



Five-year survival, performance, and neurodevelopmental outcome following cardiopulmonary resuscitation after pediatric cardiac surgery, preliminary investigation in a single-center experience

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Background and aim: Children who suffer cardiopulmonary arrest (CPA) after cardiac surgery frequently survive with return of spontaneous circulation. However, their neurodevelopmental outcomes and performance are still unclear. The aim of this study is to evaluate the midterm neurodevelopmental outcome and overall performance of children who survived CPA following cardiac surgery.

Materials and methods: In this cohort study, we followed-up children who received cardiopulmonary resuscitation (CPR) post cardiac surgery during 2012–2013. We assessed their 5-year survival, functional, and neurodevelopmental outcomes using two performance scales: Pediatric Cerebral Performance Category (PCPC) and Pediatric Overall Performance Category (POPC). Both scales ranged from 1 for normal to 6 for brain death/death. We compared CPR group with a matching group (1:1) that had similar characteristics and conditions but no CPR.

Results: Out of 758 postoperative cardiac children, 15 (2%) children had 19 episodes of CPA. Their median age was 10 months (0.5–168). Survival rates were 12/15 (80%) on hospital discharge and 10/15 (66%) after 5 years. Among 12 survivors, two patients (17%) scored 6, one (8%) scored 4, five (42%) scored 2, and four (33%) scored 1 on both PCPC and POPC. The median PCPC and POPC scores were [2, (interquartile range: 1–6) and 1, (interquartile range: 1–3, $p = 0.018$)] for CPR and matching group, respectively. Regression analysis identifies duration of CPR, number of CPR session, and late-occurring CPA as risk factors for poor outcome.

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Conclusion: Two-thirds of children requiring CPR post cardiac surgery survived after 5 years. Their neurodevelopmental and functional evaluation demonstrated worse outcome in comparison with their matching cases. CPR duration, number of CPA events, and late CPA were risk factors for poor outcome. Rehabilitation and special education programs might be needed for these groups of children with special needs.

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Keywords: Cardiopulmonary resuscitation, Neurodevelopmental outcome, Pediatric cardiac surgery

1. Introduction

Congenital heart diseases affect millions of children worldwide [1], with cardiac surgery being the mainstay management for most of these diseases. Despite the significant improvements in cardiac surgery techniques and postoperative care, complications can still occur perioperatively [2,3]. Cardiac arrest is one example of life-threatening complications that may complicate pediatric cardiac surgery [4,5]. It is generally estimated that the incidence of cardiac arrests is 0.7–3% in general pediatric intensive care unit (ICU) admissions, with a higher incidence estimated at 6–11% in pediatric cardiac ICUs (PCICUs) [6].

Both cardiac surgery and cardiac arrest are known risk factors for neurological insult and deficits in the developmental process of children [7–9]. Neurodevelopment refers to the development of neurological pathways that control performance and functioning. Impairment will lead to motor, language, or cognitive delay [10]. Because of the improvement in mortality rates of cardiac surgery, long-term sequelae such as neurodevelopmental disabilities are being observed more frequently [10,11].

There is insufficient data regarding long-term survival and neurodevelopmental outcome of children surviving cardiopulmonary arrest (CPA) post cardiac surgery. Furthermore, there are no clear recommendations regarding a need for special education or rehabilitation in this special category of affected children.

The primary objective of our study was to evaluate midterm outcome of pediatric patients who had cardiac arrest after cardiac surgery performed during 2012–2013. Additional objective was to assess neurodevelopmental and functional outcomes of these children after 5 years of follow-up and determine the possible predictors for poor outcome.

In order to evaluate neurodevelopment and functional outcome, we used previously validated

Abbreviations

ICU	Intensive care unit
CPA	Cardiopulmonary arrest
CPR	Cardiopulmonary resuscitation
PCPC	Pediatric Cerebral Performance Category
POPC	Pediatric Overall Performance Category
ROSC	Return of spontaneous circulation
RACHS	Risk adjustment for congenital heart surgery
PALS	Pediatric advanced life support

scales in large multi-institutional studies [12]. Pediatric Cerebral Performance Category (PCPC) and Pediatric Overall Performance Category (POPC) scales were developed and validated to measure and quantify morbidity after a critical illness or injury [13]. PCPC focuses on cognitive impairment, whereas POPC focuses on functional morbidity. Details of both scales can be found in [Tables S1 and S2 in the online supplementary material](#).

2. Materials and methods

After obtaining approval from the Institutional Research Board from King Abdullah International Medical Research Center of King AbdulAziz Medical City, we performed retrospective analysis and review of postoperative cardiac children who received in-hospital cardiopulmonary resuscitation (CPR) after their cardiac surgery during 2012–2013.

The data were then collected in a manner of categorizing the patients based on PCPC and POPC scales, which included assessing gross motor, fine motor, hearing, speech and language, social, emotional, behavioral development, and skills. We assessed the survival rate on discharge from hospital and within 5 years of initial in-hospital arrest, and then, we assessed neurodevelopmental and functional outcomes of survivors after 5 years to score their neurodevelopmental and performance abilities based on PCPC and POPC scales.

