of Diseases (ICD-10), Tenth Revision, and Clinical Modification diagnosis codes to identify patients with AKI and the first KRT modality using ICD-10 procedure codes (CKRT: 5A1D90Z; performance of urinary filtration, continuous, > 18 h per day; IHD: 5A1D70Z; performance of urinary filtration, intermittent, < 6 h per day).

We excluded patients without AKI diagnosis, patients who had a history of end-stage kidney disease, had or received a kidney transplant, had stage 5 chronic kidney disease (CKD) or > 1 KRT procedure in the 12 months before index admission, were treated with prolonged intermittent KRT as the first modality, received initial KRT outside the ICU, or received more than 1 KRT modality on the first KRT day (eTables 1 and 2). Patients admitted to hospitals without continuous data submission during the study period and those who died or were discharged < 3 days after KRT initiation were also excluded.

We extracted data on patient demographics, comorbidities, severity of illness, hospital characteristics, and patient outcomes. The severity of illness at hospital admission for each patient was assessed using the All Patient Refined Diagnosis-Related Group (APR-DRG), which accounts for age, procedures, and clinical severity of the primary diagnosis and all secondary diagnoses assigned during hospitalization, and is computed for

each patient at the time of hospital discharge [12–15]. The APR-DRG system categorizes a patient based on their reason for admission and the severity of illness into four levels: minor, moderate, major, and extreme, with extreme signifying the most critically ill patients. Processes of care variables, such as mechanical ventilation, extracorporeal membrane oxygenation (ECMO), intravenous fluid use, and vasopressor use, were extracted for the 3 days before and through 3 days after KRT initiation (eTable 2).

Exposure variable

The exposure variable was the annualized overall hospital-level CKRT utilization rate, defined as the number of patients treated with CKRT in the ICU divided by the total number of patients who received any KRT in the ICU per year during the study period and multiplied by 100. Patients who received both CKRT and another modality were counted only as CKRT in the numerator and the denominator. CKRT utilization rate in the hospital, rather than CKRT utilization rate per ICU, was chosen as the exposure variable since staff and technology are shared among ICUs within a hospital; since the policy implications of the relationship between CKRT utilization rate and outcome include selective referral to hospitals, rather than to specific ICUs within a hospital; and since ICU volume is collinear with other variables used to adjust for differences in case mix (*e.g.,* type of ICU) and cannot be included in the same risk-adjusted models.

Outcome measures

The primary outcome was risk-adjusted in-hospital mortality, which was censored on day 90 post-KRT initiation for patients still in the hospital. Patients directly transferred from the ICU to other institutions were classified as discharged alive. The association between CKRT utilization rate and all-cause hospital mortality was examined after categorizing CKRT utilization rates into quartiles, the reference category being the lowest quartile.

Statistical analysis

We compared patient-level and hospital-level characteristics by quartiles of CKRT utilization rates. CKRT utilization thresholds were calculated based on the overall population receiving any KRT in the ICU. Continuous and categorical data were compared using the Wilcoxon rank-sum and Chi-Squared tests. Multivariable Cox regression models were fitted to examine the association between CKRT utilization rates and hospital mortality after adjusting for covariates specified a priori as potential confounders of the relationship between CKRT utilization rates and patient outcomes. Regression models were adjusted for patient-level factors such as age, sex, race, Charlson Comorbidity Index score, medical versus surgical admission diagnosis, extreme APR-DRG severity of illness, presence or absence of coronavirus disease (COVID)-19, septic shock, use of mechanical ventilation, use of ECMO, days in the ICU before KRT initiation, number of vasopressors used in the 3-day period following KRT initiation, first KRT modality, and hospital-level factors such as teaching versus non-teaching hospital, urban versus rural population served, number of hospital beds and geographic region. To examine the change in CKRT utilization rates over time, we accounted for potential interaction effects between the year of patient discharge and CKRT utilization rates. We also examined the interaction effects between initial KRT modality and CKRT utilization rates. The lowest CKRT utilization quartile (Quartile 1) was the reference level for analyzing CKRT utilization rates and patient outcomes. All analyses were completed using R version 4.2.1 (R Foundation for Statistical Computing, Vienna, Austria).

