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ABSTRACT

Objective: To describe caregiver burden among those whose children survive in-hospital cardiac arrest and have high risk of neurologic disability, and explore factors associated with burden during the first year post-arrest.

Methods: The study is a secondary analysis of the Therapeutic Hypothermia after Paediatric Cardiac Arrest In-Hospital (THAPCA-IH) trial. 329 children who had an in-hospital cardiac arrest, chest compressions for > 2 min, and mechanical ventilation after return of circulation were recruited to THAPCA-IH. Of these, 155 survived to one year, and caregivers of 138 were assessed for burden. Caregiver burden was assessed at baseline, and 3 and 12 months post-arrest using the Infant Toddler Quality of Life Questionnaire for children < 5 years old and the Child Health Questionnaire for children > 5 years. Child functioning was assessed using the Vineland Adaptive Behaviour Scales Second Edition (VABS-II), the Paediatric Overall Performance Category (POPC) and Paediatric Cerebral Performance Category (PCPC) scales, and caregiver perception of global functioning.

Results: Of 138 children, 77 (55.8%) were male, 77 (55.8%) were white, and 109 (79.0%) were < 5 years old at the time of arrest. Caregiver burden was greater than reference norms at all time points. Worse POPC, PCPC and VABS-II scores at 3 months post-arrest were associated with greater caregiver burden at 12 months. Worse global functioning at 3 months was associated with greater burden at 12 months for children < 5 years.

Conclusions: Caregiver burden is substantial during the first year after paediatric in-hospital cardiac arrest, and associated with the extent of the child's neurobehavioural dysfunction.

Introduction

Caregiver burden is a multidimensional concept that reflects the stress and time demands of providing care for another person [1–3]. Parents providing care for children with disabilities often experience caregiver burden, which can lead to impaired parental health and decreased ability to care for the child. Children who survive a cardiac arrest may have disabilities due to the underlying condition that led to the arrest as well as neurologic injury incurring during the arrest [4–7]. The extent of a child's disability has been associated with caregiver burden after out-of-hospital cardiac arrest and other chronic complex childhood conditions [8–14]. Out-of-hospital and in-hospital arrest in children have different aetiologies, treatments and outcomes, and the associated degree and determinants of caregiver burden may be different for these two conditions [5–7]. For example, most children with out-of-hospital cardiac arrest are healthy before the arrest whereas most children with in-hospital cardiac arrest have pre-existing illness

that led to the hospitalisation in which the arrest occurred. Greater knowledge about caregiver burden after a child's in-hospital cardiac arrest would guide development of supportive interventions tailored to meet families' needs.

The Therapeutic Hypothermia after Paediatric Cardiac Arrest In-Hospital (THAPCA-IH) trial was a randomised trial comparing the efficacy of two targeted temperature management interventions on survival with good neurobehavioural function in children one year after in-hospital cardiac arrest [15]. All children recruited to the THAPCA-IH trial were comatose, required mechanical ventilation after return of circulation, and were at high risk for neurologic injury. Results of the trial showed that neither treatment arm conferred a significant benefit on survival with good neurobehavioural function. As part of the THAPCA-IH trial, we evaluated caregiver burden at baseline (reflecting pre-arrest burden), and 3 and 12 months post-arrest. We hypothesised that caregiver burden is substantial during the first year after a child's in-hospital cardiac arrest and that the extent of the child's disability is

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associated with caregiver burden. Our objective was to describe caregiver burden among those whose children survived in-hospital cardiac arrest and were at high risk of neurologic injury, and explore factors associated with burden during the first year post-arrest.

Methods

Study design

This study is a secondary analysis of the THAPCA-IH trial. Thirty-seven children's hospitals in the United States, Canada, and the United Kingdom participated between September 1, 2009 and February 27, 2015. Details of the trial were previously published [15–17]. The study was approved by the institutional review boards at all sites and the Data Coordinating Centre at the University of Utah. Parent/guardian permission was obtained for all participants.

Study population

The THAPCA-IH trial recruited 329 children [15]. Inclusion criteria were age 48 h to 18 years, occurrence of an in-hospital cardiac arrest with compressions for > 2 min, and dependence on mechanical ventilation after return of circulation. Major exclusion criteria were a Glasgow Coma Scale motor subscale score of 5 or 6 [18], inability to be randomised within 6 h of return of circulation, pre-existing terminal illness with life expectancy < 12 months, and a decision by the clinical team to withhold aggressive treatment. Of those recruited, 155 survived to one year. Caregivers (i.e., parents and/or guardians) of 138 were assessed for burden.

