

# In-Hospital Survival and Neurological Recovery Among Patients Requiring Renal Replacement Therapy in Post-Cardiac Arrest Period



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**Objectives:** Acute kidney injury (AKI) is common after cardiac arrest (CA). Few data exist on survival and neurological outcomes measured at hospital discharge of patients with severe AKI requiring renal replacement therapy (RRT) within the first 72 hours (i.e., duration of post-CA syndrome).

**Methods:** Single-center, prospective, observation cohort of patients with in- or out-of-hospital CA who survived to intensive care unit admission and were considered for targeted temperature management between 2010 and 2016 were reviewed. After excluding preexisting RRT history, patients with new RRT requirements within the first 72 hours after CA were included. Primary outcome of survival and secondary outcome of good neurological recovery defined as cerebral performance category score of 1 to 2, were compared between patients with and without RRT. Within 24 hours of initiating RRT, illness severity, as measured by Sequential Organ Failure Assessment score, Acute Physiology and Chronic Health Evaluation-II, and Charlson Comorbidity Index, was compared between survivors and nonsurvivors.

**Results:** Of 524 patients, 65 (12.4%) had new RRT requirements within 72 hours. Survival rates and good neurological recovery at discharge were comparable between RRT and non-RRT groups (19 of 65 [29%] vs. 162 of 459 [35%],  $P = 0.3$ , and 8 of 19 [42%] vs. 73 of 162 [45%], respectively). Sixty-three percent (12 of 19) of survivors requiring RRT did not need dialysis on discharge. Among patients requiring RRT, prognostic factors, including illness severity scores and indications for RRT, did not differ between survivors and nonsurvivors.

**Conclusions:** Patients with severe AKI requiring RRT during the post-CA syndrome period were not associated with any significant reduction in survival or poor neurological recovery, compared with those without RRT. Among those requiring RRT, none of the known prognostic factors predicted survival.

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KEYWORDS: cardiac arrest; neurologic outcomes; renal replacement therapy

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AKI is common after CA, and reported in up to 50% of patients during their hospitalization.<sup>1,2</sup> Up to one-third of these patients, develop severe AKI and require RRT during their post-CA hospitalization.<sup>1–3</sup>

Severe AKI after CA has been associated with increased mortality with varying relationship with neurological recovery.<sup>3</sup> However, the literature has been limited due to variations in AKI definitions and unclear onset time of AKI after CA.

The post-CA syndrome period, defined as the first 72 hours after achieving return of spontaneous circulation, has been associated with widespread activation of inflammatory mediators. Hypoperfusion and vascular hyperpermeability may occur, leading to end-organ dysfunction, and AKI.<sup>4</sup> In the later stages of hospitalization after CA, AKI is more likely to be secondary to sepsis and nephrotoxic agents, rather than CA-induced inflammation.<sup>5</sup> The prognosis of patients with severe AKI requiring RRT within this post-CA syndrome period is unknown.

In this study, we aim to estimate survival and neurological recovery at hospital discharge of patients with severe AKI requiring RRT within first 72 hours of CA.

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## METHODS

### Design

We conducted a prospective cohort study of adults with return of spontaneous circulation after in-hospital or out-of-hospital CA, who were considered for targeted temperature management at Columbia University Medical Center (an academic, tertiary-care hospital) from August 2010 through December 2016. The study was approved by the Columbia University institutional review board.

### Participants

From a consecutive sample of 528 patients with CA, we included those who required RRT within 72 hours of CA as a subgroup (Supplementary Figure S1). All patients were required to survive 72 hours for study inclusion, and study follow-up began at the end of the 72-hour period. Exclusion criteria included preexisting dialysis requirements before CA. Patients who developed new RRT requirements past 72 hours of CA were excluded due to greater likelihood of multifactorial AKI from later nephrotoxic agents or nosocomial illness. Patients on veno-arterial extracorporeal membrane oxygenation or intra-aortic balloon pump were not included in this study.

Targeted temperature management, based on the American Heart Association guidelines for the acute management of CA<sup>6</sup> is described in the Supplementary Material.

