A Comparison of Mortality Between Standard versus Low-Dose Continuous Kidney Replacement Therapy in Critically Ill Patients with Acute Kidney Injury

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Introduction

- The KDIGO guideline recommends delivering an effluent volume of 20 to 25 mL/kg/h for continuous kidney replacement therapy (CKRT) in acute kidney injury (AKI).[1)]
- The association between CKRT dose and mortality below the KDIGO guideline recommendation is not clear.
- Japan is a unique country regarding CKRT dose, as medical insurance does not allow clinicians to prescribe more than 15 to 20 liters per day of replacement fluid/dialysis solution, and the average CKRT dose would be 10.4 to 13.9 mL/kg/h, given the average body weight of Japanese individuals above 20 years old is around 60 kg.[2)]
- **The aim of this study was to assess the association between delivered CKRT dose and mortality, with or without propensity score (PS) matching, below the KDIGO guideline-recommended CKRT dose.**

Methods and Materials

Design: Single-center retrospective cohort study.
Patients: Consecutive evaluation of adult patients (≥20 years) who underwent CKRT in the medical and surgical intensive care unit (ICU) between January 1, 2012, and December 31, 2021.
Exclusion criteria: ESKD patients, patients died within 24 hours after ICU admission, extra-renal indications, or patients underwent CKRT for more than 28 days.
Exposure/Comparison: Standard (above the median) and low (below the median) CKRT dose.
Primary outcome: 28-day all-cause mortality.
Secondary outcomes: Norepinephrine-equivalent pressor dose while on CKRT, CKRT duration, and length of ICU stay.
Statistical analyses: The Kaplan-Meier method and the log-rank test with or without PS matching using 11 independent variables (age, sex, mean arterial pressure, body mass index, urine output, Acute Physiology and Chronic Health Evaluation (APACHE) II score, hemoglobin, serum albumin, blood urea nitrogen, serum creatinine, and C-reactive protein).

Results

Figure 1. Flowchart of study participants

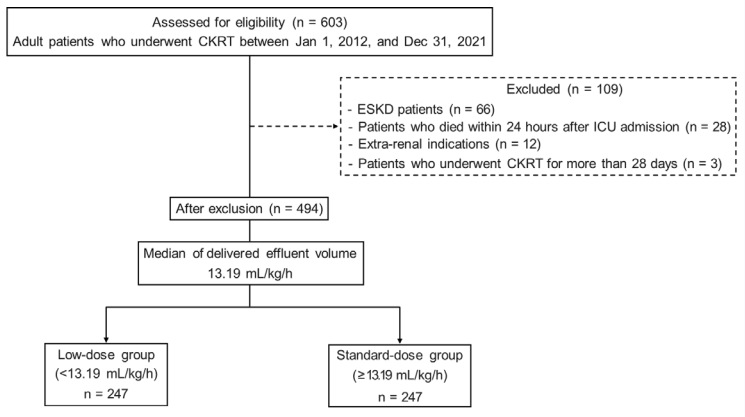


Table 1. Norepinephrine equivalent pressor dose[3)]

Drug	Dose	Norepinephrine equivalent
Epinephrine	0.1 mcg/kg/min	0.1 mcg/kg/min
Norepinephrine	0.1 mcg/kg/min	0.1 mcg/kg/min
Dopamine	15 mcg/kg/min	0.1 mcg/kg/min
Phenylephrine	1.0 mcg/kg/min	0.1 mcg/kg/min
Vasopressin	0.04 U/min	0.1 mcg/kg/min

Results (cont'd)

Table 2. Baseline patient characteristics (crude cohort and PS-matched cohort)

