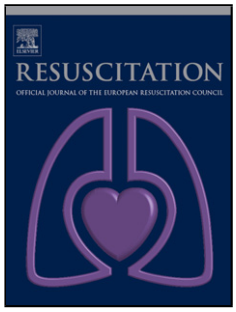

Title: Early On-Scene Management of Pediatric Out-of-Hospital Cardiac Arrest Can Result in Improved Chances for Neurologically-Intact Survival

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PII: S0300-9572(18)31080-3
DOI: https://doi.org/10.1016/j.resuscitation.2018.11.002
Reference: RESUS 7803

To appear in: *Resuscitation*

Please cite this article as: 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 Chances for Neurologically-Intact Survival, *Resuscitation* (2018), https://doi.org/10.1016/j.resuscitation.2018.11.002

Early On-Scene Management of Pediatric Out-of-Hospital Cardiac Arrest Can Result in Improved Chances for Neurologically-Intact Survival

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Running Title:
Managing Pediatric Cardiac Arrest On-Scene

ABSTRACT

Aim: To evaluate the frequency of neurologically-intact survival (SURV) following pediatric out-of-hospital cardiac arrest (POHCA) when comparing traditional early evacuation strategies to those emphasizing resuscitation efforts being performed on-scene.

Methods: Before 2014, emergency medical services (EMS) crews in a county-wide EMS agency provided limited treatment for POHCA on-scene and rapidly transported patients to appropriate hospitals. After 2014, training strongly enhanced EMS provider comfort levels with on-scene resuscitation efforts including methods to expedite protocols on-site and control positive-pressure ventilation. Frequency of SURV (hospital discharge) was compared for the two years prior to initiating the immediate on-scene care strategy to the ensuing two years following implementation.

Results: Between 01/01/2012 and 12/31/2015, 94 children experienced POHCA. There were no significant differences before and after the on-scene focus in terms of age, sex, etiology, presenting electrocardiograph, drug infusions or bystander-performed cardiopulmonary resuscitation and total scene times actually remained similar (14.3 vs. 17.67 minutes). SURV increased significantly upon implementation of the immediate on-scene management strategy and was sustained over the next two years (0.0 % to 23%; p=0.0013). Though statistically-indeterminate in this analysis, the improvement was associated with a shorter mean time to epinephrine administration among resuscitated patients (16.6 vs. 7.65 minutes).

Conclusion: Facilitating immediate on-scene management of POHCA can result in improvements in life-saving. Although a historically-controlled evaluation, the compelling appearance of neurologically-intact survivors was immediate and sustained. Targeted training, more efficient, physiologically-driven procedures, and trusted encouragement from supervisors, likely played the most significant roles and not necessarily extended scene times.

Keywords:
Pediatric Cardiac Arrest, CPR, Cardiopulmonary Arrest, Epinephrine, EMS, Emergency Medical Services, Pediatric Advanced Life Support, Intraosseous

INTRODUCTION:

Despite rapidly-responding emergency medical services (EMS) systems with advanced life support (ALS) providers, chances for neurologically-intact survival following onset of pediatric out-hospital cardiac arrest (POHCA) have remained dismal [1-7].

The scene of a POHCA frequently can be volatile and intimidating, particularly considering sporadic EMS provider experience with pediatric ALS skills and anatomical challenges of smaller blood vessels and dissimilar airways [8,9]. Typically the end-result of an evolving oxygen-deprived state and resulting progressive brady-asystolic process, POHCA (loss of circulation) generally indicates a prolonged insult [1-10]. Poor outcomes have become the expectation, often diminishing fervor for effecting success [8,9]. Even following a drowning insult, which generally carries a very favorable prognosis when bystanders rapidly perform basic cardiopulmonary resuscitation (CPR), the onset of circulatory arrest indicates that subsequent ALS interventions will generally be futile [7,11,12].

Considering these challenges, the easier ability to pick-up and carry away a child has led to the very understandable, commonplace practice to rapidly transport pediatric patients to the hospital, attempting ALS resuscitation enroute. This approach has become well-accepted in many jurisdictions, particularly in the United States (U.S.) where pediatric-capable facilities are frequently nearby, offering advantageous resources and technologies including extracorporeal membrane oxygenation (ECMO) [13,14]. In addition, recent conventional wisdom has discouraged endotracheal intubation (ETI) for POHCA while emphasizing a renewed focus on optimizing basic life support (BLS) techniques [6,15,16].

