Available online at www.sciencedirect.com

Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation

Clinical paper

Association between shockable rhythms and long-term outcome after pediatric out-of-hospital cardiac arrest in Rotterdam, the Netherlands: An 18-year observational study

M. Albrecht[a], **R.C.J. de Jonge**[a], **V.M. Nadkarni**[f], **M. de Hoog**[a], **M. Hunfeld**[a,b], **J.A.E. Kammeraad**[c], **X.R.J. Moors**[d,e], **L. van Zellem**[g], **C.M.P. Buysse**[a,*]

[a] *Pediatric Intensive Care Unit, Department of Pediatrics and Pediatric Surgery, Erasmus MC-Sophia Childrens Hospital, Rotterdam, The Netherlands*
[b] *Department of Pediatric Neurology, Erasmus MC-Sophia Childrens Hospital, Rotterdam, The Netherlands*
[c] *Department of Pediatric Cardiology, Erasmus MC-Sophia Childrens Hospital, Rotterdam, The Netherlands*
[d] *Department of Pediatric Anesthesiology, Erasmus MC-Sophia Childrens Hospital, Rotterdam, The Netherlands*
[e] *Helicopter Emergency Medical Services, Erasmus MC, Rotterdam, The Netherlands*
[f] *Department of Anesthesiology and Critical Care Medicine, The Childrens Hospital of Philadelphia, University of Pennsylvania, Philadelphia, PA, United States*
[g] *Department of Youth Health Care, Public Health Service (GGD), Amsterdam, The Netherlands*

Abstract

Introduction: Shockable rhythm following pediatric out-of-hospital cardiac arrest (pOHCA) is consistently associated with hospital and short-term survival. Little is known about the relationship between shockable rhythm and long-term outcomes (>1 year) after pOHCA. The aim was to investigate the association between first documented rhythm and long-term outcomes in a pOHCA cohort over 18 years.

Methods: All children aged 1 day–18 years who experienced non-traumatic pOHCA between 2002–2019 and were subsequently admitted to the emergency department (ED) or pediatric intensive care unit (PICU) of Erasmus MC-Sophia Children's Hospital were included. Data was abstracted retrospectively from patient files, (ground) ambulance and Helicopter Emergency Medical Service (HEMS) records, and follow-up clinics. Long-term outcome was determined using a Pediatric Cerebral Performance Category (PCPC) score at the longest available follow-up interval through august 2020. The primary outcome measure was survival with favorable neurologic outcome, defined as PCPC 1–2 or no difference between pre- and post-arrest PCPC. The association between first documented rhythm and the primary outcome was calculated in a multivariable regression model.

Results: 369 children were admitted, nine children were lost to follow-up. Median age at arrest was age 3.4 (IQR 0.8–9.9) years, 63% were male and 14% had a shockable rhythm (66% non-shockable, 20% unknown or return of spontaneous circulation (ROSC) before emergency medical service (EMS) arrival). In adolescents (aged 12–18 years), 39% had shockable rhythm. 142 (39%) of children survived to hospital discharge. On median follow-up interval of 25 months (IQR 5.1–49.6), 115/142 (81%) of hospital survivors had favorable neurologic outcome. In multivariable analysis, shockable rhythm was associated with survival with favorable long-term neurologic outcome (OR 8.9 [95%CI 3.1–25.9]).

---

[*] Corresponding author.
E-mail address: c.buysse@erasmusmc.nl (C.M.P. Buysse).
https://doi.org/10.1016/j.resuscitation.2021.05.015

Conclusion: In children with pOHCA admitted to ED or PICU shockable rhythm had significantly higher odds of survival with long-term favorable neurologic outcome compared to non-shockable rhythm. Survival to hospital discharge after pOHCA was 39% over the 18-year study period. Of survivors to discharge, 81% had favorable long-term (median 25 months, IQR 5.1–49.6) neurologic outcome. Efforts for improving outcome of pOHCA should focus on early recognition and treatment of shockable pOHCA at scene.

Keywords: Pediatric resuscitations, Shockable rhythm, Long-term outcome

Introduction

Pediatric out of hospital cardiac arrest (pOHCA) is uncommon, with incidences ranging from 9.0 to 19.7 per 100,000 person-years.[1–4] Whereas CA in adults is mostly of cardiac origin, in pediatrics it is commonly due to respiratory failure.[5]

Survival following pOHCA is poor, especially among infants,[6,7] but increasing due to 'chain-of-survival' improvements.[7–13] Children receive more bystander basic life support (BLS), more automated external defibrillators (AED's) are available and post-return of spontaneous circulation (ROSC) care has improved, despite AED use in children remaining low.[6,7,9,13,14]

Shockable rhythms in children seem more common than once thought,[15,16] especially in adolescents (aged 12–18 years) with a prevalence of 19%.[7] The positive association between shockable rhythm and short-term outcomes (ROSC, survival to hospital discharge (SHD) and outcome up to 1 year) has been reported but true long-term follow-up (>1 year after event) is lacking.[6,17]

Is increased short-term survival rate after pOHCA associated with more children with severe long-term neurological sequelae due to hypoxic ischemic brain injury[18–20]? To be able to detect a child's full potential (neurologic) recovery, a statement from the American Heart Association recently recommended one year of follow-up minimally.[21] Literature on outcomes beyond one-year following pOHCA is scarce, often small in sample size, using different and mostly crude measurements and mainly based on data prior to 2008.[17,22–27]

Since 2012 the Erasmus MC-Sophia Children's Hospital has a long-term follow-up program including all pOHCA, as part of standard of care, which led to the following subjective observations: 1) the incidence of shockable rhythms increased over time and 2) shockable pOHCA's achieve favorable long-term neurological outcome more frequently compared with non-shockable pOHCA's.

The aim of this study was to investigate the association of first documented cardiac arrest (CA) rhythm on true long-term outcome in non-traumatic pOHCA. We hypothesized that a shockable rhythm was positively associated with survival with long-term favorable neurologic outcome.

Methods

Study design

This cohort study was performed at the PICU of the Erasmus MC-Sophia Children's Hospital, a tertiary-care university children's hospital in the Netherlands. The hospital and Helicopter Emergency Medical Service (HEMS) provide health care in the southwest of the Netherlands with approximately five million inhabitants, about 25% of the Dutch population. The Medical Ethics Review Board of the Erasmus MC approved the data collection and gave a waiver for the requirement of informed consent (MEC-2019-0440).

Inclusion criteria

All children aged 24 h to 18 years with non-traumatic pOHCA, admitted to the Erasmus MC-Sophia Children's Hospital (ED or PICU) with or without CPR in progress between January 2002 and August 2019 were included. Arrests in neonates younger than 24 h were excluded as they are generally caused by perinatal asphyxia. CA was defined as the need for chest compressions for at least one minute. Cardiopulmonary resuscitation was defined as 'basic life support', in line with the European Resuscitation Council Guidelines, and if needed, followed by 'advanced pediatric life support' (APLS).[5]

Data collection

Existing CPR databases were used to combine CPR data from 2002 until 2019.[23,28] All CPR data were derived from ground ambulance records, HEMS records and hospital health record systems. Because HEMS are always deployed in the Netherlands in (suspected) pOHCA, all HEMS records between 2002 and 2019 were also analysed to get an insight of pre-hospital mortality and potential transport to other hospitals. In some rare cases of conflict between data sources (ground EMS and HEMS) HEMS data was used as golden standard.

