Association of vasopressor use during renal replacement therapy and survival

Javier A. Neyra, MD, MS[1]; Jorge Echeverri, MD, MS[2]; Daniel Bronson-Lowe, PhD[2]; Caio Plopper, MD[2]; Kai Harenski, MD[3]; Raghavan Murugan MD, MS, FRCP[4].

[1]University of Alabama at Birmingham, Birmingham, AL, USA; [2]Baxter Healthcare Corporation, Global Medical Affairs, Deerfield, IL, USA; [3]Baxter Deutschland GmbH, Unterschleissheim, Germany; [4]Program for Critical Care Nephrology, Department of Critical Care Medicine, University of Pittsburgh, Pittsburgh, PA.

Introduction

Acute renal replacement therapy (RRT) modalities could contribute differentially to hemodynamic instability. Although vasopressors are used to treat hemodynamic instability, their impact on clinical outcomes after RRT initiation is unknown. This study examined the effect of vasopressor and intravenous (IV) fluid use following RRT initiation on in-hospital mortality among critically ill adults with acute kidney injury (AKI).

Methods & Materials

The study population was adult patients with AKI who received their initial RRT in the intensive care unit (ICU) setting of a of U.S. hospital providing continuous RRT (CRRT) and intermittent hemodialysis (IHD). We used the Premier PINC AI Healthcare database and included patients who were hospitalized between January 1, 2018 and June 30, 2021. **Figure 1** shows the eligibility criteria.

Data on vasopressor and IV fluid use were extracted for the 3 days before and after RRT initiation. Cox regression was used to examine the effects of vasopressor and IV fluid use on in-hospital mortality by day 90, accounting for demographics, comorbidities, and ICU care processes. The final analysis was stratified by initial RRT modality, as the interaction between RRT modality and vasopressor use on mortality was statistically significant.