Sensitivity analysis

We performed several pre-specified sensitivity analyses to examine the robustness of the association of hospital-level CKRT utilization with hospital mortality. First, to evaluate the nature of the relationship, we fitted CKRT utilization rates as a continuous variable using restricted cubic splines with knots corresponding to the following quantiles: 0.05, 0.275, 0.50, 0.725, and 0.95. Second, we compared CKRT utilization rates below the median versus those above the median. Third, we examined CKRT utilization rates by tertiles, using the lowest tertile as the reference. Fourth, we repeated the analysis with quintiles using the lowest quintile of CKRT utilization as the reference. Fifth, we excluded patients admitted with COVID-19. Sixth, we added IV fluid use during the first three days of KRT use to the multivariable model. Seventh, we analyzed the cohort after including patients who died or were discharged during the first three days of KRT use, stratified by KRT modality. Eighth, we ran the analysis only in patients with septic shock. Ninth, we analyzed the cohort stratified by year of discharge (2018, 2019, 2020, 2021). Tenth, we incorporated CKD, CCI score, hypertension, and diabetes into the final model. Eleventh, we evaluated the effect modification of ICU KRT volume and CKRT volume on the risk-adjusted mortality. Twelfth, we assessed the effect at a fixed outcome measurement at 28 days, and finally, we evaluated the hospital clustering effect with a mixed-effects Cox model.

Results

Cohort characteristics

Among the 434,887 adults who received KRT in the ICUs of 708 acute care U.S. hospitals, we identified 49,685

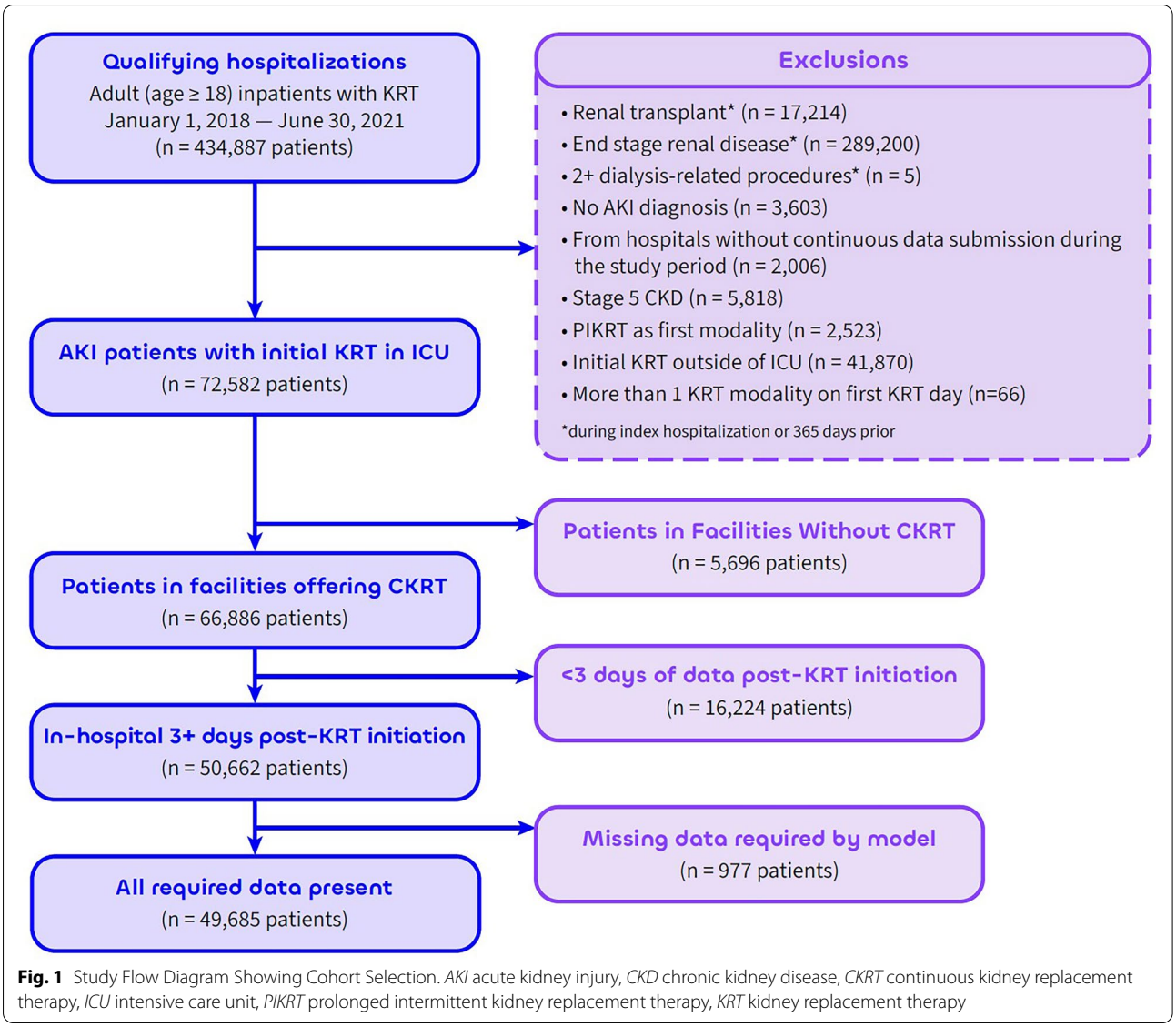

Fig. 1 Study Flow Diagram Showing Cohort Selection. *AKI* acute kidney injury, *CKD* chronic kidney disease, *CKRT* continuous kidney replacement therapy, *ICU* intensive care unit, *PIKRT* prolonged intermittent kidney replacement therapy, *KRT* kidney replacement therapy

