Clinical paper

Acute kidney injury after out of hospital pediatric cardiac arrest☆

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ABSTRACT

Importance: Many children with return of spontaneous circulation (ROSC) following cardiac arrest (CA) experience acute kidney injury (AKI). The impact of therapeutic hypothermia on the epidemiology of post-CA AKI in children has not been fully investigated.

Objective: The study aims were to: 1) describe the prevalence of severe AKI in comatose children following out-of-hospital CA (OHCA), 2) identify risk factors for severe AKI, 3) evaluate the impact of therapeutic hypothermia on the prevalence of severe AKI, and 4) evaluate the association of severe AKI with survival and functional outcomes.

Design: A post hoc secondary analysis of data from the Therapeutic Hypothermia after Pediatric Cardiac Arrest Out-of-Hospital (THAPCA-OH) trial.

Setting: Thirty-six pediatric intensive care units in the United States and Canada.

Participants: Of 282 eligible subjects with an initial creatinine obtained within 24 h of randomization, 148 were randomized to therapeutic hypothermia and 134 were randomized to therapeutic normothermia.

Main Outcomes and measures: Primary outcome was prevalence of severe AKI, as defined by stage 2 and 3 Kidney Disease Improving Global Outcomes (KDIGO) consensus definition; secondary outcome was survival with a favorable neurobehavioral outcome. For this study, risk factors and outcomes were compared between those with/without severe AKI.

Results: Of the 282 subjects enrolled, 180 (64%) developed AKI of which 117 (41% of all enrolled) developed severe AKI. Multivariable modeling found younger age, longer duration of chest compressions, higher lactate level at time of temperature intervention and higher number of vasoactive agents through day 1 of intervention associated with severe AKI. There was no difference in severe AKI between therapeutic hypothermia (39.9%) and therapeutic normothermia (43.3%) groups (p = 0.629). Survival was lower in those with severe AKI at 28 days (21% vs no severe AKI 49%, p < 0.001) and 12 months (21% vs no severe AKI 42%, p < 0.001). One year survival with favorable functional outcome was lower in those with severe AKI.

Conclusions and relevance: Severe AKI occurs frequently in children with ROSC after OHCA, especially in younger children and those with higher initial lactates and hemodynamic support. Severe AKI was associated with worse survival and functional outcome. Therapeutic hypothermia did not reduce the incidence of severe AKI.

Introduction

Return of spontaneous circulation (ROSC) following out-of-hospital cardiac arrest (OHCA) is frequently associated with the post-CA syndrome due to a systemic ischemia-reperfusion response manifesting as myocardial dysfunction, brain injury, and other organ dysfunction

[1–3]. Severe acute kidney injury (AKI) occurs in nearly 50% of adult cardiac arrest subjects [4]. AKI commonly occurs in critically ill children, including over one-third following CA, and is associated with increased morbidity and mortality [5–8]. The American Heart Association recommends treating comatose subjects following CA with either therapeutic hypothermia or therapeutic normothermia for neuroprotection [9,10]. Studies of neonates with perinatal asphyxia suggest that AKI is a risk factor for adverse neurologic outcomes [11]. Little is known about the impact of therapeutic hypothermia on the development AKI or whether AKI worsens survival or neurologic outcomes following pediatric CA.

The recently completed Therapeutic Hypothermia after Pediatric Cardiac Arrest Out-of-Hospital randomized trial (THAPCA-OH) evaluated the efficacy of targeted temperature management following pediatric OHCA [12]. This study is a secondary analysis of THAPCA-OH to describe the epidemiology of CA-associated AKI. The aims of this study were to: 1) describe the prevalence of severe AKI in comatose children following out-of-hospital CA (OHCA), 2) identify risk factors for severe AKI, 3) evaluate the impact of therapeutic hypothermia on the prevalence of severe AKI, and 4) evaluate the association of severe AKI with survival and functional outcomes.

