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Clinical paper

Long-term multidisciplinary follow-up programs in pediatric cardiac arrest survivors



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Abstract

Long-term outcome studies after pediatric cardiac arrest (CA) are few. They require a CA registry and dedicated outcome teams. Learning about the long-term outcomes is very important for developing prognostication guidelines, improving post-cardiac care, counseling caregivers about the future of their child, and creating opportunities for therapeutic intervention studies to improve outcomes.

Few PICUs worldwide provide a multidisciplinary follow-up program as routine practice at an outpatient clinic with standardized measurements, using validated instruments including neuropsychological assessments by psychologists. The primary goal of such a follow-up program should be to provide excellent care to children and their caregivers, thereby resulting in a high attendance. Pediatric psychologists, neurologists and pediatricians/pediatric intensivists should ideally be involved to screen for delayed development and psychosocial problems and offer appropriate care at the same time. Preferably, outcomes should consist of evaluation of morbidity (physical and neuropsychological), functional health and Health Related Quality Of Life (QoL) of the patient and their caregivers.

Keywords: Cardiac arrest, Children, Neuroprognostication, Long-term outcome, Follow-up

Long-term outcomes in cardiac arrest survivors

Background

There are few long-term outcome studies after pediatric cardiac arrest (CA). There are several reasons: 1) CA in children is rare, with low survival rates (e.g. 8–39% survivors to hospital discharge after out-of-hospital cardiac arrest (OHCA)), and 2) CA in children occurs in broad age categories (0–17 years) with different stages of development of the central nervous system causing challenging neuroprognostication.^{1–5} Also, long-term follow-up requires a CA registry and dedicated outcome teams.

Learning about the long-term outcomes is very important for various reasons: 1) it is necessary for the development of prognostication guidelines, 2) it can improve post-cardiac care (PCAC) if we have a better understanding of the impact of various PCAC elements on long-term outcome, 3) it helps in counseling caregivers and medical professionals about the future of their child or patient, and 4) it creates opportunities for therapeutic intervention studies to improve outcome.

An overview of the landmark studies regarding long-term outcomes

Slomine et al. described neuropsychological outcomes in a cohort of 160 children (unresponsive and mechanically ventilated after return of circulation (ROC)).⁶ One year after IHCA and OHCA, survivors had worse intelligence scores and neuropsychological testing scores compared with normative data. Children under the age of 6 achieved a median score of 67 (interquartile range: 49 – 83) on the Mullen Early Learning Composite. Notably, 56% of these children scored more than 2 standard deviations below the median norm score of 100. In case of children aged 6 or older, their overall performance on intelligence and neuropsychological tests was significantly below the norm. Specifically, the Executive Functioning and Visual Memory domains exhibited the most significant impact. Between 30% and 61% of the children scored below the median score of 70 on these domains, exceeding 2 standard deviations below the median norm score.

Hunfeld et al. investigated longitudinal functional and neuropsychological outcomes in 49 OHCA survivors as part of standard of

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<https://doi.org/10.1016/j.resplu.2024.100563>

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care.⁷ Although these OHCA survivors had a good pediatric cerebral performance category (PCPC) score 3–6 and 24 months post-OHCA (74% and 73% respectively), their IQ scores were lower compared with normative data. Similar to Slomine et al., they also obtained worse scores on attention, processing speed, and cognitive flexibility. Nevertheless, the majority of school-aged children (81%) went back to school without change in school level 24 months after OHCA.

Recently, Hickson et al. evaluated long-term outcomes (at least one year after OHCA) in 44 survivors <18 years old at time of arrest.⁸ Different domains (e.g. healthcare utilization, functional outcome, neuropsychological functioning, health-related quality of life) were assessed with validated questionnaires. As a result, survivors with unfavorable outcome at discharge had worse functional status scale (FSS) and motor function scores compared with survivors with favorable outcome. Utilization rates of rehabilitation services were higher and greater disruption of family functioning was reported too.