Data included: A) basic child characteristics (age, gender, parent's Social Economic Status (SES), pre-existing health status). The SES was calculated using a 'Status Score' divided into tertiles to interpret a 'low status (1)', 'intermediate status (2)' and 'high status (3)'.[29] The 'Status Score' is based on income, education level and unemployment rate by postal code. B) OHCA characteristics (year, location, first documented rhythm (shockable/non-shockable or unknown), witnessed, cause, bystander CPR, use of AED, CPR duration, extracorporeal CPR (ECPR), targeted temperature management, first blood lactate and pH after ROSC or at hospital arrival, regional transport, re-arrest). C) outcome (pre-hospital mortality, ROSC, SHD and neurologic outcome at the longest available follow-up interval).

At the longest available follow-up interval the neurologic outcome was determined using a Pediatric Cerebral Performance Category score (PCPC, ranging from 1 to 6) and a Functional Status Scale score (FSS, ranging from 6 to 30). The PCPC and FSS scores are internationally validated scores for assessing a child's overall cognitive and functional status after critical illness or injury.[30,31] The PCPC and FSS scores were based on one of four possible sources: 1) the prospective longitudinal follow-up outpatient clinic database (2012–2019 cohort). 2) the cross-sectional outcome database (2002–2011 cohort).[23] 3) hospital letters from outpatient clinic visits. 4) hospital discharge letters after the pOHCA. Both cross-sectional and prospective follow-up databases included validated neurocognitive and daily functioning questionnaires. Hospital letters contained more crude descriptions. The PCPC and FSS were scored by two physicians and one pediatric neurologist independently and in case of disagreement (in less than 5% of cases) agreement was reached through a consensus meeting.

Outcome measures

The primary outcome measure was survival with favorable neurologic outcome at the longest available follow-up interval. Survival with favorable neurologic outcome was defined as a PCPC score of 1−2 or no difference between pre- and post-arrest PCPC, in hospital survivors at the longest available follow-up interval. Unfavorable outcome was defined as: no ROSC, no survival to hospital discharge despite ROSC and PCPC 3−6. Secondary outcome measures were survival and favorable neurological outcome in the group of hospital-survivors.

No universal definition of favorable neurologic outcome exists. The PCPC score is mostly based on daily activity and school performance so 'favorable outcome' largely depends on a country's school system. Favorable neurologic outcome has been defined in the literature as PCPC 1−2 as well as PCPC 1−3.[9,21,32] Because in the Netherlands, a high threshold for attending a special needs classroom exists, favorable neurologic outcome was defined as PCPC 1−2.

Statistical analysis

Baseline characteristics and survival outcome were reported using descriptive statistics. Categorical variables were reported as percentages and frequencies, and differences were analyzed with Chi-square test or Fisher's exact test when applicable. Continuous data was presented as median and interquartile ranges (IQR) for skewed data, and mean and standard deviation (SD) for normal distributed data. Differences were tested using an independent sample t-test for continuous data or Mann−Whitney U test dependent on normality.

The associations of first documented rhythm, AED use, bystander BLS, year of event and the post AED guideline change period with long-term neurologic outcome were calculated with a multivariable logistic regression model. The choice of inclusion of covariates was made in three steps. First, the following covariates were considered based on existing literature: age, gender, pre-existing condition (yes or no and related to CPR event or not), SES (1, 2 or 3), event location (private or public), year of event (including before and after the AED guideline change), witnessed arrest (yes or no), bystander CPR (yes or no), bystander AED use (yes or no), CPR duration (in minutes), first documented cardiac arrest rhythm (shockable, non-shockable or unknown), cause of arrest (specific), ECPR (yes or no) and first lactate and pH after ROSC. Second, collinearity analysis to explore correlation between all covariates using a correlation matrix was performed. A cut-off value of >0.7 was used for the exclusion of variables in the model. Third, inclusion of the abovementioned potential confounders in the final models was based on $>10\%$ change of the effect estimate in the crude model. These covariates were entered one-by-one in the crude model to see the effect on the effect estimate.

Results are presented as odds ratio (OR) and 95%-confidence interval (CI).

A sensitivity analysis comparing the different definitions of favorable neurologic outcome (PCPC 1− vs PCPC 1−3, or no pre- and post-arrest difference) was performed. Stratified analysis by age group (below and above 8 years of age; infant; aged <1 year, child; aged 1−11 years and adolescent; aged 12−18 years) was also done. Lastly, a propensity score analysis using 1:1 nearest-neighbor matching of shockable to non-shockable rhythm was performed. The propensity score was estimated using a multivariable logistic regression model including the following variables: gender, age at arrest and year of event. Both groups were tested for association with long-term neurologic outcome using a multivariable logistic regression model.

Our data contained missing values for CPR duration (19%). Other covariates had <10% missing data. Variables were imputed using multiple imputation (n = 5 imputations) function based on the distribution of existing data.

A two-tailed p-value <0.05 was considered statistically significant. All analyses were conducted using SPSS software version 24 (IBM SPSS Statistics for Windows, Armonk, New York, USA).

Results

Child and CA characteristics

The target population consisted of 581 children, of whom 138 (24%) had termination of resuscitation and were pronounced deceased at scene and 74 (13%) were transported to other hospitals by HEMS. Of 369 eligible children admitted to the Erasmus MC-Sophia, 360 were included (9 children, 2%, had missing data). An overview of the inclusion is given in Fig. 1. The basic characteristics are presented in Table 1.

Most important causes of arrest were drowning (28%), 'Sudden Infant Death Syndrome' (SIDS) (15%) and arrhythmia (13%). The median age at CA was 3.4 (IQR 0.8−9.9) years and 225 (63%) were male. 152 arrests (42%) were witnessed and in 241 (68%) bystander BLS was performed. Of first documented rhythms, 14% were shockable, 66% non-shockable, 20% unknown (i.e. ROSC before arrival of EMS).

Outcome: ROSC, SHD, long-term outcome

Of the final sample of 360 children, 142 (39%) survived until hospital discharge, whereas 218 (61%) died in the ED (no ROSC, 102, 28%) or during hospital admission (116, 32%). The main cause of in-hospital mortality after ROSC was withdrawal of life-sustaining therapy (WLST) (76 children, 21%). Of the 142 survivors to hospital discharge, 7 (5%) died after discharge; 6 due to severe hypoxic encephalopathy, 1 cause unknown. The median follow-up duration was 25 months (IQR 5.1−49.6) and median age at follow-up was 6.6 years (IQR 3.4−13.4) (Table 1). 89 of 142 children (63%) had a follow-up duration of longer than 1 year post-arrest.

Table 2 shows timing and source of the long-term neurological outcome. PCPC scores are presented per category[1−6] and FSS scores as median. PCPC scores were mostly scored either at regular hospital visit (n = 47) or at prospective follow-up (n = 46). Except for the group scored at hospital discharge, median follow-up duration for the other groups exceeded 2 years (regular hospital visit 2.7 years [IQR: 0.8−5.5]; cross-sectional 3.7 [IQR 2.5−10.5] and prospective 2.3 years [IQR 1.1−3.8].

Favorable outcome versus non-favorable outcome

A higher SES score, bystander BLS, shorter CPR duration, rhythm (shockable or unknown), cause of arrest (arrhythmia, drowning, shock and seizures), lower first pH, higher lactate and ROSC before arrival to hospital were all significantly associated with favorable neurologic outcome (Table 1).