Methods

This study is a planned secondary analysis of the THAPCA-OH trial, which received Institutional Review Board approval. The THAPCA-OH trial was conducted from September 1, 2009 through December 31, 2012 in 36 enrolling pediatric intensive care units (PICU) in the United States and Canada [12]. The trial included children > 48 h and < 18 years of age who sustained an OHCA, received ≥ 2 min of chest compressions, and were admitted to a PICU mechanically ventilated after ROSC. Major exclusion criteria were inability to consent and randomize within 6 h of ROSC and a Glasgow Coma Scale motor response subscale of 5 or 6. Subjects were randomized 1:1 to either therapeutic hypothermia or therapeutic normothermia.

Temperature intervention was maintained for 120 h after randomization: therapeutic hypothermia 33 °C (range 32–34 °C) or therapeutic normothermia 36.8 °C (range 36–37.5 °C). Subjects randomized to therapeutic hypothermia were cooled to 33 °C, maintained at 32–34 °C for 48 h, rewarmed over 16–24 h to 36.8 °C and maintained at 36–37.5 °C through hour 120. Subjects randomized to therapeutic normothermia were actively maintained at 36.8 °C through 120 h. Urine output (mL/kg/hr) was calculated by calendar day from Day 1 to Day 5. Details of the study protocol were previously reported [12].

Inclusion criteria for the current study

Those with an initial serum creatinine obtained within 24 h of randomization were eligible for analysis. Subjects were excluded if they had a pre-existing renal condition or supported with Extracorporeal Life Support (ECLS).

Definition of acute kidney injury

We defined AKI using the Kidney Disease Improving Global Outcomes (KDIGO) creatinine-based consensus definitions (granular urine output data was unavailable [13,6]). Because no subjects had an immediate pre-arrest value available, baseline creatinine was calculated in the 253 subjects with available height, as (0.413 × height in cm)/100 [14]. For the 29 subjects with height unavailable, baseline creatinine was defined by subject age: 0.3 mg/dL for age < 5 years, 0.5 mg/dL for age 5–12 years, and 0.7 mg/dL for age > 12 years. The current analysis is focused on the impact of severe AKI, stage 2 or 3, as has previously been utilized by other investigators [7,15].

Outcome measures

Outcomes included 12-month survival, 12-month survival with favorable neurobehavioral function, and 12-month survival without change in neurobehavioral function. Neurobehavioral functioning was assessed using the Vineland Adaptive Behavior Scales – Second Edition (VABS-II), a caregiver report measure of daily functioning. The VABS-II includes communication, daily living, socialization, and motor skills domains and provides an overall adaptive behavior composite score. Baseline VABS-II scores were obtained within 24 h of OH-CA and were based on functioning prior to CA. Research coordinators assisted caregivers with the baseline ratings. Additionally, 12-month VABS-II scores were obtained over the telephone by trained interviewers from Kennedy Krieger Institute. The VABS-II has an age-corrected mean of 100 and standard deviation of 15. Favorable neurobehavioral functioning was defined two ways 1) survival with a 12-month VABS-II adaptive behavior composite score of ≥ 70 and 2) survival with a decrease in 12-month VABS-II by ≤ 15 points from baseline).

Statistical analysis

Time from ROSC to peak AKI was calculated and described using histograms. Time to development of severe AKI is based on the time serum creatinine was obtained, or for cases where a subject was defined as having Stage 3 AKI due to use of renal replacement therapy (RRT) an estimated time of 12:00 (noon) on the day of RRT initiation. Time from ROSC to severe AKI or death was compared between treatment groups by Kaplan-Meier survival curves utilizing a log-rank test.

Univariate associations between the presence of severe AKI and subject characteristics or outcomes were examined using Fisher's exact test (categorical variables) and Wilcoxon rank-sum test (continuous variables). Multivariable logistic regression was used to test the association of covariates with severe AKI at different time points, candidate variables with univariate associations with p-value < 0.10. Some variables were excluded from consideration due to excessively missing data, clinician preference when two factors were highly correlated (e.g. baseline versus peak lactate), or data occurring after day 1.

Predictor variables were grouped into four time periods in a stepwise model procedure: Step 1) pre-arrest, Step 2) at time of ROSC, Step 3) near time of start of temperature intervention, and Step 4) post intervention through day 1. Forward stepwise selection was performed in the four steps. In Step 1, only pre-arrest characteristics were considered. In Step 2, any characteristic kept by the model in Step 1 was included in the starting model and the candidate arrest characteristics were additionally considered. Step 3 and 4 followed similarly. In each step, a p-value < 0.1 was used as the criterion for entering the model while a p-value > 0.05 was used as the criteria for removing factors. Analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC).