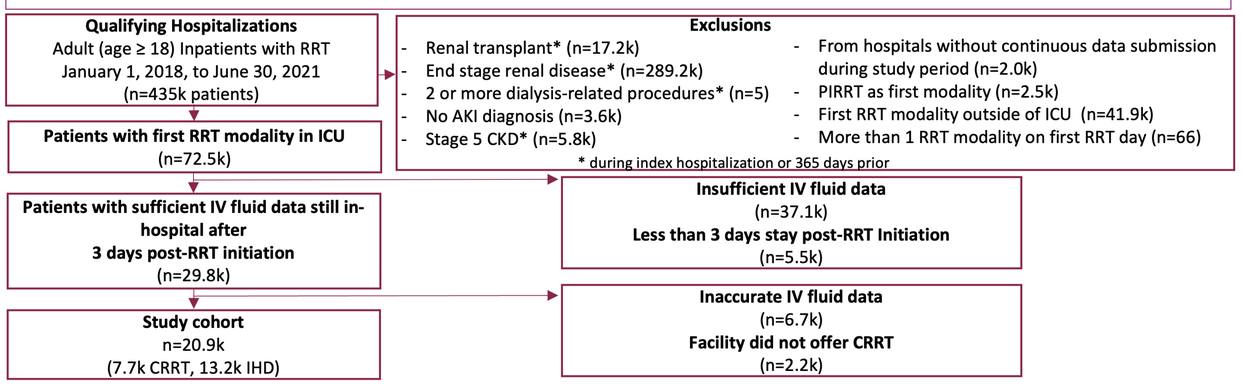

Figure 1. Eligibility criteria

Results

The final cohort included 20,882 critically ill patients whose first acute RRT occurred in the ICU, who were alive 3 days after initiation, and had complete IV fluid data (**Figure 1**). Patients who used vasopressors after RRT initiation had more sepsis, septic shock, and COVID-19, greater use of mechanical ventilation and ECMO, and greater fluid requirements before and after initiation of RRT (**Table 1**). Among all patients, 16% only received vasopressors pre-RRT, 21% only post-RRT, and 35% both pre- and post-RRT; many patients had a change in the number of vasopressors received pre- vs. post-RRT (**Figure 2**). 77% of CRRT patients and 44% of IHD patients received vasopressors after RRT initiation. In-hospital mortality, ICU length of stay and total hospital costs were higher when patients received vasopressors after RRT initiation (**Table 1**). Patients with post-RRT vasopressor use had similar 90-day survival rates regardless of pre-RRT vasopressor use (21% survival with pre-RRT use, 21% without); patients without post-RRT vasopressor use were similar (44% survival with pre-RRT use, 37% without). When combined, patients with post-RRT vasopressor use had lower 90-day survival (21%, 95%CI:19%-24%) compared to those without post-RRT vasopressor use (39%, 95%CI:34%-45%; p<0.001; **Figure 3**).

Adjusting for multiple factors, pre-RRT vasopressor use did not impact in-hospital mortality (p=0.4). After stratifying by RRT modality, the number of vasopressors used post-RRT (CRRT, 1 pressor: adjusted hazard ratio (aHR) 1.50, 95%CI:1.36-1.65; 2 pressors: aHR 1.95, 95%CI:1.77-2.15; IHD, 1: aHR 1.58, 95%CI:1.47-1.69; 2+: aHR 2.20, 95%CI:2.02-2.40), and average daily IV fluid use post-RRT (CRRT, middle tertile: aHR 1.10, 95%CI:1.00-1.20; top tertile: aHR 1.16, 95%CI:1.07-1.27; IHD, middle tertile: aHR 1.15, 95%CI:1.07-1.23; top tertile: aHR 1.13, 95%CI:1.05-1.22) were independently associated with in-hospital mortality, in both CRRT and IHD groups, respectively (**Table 2**). No interaction was observed between vasopressor use and IV fluid use on mortality.