Outcomes

The primary outcome was caregiver burden 12 months after in-hospital cardiac arrest. Caregiver burden was assessed using two scales from the Infant and Toddler Quality of Life Questionnaire (ITQOL) [19,20] for children < 5 years old, and three scales from the Child Health Questionnaire (CHQ) [21] for children > 5 years. The two scales of the ITQOL used to assess caregiver burden were (1) parent impact-emotion, and (2) parent impact-time [19]. The parent impact-emotion scale assesses how much parental anxiety or worry are caused by the child's physical and psychological problems. The parent impact-time scale assesses how much the parent's personal time is limited by the child's problems. The mean of the responses for each ITQOL scale is transformed to 0–100 with higher scores indicating lesser burden. Normative reference data from a U.S. population are not available; however, Dutch reference data exist [20].

The three scales of the CHQ used to assess caregiver burden are (1) parent impact-emotion, (2) parent impact-time, and (3) family activities [21]. The parent impact-emotion and parent impact-time scales are similar to the corresponding scales of the ITQOL. The family activities scale assesses how often the child's health or behaviour interferes with family activities. The mean of the responses for each CHQ scale is transformed to 0–100 with higher scores indicating lesser burden. Normative reference data from a U.S. population exist [21]. Details of the ITQOL and CHQ can be found at <https://www.healthactchq.com/surveys.php>.

Independent variables

Independent variables included child and caregiver socio-demographics, child clinical characteristics, family functioning and child functioning. Child clinical characteristics included pre-existing conditions, presence of congenital heart disease, occurrence of arrest post-cardiac surgery, primary aetiology of arrest, and use of extracorporeal membrane oxygenation at THAPCA-IH treatment initiation. Family functioning was assessed using the General Functioning Scale of

the Family Assessment Device (FAD-GF) [22]. Child functioning was assessed using the Vineland Adaptive Behaviour Scales Second Edition (VABS-II) [23], the Paediatric Overall Performance Category (POPC) and Paediatric Cerebral Performance Category (PCPC) scales [24], and caregiver's perception of global functioning.

The FAD-GF is a 12-item measure used to distinguish healthy and unhealthy family functioning [22]. Each item is rated using a 4-point scale. Total scores are the mean of the item responses. A score > 2 indicates unhealthy functioning.

The VABS-II is a measure of adaptive behaviour from birth through adulthood [23]. Adaptive behaviour refers to a person's performance on daily life activities necessary for personal and social independence. VABS-II domains include communication, daily living, socialisation, and motor skills. The number of items that can be performed in each domain is standardised for the child's age. In a normative U.S. population, the mean VABS-II score is 100 and standard deviation is 15. Higher scores indicate better functioning.

POPC and PCPC scales are used to assess overall health and neurological functioning, respectively [24]. Both are 6-point scales of increasing disability. Scores are 1 for good/normal, 2 for mild disability, 3 for moderate disability, 4 for severe disability, 5 for coma or vegetative state, and 6 for death.

Caregiver perception of global child functioning was assessed using items developed by the investigators. At baseline, caregivers were asked, "Compared with children of the same age, were your child's home, school or social activities limited before his/her cardiac arrest? Response choices were, 'not limited, limited a little, or limited a lot.'" At 3 and 12 months, caregivers were asked (1) "Compared with children of the same age, are your child's home, school or social activities limited now?" Response choices were, "not limited, limited a little, or limited a lot." (2) "Thinking about your child since his/her cardiac arrest, has he/she gained a lot of new skills, gained a few new skills, stayed the same, lost a few skills, or lost a lot of skills."

Procedures

Trained research coordinators at the local sites assisted caregivers with completing baseline measures (ITQOL, CHQ, FAD-GF, VABS-II, and global functioning) within 24 h of recruitment. Baseline measures were intended to reflect pre-arrest status. Research coordinators rated POPC and PCPC scores at baseline and hospital discharge. At 3 and 12 months post-arrest, caregivers completed measures (ITQOL, CHQ, VABS-II, POPC, PCPC, and global functioning) via telephone with an interviewer from the Kennedy Krieger Institute.

Statistical analyses

Baseline characteristics were summarised using frequencies and percentages for categorical variables and medians and quartiles for continuous variables. The caregiver burden scales and VABS-II were summarised at baseline, 3 months, and 12 months using the mean and standard deviation. The caregiver burden scales at each time point were compared to reference values using the *t*-test, and the difference from baseline to 3 and 12 months as well as the difference from 3 to 12 months were examined using the paired *t*-test. Spearman correlations were used to assess associations between the caregiver burden scales and the independent variables. The reference values for each caregiver burden scale were used to calculate *z*-scores at month 12. These *z*-scores were used to categorise caregiver burden as mildly elevated/normal (*z*-score –1.5 to 1.5), moderately elevated (*z*-score –3 to –1.5) or highly elevated (*z*-score < –3). All analyses were completed using SAS software v9.4 (Cary, NC).

Results

Of 138 children, 77 (55.8%) were male, 77 (55.8%) were white, and

Table 1
Descriptive Characteristics.

