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Original

Outcome of out-of-hospital cardiopulmonary arrest in children: A multicenter cohort study

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The aim of this study was to evaluate the demographic characteristics of children who experienced out-of-hospital cardiopulmonary arrest (CPA), and to assess the impact of the bystander cardiopulmonary resuscitation (CPR) on the survival rate of witnessed arrests and the effects of the arrest and CPR durations on the neurological outcomes. This multicenter, retrospective study included a total of 182 patients who underwent CPR for out-of-hospital CPA between January 2008 and December 2012 at six centers in Ankara, Turkey. The median [interquartile range (IQR)] age was 22 (5-54) months; 60.4% of the patients were males, and 44% were younger than one year of age. The witnessed arrest rate was 75.8% (138/182) and the rate of bystander CPR was 13.9% (13/93). In these patients the rate of the return of spontaneous circulation (ROSC) was higher (76.9%). Following resuscitation in the patients for whom the spontaneous circulation was able to be returned, the median (IQR) duration of arrest was 5 (1- 15) min, while it was 15 (5-40) min for the remaining patients ($p<0.001$). The ROSC rate was 94.9% in patients who underwent CPR for less than 20 min and 22% in patients requiring CPR longer than 20 min ($p<0.001$). Survival to hospital discharge was 14.3%. Of these patients, 57.7% experienced neurological disability. The short duration of an arrest and the presence of CPR are both critical for survival. We suggest that a witness to the CPA, performing early and efficient CPR, yields better results.

Key words: cardiac arrest, cardiopulmonary resuscitation, pediatrics, out-of-hospital.

The out-of-hospital cardiopulmonary arrest (CPA) is a rare, but serious condition in children, as its mortality rate is high and it may lead to serious neurological sequelae in surviving patients.[1-3] Incidence of pediatric out-of-hospital CPA is reported to be between six and 19/100,000 person-year with a survival rate of two to 24%.[4-8]

Due to the positive results achieved in adults, pediatric studies are currently the focus of concentration.[9] Between 30 and 50% of pediatric out-of-hospital CPA cases comprise infants less than one year of age. [4-6] In previous studies, the incidence and the mortality rate were reported to be much higher in children of less than one year of age, compared to those

aged between 1 and 12 years and adolescents (aged between 12 and 18 years).[5,10]

The majority of CPA cases occur in the non-public setting, such as home. The most common cause in the etiology of out-of-hospital CPA is respiratory, and the initially recorded cardiac rhythm is typically asystole/pulseless electrical activity (PEA).[5,9] Children whose arrest is witnessed and receive bystander cardiopulmonary resuscitation (CPR) have improved neurological outcomes. Bystander CPR is given in only 15 to 40% of pediatric patients.[4,10] Earlier CPR is associated with improved neurological outcomes, while prolonged periods of no-flow may result in neurological sequelae in most of the surviving patients.

To date, there have been no multi-center studies in children experiencing out-of-hospital CPA in Turkey. In this study, we aimed to evaluate the demographic characteristics of children who experienced out-of-hospital CPA, and to assess the impact of the bystander CPR on the survival rate of witnessed arrests and the effects of the arrest and CPR durations on the neurological outcomes.

Material and Methods

This multi-center, descriptive, retrospective study was conducted between January 2008 and December 2012 in the pediatric emergency and pediatric intensive care units of university hospitals and training and research Hospitals in Ankara. Children aged between one month and 18 years who experienced out-of-hospital CPA and underwent chest compression for at least one minute were included in the study.

The study protocol was approved by the Ethical Committee. The study was conducted in accordance with the principles of the Declaration of Helsinki.