This is one of the landmark studies for several reasons: it was a true long-term outcome study (median 5.6 years post-OHCA), including young adults among the survivors and outcome was assessed on the relevant domains (e.g. daily living skills, impact on parents and family functioning). Based on the relatively short cardiopulmonary resuscitation (CPR) duration for OHCA (median 5 minutes, IQR 1–7) and low response rate (25%), their study population may not be representative of the entire OHCA population.

In 2021, a pediatric core outcome set for CA in children (P-COSCA) was developed by international multidisciplinary health care providers and parents/caregivers, with the purpose to promote consistency in CA outcomes research.⁹ A core set of 5 outcomes was identified; survival, brain function, cognitive function, physical function, and basic daily life skills at different time points post-CA (Table 1).

Where are the gaps?

There are multiple gaps in knowledge regarding the long-term impact on and development of cognitive vulnerabilities throughout the lifespan of CA survivors. Moreover, the psychosocial impact and their participation in daily life are still unclear. From follow-up studies in other children with acquired brain injury (e.g., TBI or brain tumor) we know that these children may develop new deficits over time.^{10–13} Therefore, follow-up over a longer time span is needed.

Another research gap is that the pathophysiological mechanisms underlying the neuropsychological deficits in children post-CA are not well understood. During CA the brain is injured directly as a result of loss of blood flow (no-flow time) and the suboptimal flow that depends on the duration and quality of CPR. Secondary neurological injury has also been described due to reperfusion after successful

resuscitation. The neuronal injury cascade leading to cell death is a complex process, including excitotoxicity, disrupted calcium homeostasis, free radical formation, pathological protease cascades, and activation of cell death signaling pathways.^{14–15} The areas which are most vulnerable to ischemia are the cerebral cortex, watershed areas, subcortical white matter, vascular end zones, hippocampus, cerebellar Purkinje cells and basal ganglia.^{14,16–20} Unfortunately to date, no studies have been performed correlating MRI (qualitative and quantitative) results with neuropsychological findings.

A key question regarding long term outcome of CA survivors is: What are the predictors of participation in daily life and productivity in their adult life?

On a global level one must realize that there are different opinions regarding a “favorable” or “valuable” outcome based on cultural and religious beliefs, ethnicity, and personal experiences.

Follow-up programs in CA survivors

Only a few PICUs worldwide provide a multidisciplinary follow-up program as routine practice at an outpatient clinic with standardized measurements, using validated instruments including neuropsychological assessments by psychologists.^{7,21,22} Requirements for such a successful follow-up program are: 1) survivors can easily access the outpatient clinic, 2) medical care is paid for by health insurance companies, 3) dedicated multidisciplinary teams. In some European countries these requirements are already fulfilled.²³

The primary goal of such a follow-up program should be to provide excellent care (e.g. screening for delayed development and psychosocial problems and offer appropriate care at the same time) to children and their caregivers, thereby resulting in a high attendance. Pediatric psychologists, neurologists and pediatrician/pediatric intensivists should ideally be involved. Preferably, outcome should consist of evaluation of morbidity (physical and neuropsychological), functional health and Health Related Quality Of Life (QoL), also of the caregivers/family given the interdependence between child and family. No telephone interview or solely on-line surveys (e.g. in the context of research) but an on-site visit to a multidisciplinary outpatient clinic as routine practice should be organized in order to increase the quality of outcome data and maximize the attendance (and thus minimize selection bias). When on-site visits to an outpatient clinic are impossible (due to financial reasons, travel logistics, time-off-work limitations) a virtual consultation could be considered. Preferably, multidisciplinary follow-up should continue into adulthood because survivors may develop new deficits over time.

At the PICU of Erasmus MC-Sophia Children’s hospital in Rotterdam, The Netherlands, OHCA and IHCA survivors are invited to a

Table 1 – P-COSCA.

Outcome (domains)	Measure	Time point	Methods
Survival		Hospital discharge and/or 3 months after CA Between 6–12 months after CA	Caregiver report Medical records Death registry
Brain function	PCPC	Baseline Hospital discharge and/or 3 months after CA Between 6–12 months after CA	Caregiver report Medical records
Cognitive function	PedsQL Scales	Between 6–12 months after CA	Caregiver report
Physical function	PedsQL Scales		
Basic daily life skills	PedsQL Scales Daily Activities Scale		

Table 2 – Dutch follow-up program for pediatric CA survivors.