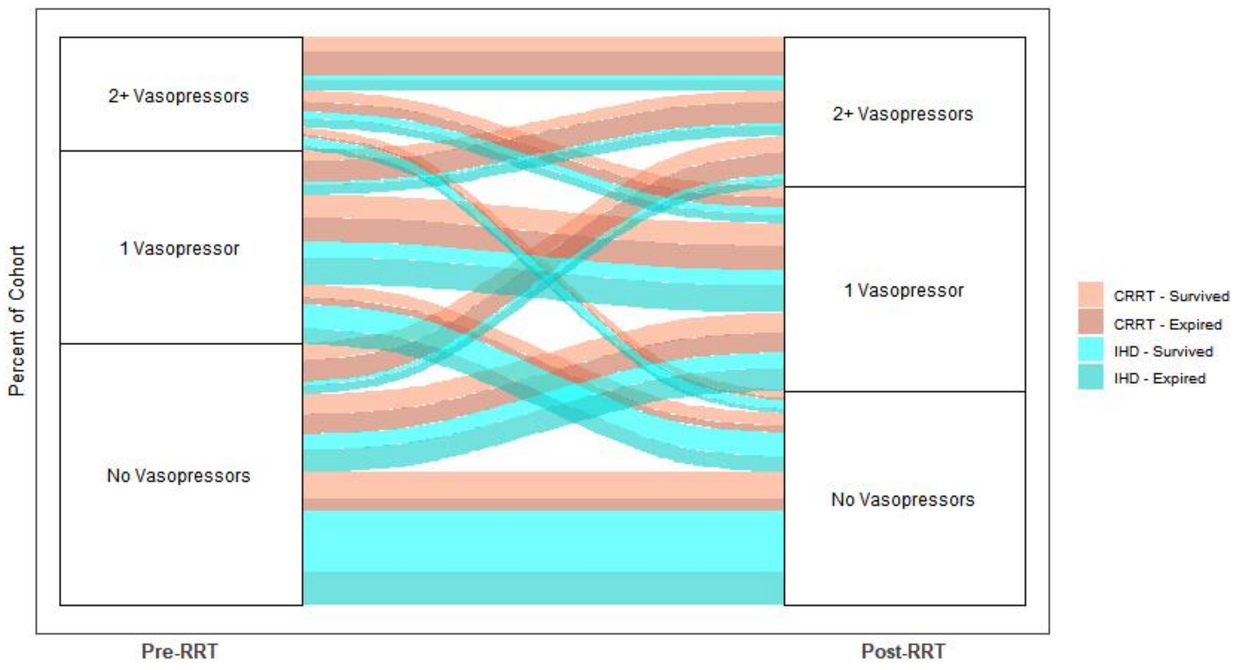

Figure 2. Vasopressor use before and after RRT initiation Alluvial diagram assessing the transition of vasopressor use categories before and after RRT initiation according to RRT modality and 90-day outcome. Pre-RRT and Post-RRT: within 3 days before and after RRT initiation, respectively.

Table 1. Characteristics and Outcomes			Vasopressor Use Post-RRT Initiation Yes	No	p-value
Total # of Patients			11,697	9,185	
% of Patients			56%	44%	
Patient Characteristics	Age, years (mean, std dev)		63 (14)	62 (15)	<0.001
	Male		62%	62%	0.36
	White, Non-Hispanic		61%	63%	0.006
Clinical Characteristics	Medical MS-DRG		48%	48%	>0.99
	Sepsis, Any		78%	60%	<0.001
	Septic Shock		67%	40%	<0.001
	COVID-19		21%	11%	<0.001
	APR-DRG Severity of Illness	Major	1.9%	6.3%	<0.001
		Extreme	98%	93%	-
	Hypertension		59%	65%	<0.001
	Diabetes		51%	54%	<0.001
	Chronic Kidney Disease		48%	56%	<0.001
	Charlson Comorbidities Index	0	6.8%	6.8%	<0.001
	Category	1-2	24%	21%	-
		3-4	27%	26%	-
		5+	42%	47%	-
	ECMO		3.5%	1.3%	<0.001
	Mechanical Ventilation		89%	70%	<0.001
	RRT Modality	CRRT	50%	19%	<0.001
		IHD	50%	81%	-
Average Daily IV Fluid Use (median ml (IQR))	Pre-RRT Initiation		1,650 (750; 3,167)	1,550 (683; 3,000)	<0.001
	Post-RRT Initiation		1,543 (750; 2,833)	900 (363; 1,729)	<0.001
Outcomes (mean)	In-hospital mortality		53%	25%	<0.001
	Length of Stay, days		24.6	24.4	0.93
	ICU Length of Stay, days		18.1	15.7	<0.001
	Total Hospital Stay Cost, $USD		135,197	110,680	<0.001