Still, the pathophysiology of POHCA infers the need for the earliest possible interventions. As most cases present with asystole, advanced airway and intravascular epinephrine are typically recommended [15]. Physiologically-speaking, delaying these indicated interventions and risking sub-optimal CPR during scene evacuation clearly seem less preferable.

Prior to 2014, *Polk County Fire-Rescue*, the EMS agency for Polk County, Florida (U.S.), like so many other agencies, provided rapid transport of POHCA patients. While outcomes for adult out-of-hospital cardiac arrest had become very respectable in Polk County, like most other U.S. jurisdictions, survival chances for children remained bleak. Resulting citizen CPR training campaigns did increase the frequency of bystander CPR somewhat, even for children, but outcomes for POHCA, remained dismal.

Hypothesizing that expediting immediate on-scene ALS interventions might improve outcomes for children, *Polk County Fire-Rescue* embarked on a new quality improvement initiative that included: 1) enhanced training/skills-retention for a targeted cadre of ALS providers who could immediately provide ETI or the i-gel^{R} (*Intersurgical Inc,* U.K.) supraglottic airway; 2) immediate intraosseous vascular access (deferring intravenous attempts); and 3) more rapid techniques for epinephrine dosing (e.g., "system one" approaches); and 4) specialized interactive training to help mitigate the emotional challenges encountered on-scene [8,17-19].

Therefore, the specific aim of this analysis was to compare the observed outcomes, and specifically the rates of survival to hospital discharge with favorable neurological status, when

POHCA patients are rapidly evacuated with care attempted enroute versus use of a strategy that focused upon rapid on-scene ALS interventions and psychological support for bystanders and rescuers alike.

METHODS:

Setting:

Located in mid-central Florida (2,010 square miles), Polk County had 642,000 residents including 18% <14 years of age with 72% designated Caucasian, 21% Hispanic and 16% African-American at the midpoint of the analysis. Mean annual income was $43,000, 50% had college or graduate degrees and 72% dwelled in single-family homes.

With annual call volumes averaging ~115,000, *Polk County Fire-Rescue* teams medically manage all aspects of dispatch, BLS first-responders and ALS-providing paramedics. Data for all cardiac arrest incidents have been collected prospectively and recorded in a comprehensive, population-based, *Utstein*-style registry utilizing the respective consensus definitions and reporting output [20,21].

Throughout the planned period of analysis (2012 through 2015), all cases of children ≤14 years of age were managed according to the 2010 *American Heart Association* (AHA) consensus guidelines for POHCA regardless of the site of care, be it off-scene or on-scene [15]. Considering that these guidelines were published in 2010 and relevant training ensued during early 2011, the POHCA cases evaluated here purposely began with those occurring after 01/01/2012 to ensure protocol consistency throughout the evaluation period while also better

ensuring steady-state performance nearly a year after system-wide implementation of the new guidelines.

Institutional Review Board:

The project was submitted and reviewed by the *University of Central Florida Institutional Review Board #1* (IRB identification # SBE-17-13224) with the last review dated June 26, 2017. All interventions were compliant with concurrent AHA guidelines [15]. Patient privacy was maintained using de-identified data and findings were considered part of an intrinsic quality assurance project conducted by a governmental public safety agency.

Specific Periods of Observations

2012-2013: Prior to 2014, POHCA patients were managed in the traditional manner involving rapid evacuation to one of several appropriate receiving facilities while attempting ALS interventions after leaving the scene.

2014-2015: In early 2014, EMS crews managed cases using the same guidelines but were strongly encouraged (and trained) to facilitate immediate ALS care on-scene (Table 1) including rapid insertion of an advanced airway, immediate intraosseous placement, early epinephrine infusion (using age-based doses) and tightly-controlled ventilatory rates [18,19,22-25].

Primary Outcomes To Be Observed:

All patients were followed to hospital discharge and beyond, but, for the purposes of this project, patients were tracked specifically for: 1) return of spontaneous circulation (ROSC), defined here as any sustained palpation of natural pulses for five minutes; and 2) the primary outcome of successful hospital discharge with favorable neurologically-intact status (SURV) using criteria equivalent to a modified Rankin-scale (mRS$\leq$3) for the older children (i.e., $\geq$9 years) or the return of age-specific normal functions and responses for the infants and younger children using methods akin to the Vineland Adaptive Behavior Scale, 2nd Edition [26]. The frequency of SURV for the two-year period (2012-13), prior to the focus on on-scene care, was compared to that for 2014-15 using two-sided tests (Fisher's Exact) with a proscribed p-value of < 0.01.