	Crude cohort				PS-matched cohort			
	Overall	Low-dose	Standard-dose	P value	Overall	Low-dose	Standard-dose	P value
N	494	247	247		182	91	91	
Age (years)	72 [62, 81]	68 [58, 77]	76 [67, 83]	<0.001	73 [64, 81]	72 [64, 82]	74 [65, 80]	0.799
Sex (Male, n(%))	309 (62.6)	185 (74.9)	124 (50.2)	<0.001	120 (65.9)	60 (65.9)	60 (65.9)	1.000
Body mass index (kg/m^2)	22.1 [19.5, 25.2]	24.8 [22.6, 27.8]	19.8 [17.5, 21.6]	<0.001	22.2 [20.4, 24.0]	22.4 [20.7, 24.1]	22.0 [20.1, 23.8]	0.316
Body weight (kg)	56.5 [48.0, 67.0]	66.0 [59.6, 75.4]	48.3 [42.0, 53.9]	<0.001	56.3 [51.4, 61.9]	58.7 [53.8, 63.7]	54.3 [49.8, 59.9]	<0.001
Mean arterial pressure (mmHg)	76 [64, 90]	76 [64, 91]	77 [63, 88]	0.505	77 [64, 91]	76 [64, 90]	77 [66, 90]	0.916
Urine output (mL/day)	322 [107, 729]	332 [110, 790]	307 [100, 643]	0.191	309 [87, 625]	338 [94, 672]	303 [81, 554]	0.463
APACHE II score	25 [19, 30]	24 [19, 30]	26 [20, 31]	0.183	25 [18, 31]	26 [19, 31]	25 [17, 31]	0.584
Baseline serum creatinine (mg/dL)	0.87 [0.68, 1.27]	0.88 [0.71, 1.27]	0.85 [0.66, 1.25]	0.191	0.87 [0.64, 1.37]	0.90 [0.64, 1.36]	0.87 [0.64, 1.31]	0.343
Cause of AKI (Acute tubular injury, n (%))	401 (81.2)	197 (79.8)	204 (82.6)	0.490	150 (82.4)	73 (80.2)	77 (84.6)	0.560
Sepsis, n (%)	233 (47.2)	104 (42.1)	129 (52.2)	0.024	86 (47.3)	34 (37.4)	52 (57.1)	0.008
Hemoglobin (g/dL)	10.1 [8.6, 12.2]	10.7 [9.0, 12.9]	9.8 [8.5, 11.4]	<0.001	9.9 [8.5, 11.6]	9.9 [8.3, 11.6]	9.8 [8.6, 11.6]	0.914
C-reactive protein (mg/dL)	10.02 [2.71, 19.75]	11.19 [3.24, 23.06]	9.19 [2.69, 18.17]	0.139	10.02 [3.56, 20.32]	8.25 [1.93, 18.90]	10.54 [4.63, 20.58]	0.123
Serum albumin (g/dL)	2.7 [2.3, 3.2]	2.7 [2.3, 3.2]	2.7 [2.3, 3.1]	0.679	2.5 [2.2, 2.9]	2.6 [2.3, 3.2]	2.4 [2.1, 2.8]	0.011
Blood urea nitrogen (mg/dL)	49 [30, 73]	49 [29, 67]	51 [32, 78]	0.139	48 [31, 69]	47 [30, 67]	48 [34, 70]	0.634
Serum creatinine (mg/dL)	2.51 [1.65, 3.70]	2.70 [1.87, 4.01]	2.33 [1.54, 3.49]	0.017	2.44 [1.63, 3.62]	2.51 [1.67, 3.60]	2.41 [1.60, 3.58]	0.714
pH on ABG	7.35 [7.27, 7.41]	7.35 [7.28, 7.41]	7.34 [7.26, 7.41]	0.878	7.35 [7.27, 7.40]	7.35 [7.25, 7.40]	7.37 [7.28, 7.40]	0.207
Bicarbonate on ABG (mEq/L)	19.0 [15.7, 22.7]	18.7 [15.6, 21.8]	19.3 [15.7, 23.0]	0.222	19.3 [16.1, 23.5]	18.1 [13.7, 21.4]	20.3 [17.2, 24.7]	0.001
CKRT modality (CVVHDF, n(%))	493 (99.8)	246 (99.6)	247 (100.0)	0.317	181 (99.5)	90 (98.9)	91 (100.0)	0.316
Vasopressor, n (%)	358 (72.5)	172 (69.6)	186 (75.3)	0.158	138 (75.8)	66 (72.5)	72 (79.1)	0.299
Delivered effluent volume (mL/kg/h)	13.19 [11.31, 16.21]	11.31 [9.93, 12.17]	16.22 [14.53, 18.31]	<0.001	13.19 [11.78, 14.78]	11.78 [10.92, 12.52]	14.78 [13.86, 16.18]	<0.001
Filtration fraction at the time of CKRT initiation (%)	10.2 [7.8, 12.0]	10.2 [7.9, 12.1]	10.0 [7.7, 11.9]	0.961	10.0 [7.7, 11.8]	9.0 [6.9, 11.2]	10.7 [8.3, 12.4]	0.003