Domains	Tests	Performed by	Timing post arrest
Health status and physical functioning	Interview	Pediatric intensivist	3–6, 12 and 24 months
	Physical and neurological exam	Pediatric neurologist	Age 5, 8, 12 and 17 years
	Questionnaires regarding health status and health perception	Patient and parents/caregivers	
Neurocognitive functioning	Neuropsychological assessment	Psychologist	3–6 and 24 months
	Questionnaires regarding executive functioning	Patient and parents/caregivers	Age 5, 8, 12 and 17 years
Motor functioning	Motor functioning testing	Physical therapist	3–6, 12 and 24 months Age 5, 8, 12 and 17 years
Quality of life, mental health, participation ¹	Questionnaires ²	Patient and parents/caregivers	3–6, 12 and 24 months Age 5, 8, 12 and 17 years

¹ Quality of life and mental health for both patient and parents.

multidisciplinary follow-up program at the outpatient clinic (Table 2).²²

In 2020 Gregorio Marañón Hospital in Madrid, Spain, also designed a follow-up program mirroring Erasmus MC-Sophia Children's hospital experience (see [supplementary files](#)).

Long-term outcomes in caregivers and siblings

It is urgently necessary not only to assess the child's outcome, but also that of caregivers and other family members. Family members may suffer from psychosocial sequelae after hospital discharge, also known as 'post-intensive-care syndrome-pediatric' (PICS-p).²⁴ They will have to cope with their grief and the trauma caused by the child's hospital admission. Additionally, families end up in a new situation where their child has neurological sequelae with a big impact on every family member. Family dynamics may change, which can result in parental separation or divorce. Caregivers may not be able to return to their jobs and sometimes they even lose their jobs due to high needs of their child, with all the financial consequences that this entails.

However, a life-threatening situation such as a pediatric CA may also bring more cohesion in the family. Caregivers are grateful that their child is still alive after this nerve-racking period.²⁵ Family functioning and well-being are important factors that have been demonstrated to have a positive effect on the child's outcome.²⁶ There is an urgent need of structural support of caregivers and siblings by a professional team of social workers and pediatric psychologists, not only during the child's hospitalization but also afterwards. A support program needs to be developed, probably first in the context of research with the ultimate goal of implementing it as a standard of care. Within this program, caregivers and siblings should be provided with information, education and support. This is called a 'parent or family empowerment program'.

Development of this process can start with the implementation of screening questionnaires for caregivers and siblings that cover different aspects:

1. The experiences of caregivers around the CA-event and during hospitalization of their child. What were their needs during this period?

2. Screening, during and after hospitalization, of psychosocial functioning and participation of caregivers. This will gain good insight of how caregivers and siblings are doing and what their needs are.

Neuroprognostication and guideline development

In addition to patient care, follow-up data can be used for research purposes as well. In future outcome studies, associations between pre-CA variables (e.g. pre-existing co-morbidity, socio-economic status), CA variables (e.g. cause, first rhythm, witnessed arrest, duration CPR), post-CA variables (e.g. first lactate and pH post-ROC, neurological exam, EEG and brain MRI findings) and long-term outcomes should be investigated in large patient samples with the ultimate goal of the development of a prediction model (Fig. 1). PCAC care could also be improved with a better understanding of the impact of various PCAC elements on long-term outcomes, which is also an argument to involve a pediatric intensivist in the multidisciplinary outcome team.

There is also a need for an accurate outcome measure at hospital discharge that is easy to apply but predictive for long-term sequelae and is also applicable to young children. Such a measure will enable clinicians to inform the child and their caregivers and provide the right care in the right place during their recovery. Often the PCPC score is used as an outcome measure. The PCPC was developed to easily measure short-term morbidity after pediatric intensive care. It is a functional outcome scale ranging from 1-6 (normal, mild, moderate/severe disability, comatose, or (brain) death), focusing on daily activity of school-going children. Obviously, when performing follow-up of CA survivors, the PCPC is a crude outcome measure. Its use in pediatric CA research causes some problems in defining 'favorable' outcome, like timing (e.g. at hospital discharge it is unknown whether a child will be able to return to the same school grade) and age. The majority of children with CA do not attend school yet and are dependent in performing daily activities.