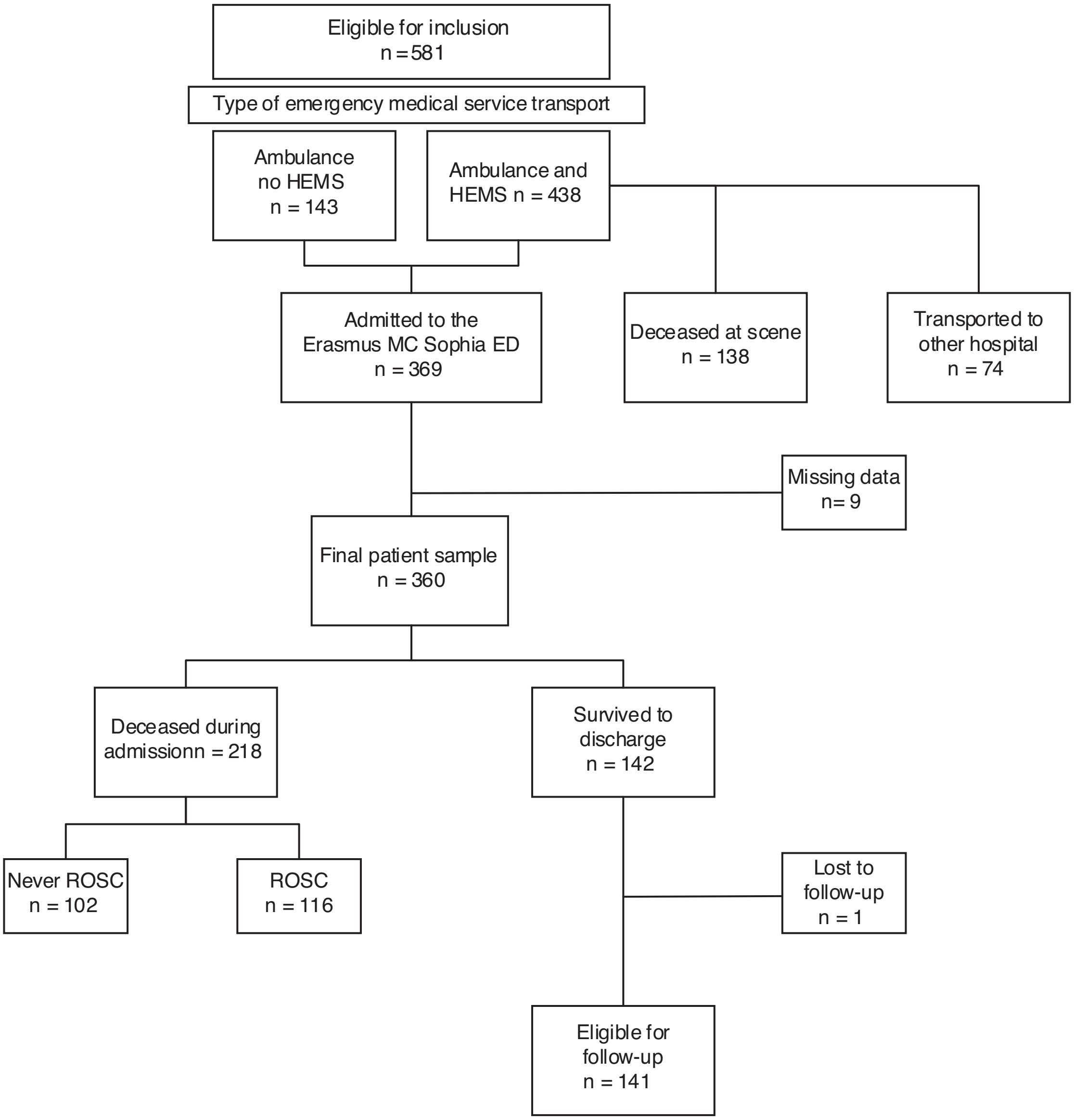

Fig. 1 – Overview of patient inclusion.
Abbreviations: ED = emergency department, HEMS = Helicopter Emergency Medical Service, ROSC = return of spontaneous circulation.

Multivariable analysis

The crude associations were adjusted for witnessed arrest, bystander CPR, age at arrest, year of arrest, first lactate, pre-existing conditions related to arrest and CPR duration. After adjustment, first documented shockable rhythm showed significantly improved odds of favorable outcome compared with non-shockable rhythm, with an OR of 8.9 [95% CI 3.1–25.9] (Table 3). Also, first documented unknown rhythm (OR 6.1 [95% CI 2.2–16.5]), a more recent year of arrest (OR 1.2 [95% CI 1.1–1.2]) and the post-guideline change period (advising AED use in all ages) (2010–2017) (OR 2.6 [95% CI 1.3–5.1]) showed significantly improved odds of favorable outcome. In the sensitivity analysis with PCPC 1–3, first documented shockable rhythm showed a stronger relationship with favorable outcome than favorable outcome defined as PCPC 1–2 (OR 13.7 [95% CI 4.6–40.9]).

Supplementary material

Stratified analysis for age are presented in the supplementary material. It proved unfeasible to create a nearest-neighbor propensity matching model (for 1:1 as well as 1 to many matching) because of the age distribution of shockable compared to non-shockable rhythm. The results are therefore not presented. The child and CA characteristics sorted by age group are presented in Supplementary Table S4. In adolescents (aged 12–18 years) the incidence of shockable rhythm was 39%. In the analysis stratified by age group an unknown rhythm was associated with favorable outcome in children <8 years (OR 5.6 [95% CI 3.6–8.8]) and children 8 years and above (OR 25.1 [95% CI 7.5–84.1) (Supplementary Table S5). Shockable rhythm was statistically significantly associated with favorable outcome in children 8 years and above (OR 22.7 [11.6–44.8). Primary and secondary

Table 1 – Patient and cardiac arrest characteristics by primary outcome measure: survival with favorable neurological outcome.