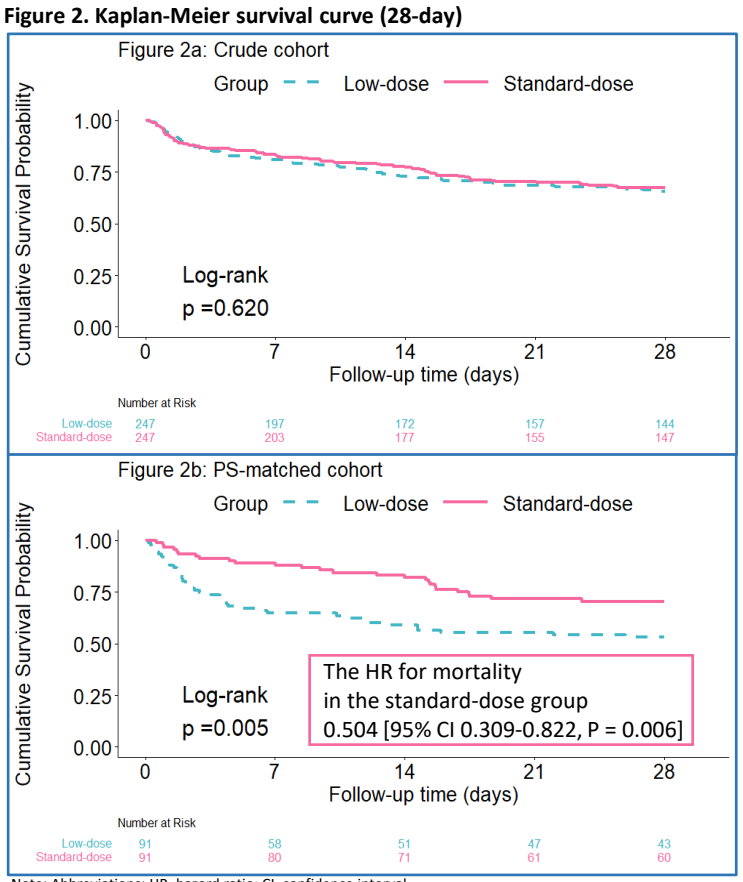
Note: Data shown as median [quartile 1, quartile 3] or number (percent). Abbreviations: APACHE, Acute Physiology and Chronic Health Evaluation; ABG, arterial blood gas; CKRT, continuous kidney replacement therapy; CVVHDF, continuous venovenous hemodiafiltration.

Table 3. Secondary outcomes (crude cohort and PS-matched cohort)

	Crude cohort				PS-matched cohort			
	Overall	Low-dose	Standard-dose	P value	Overall	Low-dose	Standard-dose	P value
N	494	247	247		182	91	91	
NE-equivalent total pressor dose (mcg)	9675 [190, 28523]	11250 [720, 35385]	8500 [56, 25265]	0.162	12665 [1213, 29658]	14600 [1845, 34555]	10350 [393, 23960]	0.252
NE-equivalent average pressor rate (mcg/kg/min)	0.05 [0.00, 0.13]	0.04 [0.00, 0.12]	0.05 [0.00, 0.14]	0.541	0.05 [0.01, 0.12]	0.06 [0.01, 0.17]	0.05 [0.00, 0.10]	0.084
Delivered CKRT duration (hour)	57.8 [30.8, 115.2]	58.3 [34.4, 115.1]	54.0 [27.8, 120.3]	0.682	59.0 [30.3, 120.5]	53.5 [26.4, 100.8]	77.8 [34.5, 139.6]	0.110
ICU stay (day)	8 [3, 15]	8 [3, 17]	7 [4, 14]	0.180	7 [4, 16]	6 [3, 16]	8 [4, 16]	0.204
Prescribed effluent volume (mL/kg/h)	13.88 [11.80, 16.51]	11.80 [10.63, 12.77]	16.35 [14.98, 18.60]	<0.001	13.97 [12.53, 15.20]	12.52 [11.89, 13.42]	15.05 [14.40, 16.34]	<0.001
Delivered/prescribed effluent volume (%)	99.0 [95.7, 100.0]	98.4 [92.8, 100.0]	99.4 [96.9, 100.0]	<0.001	98.7 [94.6, 100.0]	97.3 [87.0, 100.0]	99.4 [97.3, 100.0]	<0.001

Note: Data shown as median [quartile 1, quartile 3]. Abbreviations: NE, norepinephrine; CKRT, continuous kidney replacement therapy; ICU, intensive care unit.

Figure 2. Kaplan-Meier survival curve (28-day)



Note: Abbreviations: HR, hazard ratio; CI, confidence interval.

Discussion

- Our results showed that treatment with low-dose CKRT was associated with worse survival compared to standard-dose CKRT.
- The median delivered dose was 16.22 mL/kg/h in the standard-dose group in our study, which was lower than the dose recommended by KDIGO. However, the delivered dose is usually 10 to 20% lower than the prescribed dose due to CKRT downtime. In a previous study[4)] comparing standard (20 mL/kg/h) versus high-dose CKRT (35 mL/kg/h), the mean actual delivered dose was 17 mL/kg/h in the standard-dose group. Therefore, the standard-dose CKRT in our study is not the same as the KDIGO recommended dose but is close to the delivered dose in the real world.
- The similarity of the standard CKRT dose in our study to that in the previous study may be attributed to a higher percentage of prescribed effluent volume being delivered in our study (97-99% of prescribed effluent volume were delivered).
- Limitations: First, due to the observational nature of the study, causality could not be assessed because of unknown confounding factors. Second, our study's generalizability may be limited because of the single-center study design. Finally, there are missing data in baseline patient characteristics due to the retrospective study design.

Conclusions

- Low-dose CKRT in critically ill patients with AKI is associated with higher mortality than standard-dose CKRT.
- In countries following the KDIGO guideline-recommended CKRT dose, it is important for clinicians to avoid excessive downtime to prevent reduced delivered dose.
- In countries not following the KDIGO guideline-recommended CKRT dose, further investigation is necessary due to the potential risk of higher mortality with low-dose CKRT.

References

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