Other outcomes included time from arrival on-scene (vehicle halting at the designated address) to the moment that epinephrine was first administered as well as the time spent on-scene prior to ambulance departure and also the frequency of intubation and supraglottic airway placement.

Data Analysis

All variables using the Utstein-style template, including response intervals, identified etiology, presenting electrocardiograph (ECG), performance of CPR by bystanders and witnessed event status, were stored in a secure database system with patient confidentiality maintained through de-identified abstracting of applicable items [20,21]. Statistical analyses were performed in JMP 12.0 for the Mac. In addition to primary head-to-head comparisons of SURV in 2012 and 2013 to 2014-2015, logistic regression models were also examined to further identify any predictors of ROSC and SURV including: 1) age; 2) arrest witnessed by bystanders; 3) presenting rhythm; 4) defibrillator use; 5) time from the child being found or having onset of cardiac arrest until arrival

of the EMS crews on the scene; 6) chest compressions initiated by bystanders versus EMS crews; 7) "any treatment" by bystanders prior to EMS arrival.

RESULTS

Over the prospectively-defined four-year evaluation, EMS faced 94 consecutive POHCA patients, the great majority of whom present with asystole (80%) or with pulse electrical activity (PEA) throughout (defibrillation attempts were indicated in only 2% of cases). The median age was 12 months, with an interquartile range (IQR) of 3 to 24 months (range: 0 to 10 years). The primary etiology was 85% respiratory (including drowning arrests) as well as trauma (8%); seizure (3%) cardiac/medical (2%); and choking (2%).

Comparing 2012-2013 to 2014-15, there were no significant differences in terms of age, sex, etiology (including drowning events and trauma cases), presenting ECG, response intervals, drug sequencing, frequency of bystander CPR or relative transport distributions to the same hospitals. Advanced airways (ETI or i-gel^{R}) were placed in 40% of cases and more frequently in 2014-2015, but the numbers were too small to be determine any statistical difference before and after 2014. Due to aggressive county-wide layperson CPR training programs, the frequency of bystander CPR during the study period remained relatively high throughout all four years, being performed in 51.0% of cases (44.7% in 2012-13 and 53.6% in 2014-15; p = NS).

After implementing the focus on immediate on-scene care, the frequency of ROSC rose significantly (p=0.0033; 2-tailed Fisher's Exact) from 5.3% (2012-13) to 30.4% (2014-2015). In terms of the primary end-point, the frequency of neurologically-intact survival improved significantly (Fig. 1) from 0/38 in 2012-13 to 23.2% (13/56) in 2014-15 (p=0.0013; 2-tailed Fisher's Exact).

Among those resuscitated, the mean time from arrival at the street address to the first epinephrine infusion contracted from 16.6 minutes (2012-13) to 7.65 minutes (2014-15). Although qualitatively the mean time to epinephrine administration appeared to be inversely related to the outcome (Fig. 1), because of the small sample size, this observation was deemed statistically indeterminant in this current 4-year analysis.

Of note, actual on-scene times, measured from arrival at the street location until the time of ambulance departure from that location, were not remarkably altered with a mean scene-time of 14.85 minutes in 2012-2013 versus 17.67 minutes in 2014-2015.

As would be predicted, logistic regression analysis revealed that a shorter time elapsed from identification of the POHCA until EMS arrival was significantly associated with ROSC and SURV (both p <0.0001 for both outcomes, respectively) as well as older age (p <0.0001 for ROSC and p= 0.0236 for SURV, respectively). Interestingly, however, initial performance of CPR by EMS personnel (versus bystanders) was significantly associated with ROSC and SURV (both p<0.0001). At the same time, "any treatment" before EMS arrival was still associated with better outcomes (p<0.0001). In contrast to adult predictors, neither use of an automated external

defibrillator (only 2% of cases) or witnessed POHCA (only 13% of cases) could be demonstrated to be statistically significant factors with regard to any of the outcomes.