	Overall			Favorable outcome			Non-favorable outcome					
	(n = 360)			(n = 115)			(n = 244)					
	n[a]			n[a]			n[a]			p-Value[d]	Missings[c]	
Patient characteristics												
Age (years)[b]	360	3.4	0.8–9.9	115	3.4	1.2–12.1	245	3.2	0.7–8.6	0.429	0	
Male gender[c]	360	225	63%	115	74	64%	245	151	62%	0.489	0	
Pre-existings conditions[c]	358	155	43%	114	49	43%	244	106	43%	1.000	2	1%
- Respiratory		40	26%		12	24%		28	26%	1.000		
- Cardiac		31	20%		13	27%		18	17%	0.540		
- Neurologic		37	24%		8	16%		29	27%	0.354		
- Metabolic		3	2%		0	0%		3	3%	1.000		
- Congential malformation (non-cardiac)		32	21%		10	20%		22	21%	1.000		
- Renal		3	2%		1	2%		2	2%	1.000		
- Genetic/chromosomal		25	16%		7	14%		18	17%	0.174		
- Other		70	45%		28	57%		42	40%	0.091		
SES parents[c]	352			112			240			0.006	8	2%
- 1		128	36%		28	25%		100	42%	0.003		
- 2		153	43%		61	54%		92	38%	0.008		
- 3		71	20%		23	21%		48	20%	0.888		
Cardiac arrest characteristics												
Event location – public (versus private)[c]	360	125	35%	115	56	49%	245	69	28%	0.197	0	
Witnessed arrest[c]	358	152	42%	114	54	47%	244	98	40%	0.256	2	1%
Bystander BLS[c]	356	241	68%	115	99	86%	241	142	59%	<0.001	4	1%
Bystander AED use[c]	360	30	8%	115	10	9%	245	20	8%	0.684	0	
EMS defibrillation[c]	360	59	16%	115	23	20%	245	36	15%	0.175	0	
CPR duration (minutes)[b]	291	30.0	8.0–75.0	89	4.0	2.0–8.0	202	57.0	25.0–83.0	<0.001	69	19%
Initial rhythm[c]	351			115			237			<0.001	9	3%
- Shockable (VF)		48	14%		27	23%		21	9%	<0.001		
- Unknown/ROSC before EMS arrival		70	20%		57	50%		13	5%	<0.001		
- Non-shockable		233	66%		31	27%		202	85%	<0.001		
Asystole		172	74%		11	35%		161	80%	<0.001		
PEA		23	10%		4	13%		19	9%	0.113		
Bradycardia		38	16%		15	48%		23	11%	0.373		
Other		1	3%		1	3%		0	0%	0.331		
Cause of arrest[c]	360			115			245			<0.001	0	
- Unknown/not documented		27	8%		3	3%		24	10%	0.024		
- ALTE/SIDS		54	15%		17	15%		37	15%	1.000		
- Airway obstruction		41	11%		7	6%		34	14%	0.047		
- Arrythmia		47	13%		30	26%		17	7%	<0.001		
- Drowning		100	28%		45	39%		55	22%	0.002		
- Electrolyte abnormality		3	1%		0	0%		3	1%	0.554		
- Elevated ICP		10	3%		0	0%		10	4%	0.034		
- Hypotension/shock		30	8%		2	2%		28	11%	0.001		
- Ingestion/toxin		2	1%		2	2%		0	0%	0.103		
- Other repiratory failure		33	9%		8	7%		25	10%	0.336		
- Seizures		13	4%		1	1%		12	5%	0.043		
ECPR[c]	360	13	4%	115	4	3%	245	9	4%	1.000	0	
First pH after ROSC or after hospital arrival[b]	336	6.95	6.71–7.21	109	7.24	7.09–7.33	227	6.79	6.60–7.03	<0.001	24	7%
First lactate (mmol/L) after ROSC or after hospital arrival[b]	328	12.7	5.1–16.0	105	4.4	2.4–7.6	223	15.0	10.7–19.0	<0.001	32	9%
Post cardiac arrest characteristics												
Post-ROSC ECMO[c]	360	12	3%	115	5	4%	245	7	3%	0.534	0	
Temperature management[c]	354	149	42%	115	47	41%	239	102	43%	0.819	6	2%
Re-arrest[c]	360	13	4%	115	6	5%	245	7	3%	0.364	0	
Outcome												
Sustained ROSC[c]	360	258	72%	115	115	100%	245	143	58%	<0.001	0	
- Before arrival to hospital		204	57%		108	94%		96	39%	<0.001		
- After arrival to hospital		54	15%		7	6%		47	19%	0.001		

Table 1 *(continued)*

	Overall			Favorable outcome			Non-favorable outcome					
	(n = 360)			(n = 115)			(n = 244)					
	n[a]			n[a]			n[a]			p-Value[d]	Missings[c]	
Withdrawal of life sustaining therapies[c]	354	76	21%	115	0	0%	241	76	32%	NA	4	1%
Survival to hospital discharge[c]	360	142	39%	115	115	100%	245	27	11%	<0.001	0	
Deceased after discharge[c]	360	7	2%	115	0	0%	245	7	3%	NA	0	
Follow-up												
Follow-up (months)[b]	141	25.2	5.1–49.6	115	26.3	1.6–49.5	19	14.2	9.1–67.9	0.779		
Age at follow-up (years)[b]	141	6.6	3.4–13.4	115	8.1	3.5–14.7	19	5.3	3.0–12.1	0.300		

Abbreviations: AED = automatic external defibrillator, BLS = basic life support, EMS = emergency medical support, CPR = cardiopulmonary resuscitation, ECMO = extracorporeal cardiopulmonary support, ECPR = extracorporeal cardiopulmonary resuscitation, VF = ventricular fibrillation, ICP = intracranial, NA = not applicable pressure, PEA = pulseless electric activity, ROSC = return of spontaneous circulation.

[a] Number of subjects in whom the variable was obtained.

[b] Median (interquartile range).

[c] Number of subjects (%).

[d] p-Value: independent sample t-test for continuous data or Mann–Whitney U test dependent on normality; Fisher's exact test for dichotomous data.

Table 2 – Timing and source of long-term neurological outcome.

	Deceased after discharge (n = 7)		Scored at hospital discharge (n = 23)		Scored at a regular hospital or clinic visit (n = 47)		Scored at cross-sectional follow-up (2013–2014) (n = 18)		Scored at prospective follow-up (2011 and onwards) (n = 46)	
	Pre-arrest	Post-arrest	Pre-arrest	Post-arrest	Pre-arrest	Post-arrest	Pre-arrest	Post-arrest	Pre-arrest	Post-arrest
PCPC score[a]										
1 – Normal	5	0	18	16	39	26	17	8	40	24
2 – Mild disability	1	0	3	5	3	6	0	6	1	11
3 – Moderate disability	1	0	2	2	3	7	1	3	5	8
4 – Severe disability	0	0	0	0	2	7	0	1	0	3
5 – Coma or vegetative state	0	0	0	0	0	1	0	0	0	0
6 – Brain death	0	7	0	0	0	0	0	0	0	0
FSS score[b]	NA	NA	NA	6.0 [6.0–6.0]	NA	6.0 [6.0–11.0]	NA	6.0 [6.0–6.3]	NA	6.0 [6.0–6.3]
Follow-up (years)[b]	NA	0.6 [0.5–1.7]	NA	0.0 [0.0–0.0]	NA	2.7 [0.8–5.5]	NA	3.7 [2.5–10.5]	NA	2.3 [1.1–3.8]
Age at follow-up (years)[b]	NA	NA	NA	4.2 [1.5–8.9]	NA	6.6 [2.6–12.1]	NA	12.6 [3.8–15.0]	NA	9.0 [4.6–16.0]

Abbreviations: FSS = Functional Status Scale, PCPC = Pediatric Cerebral Performance Category.

[a] Number of subjects.

[b] Median (interquartile range). For patients deceased after discharge follow-up duration represents the median duration to date of death.

outcome measures were similarly associated with overall survival (Supplementary Table S6).

Discussion

Over an 18-year period and after a median follow-up of 25 months, this retrospective single-center study of pOHCA showed a nine times higher odds of shockable rhythms surviving with long-term favorable neurologic outcome compared to non-shockable rhythm, even after adjustment for confounders. First documented rhythms were 14% shockable (in adolescents, aged 12–18 years, 39%), 66% non-shockable and 20% unknown. SHD after pOHCA was 39%. 81% of hospital survivors achieved long-term favorable neurologic outcome and of all included children 32% survived with favorable neurologic outcome.[17,22,24]

Only few studies have true long-term follow-up and are thus comparable with the present study. We will summarize these, beyond case reports or series.[17,22–24,27]

The study of Meert et al., a secondary analysis of The Therapeutic Hypothermia after Pediatric Cardiac Arrest Out-of-Hospital (THAPCA-OH) trial, has comparable methodology as the present study as children were included after OHCA upon admission to hospital.[17] They also found that shockable rhythm was associated with greater 12-month survival and greater 12-month survival with favorable neurobehavioral functioning, assessed using the Vineland Adaptive Behavior Scales.