	Pre-arrest Caregiver Burden Measure	
	ITQOL (N = 109)	CHQ (N = 29)
Age at cardiac arrest (years), median [IQR]	0.4 [0.1–1.3]	11.5 [9.0–14.3]
Male, No. (%)	61 (56.0)	16 (55.2)
Race, No. (%)		
Black or African American	30 (27.5)	9 (31.0)
White	59 (54.1)	18 (62.1)
Other/Unknown	20 (18.3)	2 (6.9)
Ethnicity, No. (%)		
Hispanic or Latino	24 (22.0)	5 (17.2)
Not Hispanic or Latino	79 (72.5)	24 (82.8)
Unknown	6 (5.5)	0 (0.0)
Caregiver's highest education received, No. (%)		
Some high school or less	15 (13.8)	8 (27.6)
High school graduate or General Equivalency Diploma	32 (29.4)	3 (10.3)
Vocational school or some college	31 (28.4)	7 (24.1)
College degree	17 (15.6)	10 (34.5)
Graduate or doctoral degree	13 (11.9)	1 (3.4)
Question not answered	1 (0.9)	0 (0.0)
Pre-existing conditions, No. (%)		
Any pre-existing condition	100 (91.7)	25 (86.2)
Cardiac condition	82 (75.2)	13 (44.8)
Respiratory condition	33 (30.3)	9 (31.0)
Neurologic condition	26 (23.9)	14 (48.3)
Gastrointestinal condition	32 (29.4)	3 (10.3)
Prenatal condition	32 (29.4)	4 (13.8)
Other pre-existing condition	43 (39.4)	11 (37.9)
Congenital heart disease, No. (%)	75 (68.8)	7 (24.1)
Arrest post-cardiac surgery, No. (%)	47 (43.1)	4 (13.8)
Primary aetiology of arrest, No. (%)		
Cardiac	69 (63.3)	16 (55.2)
Respiratory	37 (33.9)	9 (31.0)
Other/Unknown	3 (2.8)	4 (13.8)
ECMO at treatment initiation, No. (%)	53 (48.6)	15 (51.7)
Pre-cardiac arrest VABS-II Composite Score, median [IQR]	92.0 [78.0–101.0]	98.0 [82.0–119.0]
Pre-cardiac arrest POPC, No. (%)		
Good = 1	37 (33.9)	16 (55.2)
Mild disability = 2	48 (44.0)	6 (20.7)
Moderate disability = 3	19 (17.4)	5 (17.2)
Severe disability = 4	5 (4.6)	2 (6.9)
Pre-cardiac arrest PCPC, No. (%)		
Normal = 1	61 (56.0)	21 (72.4)
Mild disability = 2	32 (29.4)	2 (6.9)
Moderate disability = 3	13 (11.9)	4 (13.8)
Severe disability = 4	3 (2.8)	2 (6.9)
Pre-cardiac arrest global child functioning: Parent perception of limitations, No. (%)		
Not limited	57 (52.2)	20 (69.0)
Limited a little	23 (21.1)	6 (20.7)
Limited a lot	16 (14.6)	3 (10.3)
Missing	13 (11.9)	0 (0.0)
Pre-cardiac arrest FAD, No. (%)		
Healthy family functioning	92 (84.4)	27 (93.1)
Unhealthy family functioning	15 (13.7)	2 (6.9)
Missing	2 (1.8)	0 (0.0)

Abbreviations: ITQOL, Infant Toddler Quality of Life; CHQ, Child Health Questionnaire; IQR, interquartile range; ECMO, extracorporeal membrane oxygenation; VABS-II, Vineland Adaptive Behaviour Scale, Second Edition; POPC, Paediatric Overall Performance Category; PCPC, Paediatric Cerebral Performance Category; FAD, Family Assessment Device.

109 (79.0%) were < 5 years old at the time of arrest (Table 1). One hundred and twenty-five (90.6%) had a pre-existing condition. Eighty-two (59.4%) had congenital heart disease and 51 (37.0%) had cardiac surgery. Aetiology of arrest was cardiac for 85 (61.6%), respiratory for 46 (33.3%) and other/unknown for 7 (5.1%). Pre-arrest adaptive behaviour was similar to reference norms for both age groups. Pre-arrest

POPC and PCPC were in the good/normal to mild disability range for 107 (77.5%) and 116 (84.1%), respectively. Children's global functioning was assessed as not limited or limited a little for 106 (76.8%). Among caregivers, 114 (82.6%) had at least a high school diploma. Family functioning was assessed as healthy for 119 (86.2%).

For children < 5 years old, pre-arrest caregiver burden was greater (i.e., lower ITQOL scores) than reference values (Table 2). Caregiver burden at 3 months post-arrest was similar to pre-arrest; caregiver burden at 12 months was improved compared to pre-arrest and 3-month values. For children > 5 years, pre-arrest caregiver burden was greater (i.e., lower CHQ parent impact-emotion and family activity scores) than reference values (Table 3). Caregiver burden at 3 months post-arrest was greater (i.e., lower parent impact-time and family activity scores) than pre-arrest values. Caregiver burden at 12 months post-arrest was improved compared to 3-months and was similar to pre-arrest. In both age groups, mean caregiver burden was greater at all times compared to reference values.