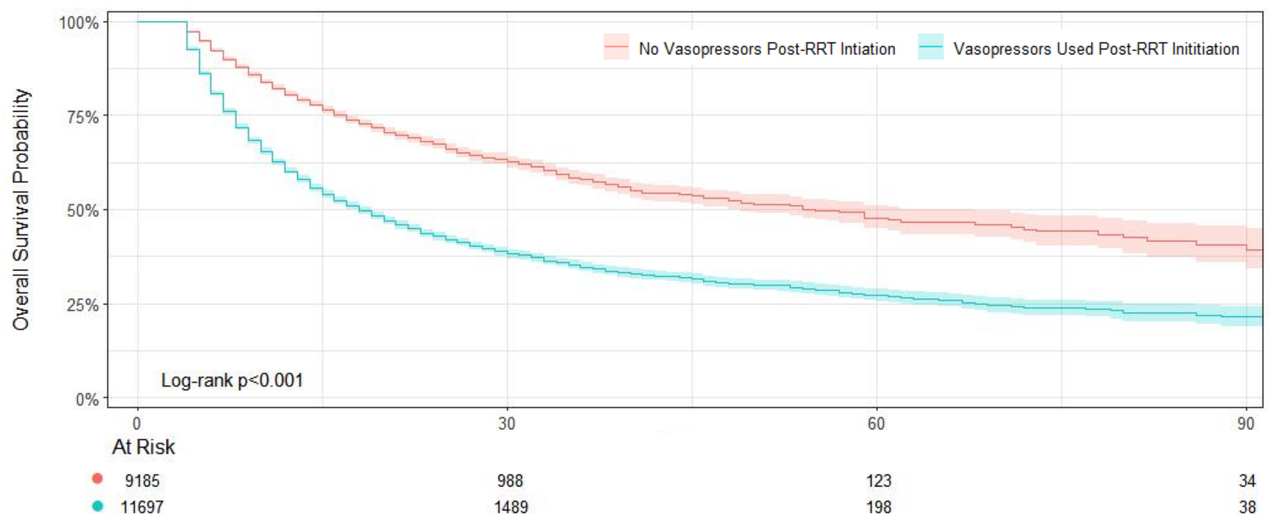

Figure 3. Patient survival by vasopressor use post-RRT initiation The Kaplan-Meier figure plots for the probability of crude in-hospital patient survival over 90 days post-RRT initiation, comparing patients with vasopressor use during the 3 days post-RRT initiation to those without. The red line represents no vasopressor use post-RRT, the blue line represents vasopressor use post-RRT, and the shading denotes a 95% CI. The probability of survival was lower among patients who required vasopressors within three days after RRT initiation compared to those without (log-rank P < 0.001).

Table 2. Final Model: Cox Regression		CRRT (n = 7,660) Hazard Ratio	95% CI	p-value	IHD (n = 13,222) Hazard Ratio	95% CI	p-value
Age (Y)		1.02	1.01, 1.02	<0.001	1.02	1.02, 1.02	<0.001
Sex	Female						
	Male	1.07	1.00, 1.14	0.041	1.17	1.10, 1.24	<0.001
White, Non-Hispanic		1.00	0.93, 1.07	>0.9	0.98	0.92, 1.04	0.500
MS-DRG Category	Surgical						
	Medical	2.33	2.17, 2.50	<0.001	2.35	2.20, 2.51	<0.001
COVID		1.26	1.17, 1.37	<0.001	1.56	1.45, 1.67	<0.001
Septic Shock		1.09	1.02, 1.18	0.015	1.17	1.10, 1.25	<0.001
ECMO		1.49	1.31, 1.70	<0.001	1.33	0.98, 1.81	0.064
Mechanical Ventilation		1.26	1.11, 1.42	<0.001	1.68	1.52, 1.84	<0.001
Days in ICU before RRT Initiation	0-1 days						
	2-3 days	1.03	0.92, 1.15	0.600	0.98	0.87, 1.11	0.800
	4-7 days	1.28	1.14, 1.44	<0.001	1.21	1.07, 1.37	0.002
	8+ days	1.47	1.30, 1.66	<0.001	1.39	1.23, 1.57	<0.001
Number of Vasopressors, post-RRT	0						
	1	1.50	1.36, 1.65	<0.001	1.58	1.47, 1.69	<0.001
	2+	1.95	1.77, 2.15	<0.001	2.20	2.02, 2.40	<0.001
Avg Total IV Fluid Use, post-RRT	Bottom tertile						
	Middle tertile	1.10	1.00, 1.20	0.047	1.15	1.07, 1.23	<0.001
	Top tertile	1.16	1.07, 1.27	<0.001	1.13	1.05, 1.22	0.002

Discussion & Conclusion

Key strengths of this study are its large sample of AKI patients requiring RRT who survived the first 3 days post RRT initiation (n=20,882) and the availability of associated IV fluid and vasopressor data. Study limitations include potential for confounding by unmeasured variables. The CRRT cohort included patients with more severe illness than the IHD cohort, although results were consistent when CRRT and IHD patients were analyzed separately.

Vasopressor use and higher average daily IV fluid use during the 3 days following RRT initiation were both independently associated with higher in-hospital mortality in patients first receiving CRRT or IHD in the ICU, regardless of vasopressor use pre-RRT. The magnitude of risk was greater in patients receiving multiple vasopressors.