Table 3 – Univariable and multivariable logistic regression analyses of all children with survival with favorable neurologic outcome as dependent variable.

	Survival with post-arrest PCPC 1–2 or ΔPCPC 0 at the longest follow-up interval[f] (n = 360)				Survival with post-arrest PCPC 1–3 or ΔPCPC 0 at the longest follow-up interval[g] (n = 360)			
	Crude		Adjusted		Crude		Adjusted	
Variable	OR [95%CI]	p-Value	OR [95%CI]	p-Value	OR [95%CI]	p-Value	OR [95%CI]	p-Value
Initial non-shockable rhythm[a]	Referent		Referent		Referent		Referent	
Initial shockable rhythm[a]	8.4 [4.2–16.8]	<0.001	8.9 [3.1–25.9]	<0.001	9.4 [4.7–18.9]	<0.001	13.7 [4.6–40.9]	<0.001
Initial unknown rhythm[a]	29.6 [14.6–60.3]	<0.001	6.1 [2.2–16.5]	<0.001	31.5 [15.1–65.8]	<0.001	5.7 [2.1–15.8]	0.001
AED use[b]	1.1 [0.5–2.4]	0.873	0.3 [0.1–1.0]	0.049	1.1 [0.5–2.4]	0.798	0.2 [0.1–0.9]	0.035
Bystander BLS[c]	4.3 [2.4–7.8]	<0.001	1.9 [0.8–4.3]	0.137	3.6 [2.1–6.2]	<0.001	1.3 [0.6–3.0]	0.492
Year of arrest[d]	1.1 [1.1–1.2]	<0.001	1.2 [1.1–1.2]	<0.001	1.1 [1.0–1.1]	<0.001	1.2 [1.1–1.2]	<0.001
Post AED guideline change[e]	2.5 [1.6–4.1]	<0.001	2.6 [1.3–5.1]	0.007	2.3 [1.5–3.7]	<0.001	2.1 [1.1–4.1]	0.028

Abbreviations: AED = automatic external defibrillator, BLS = basic life support, CPR = cardiopulmonary resuscitation, PCPC = Pediatric Cerebral Performance Category, ROSC = return of spontaneous circulation.

[a] Adjusted for witnessed arrest, bystander CPR, age at arrest, year of event, first lactate, pre-existing conditions related to event and CPR duration.

[b] Adjusted for initial rhythm (shockable/non-shockable/unknown), bystander CPR, age at arrest, year of event, first lactate, socio-economic status and CPR duration.

[c] Adjusted for initial rhythm (shockable/non-shockable/unknown), year of event, first lactate, socio-economic status and CPR duration.

[d] Adjusted for initial rhythm (shockable/non-shockable/unknown).

[e] Adjusted for initial rhythm (shockable/non-shockable/unknown), bystander CPR, age at arrest, socio-economic status and CPR duration.

[f] Favorable neurologic survival defined as a post-arrest PCPC of 1–2 or a ΔPCPC of 0.

[g] Favorable neurologic survival defined as a post-arrest PCPC of 1–3 or a ΔPCPC of 0.

Table S4 – Patient and cardiac arrest characteristics by age group.

	Infants			Children			Adolescents			
	(n = 95)			(n = 187)			(n = 78)			
	n[a]			n[a]			n[a]			p-Value[d]
Patient characteristics										
Male gender[c]	95	58	61%	187	119	64%	78	48	62%	0.887
Pre-existings conditions[c]	95	38	40%	186	69	37%	77	48	62%	0.001
Respiratory		5	13%		20	29%		15	31%	0.015
Cardiac		11	29%		13	19%		7	15%	0.405
Neurologic		5	13%		16	23%		16	33%	0.004
Metabolic		0	0%		1	1%		2	4%	0.182
Congential malformation (non-cardiac)		14	37%		15	22%		3	6%	0.044
Renal		2	5%		1	1%		1	2%	0.110
Genetic/Chromosomal		11	29%		9	13%		5	10%	0.080
Other		18	47%		30	43%		22	46%	0.165
SES parents[c]	93			182			77			0.254
1		38	41%		68	37%		22	29%	0.237
2		33	35%		80	44%		40	52%	0.099
3		22	24%		34	19%		15	19%	0.616
Cardiac arrest characteristics										
Event location – public (versus private)[c]	95	15	16%	187	78	42%	78	34	44%	<0.001
Witnessed arrest[c]	95	46	48%	185	63	34%	78	43	55%	0.003
Bystander BLS[c]	95	63	66%	185	123	66%	76	55	72%	0.617
Bystander AED use[c]	95	5	5%	187	11	6%	78	14	18%	0.005
EMS defibrillation[c]	95	4	4%	187	22	12%	78	33	42%	<0.001
CPR duration (minutes)[b]	71	38.0	10.0–75.0	160	35.0	8.0–75.0	60	15.0	6.0–60.0	0.141
Initial rhythm[c]	93			181			77			<0.001
Shockable (VF)		4	4%		14	8%		30	39%	<0.001
Unknown/ROSC before EMS arrival		23	25%		41	23%		6	8%	0.006
Non-shockable		66	71%		126	70%		41	53%	0.025
Asystole		48	73%		91	72%		32	78%	0.356
PEA		6	9%		13	10%		4	10%	0.958
Bradycardia		12	18%		22	17%		4	10%	0.186

Table S4 *(continued)*

	Infants			Children			Adolescents			
	(n = 95)			(n = 187)			(n = 78)			
	n[a]			n[a]			n[a]			p-Value[d]
Other		2	17%		1	5%		1	25%	0.219
Cause of arrest[c]	95			187			78			<0.001
Unknown/Not documented		7	7%		15	8%		5	6%	0.932
ALTE/SIDS		49	52%		5	3%		0	0%	<0.001
Airway obstruction		10	11%		20	11%		11	14%	0.687
Arrythmia		3	3%		15	8%		29	37%	<0.001
Drowning		1	1%		91	49%		8	10%	<0.001
Electrolyte abnormality		0	0%		1	1%		2	3%	0.183
Elevated ICP		0	0%		3	2%		7	9%	0.002
Hypotension/Shock		12	13%		14	7%		4	5%	0.225
Ingestion/Toxin		0	0%		2	1%		0	0%	0.725
Other repiratory failure		10	11%		15	8%		8	10%	0.716
Seizures		3	3%		6	3%		4	5%	0.701
ECPR[c]	95	2	2%	187	9	5%	78	2	3%	0.568
First pH after ROSC or after hospital arrival[b]	87	6.87	6.61–7.14	175	6.94	6.72–7.19	76	7.11	6.86– 7.28	0.001
First lactate (mmol/L) after ROSC or after hospital arrival[b]	85	15.0	9.1–19.0	173	13.1	5.4–16.0	72	6.4	4.0–15.0	0.001
Post cardiac arrest characteristics										
Post-ROSC ECMO[c]	95	12	13%	187	9	5%	78	3	4%	0.072
Temperature management[c]	92	33	36%	185	77	42%	77	39	51%	0.156
Re-arrest[c]	95	3	3%	187	6	3%	78	4	5%	0.701
Outcome										
Sustained ROSC[c]	95	63	66%	187	133	71%	78	62	79%	0.155
Before arrival to hospital		51	54%		98	52%		55	71%	0.106
After arrival to hospital		12	13%		35	19%		7	9%	0.109
Withdrawal of life sustaining therapies[c]	95	22	23%	187	32	17%	78	22	28%	0.312
Survival to hospital discharge[c]	95	29	31%	187	75	40%	78	31	40%	0.159
Deceased after discharge[c]	95	1	1%	187	6	3%	78	0	0%	0.238
Surival with favorable neurologic outcome at the longest follow-up[c]	95	26	27%	187	60	32%	77	29	38%	0.405
Follow-up										
Follow-up (months)[b]	30	28.3	5.7–57.3	81	23.1	3.6–49.5	31	25.7	8.1–32.0	0.647
Age at follow up (years)[b]	30	2.4	0.9–5.1	81	5.5	3.6–10.3	31	17.2	15.9–18.8	<0.001