By using the medical records of the patients in six centers, the following data were recorded: demographic characteristics including age, sex, and presence of underlying chronic disorder; the event features, including the arrest location, arrest duration, arrest day (weekday-weekend), whether the arrest was witnessed and if witnessed, who the witness was (healthcare personnel, family), was CPR performed by the person who witnessed the event, the initial location of resuscitation (i.e., home, outside, ambulance) and the first detected rhythm in the patient (asystole, bradycardia, PEA, ventricular fibrillation (VF), pulseless ventricular tachycardia (VT), unidentified); the etiology of the arrest, including respiratory failure (upper airway disease, pulmonary disease, hypoventilation), circulatory failure, central nervous system disease, poisoning, and trauma; the interventions performed, including airway management (mouth to mouth, bag-mask, intubation) and drugs used (epinephrine, sodium bicarbonate, lidocaine, amiodarone, calcium, glucose, atropine, fluids).

The medical records were also used to identify how the patients were delivered to hospital. In Turkey, when individuals require pre-hospital emergency health care, the emergency medical service (EMS) phone number, 112, is called and help is requested. An ambulance and medical intervention (usually paramedics) is sent to the patient in the shortest possible time, and the patient is taken to hospital. In the present study, EMS ambulances transported some of our patients, while others were taken to hospital by their relatives.

Arterial blood gas measurements, the mean resuscitation time, the mean number of days under mechanical ventilation, the number of the patient's arrests until discharge from hospital, and the length of hospital stay were recorded in the patients whose spontaneous circulation returned following resuscitation.

In all patients whose spontaneous circulation returned following the initial resuscitation, a Glasgow Coma Score was obtained within the first three hours to assess their neurological status. The Pediatric Cerebral Performance Scale (PCPC) was performed on patients whose spontaneous circulation returned following resuscitation and were discharged from hospital. PCPC scores measure the degree of cognitive function and range from 1 to 6, where 1 is normal, 2 is mild disability, 3 is moderate disability, 4 is severe disability, 5 is coma or vegetative state, and 6 is brain death. The score of 1–2 indicate good neurological status, while 3-5 indicate poor neurological status.[11]

Statistical Analysis

Statistical analysis was performed using the

Table I. Description of Pediatric Cardiac Arrest Victims (n=182).

Factor	Variable	n	(%)
Age category			
	>1 month-1 year	80	(44.0%)
	1-12 years	80	(44.0%)
	13-18 years	22	(12.0%)
Gender			
	Male	110	(60.4%)
	Female	72	(39.6%)
Arrest site			
	Home	97	(53.3%)
	Outside	35	(19.2%)
	During transport	50	(27.5%)
Witness status			
	Witnessed bystander	93	(51.1%)
	Witnessed- EMS	45	(24.7%)
	Not witnessed	44	(24.2%)
Type of admission to the hospital			
	EMS	99	(54.4%)
	With their own means	83	(45.6%)
Time of arrest			
	08:00-16:59	82	(45.1%)
	17:00-07:59	100	(54.9%)
Day of arrest			
	Weekday	130	(71.4%)
	Weekend	52	(28.6%)
Causes of Cardiac Arrest			
	Respiratory failure	100	(55.0%)
	Circulatory failure	38	(20.9%)
	CNS disease	30	(16.5%)
	Trauma	11	(6.0%)
	Poisoning	3	(1.6%)

CNS: central nervous system; EMS: emergency medical service.

SPSS (Statistical Package for Social Sciences) for Windows 20 (SPSS Inc., Chicago, IL, USA) program. Normal distribution of data was evaluated with the Kolmogorov-Smirnov normality tests. Normally distributed variables were expressed in mean ± SD, while abnormally distributed variables were expressed in median (Interquartile range). The Mann-Whitney U-test was used to compare abnormally distributed variables between two groups. The Pearson chi-square test was used to compare categorical variables. A p value of <0.05 was considered statistically significant.

Results

During the study period, CPR was performed on 182 cases with out-of-hospital CPA. The patients' characteristics and descriptions are presented in Table I. Of all patients, 80 (44%) were less than 12 months old, while 60.4% were males. Ninety-seven (53.3%) events occurred in the home setting. The majority, 138 (75.8%) of the patients, were witnessed. Of these 51.1% were witnessed by a bystander and 24.7% by EMS. Of the 182 cases, 83 (45.6%) were delivered to the hospital independently.