For caregivers of children < 5 years old, 24 (22.4%) reported moderate to highly elevated burden for the parent impact-emotion domain and 22 (20.6%) the parent impact-time domain at 12 months post-arrest (Fig. 1). For caregivers of children > 5 years old, 12 (38.7%) reported moderate to highly elevated burden for the parent impact-emotion domain, 11 (35.4%) for the parent impact-time domain, and 16 (51.6%) for the family activities domain.

Several measures of child function prior to 3 months post-arrest correlated moderately with caregiver burden at 3 months (Table 4). Worse pre-arrest POPC and PCPC correlated with greater caregiver worry (i.e., parent impact-emotion) for children < 5 years old. Worse POPC and/or PCPC at hospital discharge correlated with greater caregiver worry and limitation in personal time (i.e., parent-impact-time) for children in both age groups. Worse POPC, PCPC, VABS-II and global functioning at 3 months post-arrest correlated with greater caregiver worry and limitation in personal time for children in both age groups. Higher caregiver education correlated with greater caregiver worry for children < 5 years old and greater caregiver burden in all domains for children > 5 years old. Healthy family functioning correlated with greater caregiver worry and limitation in personal time for children < 5 years old. Race, ethnicity, and the presence of pre-existing conditions did not correlate with caregiver burden (Data not shown).

Several measures of child function prior to 12 months post-arrest correlated moderately with caregiver burden at 12 months (Table 5). Worse pre-arrest POPC and PCPC correlated with greater limitation in caregiver personal time for children > 5 years old. Worse POPC and/or PCPC at hospital discharge correlated with greater caregiver worry and limitation in personal time for children in both age groups. Worse POPC, PCPC, VABS-II and global functioning at 3 months and 12 months post-arrest correlated with greater caregiver burden in all domains for children < 5 years old, and with greater burden in most domains for children > 5 years old. Higher caregiver education correlated with greater limitation in caregiver personal time for children < 5 years old and greater caregiver worry and interference with family activities for children > 5 years old. Family functioning did not correlate with caregiver burden at 12 months. Race, ethnicity and the presence of pre-existing conditions also did not correlate with burden (Data not shown).

Discussion

Our findings demonstrate that caregiver burden is substantial during the first year after paediatric in-hospital cardiac arrest. The extent of the child's disability 3 months post-arrest was associated with caregiver burden at 12 months. Higher caregiver education was associated with greater burden 3 and 12 months post-arrest. Healthy family functioning was associated with greater burden 3 months post-arrest for caregivers of children < 5 years old, but not associated with burden by 12 months. Race, ethnicity and the presence of pre-existing conditions

Table 2
Infant Toddler Quality of Life Caregiver Burden Measures over Time.

	Reference	Time point								
		Pre-cardiac arrest	P-value ^a	Month 3	P-value ^a	P-value ^b	Month 12	P-value ^a	P-value ^b	P-value ^c
ITQOL Parent Impact – Emotional										
N		106		109			107 ^d			
Standardized score, mean (SD)	92.1 (10.84)	73.7 (25.56)	< 0.001	76.3 (23.65)	< 0.001	0.431	85.5 (16.67)	< 0.001	< 0.001	< 0.001
ITQOL Parent Impact – Time										
N		107		109			107 ^d			
Standardized score, mean (SD)	93 (10.92)	81.5 (22.71)	< 0.001	80.4 (22.45)	< 0.001	0.590	87.4 (18.76)	0.003	0.025	0.003
VABS-II Composite Score										
N		109		109			107			
Standardized score, mean (SD)	100 (15)	89.8 (16.44)		80.0 (18.63)			80.3 (17.17)			

Abbreviations: ITQOL, Infant Toddler Quality of Life, VABS-II, Vineland Adaptive Behaviour Scale, Second Edition.

^a P-value from *t*-test comparing caregiver burden measure to reference.

^b P-value from paired *t*-test comparing caregiver burden measure to pre-arrest.

^c P-value from paired *t*-test comparing the change in caregiver burden measure from month 3 to month 12.

^d Two children whose caregivers completed the ITQOL at 3 months were administered the CHQ at 12 months because the children turned 5 years between the 3- and 12-month assessments.

Table 3
Child Health Questionnaire Caregiver Burden Measures over Time.