Results

Patient characteristics

Of 294 THAPCA-OH eligible subjects, 12 were excluded; eight for pre-existing renal condition, four for ECLS. Of 282 eligible subjects; 148 were randomized to therapeutic hypothermia and 134 to therapeutic normothermia. The median age at randomization was 2 years (IQR 0.4–8.8 years); 38% were < 1 year. One hundred thirty (46%) of subjects had a pre-existing medical condition (Table 1). The most common etiologies of CA were respiratory related in 89 (31.6%), drowning in 71 (25.2%) and sudden unexplained infant death (SUID) in 45 (16.0%) (Table 1). Asystole was the first documented rhythm in nearly 60% of cases.

Table 1
Demographics and Diagnostic Data.

| | Overall (N = 282) | Severe AKI | | |
		Yes (N = 117)	No (N = 165)	P-value
Age Group at Randomization				
< 1 year	106 (37.6%)	70 (59.8%)	36 (21.8%)	< 0.001[1]
1–4 years	89 (31.6%)	27 (23.1%)	62 (37.6%)	0.013[1]
5–12 years	43 (15.2%)	8 (6.8%)	35 (21.2%)	< 0.001[1]
> 13 years	44 (15.6%)	12 (10.3%)	32 (19.4%)	0.045[1]
Male sex	188 (66.7%)	77 (65.8%)	111 (67.3%)	0.799[1]
Preexisting conditions				
None	152 (53.9%)	63 (53.8%)	89 (53.9%)	1.000[1]
Lung or airway disease	63 (22.3%)	27 (23.1%)	36 (21.8%)	0.885[1]
Neurologic condition	43 (15.2%)	16 (13.7%)	27 (16.4%)	0.615[1]
Gastrointestinal disorder	36 (12.8%)	19 (16.2%)	17 (10.3%)	0.151[1]
Prenatal condition	30 (10.6%)	19 (16.2%)	11 (6.7%)	0.017[1]
Congenital heart disease	30 (10.6%)	16 (13.7%)	14 (8.5%)	0.175[1]
Other	59 (20.9%)	28 (23.9%)	31 (18.8%)	0.303[1]
Primary etiology of cardiac arrest				
Cardiac	35 (12.4%)	13 (11.1%)	22 (13.3%)	0.714[1]
ALTE/SUID	45 (16.0%)	32 (27.4%)	13 (7.9%)	< 0.001[1]
Drowning	71 (25.2%)	15 (12.8%)	56 (33.9%)	< 0.001[1]
Other Respiratory	89 (31.6%)	39 (33.3%)	50 (30.3%)	0.605[1]
Other/Unknown	42 (14.9%)	18 (15.4%)	24 (14.5%)	0.866[1]

[1] P-value is based on Fisher's exact test.

Prevalence of AKI

One hundred eighty subjects (64%) had AKI. Of the 180 subjects, 63 had stage 1, 52 had AKI stage 2, and 65 had AKI stage 3 – we combined stage 2 and 3 to define severe AKI; therefore, 117 (41%) had severe AKI, including 10 subjects (3.5%) who received renal replacement therapy.

Risk factors for severe AKI

Subjects who developed severe AKI were younger (mean, 3.0 years; SD, 4.9 vs mean, 6.1; SD, 5.6, p < 0.001) with 70 of 117 (60%) less than one year of age. Subjects with a prenatal condition were more likely to develop severe AKI (Table 1). The primary etiology of the CA differed between subjects who developed severe AKI and those who did not (Table 1). Drowning subjects were least likely to develop severe AKI (odds ratio, 0.3; CI, 0.2–0.5) and SUID subjects were most likely (odds ratio, 4.4; CI, 2.2–8.8). SUID accounted for 27% (32/117) of the severe AKI cases. In a sensitivity analysis excluding subjects with CA etiology of SUID an association between severe AKI and age remained (Appendix Table 1 in Supplementary material).