patients whose initial KRT occurred in the ICU, either as IHD or CKRT, were treated in the 426 hospitals that offered both CKRT and IHD, and were still in the hospital 3 days after KRT initiation. Figure 1 illustrates the flowchart of patient entry into the study and the exclusion criteria. CKRT was utilized as a first modality in 18,120 (36.5%) patients in the entire cohort; the median (interquartile range [IQR]) of hospital-level CKRT utilization was 17% (IQR, 8% to 31.5%) (eFigure 1). The percentage of hospitals within the lowest quartile of CKRT utilization decreased between 2018 and 2021, while the percentage of hospitals in the highest quartile increased (eFigure 2A). This shift was notably present in 2020 and 2021. However, most hospitals only increased by one quartile yearly, and more significant transitions were rare (eFigure 2B).

Patient characteristics

The mean age was 62.4 (SD, ± 14.7) years; 61.7% were males, 62.7% were white non-Hispanic, and 45.6% of patients had surgical admissions. Most patients had sepsis (63.9%), and nearly one-half had septic shock (49.8%). 91% of patients had extreme APR-DRG severity of illness category, and 70.7% were mechanically ventilated (Table 1). Patients in the highest quartile were younger, had more surgical admissions, had a greater prevalence of sepsis, septic shock, COVID-19 infection, ECMO, mechanical ventilation and vasopressor use, and were more severely ill compared with the lowest quartile. The

Table 1 Patient Characteristics by Quartiles of Hospital-level CKRT Utilization

Characteristic	No. (%)					*P*-value
	Overall (*n* = 49,685)	First Quartile (*n* = 10,560)	Second Quartile (*n* = 8,695)	Third Quartile (*n* = 11,909)	Fourth Quartile (*n* = 18,521)	
Age, years, mean (SD)	62.4 (14.7)	63.6 (14.7)	62.9 (14.6)	62.9 (14.5)	61.3 (14.6)	< 0.001
Male	30,659 (61.7)	6357 (60.2)	5329 (61.3)	7325 (61.5)	11,648 (62.9)	< 0.001
White, Non-Hispanic	31,156 (62.7)	6660 (63.1)	5627 (64.7)	7578 (63.6)	11,291 (61.0)	< 0.001
Clinical Characteristics						
Medical MS-DRG	27,052 (54.4)	6347 (60.1)	4949 (56.9)	6494 (54.5)	9262 (50.0)	< 0.001
Sepsis, Any	31,751 (63.9)	6712 (63.6)	5476 (63.0)	7558 (63.5)	12,005 (64.8)	0.009
Septic Shock	24,762 (49.8)	5075 (48.1)	4163 (47.9)	5830 (49.0)	9694 (52.3)	< 0.001
COVID-19	6148 (12.4)	1157 (11.0)	918 (10.6)	1373 (11.5)	2700 (14.6)	< 0.001
APR-DRG Severity of Illness						
Minor (reference)	4 (< 0.1)	0 (0)	2 (< 0.1)	1 (< 0.1)	1 (< 0.1)	< 0.001
Moderate	316 (0.6)	86 (0.8)	72 (0.8)	83 (0.7)	75 (0.4)	
Major	4144 (8.3)	1150 (10.9)	824 (9.5)	961 (8.1)	1209 (6.5)	
Extreme	45,221 (91)	9324 (88.3)	7,797 (89.7)	10,864 (91.2)	17,236 (93.1)	
ECMO	1209 (2.4)	70 (0.7)	100 (1.2)	218 (1.8)	821 (4.4)	< 0.001
Mechanical Ventilation	35,106 (70.7)	6792 (64.3)	5827 (67.0)	8462 (71.1)	14,025 (75.7)	< 0.001
Vasopressor Use, Any	19,141 (38.5)	3882 (36.8)	3224 (37.1)	4551 (38.2)	7484 (40.4)	< 0.001
Vasopressor Use Post-KRT Initiation						
0	34,757 (70)	7613 (72.1)	6284 (72.3)	8403 (70.6)	12,457 (67.3)	< 0.001
1	8832 (17.8)	1963 (18.6)	1571 (18.1)	2058 (17.3)	3240 (17.5)	
2 +	6096 (12.3)	984 (9.3)	840 (9.7)	1448 (12.2)	2824 (15.2)	
Hypertension	30,739 (61.9)	6765 (64.1)	5555 (63.9)	7386 (62)	11,033 (59.6)	< 0.001
Diabetes	26,490 (53.3)	5908 (55.9)	4742 (54.5)	6357 (53.4)	9483 (51.2)	< 0.001
Chronic Kidney Disease	26,642 (53.6)	6034 (57.1)	4817 (55.4)	6367 (53.5)	9424 (50.9)	< 0.001
Charlson Comorbidities Index score						
0	3322 (6.7)	697 (6.6)	562 (6.5)	773 (6.5)	1290 (7)	< 0.001
1–2	10,943 (22)	2302 (21.8)	1876 (21.6)	2660 (22.3)	4105 (22.2)	
3–4	13,234 (26.6)	2695 (25.5)	2259 (26)	3207 (26.9)	5073 (27.4)	
5 +	22,186 (44.7)	4866 (46.1)	3998 (46)	5269 (44.2)	8053 (43.5)	
CKRT as initial modality	18,120 (36.5)	639 (6.1)	1805 (20.8)	4414 (37.1)	11,262 (60.8)	< 0.001
Hospital Characteristics						
Teaching Facility	29,544 (59.5)	4783 (45.3)	4058 (46.7)	6703 (56.3)	14,000 (75.6)	< 0.001
Urban Population	45,714 (92)	9360 (88.6)	8012 (92.1)	11,183 (93.9)	17,159 (92.6)	< 0.001
Bed Count						
< 300	11,002 (22.1)	4110 (38.9)	2569 (29.5)	2120 (17.8)	2203 (11.9)	< 0.001
300–499	13,880 (27.9)	3074 (29.1)	2474 (28.5)	4111 (34.5)	4221 (22.8)	
500 +	24,803 (49.9)	3376 (32)	3652 (42)	5678 (47.7)	12,097 (65.3)	
Geographic Region						
Northeast	6967 (14)	1274 (12.1)	1017 (11.7)	1677 (14.1)	2999 (16.2)	< 0.001
Midwest	11,660 (23.5)	1947 (18.4)	2003 (23)	2701 (22.7)	5009 (27)	
South	23,459 (47.2)	4869 (46.1)	3994 (45.9)	6165 (51.8)	8431 (45.5)	
West	7599 (15.3)	2470 (23.4)	1681 (19.3)	1,366 (11.5)	2082 (11.2)	
Outcomes						
Hospital Length of Stay, days, median (IQR)	17 (11, 27)	16 (10, 24)	16 (10, 25)	17 (11, 27)	19 (12, 30)	< 0.001
ICU Length of Stay, days, median (IQR)	10 (6, 18)	9 (5, 16)	9 (5, 16)	10 (5, 17)	11 (6, 20)	< 0.001
In-hospital mortality	16,799 (33.8)	3135 (29.7)	2735 (31.5)	4080 (34.3)	6849 (37.0)	< 0.001