	Reference	Time point								
		Pre-cardiac arrest	P-value ^a	Month 3	P-value ^a	P-value ^b	Month 12	P-value ^a	P-value ^b	P-value ^c
CHQ Parent Impact – Emotional										
N		29		29			31 ^d			
Standardized score, mean (SD)	80.3 (19.1)	54.3 (28.92)	< 0.001	44.3 (34.08)	< 0.001	0.230	61.6 (28.52)	< 0.001	< 0.336	< 0.008
CHQ Parent Impact – Time										
N		29		29			31 ^d			
Standardized score, mean (SD)	87.8 (19.9)	77.0 (29.09)	< 0.056	50.6 (35.58)	< 0.001	< 0.001	68.5 (33.59)	0.003	0.140	0.033
CHQ Family Activities										
N		29		29			31 ^d			
Standardized score, mean (SD)	89.7 (18.6)	70.3 (27.59)	< 0.001	54.5 (26.49)	< 0.001	0.031	65.9 (24.28)	< 0.001	0.380	0.035
VABS-II Composite Score										
N		29		29			31 ^d			
Standardized score, mean (SD)	100 (15)	96.3 (28.17)		75.4 (22.76)			82.3 (25.68)			

Abbreviations: CHQ, Child Health Questionnaire, VABS-II, Vineland Adaptive Behaviour Scale, Second Edition.

^a P-value from *t*-test comparing caregiver burden measure to reference.

^b P-value from paired *t*-test comparing caregiver burden measure to pre-arrest.

^c P-value from paired *t*-test comparing the change in caregiver burden measure from month 3 to month 12.

^d Two children whose caregivers completed the ITQOL at 3 months were administered the CHQ at 12 months because the children turned 5 years between the 3- and 12-month assessments.

were not associated with caregiver burden.

Although caregiver burden persists throughout the first year after paediatric in-hospital cardiac arrest, the temporal pattern of burden was different for caregivers of children < 5 years and > 5 years old. For caregivers of children < 5 years old, burden at 3 months post-arrest was similar to pre-arrest baseline, and declined to less than baseline by 12-months. Many of these younger children had congenital heart disease and were post-operative (43.1%) at the time of arrest. At baseline, the high level of burden may reflect caring for a child with an unrepaired heart defect. By 12-months, these children would have recovered from their surgery and despite the cardiac arrest during the hospitalisation, their care at 12 months resulted in less burden than prior to their cardiac repair. Prior research has shown that young children with congenital heart disease have functional disabilities and that their parents have increased illness-related stress, although the time course of parental stress, coping and adaptation have not been well characterised [25,26].

For caregivers of children > 5 years old, burden was greater at 3 months post-arrest than pre-arrest baseline, and declined to baseline by 12 months. The decline in burden at 12 months post-arrest to baseline suggests that for many caregivers the child's arrest did not contribute to burden in the long-term beyond that already present due to the illness

that led to the arrest. It is also possible that the small number of children in the > 5 year age group (n = 29) made differences in burden difficult to demonstrate. Importantly, caregiver burden was significantly more than reference norms at all time points in both age groups.

Consistent with results exploring caregiver burden in the Therapeutic Hypothermia after Paediatric Cardiac Arrest Out-of-Hospital (THAPCA-OH) trial [8], caregiver-reported disability (VABS-II) and global functioning were moderately associated with caregiver burden. In contrast to the THAPCA-IH trial, most children in THAPCA-OH were healthy pre-arrest [27] and many survivors had severe disability post-arrest [28,29]; caregiver burden at pre-arrest baseline was similar to reference norms and persistently elevated above baseline at 3 and 12 months post-arrest. The greater burden perceived by caregivers after a child's out-of-hospital arrest may be related to a greater degree of post-arrest disability and the experience of caring for a disabled child when the child was previously healthy.

A higher level of caregiver education was associated with greater caregiver burden after paediatric in-hospital cardiac arrest. Highly educated caregivers may have greater recognition of their child's cognitive disabilities; and hence, greater anxiety, worry, and time committed to their child's care. Among parents of children with cancer,