DISCUSSION

Although this analysis carries the typical limitations of a historical control and a bundled approach to care, its findings still remain compelling. After experiencing negligible survival chances for many years, and well before the defined period of analysis, the sudden appearance of a large number of neurologically-intact survivors following the renewed focus on rapid on-site care was immediate, sustained and significant. Whatever the key independent variables might have been, the actions taken to focus on optimal, early on-scene care clearly made an irrefutable improvement for the community involved. Most importantly, the findings also help to diminish pervasive pessimism about the chances of survival following POHCA [18].

While one may broadly attribute the outcome improvements to the classic nuances associated with a historical control design such as better training, better logistical organization, a "Hawthorne effect" and/or progressive experience of the team, all of those pivotal components of training and accompanying logistical techniques to expedite the rapid provision of the indicated care, including ALS interventions, did, in fact constitute the central intent of this evaluation.

Though indeterminate statistically in this limited sample size, the observed trend (Fig. 1). between progressively-improving survival rates and earlier infusion of epinephrine (Fig. 1) remains a compelling and hypothesis-generating finding, and it supports what others have also observed [27-29]. Even if just a surrogate marker for other factors such as earlier delivery of care or suboptimal CPR while evacuating and transporting, this observation still deserves further attention [30-32]. Also, whether ALS interventions are the key factor or not, the "system-one" dosing strategy employed here not only expedited indicated care delivery, but it helps to avoid dosing errors and allows for simpler therapeutic decision-making at the typically volatile POHCA scene [18,19,33,34].

Crews were also purposefully cross-trained to monitor each other with respect to avoiding overzealous positive-pressure ventilation (PPV) delivery [23-25,35-39]. Poor outcomes for cardiac arrest patients, adults and children alike, have been attributed in part to excess PPV during the low flow state of basic CPR and other compromised circulatory states [23-25,35-39]. It has been conjectured further that the common emphasis on POHCA being due to an underlying "respiratory" cause might bias rescuers to provide more breaths for the child than necessary [23,39]. Also, PPV-induced impairment to flow during CPR can be frequently exacerbated by any accompanying hypovolemia, common in childhood critical illness and POHCA [4-6,23,35]. Regardless, once any patient has reached a state of circulatory arrest, frequent PPV is detrimental. Successful ETI may even facilitate this harmful effect when ventilation is not appropriately controlled. This may explain poor outcomes, not only in terms of prior POHCA airway studies, but also poor outcomes for children day-to-day, intubated or not [6,23,25,37,38].

While uncontrolled ventilation practices have, in part, been responsible for controversies regarding ETI, EMS-oriented training and frequency of skills utilization are also key factors [39]. Concerns regarding prehospital ETI are appropriate if systems are not designed to enhance skills utilization and control ventilation [23,39]. In this program, ALS providers received frequent simulation practice utilizing high-fidelity pediatric models with anterior-positioned vocal cords and teams were deployed to facilitate more frequent experience with ETI (and i-gel^{R} back-up). A direct association between rapid advanced airway placement and improved SURV could not be determined statistically with this sample, but enhanced skills experience and controlled ventilation should still be considered another hypothesis-generating component.

In Polk County, quality chest compressions and accompanying pit-crew approaches, recognized factors in successful resuscitation, had already been emphasized and closely-monitored in the pre-2012 era with implementation of the 2010 AHA guidelines. However, one could argue that CPR during rapid evacuation and transport would have compromised CPR quality. Therefore, more optimal performance of CPR on-scene might have been a major contributing factor.

If the main conclusions drawn from this analysis are to simply re-emphasize a focus on delivering indicated care more rapidly on-scene (versus attempting rapid transport), they do not necessarily imply that a longer on-scene is better. Earlier reports have correlated improved outcomes with longer on-scene intervals [30]. However, these findings may simply reflect a matured system that effectively provides the indicated care on-site than the crude measurement of time spent on-scene. In this current evaluation, on-scene intervals were not much longer than

in the rapid transport phase. In most cases, the logistics of arriving and retrieving stretchers and equipment, locating the patient and later securing the lifeless child while trying to perform CPR and ventilation during evacuation to the ambulance can be a lengthy undertaking. Preparing for travel and strapping-in/securing the patient (and accompanying guardians) can take a finite amount of time and even constitute the majority of on-scene time. Future studies should therefore delineate actual "bedside' time versus the other aspects of on-scene time. It should also account for care provided beyond the original scene including care given in back of the ambulance and attempting resuscitation before scene departure. Nonetheless, the findings here infer a emphasis on providing expedited on-scene care and not simply spending more time on-scene.