The initial rhythm or bystander initiated chest compressions did not differ between severe AKI/no severe AKI groups (Table 2), however, the estimated duration of chest compressions and chest compressions on arrival to first hospital were associated with severe AKI. Children with severe AKI had a higher incidence of organ dysfunction as reflected by increased ALT, lactate and vasopressor requirements (Table 2). They were more likely to receive vancomycin and more doses of epinephrine (severe AKI: 4 [IQR 2, 6] doses vs no severe AKI: 3 [IQR 1, 4] doses).

In multivariable modeling of prearrest and arrest periods variables (Step 1 and 2), only age and duration of chest compressions were associated with severe AKI. When additional variables were added reflecting a later point in time around temperature intervention (Step 3), lactate was associated with severe AKI development along with age but not duration of chest compressions. When variables beyond the intervention period were added through day 1 (Step 4), the number of

vasoactive agents administered was associated with severe AKI (Table 3) along with age and lactate concentration. Of note, predictive ability of the model as assessed by area under the curve (AUC) improved only modestly from 70.9% to 78.9% when factors other than the child's age were added.

Impact of hypothermia on severe AKI

There was no difference in rates of severe AKI between the temperature treatment groups (therapeutic hypothermia 39.9% vs therapeutic normothermia 43.3%; p = 0.629). Day-by-day rates of severe AKI were higher in the therapeutic normothermia group on Days 1 and 2 and the therapeutic hypothermia group on Day 5, but not significant different. Rates of a combined outcome of severe AKI or death did not differ over time in the therapeutic normothermia group versus the hypothermia group (Fig. 1; p = 0.27).

Half of subjects with severe AKI developed peak AKI within the first 24 h after ROSC (Fig. 2). A secondary peak of AKI occurred 96 h after ROSC and was more commonly observed following rewarming in the hypothermia group (Fig. 2).

Association of AKI and outcomes

Rates of survival at 28 days and at 12 months were higher in those without severe AKI (severe AKI 21% vs no severe AKI 49% at 28 days, p < 0.001, and severe AKI 21% and no severe AKI 42% at 12 months, p < 0.001; Table 4). There was no difference in survival with VABS-II within 15 points of baseline at one year (p = 0.099), however, there was a statistically significant association of lower one year survival with favorable neurobehavioral outcome in subjects who developed severe AKI (p = 0.008; Table 4).

Discussion

The current study shows that AKI occurs commonly in comatose pediatric subjects following OHCA, with 64% developing AKI and 41% developing severe AKI. Children with severe AKI were younger and had laboratory and clinical findings consistent with other severe end organ injury. Therapeutic hypothermia was not associated with decreased occurrence or severity of AKI.

AKI prevalence in our study was significantly higher than a recent report by Neumayr et al., who describe that 21.4% of subjects meet criteria for AKI after OHCA [8]. The higher prevalence of AKI in our cohort could be explained by different criteria to define AKI in the two studies, and differing inclusion and exclusion criteria. Our results are also consistent with the prevalence of AKI in neonates following perinatal asphyxia [11,16]. A recent publication investigating AKI and OHCA in adults showed a similar rate of AKI of 46%, which was associated with poor outcomes [17]. The lack of benefit of therapeutic hypothermia on AKI development is in contrast to Tanigasalam el al.'s findings that neonates who received therapeutic hypothermia had reduced occurrences of AKI and lower mortality [16]. Additionally, adult data regarding renal transplant from deceased organ donors demonstrate a protective benefit of hypothermia for the transplanted kidney [18]. The benefit of hypothermia in these studies may reflect a difference in the etiology of arrest, age and developmental differences, timing of cooling, and other factors.

Our findings demonstrate that severe AKI is associated with injury and dysfunction of other organs, consistent with the severe systemic ischemia/reperfusion injury following ROSC (Table 2). Higher lactate levels and more vasopressor medications are independent risk factors for post-OHCA AKI suggesting a key role of early hemodynamic insufficiency after ROSC in the development of severe AKI. The additional finding that SUID is associated with higher risk of AKI independent of age suggests that the duration of hemodynamic insufficiency may contribute to AKI as these individuals may be pulseless for an extended

Table 2
Physiologic and Therapeutic Data.