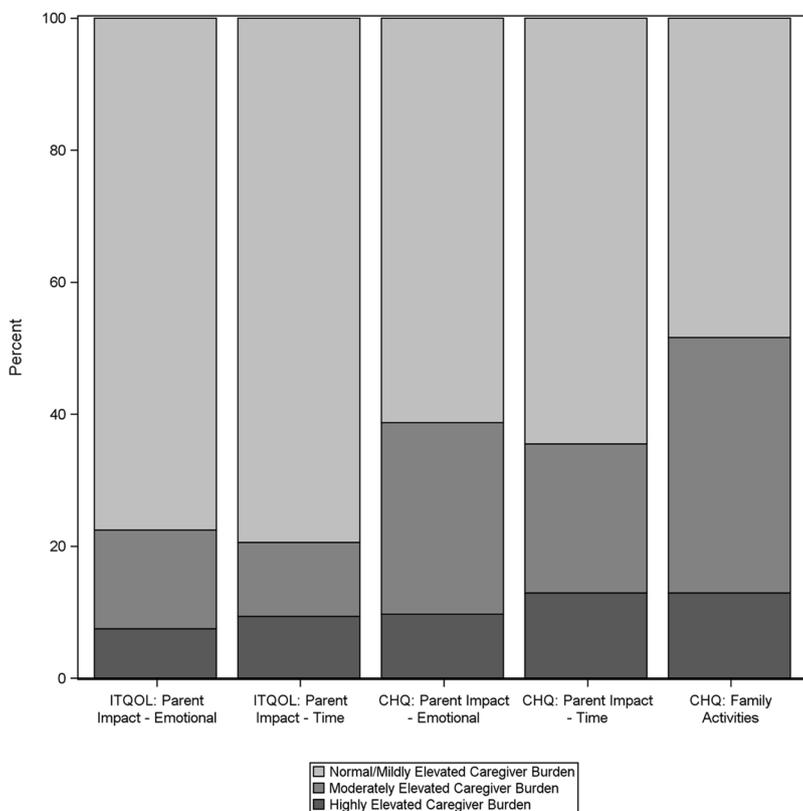


Fig. 1. Caregiver Burden 12 Months after a Child's In-Hospital Cardiac Arrest.
 Legend: Percent of caregivers reporting normal/mild, moderate, and high levels of burden for each assessed caregiver burden domain 12 months after their child's cardiac arrest.
 Abbreviations: ITQOL, Infant Toddler Quality of Life; CHQ, Child Health Questionnaire.

both higher and lower levels of education have been associated with increased parental distress and caregiving demands [30–33]. These findings suggest that general education may not protect against caregiver burden and that supportive interventions may be needed regardless of education level.

Healthy family functioning pre-arrest was associated with greater caregiver burden at 3 months post-arrest for children < 5 years old. The relationship between family functioning and caregiver burden is complex [2]. Greater burden can lead to unhealthy family functioning and

vice versa. On the other hand, the challenges of managing a chronic condition can improve aspects of family functioning such as problem solving [2,34]. Thus, caregiver burden may be associated with families learning to function together better. Neither caregiver education nor family functioning were associated with burden after paediatric out-of-hospital arrest [8]. Children with out-of-hospital arrest have a greater degree of disability post-arrest which may be a more important determinant of burden, potentially masking other factors.

Table 4
 Month 3 Caregiver Burden Measure Correlations.

Covariate	ITQOL Parent Impact – Emotion	ITQOL Parent Impact – Time	CHQ Parent Impact – Emotion	CHQ Parent Impact – Time	CHQ Family Activities
Pre-cardiac arrest					
Age at randomization (years)	0.006	–0.030	–0.154	–0.039	–0.142
Caregiver's highest education received	–0.248*	–0.125	–0.431*	–0.496*	–0.568*
Global child functioning: Parent perception of limitations	–0.090	–0.139	–0.146	–0.114	–0.144
Average FAD score	0.197*	0.194*	–0.346	–0.306	–0.180
VABS-II Composite Score	0.162	–0.034	0.088	–0.009	–0.171
POPC	–0.198*	–0.114	–0.016	0.060	0.140
PCPC	–0.192*	–0.091	–0.114	0.050	0.081
Hospital discharge					
POPC	–0.403*	–0.204*	–0.330	–0.214	–0.060
PCPC	–0.346*	–0.142	–0.484*	–0.369*	–0.163
Month 3					
VABS-II Composite Score	0.444*	0.363*	0.640*	0.591*	0.409*
POPC	–0.465*	–0.469*	–0.706*	–0.574*	–0.327
PCPC	–0.431*	–0.341*	–0.644*	–0.590*	–0.424*
Global child functioning: Parent perception of limitations	–0.492*	–0.383*	–0.603*	–0.415*	–0.265
Global child functioning: Parent perception of skills	–0.235*	–0.339*	–0.610*	–0.420*	–0.342

Abbreviations; ITQOL, Infant Toddler Quality of Life; CHQ, Child Health Questionnaire; FAD, Family Assessment Device; VABS-II, Vineland Adaptive Behaviour Scale, Second Edition; POPC, Paediatric Overall Performance Category; PCPC, Paediatric Cerebral Performance Category.

* Indicates p-value < 0.05.

Table 5
Month 12 Caregiver Burden Measure Correlations.