Table 1 (continued)

SD Standard Deviation, *IQR* Interquartile range, *APR-DRG* All Patient Refined-Diagnosis Related Groups, *COVID* Coronavirus Disease, *CKRT* Continuous Kidney Replacement Therapy, *ECMO* Extracorporeal Membrane Oxygenation, ICU Intensive Care Unit, *MS-DRG* Medicare Severity Diagnosis Related Groups, *KRT* Kidney Replacement Therapy

prevalence of chronic conditions such as hypertension, diabetes and CKD, as well as the CCI score, was slightly lower among patients in the highest CKRT utilization quartile than in lower quartiles. CKRT was used as the first KRT modality in 61% of patients in the highest quartile compared with only 6.1% in the lowest quartile. The number of patients by KRT modality according to CKRT utilization quartiles and ICU KRT volume is depicted in eTables 12 and 13.

Hospital characteristics

Academic hospitals serving urban populations with greater than 500 beds were mostly in the fourth quartile of CKRT utilization. There was also variation by hospital geographic region; CKRT utilization rates were higher in the South and Midwest regions.

Outcomes

The length of stay at the hospital (Q4 vs. Q1, 19 [IQR, 12–30 days] vs.16 [IQR, 10–24] days; $P < 0.001$) and ICU (Q4 vs. Q1, [6–20] vs. [5–16] days; $P < 0.001$) was longer for the highest quartile compared with the first quartile. Crude hospital mortality in the first, second, third, and fourth quartiles was 30%, 31%, 34%, and 37%, respectively ($P < 0.001$) (Table 1).

Multivariable regression of hospital-level CKRT Utilization with 90-day mortality

After multivariable adjustment, patients admitted to a hospital with higher CKRT utilization rates had a significantly reduced risk of death compared with those in hospitals with lower CKRT utilization rates. Specifically, compared with patients admitted to a hospital in the lowest CKRT utilization quartile, patients admitted to a hospital in the third (adjusted hazard ratio [aHR], 0.94, 95% CI: 0.89–0.98) and fourth (aHR, 0.85, 95% CI: 0.81–0.90; eFigure 3) CKRT utilization quartiles had a lower adjusted risk of death (Table 2). There was no significant interaction between the quartiles of the CKRT utilization rate and the year of discharge or the first KRT modality in terms of the mortality outcome.