Abbreviations: VF = Ventricular fibrillation, PEA = Pulseless electric activity, AED = Automatic external defibrillator, EMS = Emergency medical support, CPR = Cardiopulmonary resuscitation, ICP = Intracranial pressure, ECMO = Extracorporeal cardiopulmonary support, ECPR = Extracorporeal cardiopulmonary resuscitation, ROSC = Return of spontaneous circulation.

[a] Number of subjects in whom the variable was obtained.

[b] Median (interquartile range).

[c] Number of subjects (%).

[d] p-Value: independent sample t-test for continuous data or Mann–Whitney U test dependent on normality; Fisher's exact test for dichotomous data.

However, there are important differences: 1. Inclusion criteria; in THAPCA children were included when unresponsive and mechanically ventilated after ROSC, creating a specific pOHCA population. 2. Furthermore; only a fraction of eligible children presenting to the hospital were included (295/1355, 22%). 3. THAPCA was a randomized trial comparing the efficacy of therapeutic hypothermia with therapeutic normothermia on survival with good neurobehavioral outcome in children 1 year after event. 4. Inclusion period; 2009–2012 in THAPCA versus 2002–2019 in present study. 5. Follow-up interval; 1 year in THAPCA versus cross-sectional with a median of 25 months in present study. Additional cognitive evaluations of the THAPCA cohort were performed by Slomine et al.[25,26] They found significant neuropsychological and neurobehavioral deficits in initially comatose pOHCA survivors although they were classified one year post-arrest as having favorable neurologic outcome. In addition they observed 3-month outcomes to be predictive of outcomes after 1 year.[33] Van Zellem studying in- and out-of-hospital arrests et al. used different IQ tests, neuropsychological tests and questionnaires, incomparable with the PCPC scoring system.[23] Lopez-Herce et al. found in 95 children (multicenter, 1998–1999), 17% favorable neurologic outcome after one year.[24] Michiels et al. found in a 36-year inclusion period (1976–2007) and a median of 4 years of follow-up, 2% favorable neurologic outcome.[22] Both described favorable neurologic outcome as PCPC scores of 1–2. Finally, Suominen et al. studied only arrests caused by drowning between 1985 and 2007.[27] Only 4 of 21 children had no neurologic or cognitive deficit after a median of 8 years of follow-up.

What are the implications of the present study?

Table S5 – Univariable and multivariable logistic regression analyses of all children with survival with favorable neurologic outcome as dependent variable by age.

	Survival with post-arrest PCPC 1-2 or ΔPCPC 0 at the longest follow-up interval[f]							
	Crude		Adjusted[a,b,c,d,e]		Crude		Adjusted[a,b,c,d,e]	
Variable	OR [95%CI]	p-Value	OR [95%CI]	p-Value	OR [95%CI]	p-Value	OR [95%CI]	p-Value
	Below 8 years (n = 256)				8 years and above (n = 104)			
Initial non-shockable rhythm[a]	referent		referent		referent		referent	
Initial shockable rhythm[a]	1.0 [0.4–2.4]	0.974	0.6 [0.2–1.7]	0.327	14.2 [9.2– 21.8]	<0.001	22.7 [11.6–44.8]	<0.001
Initial unknown rhythm[a]	27.2 [20.0–37.1]	<0.001	5.6 [3.6–8.8]	<0.001	49.0 [19.3–124.3]	<0.001	25.1 [7.5–84.1]	<0.001
AED use[b]	0.2 [0.1–0.4]	<0.001	0.1 [0.0–0.2]	<0.001	2.6 [1.7–4.0]	<0.001	1.3 [0.5–2.9]	0.592
Bystander BLS[c]	4.7 [3.5–6.4]	<0.001	2.0 [1.3–3.1]	0.001	3.7 [2.5–5.6]	<0.001	2.1 [1.1–4.2]	0.022
Year of event[d]	1.1 [1.1–1.1]	<0.001	1.2 [1.1–1.2]	<0.001	1.1 [1.1–1.2]	<0.001	1.2 [1.1–1.2]	<0.001
Post AED guideline change[e]	2.6 [2.1–3.3]	<0.001	2.8 [2.0–3.9]	<0.001	2.1 [1.5–3.1]	<0.001	2.4 [1.4–4.3]	0.002

Abbreviations: AED = Automatic external defibrillator, BLS = Basic life support, CPR = Cardiopulmonary resuscitation, PCPC = Pediatric Cerebral Performance Category, ROSC = Return of spontaneous circulation.

[a] Adjusted for witnessed arrest, bystander CPR, age at arrest, year of event, first lactate, pre-existing conditions related to event and CPR duration.

[b] Adjusted for initial rhythm (shockable/non-shockable/unknown), bystander CPR, age at arrest, year of event, first lactate, socio-economic status and CPR duration.

[c] Adjusted for initial rhythm (shockable/non-shockable/unknown), year of event, first lactate, socio-economic status and CPR duration.

[d] Adjusted for initial rhythm (shockable/non-shockable/unknown).

[e] Adjusted for initial rhythm (shockable/non-shockable/unknown), bystander CPR, age at arrest, socio-economic status and CPR duration.

Table S6 – Univariable and multivariable logistic regression analyses of favorable neurologic outcome among hospital-survivors and total survival.

	Favorable neurologic outcome (PCPC 1-2 or ΔPCPC 0) among discharged patients at the longest follow-up interval[g] (n = 142)				Total survival[h] (n = 360)			
	Crude		Adjusted[a,c,d,e]		Crude		Adjusted[b,c,d,e]	
Variable	OR [95%CI]	p-Value	OR [95%CI]	p-Value	OR [95%CI]	p-Value	OR [95%CI]	p-Value
Primary outcome measure								
Initial non-shockable rhythm[a,b]	referent		referent		referent		referent	
Initial shockable rhythm[a,b]	5.5 [1.5–20.1]	0.011	1.8 [0.2–15.2]	0.589	7.4 [3.8–14.5]	<0.001	9.6 [3.5–26.2]	<0.001
Initial unkown rhythm[a,b]	8.7 [2.7–14.0]	<0.001	8.8 [1.6–48.3]	0.011	25.6 [12.1–54.1]	<0.001	5.1 [1.9–13.6]	0.001
Secondary outcome measure								
AED use[c]	0.7 [0.2–2.9]	0.652	0.1 [0.0–1.3]	0.087	1.2 [0.5–2.5]	0.672	0.3 [0.1–1.0]	0.051
Bystander BLS[d]	2.4 [0.9–6.7]	0.092	1.6 [0.4–6.7]	0.521	3.9 [2.3–6.7]	<0.001	1.6 [0.7–3.5]	0.221
Year of event[e]	1.1 [1.0–1.2]	0.018	1.2 [1.1–1.3]	0.003	1.1 [1.0–1.1]	<0.001	1.1 [1.1–1.2]	<0.001
Post AED guideline change[f]	3.5 [1.5–8.5]	0.005	4.5 [1.5–13.5]	0.007	2.3 [1.5–3.7]	<0.001	1.8 [0.9–3.4]	0.068

Abbreviations: AED = Automatic external defibrillator, BLS = Basic life support, CPR = Cardiopulmonary resuscitation, PCPC = Pediatric Cerebral Performance Category, ROSC = Return of spontaneous circulation.