In future long-term outcomes studies after CA, the study population should ideally represent the entire OHCA and IHCA population, including non-survivors (and cause of mortality) after return of circulation (ROC), in a prospective CA registry. A substantial number of

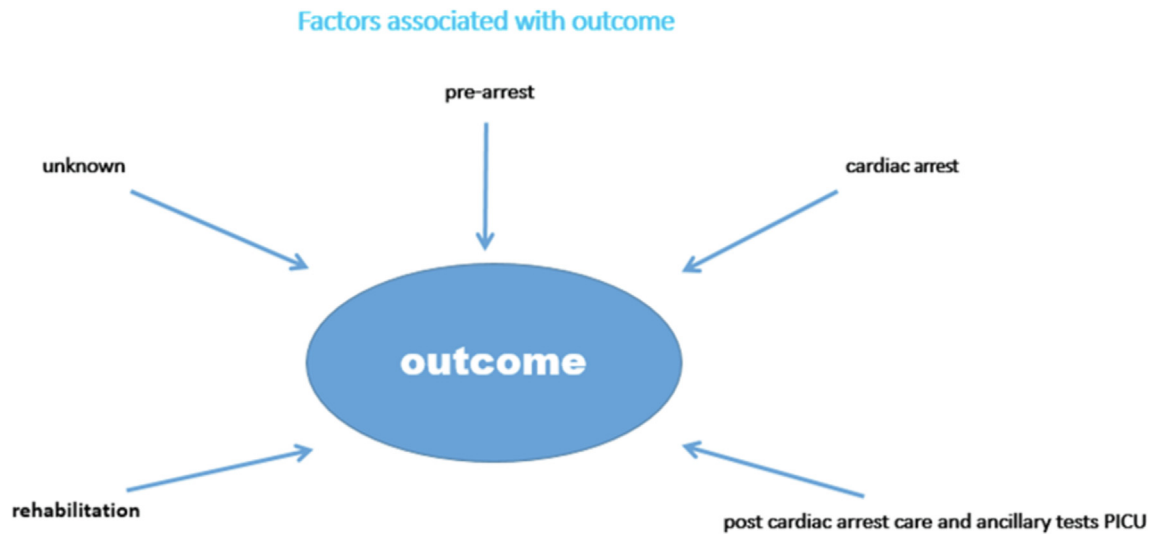


Fig. 1 – Factors associated with outcome.

children who achieve ROC die prior to hospital discharge. Causes of death at the PICU are mostly WLST, based on poor neurological prognosis or brain death.^{27–28} Lower percentage of WLST in a CA cohort may lead to more severe long-term neurological deficits. In addition, *after* hospital discharge it is important to understand the cause of death in non-survivors (e.g. was it related to the CPR event?). In which case, these non-survivors should be added to the unfavorable outcome group.

Conclusion and future perspectives

Long-term outcome studies after pediatric CA are few. They require a CA registry and a follow-up program. Requirements for a successful follow-up program are: 1) survivors can easily access the outpatient clinic, 2) medical care is paid for by health insurance companies, 3) dedicated multidisciplinary outcome teams, 4) it should be organized as routine practice with standardized measurements, using validated instruments including neuropsychological assessments. In some European countries these requirements are already fulfilled. The different follow-up clinics need to collaborate so that outcomes can be compared in large patient samples and PCAC, neuroprognostication and long-term outcome can be optimized.

CRedit authorship contribution statement

M. Hunfeld: Writing – review & editing. **K. Dulfer:** Writing – review & editing. **J. Del Castillo:** Writing – review & editing. **M. Vázquez:** Writing – review & editing. **C.M.P. Buysse:** Writing – original draft.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.resplu.2024.100563>.

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