Sensitivity analysis

In the cubic spline model, a non-linear relationship suggested that higher hospital-level CKRT utilization is associated with lower patient-level mortality (Fig. 2). Patients from hospitals with a CKRT utilization rate above the median had a lower risk of mortality (aHR, 0.90, 95%CI: 0.87–0.93 ≥ vs. < median). Using tertiles or quintiles, the highest tertile (aHR, 0.87, 95%CI: 0.83–0.91) or quintile (aHR, 0.85, 95%CI: 0.81- 0.90) of CKRT use was associated with a lower risk of death compared with the lowest tertile or quintile, respectively (eFigure 4). A similar association was seen after excluding patients with COVID-19 infection, after adding IV fluid use to the model, when including all patients irrespective of death or discharge during the first 3 days of KRT use, after evaluating only patients with septic shock, and when the analysis was stratified by year of hospital discharge (Table 3). Incorporating CKD, CCI score category, hypertension, and diabetes into the final model did not alter the relationship between the quartiles of CKRT utilization and mortality (eTable 3).

There was a statistically significant interaction between ICU CKRT utilization quartiles and the overall ICU KRT volume per month quartiles. When stratifying by quartiles of ICU KRT volume per month, the dose–response pattern of lower mortality as CKRT utilization increased was only seen for the highest ICU KRT volume quartile (eTable 4–8). In contrast, there was no statistically significant interaction between ICU CKRT utilization quartiles and ICU CKRT volume per month quartiles (eTable 9–11). Findings remained consistent when using 28-day mortality as the outcome measure in the final model (eTable 14). Finally, the mixed effect model showed a similar pattern to the primary analysis, but only the highest quartile of CKRT utilization exhibited a statistically significant association with lower mortality (eTable 15).

Discussion

This large, real-world US observational study showed that among critically ill adults with AKI receiving KRT, admission to a hospital with a high CKRT utilization rate was associated with lower hospital mortality compared to admission to a hospital with lower CKRT utilization rates. To our knowledge, this is the first multicenter study to demonstrate an association between CKRT utilization rates and patient outcomes. Our findings were robust to several sensitivity analyses and aligned with established hospital volume-outcome relationships in other care processes, such as mechanical ventilation, surgical procedures, and in-center hemodialysis [8, 9, 16]. Critically ill patients with AKI requiring CKRT have an associated mortality exceeding 50% [17, 18]. Several factors contribute to this high mortality, including patient comorbidities and acute multiple organ dysfunction, and no

Table 2 Multivariable Regression of CKRT Utilization with Hospital Mortality

Variable	Adjusted Hazard Ratio	95% Confidence Interval	P value
Hospital-level CKRT utilization			
First Quartile (reference)	–	–	–
Second Quartile	1.00	0.95, 1.05	> 0.9
Third Quartile	0.94	0.89, 0.98	0.009
Fourth Quartile	0.85	0.81, 0.90	< 0.001
Age	1.02	1.02, 1.02	< 0.001
Male vs. female	1.10	1.07, 1.14	< 0.001
White, Non-Hispanic	0.96	0.93, 0.99	0.009
MS-DRG Category: Medical vs. Surgical	2.19	2.11, 2.26	< 0.001
Extreme APR-DRG Severity of Illness	2.25	1.98, 2.56	< 0.001
COVID-19	1.51	1.46, 1.57	< 0.001
Septic Shock	1.22	1.18, 1.26	< 0.001
ECMO	1.59	1.47, 1.72	< 0.001
Mechanical Ventilation	1.72	1.64, 1.81	< 0.001
Days in ICU before KRT Initiation			
0–1 (reference)			
2–3	0.87	0.83, 0.91	< 0.001
4–7	1.05	1.01, 1.10	0.024
≥ 8	1.18	1.13, 1.24	< 0.001
Number of Vasopressors, post-KRT			
1 vs. 0	1.46	1.40, 1.52	< 0.001
2 + vs. 0	1.90	1.81, 1.98	< 0.001
First KRT modality			
IHD vs. CKRT	0.73	0.70, 0.76	< 0.001
Teaching Status			
Non-Teaching vs. Teaching hospital	0.99	0.96, 1.03	0.700
Population Served			
Rural vs. urban	0.95	0.89, 1.00	0.065
Hospital no. of beds			
1–299 (reference)			
300–499	1.00	0.96, 1.05	> 0.9
500 +	1.00	0.96, 1.05	> 0.9
Geographic region			
Northeast (reference)			
Midwest	0.85	0.80, 0.89	< 0.001
South	0.91	0.87, 0.95	< 0.001
West	0.91	0.86, 0.97	0.001