[a] Adjusted for follow-up duration, witnessed arrest, bystander CPR, age at arrest, year of event, first lactate, pre-existing conditions related to event and CPR duration.

[b] Adjusted for witnessed arrest, bystander CPR, age at arrest, year of event, first lactate, pre-existing conditions related to event and CPR duration.

[c] Adjusted for initial rhythm (shockable/non-shockable/unknown), bystander CPR, age at arrest, year of event, first lactate, socio-economic status and CPR duration.

[d] Adjusted for initial rhythm (shockable/non-shockable/unknown), year of event, first lactate, socio-economic status and CPR duration.

[e] Adjusted for initial rhythm (shockable/non-shockable/unknown).

[f] Adjusted for initial rhythm (shockable/non-shockable/unknown), bystander CPR, age at arrest, socio-economic status and CPR duration.

[g] Favorable neurologic survival defined as a post-arrest PCPC of 1-2 or a ΔPCPC of 0.

[h] Total survival amongst the included study population.

First, shockable rhythm was shown to significantly and relevantly improve odds of true long-term favorable outcome. With favorable outcome defined as PCPC 1–3 the relationship was even stronger. And most notably in children eight years and above, shockable rhythm was statistically significantly associated with favorable outcome with OR 22.7 [11.6–44.8). This can be explained by the relatively high incidence of shockable rhythm in adolescents (aged 12–18 years) (39%). Also young children are less likely to have an AED used during CPR than older children, possibly because arrests are more often occurring at home rather than in public locations where AEDs are available. In a cohort study from an OHCA registry in Japan, the proportion of adults with a favorable neurological outcome 30 days after event was significantly higher in those who received public-access defibrillation than those who did not (845 [37.7%] vs 5676 [22.6%].[34]

Our results might implicate that the efforts for improving outcome of pOHCA should focus on early recognition and treatment of shockable OHCA at scene and the importance of improvements in the chain of survival (e.g. bystander BLS, public access to and use of AED and adequate EMS response).[35,36]

Second, a remarkable finding was that 81% of survivors to hospital discharge achieved long-term favorable neurologic outcome beyond 1 year. This could be due to the setting in the Netherlands (e.g. high incidence in AED use and bystander CPR, the availability of HEMS 24/7, short transfer time from the scene to the hospital). Another possible explanation could be that in our study cohort the main cause of in-hospital mortality after ROSC was WLST (21%), probably due to poor neurologic prognosis. Less WLST could lead to higher survival to discharge numbers, but with more severe neurologically damaged children surviving long-term. Accurate neurological prognostication in a comatose child after OHCA remains challenging and no international pediatric guidelines exist.[21,37,38] Potentially inaccurate prognostication and WLST may bias outcome.[28,37,39,40]

Third, the median age at time of follow-up was 6.6 years (IQR 3.4 −13.4), which is relatively young in childhood and thus growing into deficits might not yet be present. Moreover, neurologic outcome was measured by PCPC, which is a crude outcome scale ranging from 1 to 6 (from no disabilities to brain death). It is unknown whether PCPC reflected how these children function in daily life and if it was associated with detailed neuropsychological functioning. In our opinion, it is crucial to identify how these pOHCA survivors will function on different physical and neuropsychological domains when reaching adolescence or young adulthood. Will they be able to live independently and happy, have a job and start a family? The importance to understand the influence of an arrest on long-term education and development as children grow into adulthood seems clear.[21] True long-term follow-up is time and resource consuming, with the potential of losing children to follow-up.[21] Long-term follow-up outpatient clinics have to be set up also beyond the 18 year boundary to support this group in maximizing outcome.

Our study has several limitations. First, it was an observational, retrospective single center study. Secondly, there were missing data due to the incomplete documentation of the CPR-event (e.g. CPR duration), which required imputation in up to 10% of the data. We minimized this potential bias by doing supplemental analyses with and without imputation. Additionally, we were not able to report and correct for some important CPR characteristics (e.g. quality of CPR, post-ROSC care). Finally, our study is not a complete regional or national pOHCA study since only children admitted to our hospital (with or without CPR in progress) were included. This could have led to selection bias by not including those children who died at scene or transferred to another hospital.

Conclusion

Shockable pOHCA had an almost nine times higher odds of long-term favorable neurologic survival compared to non-shockable rhythm, adjusted for confounding. The overall SHD after pOHCA was 39% over the 18-year study period, of which 81% of survivors achieved long-term (median 25 months, IQR 5.1−49.6) favorable neurologic outcome. This indicates the efforts for improving outcome of pOHCA should focus on early recognition and treatment of shockable pOHCA at scene.

CRediT author statement

The contributions of the authors were as follows: M. Albrecht, R. De Jonge and C. Buysse had the original idea for the study. M. Albrecht, as first author, participated in its design, performed the statistical analysis, interpreted the data, drafted and critically revised the article. All co-authors revised the manuscript critically for important intellectual content. C. Buysse provided supervision. All authors read and approved the final article. All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

Acknowledgements

Dr. Buysse and M. Albrecht report a grant for the data collection of this study by The Laerdal Foundation. The Laerdal Foundation had no role in design and conduct of the study; collection, management, analysis and interpretation of the data; and preparation, review or approval of the manuscript. Dr. Nadkarni reports grants from Zoll Medical Corp, American Heart Association/Resuscitation Quality Improvement Program, Nihon Kohden Corp, National Institutes of Health, and Agency for Healthcare Quality Improvement. All are unrelated to this study. The other authors report no conflicts.

REFERENCES

1. Sirbaugh PE, Pepe PE, Shook JE, et al. A prospective, population-based study of the demographics, epidemiology, management, and outcome of out-of-hospital pediatric cardiopulmonary arrest. Ann Emerg Med 1999;33:174−84.
2. Kuisma M, Suominen P, Korpela R. Pediatric out-of-hospital cardiac arrests—epidemiology and outcome. Resuscitation 1995;30:141−50.
3. Gerein RB, Osmond MH, Stiell IG, Nesbitt LP, Burns S, Grp OS. What are the etiology and epidemiology of out-of-hospital pediatric cardiopulmonary arrest in Ontario, Canada? Acad Emerg Med 2006;13:653−8.
4. Bardai A, Berdowski J, van der Werf C, et al. Incidence, causes, and outcomes of out-of-hospital cardiac arrest in children. A comprehensive, prospective, population-based study in the Netherlands. J Am Coll Cardiol 2011;57:1822−8.
5. Maconochie IK, Bingham R, Eich C, et al. European Resuscitation Council guidelines for resuscitation 2015: section 6. Paediatric life support. Resuscitation 2015;95:223−48.
6. Atkins DL, Everson-Stewart S, Sears GK, et al. Epidemiology and outcomes from out-of-hospital cardiac arrest in children: the resuscitation outcomes consortium epistry-cardiac arrest. Circulation 2009;119:1484−91.
7. Fink EL, Prince DK, Kaltman JR, et al. Unchanged pediatric out-of-hospital cardiac arrest incidence and survival rates with regional variation in North America. Resuscitation 2016;107:121−8.
8. Fukuda T, Ohashi-Fukuda N, Kobayashi H, et al. Public access defibrillation and outcomes after pediatric out-of-hospital cardiac arrest. Resuscitation 2017;111:1−7.
9. Naim MY, Burke RV, McNally BF, et al. Association of Bystander Cardiopulmonary Resuscitation with overall and neurologically

favorable survival after pediatric out-of-hospital cardiac arrest in the United States: a report from the Cardiac Arrest Registry to enhance survival surveillance registry. JAMA Pediatr 2017;171:133–41.