In addition, CPA most commonly (54.9%) occurred at night - from 5:00 PM to 7:59 AM. The weekday arrest rate was 130 (71.4%), while the weekend rate was 52 (28.6%). The most frequent cause of arrest was respiratory failure with 100 patients (55%).

Table II shows the patients' characteristics in relation to the outcome of CPR. Return of spontaneous circulation (ROSC) was achieved in 83 cases (45.6%) and not achieved in 99 cases (54.4%). The median (IQR) age was 22 (5-54) months. One hundred cases (61.0%) had chronic pre-existing conditions. In these cases, spontaneous circulation was unable to be returned (p=0.053). In both groups, the age, sex, and frequency of chronic conditions were similar.

Arrest characteristics are described in Table III. The return of spontaneous circulation was achieved in 74.7% of the cases who experienced CPA on a weekday, and in 25.3% at the weekend (p=0.413). The patients for whom spontaneous circulation was unable to be achieved 37.4%, were admitted during the daytime, while 62.6% were admitted at night (p=0.053). Of the patients for whom spontaneous circulation were able to be returned, 70 (84.3%) were witnessed and 13 (15.7%) were not; whereas, of those for whom spontaneous circulation did not return 68 (68.7%) were witnessed and 31 (31.3%) were not (p=0.015). In ten (12.1%) of the patients for whom spontaneous circulation was achieved, resuscitation was carried out by bystanders; whereas, in 73 (87.9%), it was given by the EMS personnel (p=0.022). In the cases of out-of-hospital CPA, who were admitted to the hospital by their relatives, the rate of ROSC was 30 (36.1%), whereas, in the cases transferred to the hospitals by EMS, the rate was 53 (68.9%) (p=0.025). The initially identified rhythm was asystole in 116 cases, bradycardia in 39 cases, and VT/VF in four. The rhythm was not specified in 23 cases. The ROSC was found in 31% of the patients for whom the initially identified rhythm was asystole, in 79.5% of those with bradycardia, and in 75% of those with VT/VF (p<0.001)

Table II. Outcome of CPR and Patients' Characteristics.

	Total arrests n=182	Success (ROSC Achieved n=83 (45.6%)		Not achieved n=99 (54.4%)		
		n	%	n	%	p value
Age (month)						
Median (IQR)	22 (5- 54)	24 (5- 72)		18 (6- 48)		0,368*
Range	1-216	1-204		1-216		
1 – 12 mo	80	34	42.5	46	57.5	0.380**
13 - 144 mo	80	36	45.0	44	55.0	
145- 216 mo	22	13	59.1	9	40.9	
Gender						0.447**
Male	110	53	48.2	57	51.8	
Female	72	30	41.7	42	58.3	
Any chronic pre-existing condition	100	39	39.0	61	61.0	0.053**
Pre-existing conditions						
Lung or airway disease	5	3	60.0	2	40.0	
Heart disease	25	11	44.0	14	56.0	
Hematological	6	2	33.3	4	66.7	
Metabolic	25	5	20.0	20	80.0	
Neurological	39	18	46.2	21	53.8	

ROSC: Return of spontaneous circulation; IQR: interquartile range
** Mann-Whitney U Test ** Chi-square Test*

(Table III).

We also found that mouth-to-mouth breathing was used in six (3.3%) patients, bag-mask ventilation in 21 (11.5%) patients, and endotracheal intubation in 155 (85.2%) patients for maintaining the airway during resuscitation. Almost all of these patients (98.7%, n=153) were intubated at emergency services. The airway management given by EMS personnel was maintained by bag-mask. The ROSC was present in 68 patients (46.3%) who were administered fluid bolus and in 79 patients (53.7%) for whom spontaneous circulation was unable to be returned (p=0.717). All patients (100%, n=182) received epinephrine during resuscitation. Drugs used during arrest are shown in Table III.

Following resuscitation in the patients for whom the spontaneous circulation were able to be returned, the median (IQR) duration of arrest was 5 (1- 15) min, while it was 15 (5-40) min for the remaining patients (p<0.001). In the patients with a resuscitation period of less than 20 min, the spontaneous circulation returned in 94.9% and did not return in 5.1%. In the patients with a resuscitation period longer than 20 min, the spontaneous circulation returned in 22.0% and did not return in 78.0% (p<0.001) (Table III).