### Measurements

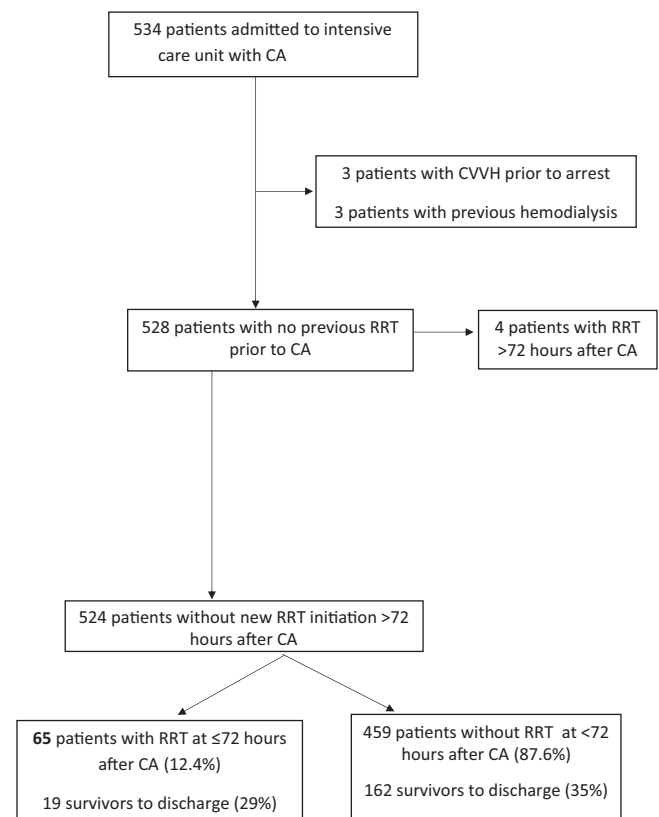
Variables were collected per Utstein guidelines.<sup>6</sup> AKI was determined by Kidney Disease: Improving Global Outcomes criteria.<sup>7</sup> The exposure variable of interest was whether RRT was initiated within 72 hours of CA event. Charlson Comorbidity indices were determined to assess pre-CA comorbidities.<sup>8</sup> Serum creatinine (mg/dl) obtained by Jaffe method was recorded at the time of admission, at 48 hours, at peak value within 72 hours, and at discharge. Preexisting renal disease was defined as the available nadir value before intensive care unit admission. Illness severity within 24 hours of initiating continuous veno-venous hemofiltration was calculated by the Sequential Organ Failure Assessment score, Acute Physiology and Chronic Health Evaluation–II scores, and number of vasopressors at RRT initiation.<sup>9,10</sup> Two reviewers (S.G. and V.Y.) documented indications for RRT using assessments obtained from board-certified nephrologists. Indications for RRT were categorized into the following: (i) volume overload, (ii) oliguria, (iii) anuria, (iv) acidosis, (v) hyperkalemia, and (vi) uremia. Neurologic outcome was assessed at discharge by cerebral performance category score.

### Statistical Analysis

Primary outcome of survival and secondary outcome of good neurological recovery, defined as cerebral performance category score of 1 to 2, were compared between patients with and without RRT. Among patients requiring RRT, illness severity scores, indications for RRT, and other patient characteristics were compared between survivors and nonsurvivors. Chi-square test and the Wilcoxon rank-sum test were used. A *P* value <0.05 was considered as statistically significant, and analyses were performed using STATA software (StataCorp, College Station, TX).

## RESULTS

Of 524 patients with CA included, 65 (12.4%) had new RRT requirements within 72 hours of arrest (Figure 1). Each of these patients received continuous veno-venous hemofiltration as their RRT modality, as was clinically indicated for critical illness and recent cardiac instability. Compared with the 459 patients who did not require RRT, those requiring RRT were younger, more often men, and had higher prevalence of preexisting renal disease (baseline estimated glomerular filtration rate<sup>7</sup> <60 ml/min per 1.73 m<sup>2</sup>). The RRT group also had patients with significantly higher rates



**Figure 1.** Patient selection for the prospective cohort. CA, cardiac arrest; CVVH, continuous veno-venous hemofiltration; RRT, renal replacement therapy.

of in-hospital arrests, ventricular tachycardia/fibrillation as their initial rhythm, bystander cardiopulmonary resuscitation and defibrillation, and a slight trend toward targeted temperature management administration (Table 1).

### Survival and Neurological Recovery at Hospital Discharge

Survival rates to hospital discharge were comparable between RRT and non-RRT groups (19 of 65 [29%] vs.