10. Tijssen JA, Prince DK, Morrison LJ, et al. Time on the scene and interventions are associated with improved survival in pediatric out-of-hospital cardiac arrest. Resuscitation 2015;94:1–7.
11. Cummins RO, Ornato JP, Thies WH, Pepe PE. Improving survival from sudden cardiac arrest: the "chain of survival" concept. A statement for health professionals from the Advanced Cardiac Life Support Subcommittee and the Emergency Cardiac Care Committee, American Heart Association. Circulation 1991;83:1832–47.
12. Kitamura T, Iwami T, Kawamura T, et al. Conventional and chest-compression-only cardiopulmonary resuscitation by bystanders for children who have out-of-hospital cardiac arrests: a prospective, nationwide, population-based cohort study. Lancet 2010;375:1347–54.
13. Goto Y, Funada A, Goto Y. Duration of prehospital cardiopulmonary resuscitation and favorable neurological outcomes for pediatric out-of-hospital cardiac arrests: a nationwide, population-based cohort study. Circulation 2016;134:2046–59.
14. Kiyohara K, Nitta M, Sato Y, et al. Ten-year trends of public-access defibrillation in Japanese school-aged patients having neurologically favorable survival after out-of-hospital cardiac arrest. Am J Cardiol 2018;122:890–7.
15. Soar J, Donnino MW, Maconochie I, et al. 2018 International consensus on cardiopulmonary resuscitation and emergency cardiovascular care science with treatment recommendations summary. Resuscitation 2018;133:194–206.
16. Topjian AA, Nadkarni VM, Berg RA. Cardiopulmonary resuscitation in children. Curr Opin Crit Care 2009;15:203–8.
17. Meert KL, Telford R, Holubkov R, et al. Pediatric out-of-hospital cardiac arrest characteristics and their association with survival and neurobehavioral outcome. Pediatr Crit Care Med 2016;17:e543–50.
18. Girotra S, Spertus JA, Li Y, et al. Survival trends in pediatric in-hospital cardiac arrests: an analysis from get with the guidelines-resuscitation. Circ Cardiovasc Qual Outcomes 2013;6:42–9.
19. Sekhon MS, Ainslie PN, Griesdale DE. Clinical pathophysiology of hypoxic ischemic brain injury after cardiac arrest: a "two-hit" model. Crit Care 2017;21:90.
20. Tress EE, Kochanek PM, Saladino RA, Manole MD. Cardiac arrest in children. J Emerg Trauma Shock 2010;3:267–72.
21. Topjian AA, Scholefield BR, Pinto NP, et al. P-COSCA (pediatric core outcome set for cardiac arrest) in children: an advisory statement from the International Liaison Committee on resuscitation. Circulation 2020;142:e246–61.
22. Michiels E, Quan L, Dumas F, Rea T. Long-term neurologic outcomes following paediatric out-of-hospital cardiac arrest. Resuscitation 2016;102:122–6.
23. van Zellem L, Buysse C, Madderom M, et al. Long-term neuropsychological outcomes in children and adolescents after cardiac arrest. Intensive Care Med 2015;41:1057–66.
24. Lopez-Herce J, Garcia C, Dominguez P, et al. Outcome of out-of-hospital cardiorespiratory arrest in children. Pediatr Emerg Care 2005;21:807–15.
25. Slomine BS, Silverstein FS, Christensen JR, et al. Neurobehavioral outcomes in children after out-of-hospital cardiac arrest. Pediatrics 2016137:.
26. Slomine BS, Silverstein FS, Christensen JR, et al. Neuropsychological outcomes of children 1 year after pediatric cardiac arrest: secondary analysis of 2 randomized clinical trials. JAMA Neurol 2018;75:1502–10.
27. Suominen PK, Sutinen N, Valle S, Olkkola KT, Lonnqvist T. Neurocognitive long term follow-up study on drowned children. Resuscitation 2014;85:1059–64.
28. Hunfeld M, Nadkarni VM, Topjian A, et al. Timing and cause of death in children following return of circulation after out-of-hospital cardiac arrest: a single-center retrospective cohort study. Pediatr Crit Care Med 2020.
29. Statistics Netherlands 2019. Available from: https://www.cbs.nl/en-gb.
30. Fiser DH, Long N, Roberson PK, Hefley G, Zolten K, Brodie-Fowler M. Relationship of pediatric overall performance category and pediatric cerebral performance category scores at pediatric intensive care unit discharge with outcome measures collected at hospital discharge and 1- and 6-month follow-up assessments. Crit Care Med 2000;28:2616–20.
31. Pollack MM, Holubkov R, Funai T, et al. Relationship between the functional status scale and the pediatric overall performance category and pediatric cerebral performance category scales. JAMA Pediatr 2014;168:671–6.
32. Berg RA, Nadkarni VM, Clark AE, et al. Incidence and outcomes of cardiopulmonary resuscitation in PICUs. Crit Care Med 2016;44:798–808.
33. Slomine BS, Silverstein FS, Page K, et al. Relationships between three and twelve month outcomes in children enrolled in the therapeutic hypothermia after pediatric cardiac arrest trials. Resuscitation 2019;139:329–36.
34. Nakashima T, Noguchi T, Tahara Y, et al. Public-access defibrillation and neurological outcomes in patients with out-of-hospital cardiac arrest in Japan: a population-based cohort study. Lancet 2019;394:2255–62.
35. Blom MT, Beesems SG, Homma PC, et al. Improved survival after out-of-hospital cardiac arrest and use of automated external defibrillators. Circulation 2014;130:1868–75.
36. Banerjee PR, Ganti L, Pepe PE, Singh A, Roka A, Vittone RA. Early on-scene management of pediatric out-of-hospital cardiac arrest can result in improved likelihood for neurologically-intact survival. Resuscitation 2019;135:162–7.
37. Geocadin RG, Callaway CW, Fink EL, et al. Standards for studies of neurological prognostication in comatose survivors of cardiac arrest: a scientific statement from the American Heart Association. Circulation 2019 CIR0000000000000702.
38. Hunfeld M, Muusers MAC, Catsman CE, Castillo JD, Tibboel D, Buysse CMP. The current practice regarding neuro-prognostication for comatose children after cardiac arrest differs between and within European PICUs: a survey. Eur J Paediatr Neurol 2020;28:44–51.
39. Kirschen MP, Walter JK. Ethical issues in neuroprognostication after severe pediatric brain injury. Semin Pediatr Neurol 2015;22:187–95.
40. Ostendorf AP, Hartman ME, Friess SH. Early electroencephalographic findings correlate with neurologic outcome in children following cardiac arrest. Pediatr Crit Care Med 2016;17:667–76.