Laboratory Data and Organ Dysfunction

The median (IQR) duration of using mechanical ventilator (MV) was found to be 6 (2- 16) days and the length of hospital stay as 6 (1- 27) days in ROSC patients. Following CPR, there was respiratory failure in 55 (66.3%), cardiovascular failure in 51 (61.4%), neurological dysfunction in 50 (60.2%), liver injury in 27 (32.5%), hematological dysfunction in 26 (31.3%) and renal injury in 23 patients (27.7%).

Following CPR, 68 (67.5%) of the 83 surviving patients were comatose with a median (IQR) GCS score of 3 (3-4). Neuroprotective therapies, such as temperature-targeted management (TTM), were utilized in 16 patients (19.3%). Hypertonic saline was given to 16 patients (19.3%); mannitol to 12 patients (14.5%), and steroids to 12 patients (14.5%).

In certain patients, CPR was performed more than once. The number of patients undergoing CPR twice was 36; seven underwent CPR three times, and three had CPR four times. The survival rate was very low in patients who underwent CPR two or more times (p< 0.001).

Outcome

Of all patients, 26 (14.3%) were discharged from hospital. In 24 (92.4%) of the discharged patients, the arrest was witnessed. The median (IQR) length of hospital stay was 37 (15.3-55.3) days in survivors.

Among 26 patients who were discharged home, seven (26.9%) had good PCPC scores; four (15.4%) had no change compared to the previous abnormal neurological status, and 15 (57.7%) had a poor outcome (PCPC score 3-5). One of the six patients with brain death also became an organ donor.

We found that there was no statistically significant difference in comparison of arrest and duration of CPR in patients discharged home with good or poor neurological status (p= 0.061, p= 0.198, respectively).

Discussion

Out-of-hospital CPA is an unusual occurrence in children.[5,8] Despite the CPR guidelines developed for the treatment of children within the past three decades, the results are still underwhelming.[9] In our study, similar to others, the survival rate was found to be low. VF was very rare as the initially identified rhythm, most of the arrests occur at home, and the rate of bystander CPR was low. The rate of ROSC also increases when the CPR is performed by the witness; however, the survival rate remains unchanged. In this study, patients undergoing CPR for longer than 20 min duration had poor neurological sequelae with a low survival rate.

The demographic data in this study were similar to other studies among out-of-hospital CPA cases. In many studies, 30 to 50% of patients were aged less than one year. The significantly high rate in this age group is associated with sudden infant death syndrome.[4, 6, 10,12,13] In our study, we showed that 44.0% of our cases were less than one year of age. Similar to previous studies, it was more frequent amongst the male sex.[5,7,8,12,14,15] In addition, most of the arrests occurred at home, consistent with the previous reports.[5,7,9,12,14,15]

In addition, the patients in our study were delivered to the hospitals either by their

Table III. Cardiac Arrest Event Characteristics and Relationship to ROSC.