	Overall '(N = 282)	Severe AKI		P-value
		Yes (N = 117)	No (N = 165)	
Initial rhythm noted by EMS or hospital				
Asystole	168 (59.6%)	74 (63.2%)	94 (57.0%)	0.325[1]
Bradycardia	18 (6.4%)	9 (7.7%)	9 (5.5%)	0.468[1]
Pulseless electrical activity (PEA)	40 (14.2%)	16 (13.7%)	24 (14.5%)	0.864[1]
Ventricular fibrillation or tachycardia	22 (7.8%)	5 (4.3%)	17 (10.3%)	0.073[1]
Unknown	34 (12.1%)	13 (11.1%)	21 (12.7%)	0.715[1]
Bystander witnessed cardiac arrest	102/268 (38.1%)	37/110 (33.6%)	65/158 (41.1%)	0.250[1]
Chest compressions administered by bystander	178/272 (65.4%)	67/112 (59.8%)	111/160 (69.4%)	0.120[1]
Estimated duration of chest compressions in 272 patients (minutes) – Median (Q1, Q3)	25.0 (17.0, 37.0)	26.0 (20.0, 45.0)	25.0 (15.0, 35.0)	0.014[2]
Chest compressions still required at time of arrival at first hospital	189/276 (68.5%)	89/114 (78.1%)	100/162 (61.7%)	0.006[1]
Total number of doses of epinephrine administered by EMS and at hospital in 253 patients – Median (Q1, Q3)	3.0 (2.0, 5.0)	4.0 (2.0, 6.0)	3.0 (1.0, 4.0)	0.003[2]
Assigned to Hypothermia treatment	148 (52.5%)	59 (50.4%)	89 (53.9%)	0.629[1]
Aminoglycoside (Day 0–1)	3 (1.1%)	2 (1.7%)	1 (0.6%)	0.572[1]
Vancomycin (Day 0–1)	93 (33.0%)	48 (41.0%)	45 (27.3%)	0.020[1]
Baseline Lactate[3] in 273 patients (mmol/L) – Median (Q1, Q3)	5.6 (3.2, 10.0)	9.0 (4.5, 13.5)	4.2 (2.8, 7.6)	< 0.001[2]
Peak Lactate (Day 0–1) in 275 patients (mmol/L) – Median (Q1, Q3)	6.5 (3.5, 10.7)	9.7 (4.8, 14.1)	4.8 (2.9, 7.9)	< 0.001[2]
Baseline glucose in 258 patients concentration (mmol/L) – Median (Q1, Q3)	250 (179, 321)	241 (168, 324)	252 (193, 317)	0.726[2]
Baseline ALT in 245 patients concentration (U/L) – Median (Q1, Q3)	113 (59, 251)	147 (80, 335)	95 (51, 196)	0.002[2]
Peak ALT (Day 0–5) in 279 patients concentration (U/L) – Median (Q1, Q3)	139 (71, 331)	193 (99, 417)	108 (60, 207)	< 0.001[2]
Milrinone (Day 0–1)	41 (14.5%)	17 (14.5%)	24 (14.5%)	1.000[1]
Vasopressin (Day 0–1)	58 (20.6%)	28 (23.9%)	30 (18.2%)	0.295[1]
Vasoactive Agents (Day 0–1)				
Epinephrine	139 (49.3%)	71 (60.7%)	68 (41.2%)	0.002[1]
Dopamine	107 (37.9%)	50 (42.7%)	57 (34.5%)	0.173[1]
Norepinephrine	48 (17.0%)	26 (22.2%)	22 (13.3%)	0.055[1]
Dobutamine	14 (5.0%)	7 (6.0%)	7 (4.2%)	0.583[1]
Phenylephrine	5 (1.8%)	3 (2.6%)	2 (1.2%)	0.652[1]
Number of Vasoactive Agents (Day 0–1)				0.001[1]
0	99 (35.1%)	26 (22.2%)	73 (44.2%)	
1	73 (25.9%)	34 (29.1%)	39 (23.6%)	
2	90 (31.9%)	48 (41.0%)	42 (25.5%)	
3	20 (7.1%)	9 (7.7%)	11 (6.7%)	

[1] P-value is based on Fisher's exact test.
[2] P-value is based on the Wilcoxon rank-sum test.
[3] First non-missing lactate value occurring ≤8 h after randomization.

Table 3
Logistic Regression Models for Severe AKI Outcome.