**Table 1.** Comparing patient characteristics and outcomes between patients with and without RRT

Characteristics, n (%)	No RRT, n = 459 (87.6%)	RRT, n = 65 (12.4%)	P
Age, mean ± SD	64.2 ± 17.7	59.8 ± 16.1	<b>0.04</b>
Men	244 (53.2)	45 (69.2)	<b>0.02</b>
Pre-arrest comorbidities			
Myocardial infarction	70 (15.3)	4 (6.2)	0.05
Heart failure	125 (27.2)	20 (30.8)	0.55
Hypertension	283 (61.7)	41 (63.1)	0.83
Renal disease	102 (22.2)	24 (36.9)	<b>0.01</b>
NIDDM	107 (23.3)	14 (21.5)	0.75
Liver disease	20 (4.4)	5 (7.7)	0.24
Cerebrovascular disease	66 (14.4)	4 (6.2)	0.07
PVD	39 (8.5)	8 (12.3)	0.31
Obesity (BMI >30 m/kg <sup>2</sup> )	42 (9.2)	8 (12.3)	0.42
Dementia	64 (13.9)	3 (4.6)	<b>0.04</b>
Smoking status			0.17
Nonsmoker	177 (44.5)	35 (57.4)	
Former smoker	135 (33.9)	16 (26.2)	
Current smoker	86 (21.6)	10 (16.4)	
Pre-arrest CPC			0.07
- CPC 1	253 (55.7)	43 (66.2)	
- CPC 2	86 (18.9)	15 (23.1)	
- CPC 3	108 (23.8)	7 (10.8)	
- CPC 4	7 (1.5)	0 (0)	
In-hospital arrests	144 (31.4)	35 (53.9)	<b>&lt;0.01</b>
Witnessed arrest	352 (78.2)	53 (81.5)	0.54
CPR provided			
-No CPR	169 (37.1)	10 (15.4)	
-Yes, by a bystander	98 (21.5)	9 (13.9)	
-Yes, with medical personnel	189 (41.5)	46 (70.8)	
Defibrillation use	148 (33.3)	24 (38.1)	0.45
Initial rhythm			
- VT/VF/AED Advised Shock	93 (22.0)	20 (34.5)	
- PEA	212 (50.1)	25 (43.1)	
- Asystole	118 (27.9)	13 (22.4)	
ROSC, mean ± SD	21.6 (16.4)	24.5 (26.6)	0.65
Temperature management	319 (69.5)	53 (81.5)	0.05
Survival to discharge	162 (35.3)	19 (29.2)	0.34
CPC for 181 survivors at discharge, n (%)			
- CPC 1	32 (19.8)	4 (21.1)	
- CPC 2	41 (25.3)	3 (15.8)	
- CPC 3	59 (36.4)	11 (57.9)	
- CPC 4	30 (18.5)	1 (5.3)	

AED, automated external defibrillators; BMI, body mass index; CPC, cerebral performance score; CPR, cardiopulmonary resuscitation; NIDDM, non-insulin-dependent diabetes mellitus; PEA, pulseless electrical activity; PVD, peripheral vascular disease; ROSC, return of spontaneous circulation; RRT, renal replacement therapy; VT/VF, ventricular tachycardia/ventricular fibrillation. *P* < 0.05 are in bold.

162 of 459 [35%], *P* = 0.3). Rates of good neurological function at discharge among all survivors (181 of 524 [34.5%]) were also similar in the RRT and non-RRT groups (8 of 19 [42%] vs. 73 of 162 [45%], *P* = 0.8). Among patients requiring RRT, survivors and non-survivors had no significant differences in prognostic factors, including patient characteristics (Supplementary Table S1), illness severity scores (Sequential Organ Failure Assessment, Acute Physiology and Chronic Health Evaluation–II, Charlson Comorbidity Index), serum creatinine levels at any estimated time points, early RRT (defined as within 48 hours of arrest), or indications for dialysis within 24 hours of RRT initiation (Table 2). Sixty-three percent of survivors (12 of 19) in the RRT group did not require long-term dialysis on discharge.