	Total arrests n=182	Success (ROSC Achieved n=83 (45.6%)	Success (ROSC Not achieved n=99 (54.4%)	p value
		n (%)	n (%)	
Day of arrest (if unavailable, using CPR, ROSC, or arrival at hospital)[b]				0.413*
Weekday	130	62 (74.7)	68 (68.7)	
Weekend	52	21 (25.3)	31 (31.3)	
Time of arrest (if unavailable, using CPR, ROSC, or arrival at hospital)[b]				0.053*
Day (08:00-16:59)	80	43 (51.8)	37 (37.4)	
Night (17:00-07:59)	102	40 (48.2)	62 (62.6)	
Witness status[b]				
Witnessed	138	70 (84.3)	68 (68.7)	0.015*
Not witnessed	44	13 (15.7)	31 (31.3)	
The initial resuscitator[b]				0.022*
Non-health person	13	10 (12.1)	3(3.0)	
Health care personnel	169	73 (87.9)	96 (97.0)	
Type of delivery to the hospital[b]				0.025*
EMS	99	53 (68.9)	46 (46.5)	
Patient relatives	83	30 (36.1)	53 (53.5)	
First monitored rhythm[a]				< 0.001*
Asystole	116	36 (31.0)	80 (69.0)	
Bradycardia	39	31 (79.5)	8 (20.5)	
Ventricular fibrillation/ tachycardia	4	3 (75.0)	1 (25.0)	
Other / Unknown	23	13 (56.5)	10 (43.5)	
Drugs administered during arrest except Adrenalin[a]				
Fluid bolus	147	68 (46.3)	79 (53.7)	0.717*
Atropine	23	10 (43.5)	13 (56.5)	0.827*
Sodium bicarbonate	114	35 (30.7)	79 (69.3)	<0.001*
Calcium	15	6 (40.0)	9 (60.0)	0.649*
Lidocaine	3	2 (66.7)	1 (33.3)	0.593*
Amiodarone	3	3 (100.0)	0	0.093*
Glucose	11	2 (18.2)	9 (81.8)	0.069*
The duration of arrest [Median (IQR)]	10 (1- 28.8)	5 (1- 15)	15 (5- 40)	<0.001**
The duration of CPR				
Median (IQR)	30 (20- 45)	15 (10- 25)	40 (30- 45)	<0.001**
1- 20 min	59	56 (94.9)	3 (5.1)	<0.001*
>20 min	123	27 (22.0)	96 (78.0)	

CPR: cardiopulmonary resuscitation; EMS: emergency medical service; ROSC: return of spontaneous circulation; SD: standard deviation; IQR: interquartile range.
[a]*raw percentages given*, [b]*column* percentages given
** Chi-square Test ** Mann-Whitney U Test*

relatives or by EMS. Fifty-three patients (63.9%) delivered by their families did not survive; this result was considered to be related to the longer duration of arrest, compared to the patients admitted through EMS.

In their study, Gerein et al.[8] determined a rate of 30% for chronic disorders; in our study, the ratio of underlying disorders was 54.9%. In children with underlying disorders, even a simple problem may lead to the disturbance of balance and rapid impairment of the overall condition. Therefore, the increased risk of out-of-hospital CPA is an expected outcome in patients with underlying disorders.

In a study, Kitamura et al.[16] reported that the ROSC rate was lower in nighttime arrests. We also found that the ROSC rate was lower at nighttime. This can be attributed to the fact that arrests occurring at night are able to be diagnosed and managed in a delayed fashion.

Several studies have reported survival rates of between 2 and 24%.[6, 8, 24-27] In the study of Kendirli et al.[28], ROSC was found in 10 (41.7%) of 24 out-of-hospital CPA cases and only two (8%) were discharged from hospital. In South Korea, the outcomes of pediatric out-of-hospital CPA cases have improved in the past five years; the ROSC rate following CPR was reported to increase from 17.6% to 35.2% and the discharge rate from 4.4% to 12.8%.[14,29] The ROSC was obtained in 83 patients (45.6%), following the initial CPR, who experienced out-of-hospital CPA, and 26 (31.3%) of these patients were discharged from hospital. Therefore, we conclude that the survival rate of 14.3% in our study is consistent with the previous study findings. The arrest being witnessed and the immediate initiation of CPR are related to both ROSC and a good neurological outcome [4, 10, 17-23]. Unfortunately, bystander CPR is performed in only 15 to 40% of the pediatric out-of-hospital CPA cases.[4,5,10] In a study conducted in Canada between 1991 and 2002, Gerein et al.[8] reported 503 out-of-hospital CPA cases. Of these patients, 34% were witnessed, 80.7% were witnessed by a bystander, and 18.1% by EMS. Bystander CPR was performed in 32.4% of the cases. In another study carried out in USA between 2002 and 2003, Foltin et al. [24] described 147 out-of-hospital CPA cases and reported the bystander CPR rate to be 30%. In the study by Park et al.[14], 33.7% of the cases were witnessed and bystander CPR was performed in only 2.9% of these cases with a survival rate of 5%. In our study, the witnessed arrests were at a rate of 75.8% (138/182); of these 67.4% were witnessed by a bystander, and the rate of CPR being performed by a bystander was 13.9%.[14] The ROSC was observed in 76.9% of the cases for whom bystander CPR was performed; however, the rate of discharge from hospital was 15.4%. It was found that CPR carried out by the witness increased the ROSC rate; however, it did not improve the survival rate. When an arrest case is witnessed, the period of no-flow is shorter; moreover, early and efficient CPR increases the patient's probability of survival.