Covariate	ITQOL Parent Impact – Emotion	ITQOL Parent Impact – Time	CHQ Parent Impact – Emotion	CHQ Parent Impact – Time	CHQ Family Activities
Pre-cardiac arrest					
Age at randomization (years)	–0.045	–0.055	–0.322	–0.186	–0.253
Caregiver's highest education received	–0.173	–0.218*	–0.390*	–0.148	–0.362*
Global child functioning: Parent perception of limitations	–0.104	–0.086	–0.176	–0.080	–0.106
Average FAD score	–0.054	0.004	–0.237	–0.208	–0.241
VABS-II Composite Score	0.144	0.085	0.157	0.314	0.196
POPC	–0.126	–0.076	–0.139	–0.423*	–0.232
PCPC	–0.151	–0.137	–0.246	–0.456*	–0.344
Hospital discharge					
POPC	–0.311*	–0.316*	–0.250	–0.303	–0.191
PCPC	–0.254*	–0.215*	–0.364*	–0.427*	–0.291
Month 3					
VABS-II Composite Score	0.431*	0.300*	0.548*	0.504*	0.429*
POPC	–0.456*	–0.402*	–0.318	–0.532*	–0.377*
PCPC	–0.382*	–0.311*	–0.456*	–0.568*	–0.346
Global child functioning: Parent perception of limitations	–0.305*	–0.243*	–0.115	–0.150	–0.092
Global child functioning: Parent perception of skills	–0.203*	–0.207*	–0.220	–0.165	–0.174
Corresponding caregiver burden measure	0.571*	0.356*	0.555*	0.361	0.460*
Month 12					
VABS-II Composite Score	0.466*	0.265*	0.432*	0.587*	0.466*
POPC	–0.482*	–0.420*	–0.310	–0.556*	–0.365*
PCPC	–0.397*	–0.287*	–0.439*	–0.611*	–0.431*
Global child functioning: Parent perception of limitations	–0.367*	–0.311*	–0.417*	–0.548*	–0.453*
Global child functioning: Parent perception of skills	–0.233*	–0.211*	–0.502*	–0.419*	–0.470*

Abbreviations: ITQOL, Infant Toddler Quality of Life; CHQ, Child Health Questionnaire; FAD, Family Assessment Device; VABS-II, Vineland Adaptive Behaviour Scale, Second Edition; POPC, Paediatric Overall Performance Category; PCPC, Paediatric Cerebral Performance Category.

* Indicates p -value < 0.05.

Limitations

Limitations of this study include using different caregiver burden measures for younger and older children. Separating the primary outcome by age group could have reduced the statistical power to detect some meaningful associations. Normative reference data from a U.S. population are not available for the ITQOL. Other limitations include the select population of children included in THAPCA-IH. However, because these children were at high risk for neurologic injury, knowledge about burden for this population will be most useful to caregivers and clinicians. Other potential risk factors for caregiver burden exist that were not evaluated. Caregiving can have a positive impact on caregivers [35] which was also not evaluated.

Conclusions

Caregiver burden is substantial during the first year after paediatric in-hospital cardiac arrest. Standardised measures of the child's neuro-behavioural function as well as caregivers' subjective perceptions of their child's global function were associated with caregiver burden.