APR-DRG All Patient Refined-Diagnosis Related Groups, *CI* Confidence Interval, *COVID* Coronavirus Disease, *CKRT* Continuous Kidney Replacement Therapy, *ECMO* Extracorporeal Membrane Oxygenation, *HR* Hazard Ratio, *ICU* Intensive Care Unit, *IHD* Intermittent Hemodialysis, *MS-DRG* Medicare Severity Diagnosis Related Groups, *KRT* Kidney Replacement Therapy

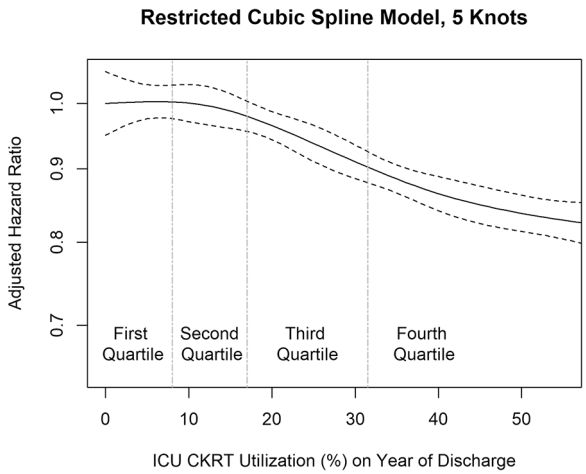

Fig. 2 Restricted Cubic Spline Model. The figure illustrates the association of CKRT utilization rates as a continuous variable using restricted cubic splines with knots corresponding to the following quintiles: 0.05, 0.275, 0.50, 0.725, and 0.95. The solid line represents the changes in the adjusted hazard ratio for each one percentage point increase in the hospital's CKRT utilization. The dashed lines above and below the solid line are the 95% confidence intervals. The plot was truncated at the 95th percentile of CKRT utilization (59%). The hazard ratios were adjusted for all of the covariates in the final model. The quartiles identified by the vertical lines represent the quartiles of CKRT utilization for comparison

intervention has been proven to reduce this outcome. Randomized clinical trials investigating the timing, dose, and modality of KRT have been null [2, 3, 18]. Our findings suggest that the annual hospital CKRT utilization rate, which indirectly reflects CKRT processes of care, could be another important determinant of outcomes among critically ill adults with AKI. The findings of this study may have implications for the use of acute KRT in hospitals and could spark discussions about best KRT practices in the ICU. Currently, various cost-effectiveness models from the payer perspective have shown promising results [19, 20]. Future budget impact studies may further clarify the economic effects for healthcare institutions. One should note that this study was not designed to draw conclusions about the superiority of CKRT compared to IHD in critically ill patients, as the choice of KRT modality largely depends on individual patient characteristics and the clinical context.

There are many possible causes for the association between hospital CKRT utilization rate and mortality. Hospitals with high CKRT utilization rates may be more adherent to best practices, including higher nurse-to-patient ratio, multidisciplinary care teams, CKRT quality assurance, and clinician/staff training [21–23]. Indeed, multiple observational studies have shown that implementing CKRT quality programs improves processes of

Table 3 Sensitivity Analysis of Association of Hospital-level CKRT use with Mortality