### DISCUSSION

Survival and neurological status at discharge were not significantly different in patients requiring RRT within the first 72 hours due to severe AKI, compared with those who did not need RRT. Among patients requiring RRT, 1 of 3 survive to discharge, with more than a quarter achieving good neurological recovery, and 2 of 3 of all patients with CA on RRT did not require long-term dialysis at the time of discharge. In contrast to previous

**Table 2.** Comparing indications for RRT and severity of illness between RRT survivors and nonsurvivors (*n* = 65)

Characteristics, n (%)	Survivors, n = 19 (29.2%)	Nonsurvivors, n = 46 (70.8%)	P
Serum creatinine, mean ± SD			
Baseline	1.66 ± 1.02	1.88 ± 1.35	0.57
48 h after cardiac arrest	3.97 ± 2.62	3.35 ± 1.60	0.52
Peak	4.11 ± 2.61	3.44 ± 1.56	0.41
On discharge (survivors only)	2.30 ± 1.54	–	–
Illness severity score, mean ± SD			
SOFA	14.47 ± 2.17	14.26 ± 2.55	0.75
APACHE-II	32.32 ± 5.83	33.48 ± 5.76	0.44
Number of pressors, mean ± SD	2.4 ± 1.42	2.5 ± 0.98	0.81
Furosemide infusion prior to RRT initiation	3 (15.8)	6 (13.0)	0.71
Early dialysis initiation (within 48 hours of arrest)	13 (68.4)	36 (78.3)	0.40
Indications for dialysis on RRT initiation			
Volume overload	7 (36.8)	12 (26.1)	0.39
Oliguria	5 (26.3)	6 (13.0)	0.28
Anuria	3 (15.8)	17 (37.0)	0.09
Acidosis	6 (31.6)	17 (37.0)	0.68
Hyperkalemia	4 (21.1)	11 (23.9)	1.00
Uremia	0 (0)	1 (2.2)	1.00
Dialysis on discharge (survivors only)	7 (36.8)	–	–

APACHE-II, Acute Physiology and Chronic Health Evaluation–II; RRT, renal replacement therapy; SOFA, Sequential Organ Failure Assessment.

literature, we did not find a difference in measured outcomes between oliguric and anuric AKI.<sup>11,12</sup>

Our study is the first looking at the utility of RRT for severe AKI developed in the early post-CA period. The kidney is particularly susceptible to post-resuscitation changes; interstitial inflammation and microvasculopathy resulting in incomplete tubular cell repair, fibrosis, and renal insufficiency.<sup>11</sup> AKI may have an impact on neurological recovery, although clinical results vary.<sup>13,14</sup> In experimental modes of renal injury, AKI contributes to hippocampal inflammatory injury and altered blood-brain barrier permeability.<sup>14</sup> There is some additional evidence that RRT may improve neurologic outcomes by removal of inflammatory mediators in the post-CA period.<sup>15–17</sup>

Further, severity of illness should not be a sole indicator to withhold RRT in the post-CA period. Among our post-CA RRT patients, survivors to discharge did not differ significantly from nonsurvivors, neither by severity of illness nor by indication for dialysis.

Our study has limitations. Although it is one of the largest studies dedicated to the utility of RRT after CA, our study size is nonetheless relatively small, and may not have enough power to detect the differences. Preexisting renal disease was defined as the available nadir value before intensive care unit admission, as outpatient creatinine values were not always available. All patients received only continuous veno-venous hemofiltration in the acute CA period, as these patients were critically ill and had had recent profound cardiac instability. Our results cannot be extrapolated to other types of RRT. Creatinine was measured nonenzymatically. We did not assess outcomes with time to intermittent hemodialysis transition later in hospitalization, nor did we assess length of stay while assessing in-hospital survival. Data regarding administration of nephrotoxins before or during CA were not collected, nor were resuscitation fluids. These factors could further refine outcomes in patients with AKI after CA.

CA is plagued with early withdrawal of life-sustaining treatments; of the 297 non-RRT patients who died, 25 patients met criteria for RRT within 72 hours but did not receive treatment, due to poor projected neurologic prognosis. This is consistent with other studies reporting only 40% of patients with CA with AKI are started on RRT because of predicted poor neurological recovery, and mortality was more than double in patients with acute renal failure without RRT.<sup>4</sup>

Long-term neurologic and renal outcomes of patients requiring RRT post-CA are still unknown, and merit further study.

## DISCLOSURE

JC reports personal fees from SAGE; grants from DANA, McDonnell, SHINE, I-SPOT, ESETT, and SAGE; and other from ICE Neurosystems, outside the submitted work. All the other authors declared no competing interests.

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## SUPPLEMENTARY MATERIAL

**Figure S1.** Patient selection for the prospective renal replacement therapy (RRT) cohort after cardiac arrest (CA). CVVH, continuous veno-venous hemofiltration.

**Table S1.** Comparing various clinical characteristics of survivors and nonsurvivors among patients who received RRT ( $n = 65$ ).

### Supplemental Section 1.

Supplementary material is linked to the online version of the paper at [www.kireports.org](http://www.kireports.org).

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