Conflict of interest

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References

- Raina P, O'Donnell M, Schweltnus H, Rosenbaum P, King G, Brehaut J, et al. Caregiving process and caregiver burden: conceptual models to guide research and practice. *BMC Pediatr* 2004;4:1.
- Pilapil M, Coletti DJ, Rabey C, DeLaet D. Caring for the caregiver: supporting families of youth with special health care needs. *Curr Probl Pediatr Adolesc Health Care* 2017;47:190–9.
- Chambers HG, Chambers JA. Effects of caregiving on the families of children and adults with disabilities. *Phys Med Rehabil Clin N Am* 2015;26:1–19.
- Phillips RS, Scott B, Carter SJ, Taylor M, Peirce E, Davies P, et al. Systematic review and meta-analysis of outcomes after cardiopulmonary arrest in childhood. *PLoS One* 2015;10:e0130327.
- Moler FW, Meert K, Donaldson AE, Nadkarni V, Brilli RJ, Dalton HJ, et al. In-hospital versus out-of-hospital pediatric cardiac arrest: a multicenter cohort study. *Crit Care Med* 2009;37:2259–67.
- Meert KL, Donaldson A, Nadkarni V, Tieves KS, Schleien CL, Brilli RJ, et al. Multicenter cohort study of in-hospital pediatric cardiac arrest. *Pediatr Crit Care Med* 2009;10:544–53.
- Moler FW, Donaldson AE, Meert K, Brilli RJ, Nadkarni V, Shaffner DH, et al. Multicenter cohort study of pediatric out-of-hospital cardiac arrest. *Crit Care Med* 2011;39:141–9.
- Meert KL, Slomine BS, Christensen JR, Telford R, Holubkov R, Dean JM, et al. Family burden after out-of-hospital cardiac arrest in children. *Pediatr Crit Care Med* 2016;17:498–507.
- Rashid M, Goez HR, Mabood N, Damanhoury S, Yager JY, Joyce AS, et al. The impact of pediatric traumatic brain injury (TBI) on family functioning: a systematic review. *J Pediatr Rehabil Med* 2014;7:241–54.
- Kuo DZ, Cohen E, Agrawal R, Berry JG, Casey PH. A national profile of caregiver challenges among more medically complex children with special health care needs. *Arch Pediatr Adolesc Med* 2011;165:1020–6.
- Stacin T, Wade SL, Walz NC, Yeates KO, Taylor HG. Family adaptation 18 months after traumatic brain injury in early childhood. *J Dev Behav Pediatr* 2010;31:317–25.
- Aitken ME, McCarthy ML, Slomine BS, Ding R, Durbin DR, Jaffe KM, et al. Family burden after traumatic brain injury in children. *Pediatrics* 2009;123:199–206.
- Wade SL, Gerry Taylor H, Yeates KO, Drotar D, Stancin T, Minich NM, et al. Long-term parental and family adaptation following pediatric brain injury. *J Pediatr Psychol* 2006;31:1072–83.
- Guyard A, Fauconnier J, Mermet MA, Cans C. Impact on parents of cerebral palsy in children: a literature review. *Arch Pediatr* 2011;18:204–14.
- Moler FW, Silverstein FS, Holubkov R, Slomine BS, Christensen JR, Nadkarni VM, et al. Therapeutic hypothermia after in-hospital cardiac arrest in children. *N Engl J Med* 2017;376:318–29.
- Moler FW, Silverstein FS, Meert KL, Clark AE, Holubkov R, Browning B, et al. Rationale, timeline, study design, and protocol overview of the Therapeutic Hypothermia after Paediatric Cardiac Arrest trials. *Pediatr Crit Care Med* 2013;14:e304–15.
- Holubkov R, Clark AE, Moler FW, Slomine BS, Christensen JR, Silverstein FS, et al. Efficacy outcome selection in the therapeutic hypothermia after paediatric cardiac arrest trials. *Pediatr Crit Care Med* 2015;16:1–10.
- Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. *Lancet* 1974;2:81–4.
- HealthActCHQ. Confidential Scoring Rules. Infant and Toddler Quality of Life Questionnaire-97 (ITQOL-97). Boston, MA: HealthActCHQ; 2008.
- Raat H, Landgraf JM, Oostenbrink R, Moll HA, Essink-Bot ML. Reliability and validity of the Infant and Toddler Quality of Life Questionnaire (ITQOL) in a general population and respiratory disease sample. *Qual Life Res* 2007;16:445–60.
- HealthActCHQ. The CHQ Scoring and Interpretation Manual. Boston, MA: HealthActCHQ; 2008.
- Epstein N, Baldwin L, Bishop D. The McMaster family assessment device. *J Marital Fam Ther* 1983;9:171–80.
- Sparrow S, Cicchetti D, Balla D. Vineland Adaptive Behavior Scales. 2nd ed. Minneapolis, MN: Pearson Assessment; 2005.
- Fisher DH. Assessing the outcome of pediatric intensive care. *J Pediatr* 1992;121:68–74.
- Limperopoulos C, Majnemer A, Shevell MI, Rosenblatt B, Rohlicek C, Tchervenkov C, et al. Functional limitations in young children with congenital heart defects after cardiac surgery. *Pediatrics* 2001;108:1325–31.
- Caris EC, Dempster N, Wernovsky G, Butz C, Neely T, Allen R, et al. Anxiety scores in caregivers of children with hypoplastic left heart syndrome. *Congenit Heart Dis* 2016;11:727–32.
- Moler FW, Silverstein FS, Holubkov R, Slomine BS, Christensen JR, Nadkarni VM, et al. Therapeutic hypothermia after out-of-hospital cardiac arrest in children. *N Engl J Med* 2015;372:1898–908.
- Slomine BS, Silverstein FS, Christensen JR, Holubkov R, Page K, Dean JM, et al. Neurobehavioral outcomes in children after out-of-hospital cardiac arrest. *Pediatrics* 2016;137. pii:e20153412.
- Silverstein FS, Slomine BS, Christensen J, Holubkov R, Page K, Dean JM, et al. Functional outcomes trajectories after out-of-hospital pediatric cardiac arrest. *Crit Care Med* 2016;44:e1165–74.
- Klassen A, Raina P, Reineking S, Dix D, Pritchard S, O'Donnell M. Developing a literature base to understand the caregiving experience of parents of children with cancer: a systematic review of factors related to parental health and well-being. *Support Care Cancer* 2007;15:807–18.
- Choi EK, Yoon SJ, Kim JH, Park HJ, Kim JY, Yu ES. Depression and distress in caregivers of children with brain tumors undergoing treatment: psychosocial factors as moderators. *Psychooncology* 2016;25:544–50.
- Mu PF, Ma FC, Hwang B, Chao YM. Families of children with cancer: the impact of anxiety experienced by fathers. *Cancer Nurs* 2002;25:66–73.
- Svavarsdottir EK. Surviving childhood cancer: parents' perceptions of their child's health. *J Pediatr Oncol Nurs* 2005;22:80–8.
- Blair C, Freeman C, Cull A. The families of anorexia nervosa and cystic fibrosis patients. *Psychol Med* 1995;25:985–93.
- Murphy NA, Christian B, Caplin DA, Young PC. The health of caregivers for children with disabilities: caregiver perspectives. *Child Care Health Dev* 2007;33:180–7.