Variable	Adjusted Hazard Ratio[a]	95% Confidence Interval	P value
By median ($n=49,685$)			
Below median (reference)			
Above the median	0.90	0.87, 0.93	< 0.001
By tertiles ($n=49,685$)			
Low tertile (reference)			
Middle tertile	0.97	0.93, 1.02	0.2
High tertile	0.87	0.83, 0.91	< 0.001
By quintiles ($n=49,685$)			
Quintile 1 (reference)			
Quintile 2	1.01	0.95, 1.07	0.8
Quintile 3	0.98	0.92, 1.03	0.4
Quintile 4	0.92	0.87, 0.97	0.002
Quintile 5	0.85	0.81, 0.90	< 0.001
After excluding COVID-19 patients ($n=43,537$)			
Quartile 1 (reference)			
Quartile 2	1.01	0.95, 1.07	0.9
Quartile 3	0.95	0.89, 1.00	0.06
Quartile 4	0.86	0.81, 0.91	< 0.001
After restricting the analysis to patients who had IV fluid use within 3 days of KRT ($n=20,857$)			
Quartile 1 (reference)			
Quartile 2	1.03	0.96, 1.11	0.4
Quartile 3	0.94	0.88, 1.01	0.09
Quartile 4	0.88	0.82, 0.94	< 0.001
After including all patients irrespective of survival in first three days CKRT cohort ($n=26,351$)			
Quartile 1 (reference)			
Quartile 2	0.97	0.93, 1.06	0.5
Quartile 3	0.87	0.86, 0.94	< 0.001
Quartile 4	0.77	0.71, 0.84	< 0.001
After including all patients irrespective of survival in first three days IHD cohort ($n=39,165$)			
Quartile 1 (reference)			
Quartile 2	0.96	0.92, 1.01	0.08
Quartile 3	0.90	0.86, 0.94	< 0.001
Quartile 4	0.87	0.83, 0.91	< 0.001
Patients with septic shock only ($n=24,762$)			
Quartile 1 (reference)	1.00	0.94, 1.07	> 0.9
Quartile 2	0.89	0.84, 0.95	< 0.001
Quartile 3	0.86	0.81, 0.91	< 0.001
Quartile 4	1.00	0.94, 1.07	> 0.9
Analysis by discharged year 2018 ($n=12,392$)			
Quartile 1 (reference)			
Quartile 2	0.94	0.85, 1.05	0.3
Quartile 3	0.86	0.77, 0.95	0.002
Quartile 4	0.83	0.74, 0.92	< 0.001
Analysis by discharged year 2019 ($n=13,117$)			
Quartile 1 (reference)			
Quartile 2	0.97	0.87, 1.09	0.6
Quartile 3	0.91	0.82, 1.01	0.07
Quartile 4	0.83	0.75, 0.93	0.001
Analysis by discharged year 2020 ($n=15,870$)			
Quartile 1 (reference)			
Quartile 2	1.02	0.93, 1.12	0.7
Quartile 3	0.95	0.87, 1.03	0.2
Quartile 4	0.87	0.80, 0.95	0.001
Analysis by discharged year 2021 ($n=8306$)			
Quartile 1 (reference)			
Quartile 2	1.09	0.95, 1.24	0.2
Quartile 3	0.98	0.87, 1.10	0.7
Quartile 4	0.86	0.76, 0.96	0.01

[a] Adjusted for differences in age, sex, race, medical diagnosis, Extreme APR-DRG Severity of illness, COVID-19 infection, septic shock, ECMO use, mechanical ventilation use, days in the ICU before KRT, no. of vasopressors used after KRT initiation, initial KRT modality, hospital teaching status, urban population, number of hospital beds and geographic region

CKRT delivery and could potentially reduce mortality [22–24]. Clinicians practicing in hospitals with higher CKRT utilization rates may also gain experience in CKRT prescription and delivery, which could translate into improved clinical outcomes [22, 25]. More experienced clinicians may be better at preventing, recognizing and treating complications of CKRT or may be better at translating evidence into practice. However, globally, CKRT utilization has varied across regions due to the lack of conclusive survival benefits compared with IHD, technology availability, and user expertise.

The observed relationship between CKRT utilization rate and mortality was independent of the hospital type (teaching vs. non-teaching), geographic region, and year of hospital admission. Larger hospitals tended to have higher CKRT utilization and treated patients with a higher acuity of illness. This could explain the higher mortality and longer stays in the non-adjusted analysis (Table 1). However, the structure, process, and organization of CKRT care delivery within hospitals are essential to identify best practices to improve clinical and process outcomes. The observed association may reflect not only the volume/utilization of CKRT, but also other factors related to hospital characteristics such as staffing models, resource availability, and the prevailing clinical culture within the institution. Importantly, protocols

or multidisciplinary care models could be exportable between hospitals with higher and lower CKRT utilization. If that is the case, low-CKRT utilization hospitals might achieve the same outcomes as high-CKRT utilization hospitals by adopting the best evidence-based practices. An alternative strategy used in trauma and neonatal care would involve regionalization of care for patients requiring CKRT and developing regional models of excellence. Nonetheless, the overall effect of these quality assurance strategies on CKRT processes and patient outcomes needs to be formally tested in implementation studies.

We also noticed a chronological increase in the overall CKRT utilization during the study period, with a greater percentage of hospitals having higher CKRT utilization in 2020 and 2021. This finding coincided with the COVID-19 pandemic, during which a higher demand for CKRT was due to the highly ill population [26]. However, the association of higher hospital-level CKRT utilization with lower patient-level mortality was significant and independent of the year of hospital admission/KRT use and remained significant after we excluded patients with COVID-19 infection in sensitivity analyses.