Predictors[a]	Through Step 1 Model AUC = 70.9%		Through Step 2 Model AUC = 73.6%		Through Step 3 Model AUC = 78.2%		Through Step 4 Model AUC = 78.9%	
	Odds Ratio (95% CI)	P-value	Odds Ratio (95% CI)	P-value	Odds Ratio (95% CI)	P-value	Odds Ratio (95% CI)	P-value
Step 1: Pre-arrest								
Age in years		< .001		< .001		< .001		< .001
< 1 year	Reference		Reference		Reference		Reference	
1–4 years	0.22 (0.12, 0.41)		0.23 (0.12, 0.42)		0.26 (0.13, 0.51)		0.23 (0.12, 0.47)	
5–12 years	0.12 (0.05, 0.28)		0.11 (0.04, 0.27)		0.13 (0.05, 0.34)		0.12 (0.04, 0.30)	
> 13 years	0.19 (0.09, 0.42)		0.23 (0.10, 0.50)		0.35 (0.15, 0.81)		0.29 (0.12, 0.70)	
Step 2: At time of ROSC								
Estimated duration of chest compressions[b]			1.02 (1.00, 1.04)	0.01	1.01 (0.99, 1.03)	0.27	1.01 (0.99, 1.03)	0.36
Step 3: Post-arrest, near intervention start								
Baseline Lactate[c] (mmol/L)					1.14 (1.07, 1.22)	< .001	1.12 (1.05, 1.20)	0.001
Step 4: Day 0–1								
Number of Vasoactive Agents (Day 0–1)							1.50 (1.09, 2.05)	0.01

[a] Predictors considered for logistic regression models: age, preexisting prenatal condition, etiology of arrest, initial rhythm, doses of epinephrine, estimated duration of chest compressions, chest compressions still required at time of arrival at first hospital, baseline lactate, vancomycin used (day 0 or 1), number of vasoactive agents used (day 0 or 1).
[b] Replacement of 'estimated duration of chest compressions' with 'total number of epinephrine doses' in step 2 resulted in the selection of the same predictors and similar odds ratio estimates in steps 3 and 4.
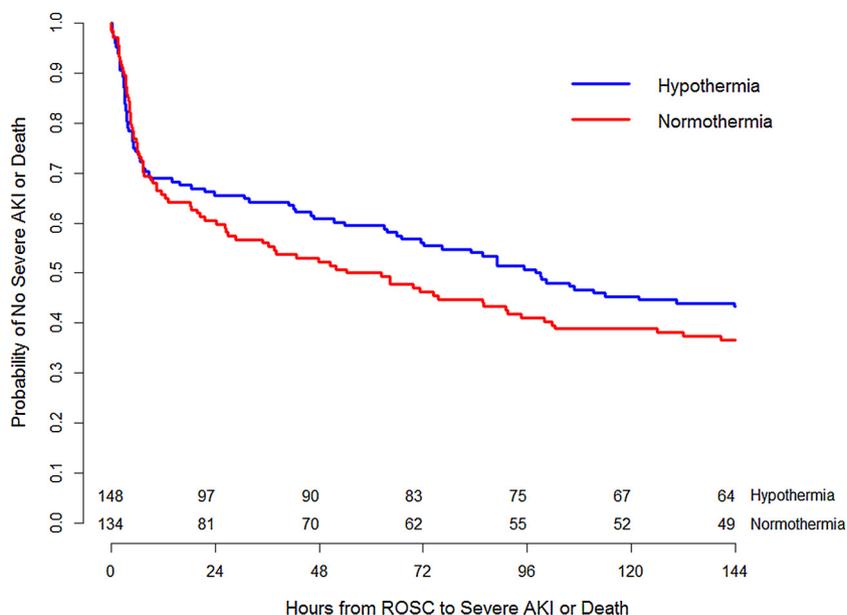[c] First non-missing lactate value occurring ≤8 h after randomization.