As ECMO has been rolled out more recently for children with some successes, there may be a renewed role for rapid transport. However, that poses a different question than that posed by the current evaluation. Also, based on the dramatic findings here, one might still argue for rapid on-scene interventions initially, whether ECMO resources are available or not.

Despite the face-value results, *caveat emptor* still applies. Two positively-influencing factors, bystander CPR and the proportion of patients involved in drowning incidents, remain intrinsic considerations. The frequency of bystander CPR, a well-known driver of better outcomes, increased slightly over the course of our project, but those differences were neither very large nor statistically significant. More specifically, the incremental number of survivors who received bystander CPR could not fully account for the profound improvements observed overall.

The same considerations apply to drowning events. Generally, a rapid-onset asphyxial event, drowning can be far more reversible than most critical pediatric crises when early bystander CPR is performed [7,11,12]. The number of drowning cases did increase somewhat over the course of the evaluation, but again these were neither statistically significant differences nor large enough to account for the overall differences in outcome. Also, once drowning events without bystander CPR progress onto POHCA, the historical prognosis is dismal. In essence, even if contributory, the frequency of bystander CPR and drowning cases would not entirely explain the longstanding negligible survival rates for many years prior, with or without bystander CPR or a drowning etiology.

CONCLUSIONS:

Dealing with critically ill children is, understandably, anxiety-provoking, both technically and environmentally, but the typical resulting practice of early evacuation from the scene may be detrimental. Based on this study and inferences from other published data, encouraging immediate, efficient and psychologically-supported on-scene management of POHCA can result in substantial improvements in life-saving. Although this analysis involved a historically-controlled design, the immediate appearance of neuro-intact survivors was profound and it was sustained while no other factors changed significantly. Specialized training involving pre-planned efficiencies (Table 1) and trusted encouragement from medical supervisors were part of a bundled approach that had the most significant role.

Funding Sources: None

Declaration of Conflict of Interest: None to disclose

CONFLICT OF INTEREST STATEMENT:

None of the authors have any conflict of interest to disclose and there were no external sources of funding or sponsors for the project.

ACKNOWLEDGEMENTS:

The authors extend their deepest gratitude to the men and women of the *Polk County Fire-Rescue* EMS system whose day-to-day dedication to an extraordinary level of public service made this project and the resulting life-saving possible. They also express their deepest sympathy to the families who experienced the tragedy of childhood cardiac arrest as well as our strongest appreciation for those families and the receiving facilities who uniformly provided the critical outcome information that we needed to report the results. The authors also thank Gary Ball and Lisa Correll, the *Polk County Fire-Rescue* data analysts who maintained the *Utstein-style* registry and tabulated the data for the investigators.

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TABLE I: Modified strategies in the EMS system that were established to facilitate more immediate on-scene resuscitative care including advanced life support (ALS) interventions.

- EMS system changes involved creation of a cadre of highly-skilled paramedics with rapid ALS capabilities who repeatedly received additional training in high-fidelity simulated endotracheal intubation and supraglottic airway placement that included difficult airways and anteriorly-oriented pediatric vocal cords.
- Additional proficiency training in supra-glottic airway (i-gel^{R}) use and appropriate bag-valve device use (two-person, tight seal) delivering a breath large enough to create chest wall rise (given over 1-2 seconds) followed by a quick release to permit rapid expulsion of expired air.
- Use of controlled ventilatory rates (i.e., ~1 breath every 10 seconds) that were closely monitored by all to ensure a disciplined approach in an otherwise charged environment.[23]
- Rapid intraosseous insertion into proximal tibia and earliest possible adrenaline (epinephrine) infusion immediately followed by saline fluid bolus infusion.
- Dosing of epinephrine using a proscribed "system-one thinking" approach that was predetermined by the patient's approximate age.[18,19]
- Interactive training with special psychological tools and methods for providing better reassurances and successful interface with family members and other bystanders along with team support training among all responding crew members.
- Use of a "pit-crew" type of approach as previously described.[22]

FIGURE 1: Comparison of return of spontaneous circulation (ROSC) and neurologically-intact survival when using a traditional rapid scene evacuation approaches to pediatric out-of-hospital cardiac arrest (2012 and 2013) versus a focus on immediate on-site delivery of indicated care including advanced life support interventions on-scene (2014 and 2015).