Limitations of our study include potential biases due to patient selection, hospital referrals, hospital-level processes and coding. The observational design of this study limits the ability to establish causal relationships due to unmeasured confounding. Owing to its relatively low frequency (≈ 3.5%), patients receiving PIKRT were excluded from the analysis. Study hospitals were not a random sample of all hospitals in the United States. They participated in the PINC-AI database to receive regular information about risk-adjusted outcomes for benchmarking and quality control. Thus, smaller hospitals may have been underrepresented. The fact that we observed a utilization-outcome relationship in this cohort suggests that the effect of hospital-level CKRT utilization rates on patient-level survival might be more significant if additional smaller hospitals were included. While it is possible that a few hospitals with lower CKRT utilization and poor outcomes drove the association, this is unlikely because of the apparent "dose–response" relationship between CKRT utilization and mortality rates across quartiles and in the fitted cubic spline. Patient referral practices could influence the results of this study. Hospitals with higher CKRT utilization could be more likely to receive patients transferred from another hospital for CKRT and less likely to transfer patients from their ICUs than other hospitals. Because patients transferred to ICUs have a higher rate of death than predicted based on severity-of-illness measures, the referral bias of this study would tend to make the hypothesis null and, therefore, strengthen our conclusions.

The improved risk-adjusted survival at high CKRT utilization hospitals may simply reflect more accurate coding or even "up-coding" of the severity of illness at these centers. However, outcomes at PINC-AI participating hospitals are not publicly reported, reducing the incentive to up-code the severity of illness. The extensive procedures for training, standardized data entry, and quality control in the PINC-AI database further reduce the likelihood that differences in coding affected the risk adjustment or the results of the study. Moreover, using the PINC-AI database which is limited in its provision of comprehensive clinical details, we were not able to identify the causes of why some hospitals used more CKRT than others. This could be for several reasons, including stricter initiation criteria, treating sicker patients earlier, etc. However, PINC-AI data offer robust demographics, diagnostic classifiers, and hospital characteristics, enabling us to conduct various sensitivity analyses to assess confounders and potential selection bias. In addition, we were not able to account for differences in institutional factors such as staff training and adherence to best practices, which could explain why facilities with higher CKRT utilization had better survival rates. The absence of standardized practices for CKRT in real-world clinical settings may have introduced potential indication bias, which should be further addressed with prospective research.

Finally, the utilized definition of the primary exposure variable presents several limitations that constrain the inferences regarding the association between facility CKRT utilization clinical outcomes. For example, the finding of lower mortality in facilities with higher CKRT utilization does not necessarily suggest that the volume of the center is what matters but rather how frequently they use CKRT in relation to IHD. In addition, we observed an effect modification of total KRT volume per month on the association between CKRT utilization and mortality, which could mean that the underpinned relationship may only apply to facilities with a specific number of KRT sessions per month.

Conclusions

In conclusion, for critically ill adult patients with AKI treated with KRT in the ICU, care at a hospital with higher CKRT utilization rates is associated with a lower likelihood of mortality. The study was conducted in hospitals with capability for both IHD and CKRT, and the finding was independent of the type of hospital (teaching vs. non-teaching), the number of beds, the year of admission, and the region. It is possible that

clinician and staff experience and/or specific care processes common to higher-CKRT utilization hospitals explain the observed association. However, additional research is needed to determine these care processes and assess the ability to effectively export them to hospitals with lower CKRT utilization, as well as to investigate the feasibility of regionalizing CKRT care in the ICU for standardization in quality assurance.

Supplementary Information
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Author contributions
Dr. Bronson-Lowe had full access to the data and took full responsibility for the data and the accuracy of the data analysis. ***Study concept and design***: Murugan, Neyra, Echeverri. ***Acquisition of data***: Echeverri, Bronson-Lowe. ***Analysis and interpretation of data***: Neyra, Murugan, Bronson-Lowe, Echeverri. ***Drafting of the manuscript***: Neyra and Murugan. ***Critical revision of the manuscript for important intellectual content***: Neyra, Murugan, Echeverri, Bronson-Lowe, Plopper, Harenski. ***Statistical analysis***: Bronson-Lowe. ***Administrative, technical, or material support***: Echeverri. ***Study supervision***: Echeverri, Neyra, and Murugan. All authors critically reviewed and approved the final version for submission.

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Declarations

Conflict of interest
Echeverri and Harenski are full-time employees at Vantive Health LLC, formerly the Baxter Kidney Care segment. Bronson-Lowe and Plopper are full-time employees of Baxter International. Neyra and Murugan are authors of the publication and have received consulting fees from Baxter Healthcare Corporation for the data analysis. Murugan received research grants from the United States National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and Baxter, Inc., and consulting fees from Baxter Inc., AM Pharma Inc., Bioporto Inc. La Jolla Inc., Fresenius Medical Care, and Novartis Inc., unrelated to this study. Neyra has received consulting fees from Baxter and has a consulting agreement with CovarsaDx. Neyra has received grants from NIDDK.

Ethical approval
The PINC-AI database is a limited dataset compliant with the Health Insurance Portability and Accountability Act; therefore, it is not subject to institutional review board approval.

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