Ventricular rhythm is quite rarely observed in children; the initially identified rhythm in the arrest is usually asystole or PEA.[9] In various studies, a VT/VF incidence of 4 to 8% was reported in pediatric out-of-hospital CPA cases.[5,7,8,12,14,15] Similarly, the incidence was 2% in the study conducted by Foltin et al.[24] and Park et al. [14] also identified 2% incidence of a rhythm which could be shocked. In our study, the incidence of VT/VF was 2.2%. These low VT/VF rates are due to the causes of arrest being more likely related to respiratory and circulatory failure, rather than to any cardiac pathology.

Moreover, it is well-established that short duration of the arrest is critical for the survival rate. Schindler et al.[27] reported patients who survived to hospital discharge had a significantly shorter interval between arrest and arrival at the hospital. In our study, the median (IQR) duration of arrest was found to be significantly lower in the patients in whom the ROSC was able to be achieved [5 (1- 15) min], compared to those in whom the ROSC was unable to be achieved [15 (5-40) min] ($p<0.001$).

The duration of resuscitation being short in out-of-hospital CPA cases was found to be significant for ROSC. Schindler et al.[27] also showed that the short resuscitation period in the emergency setting was an important indicator of survival. None of the patients with CPR duration of longer than 20 min were able to survive. Innes et al.[30] also reported that none of the cases with in-hospital or out-of-hospital CPA, whose CPR duration was longer than 30

min, survived. Abramson et al.[31] reported that a delay time of >6 min. with subsequent CPR time of 6–15 min. until return of spontaneous circulation had a 19% survival with good neurological outcome. In a study conducted by Matos et al.[32] favorable neurological outcome was achieved in 11.0% of all children after CPR for >15 minutes and in 9.5% after 35 minutes. In our study, the ROSC was identified in 94.9% of the patients who underwent CPR for less than 20 minute. In cases where CPR lasts longer than 20 min, 5.7% were discharged from hospital; however, all of them were in a poor neurological state. We found that there was no statistically significant difference in comparison of arrest and duration of CPR in patients discharged home with good or poor neurological status. This result may be due to the small number of patients.

Nonetheless, there are some limitations to this study. First, it was conducted in only one geographical region of Turkey. Therefore, the results may not be applicable to other regions of the country. Second, some data were unable to be reached due to the retrospective design of the study. In non-witnessed CPA in particular, the reliability of the time of the arrest is controversial. Although in most of the cases etiology is clear, there are some cases where the cause of death can only be ascertained by autopsy. Third, due to the absence of emergency physicians in the ambulances, pediatric patients were unable to be intervened. We were also unable to capture the quality of CPR performed on the children in our study. Fourth, we determined the neurological outcome during discharge with a simple PCP score. Ideally, outcome would be assessed at follow-up visits at one year or longer with detailed neurobehavioral tests. Finally, we were unable to identify the initial cardiac arrest rhythm in all patients. In 12.6% patients, the initial rhythm data were missing and important data were not recorded. This may be due to the level of training of EMS staff.

In conclusion, despite the development of novel treatments and guidelines on out-of-hospital CPA arrests, the results are not still favorable for neurological outcomes and survival rates. Our study shows that ROSC rate is increased in witnessed arrests, shorter CPR time in under 20 minute arrests. Early intervention is important but survival rate can be expected to increase with the correct and effective intervention. For this reason, we think that everyone should be given basic life support education.

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