Fig. 1. Hours to Severe AKI or Death.
The two lines represent Kaplan-Meier rates from 0 to 144 h after ROSC for patients in each study arm (p = 0.27 by log-rank test).
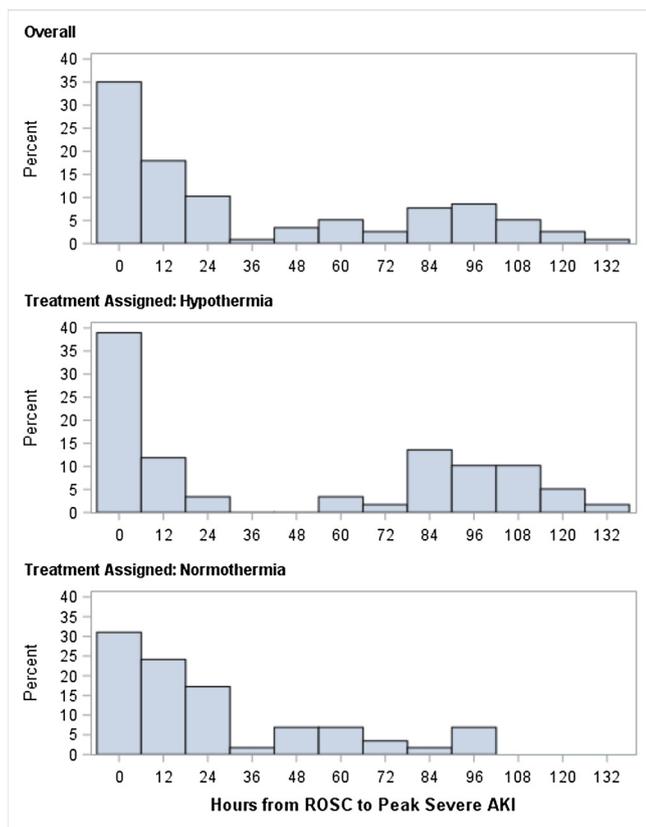

Fig. 2. Hours from ROSC to Peak Severe AKI.
Time in hours from ROSC to peak severe AKI did not differ between treatment groups (p = 0.25, Wilcoxon rank-sum test).

time prior compared to individuals with etiologies that occur near bystanders.

This secondary analysis of the THAPCA-OHCA trial represents the largest prospective cohort of children who experienced OHCA-associated AKI. We anticipate that randomization balanced known and unknown risk factors for AKI in the two temperature intervention

Table 4
Association of Severe AKI with Outcomes.

		Severe AKI		
	Overall	Yes	No	P-value
Survival at 12 months with VABS-II > = 70	40/251 (15.9%)	9/106 (8.5%)	31/145 (21.4%)	0.008[1]
Survival with VABS-II decreased no more than 15 points or improved	35/273 (12.8%)	10/115 (8.7%)	25/158 (15.8%)	0.099[1]
Survival at 12 months	91/275 (33.1%)	24/116 (20.7%)	67/159 (42.1%)	< .001[1]
Survival at 28 days	106/282 (37.6%)	25/117 (21.4%)	81/165 (49.1%)	< .001[1]

[1] P-value is based on Fisher's exact test.

groups, limiting confounding. One limitation of our analysis is the large proportion of early deaths may have resulted in underestimation of AKI at later time points. We attempted to correct for this by combining the outcomes of death and severe AKI, which did not demonstrate therapeutic hypothermia delayed the time to death or development of severe AKI compared to therapeutic normothermia (Fig. 1). Another limitation is that the THAPCA-OH trial population excluded all cases that were not comatose at the time of randomization up to 6 h following ROSC, which may have overestimated AKI for the overall OHCA population by selecting a cohort of subjects with more severe ischemia/reperfusion insult as result of CA. Other limitations are use of an estimate for baseline SCr, and we utilized modified KDIGO criteria, with SCr alone, to define AKI (sufficient urine output data not available). Finally, our data represents the OHCA cohort only. The association of AKI and In-hospital CA is currently being investigated.

In summary, our findings demonstrate that AKI frequently affects comatose children following OHCA, and therapeutic hypothermia does not decrease the rate of severe AKI. Younger children, longer duration of chest compressions, higher lactate concentration in the post arrest period, and high degree of hemodynamic support were independent risk factors for developing AKI post-OHCA. Development of severe AKI was associated with increased 28-day and 12-month mortality, and lower survival with favorable neurobehavioral outcome.

Conflict of interest

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.resuscitation.2018.07.362.

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