The inclusion criteria were all patients who had witnessed cardiac arrest post cardiac surgery and received in-hospital CPR during the study time frame. We excluded all patients who had cardiac arrest outside the hospital setting after discharge, brief cardiac arrest for <1 minute, and nonsurgical cases. Patients who expired in hospital or after hospital discharge were counted in PCPC and POPC data analysis and they were given a score of 6. We matched the CPR cases with comparable patients (matching group) of similar age, weight, and surgical risk category, but did not suffer cardiac arrest, with a ratio of 1:1. We classified surgical risk category of our patients using Risk Adjustment for Congenital Heart Surgery score with 1 representing simple cases and 6 representing most complex surgical cases [14].

Lastly, within CPR group, we compared cases who had poor outcome defined as death or POPC/PCPC score ≥ 5 with cases who had acceptable outcome defined as POPC/PCPC score < 5 to identify possible risk factors associated with poor outcome after CPR.

We used SPSS version 20 (SPSS Inc., Chicago, IL, USA) for statistical analysis. Mann-Whitney

U test was used in the analysis on nonparametric data; Student *t* test and Fisher exact test were used to analyze continuous and categorical data, respectively. A *p* value of < 0.05 (alpha) was considered significant. Logistic regression analysis was used to identify possible risk factors for poor outcome in the CPR group.

3. Results

During the 2-year study period, out of 758 post-operative PCICU admissions, 15 patients (2%) had 19 episodes of CPA. All events occurred within PCICU. CPR was initiated for all cases following the Pediatric Advanced Life Support guidelines.

Out of these 15 patients, three had multiple CPR, whereas the rest had single CPR. Out of 19 arrests, 16 (84%) patients were successfully resuscitated and 12 (80%) patients survived to discharge. Out of the three patients who had multiple CPR, one patient had return of spontaneous circulation and survived, whereas two patients expired. One patient did not survive out of 12 single-CPR patients as seen in Fig. 1. The causes of arrest in our patients were mainly cardiac (66%) and respiratory (33%).

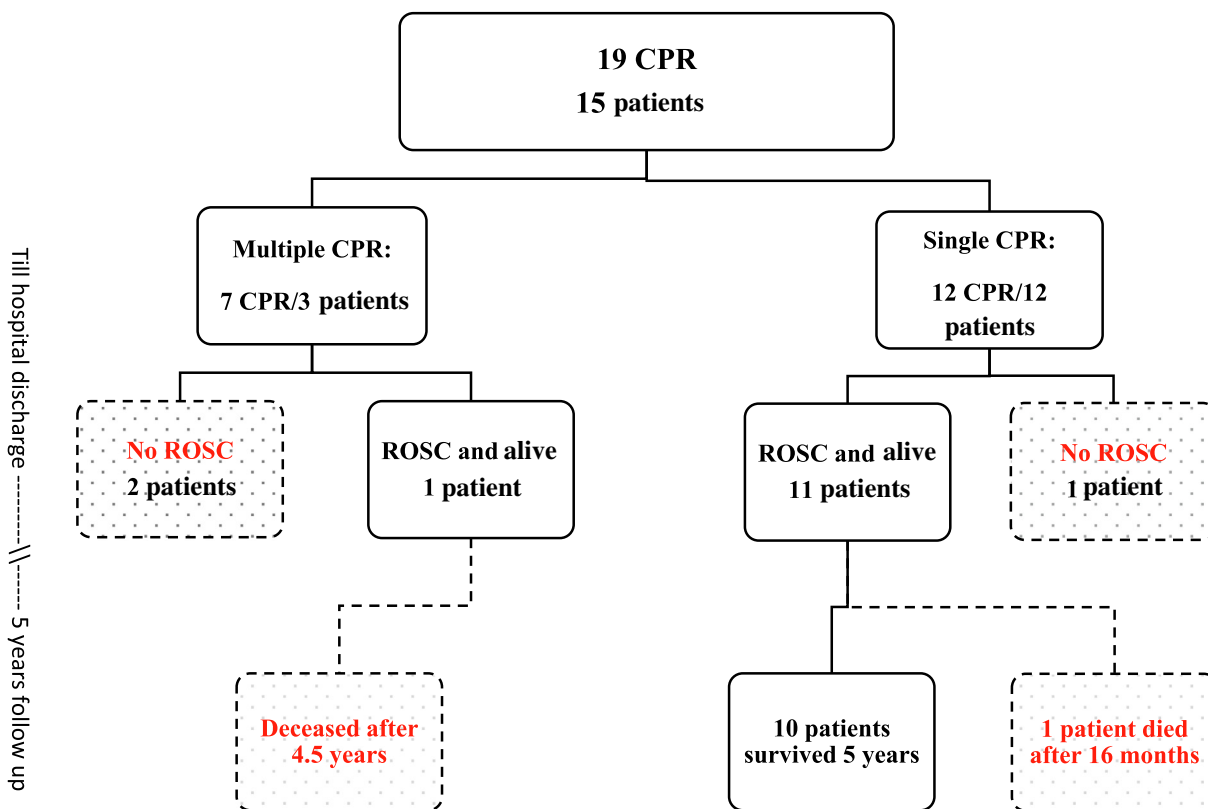


Figure 1. Details of cardiopulmonary resuscitation group until hospital discharge and then within 5 years of follow-up. CPR = cardiopulmonary resuscitation; ROSC = return of spontaneous circulation.

Table 1. Details of diagnosis and surgical procedures for cardiopulmonary resuscitation group.

#	Age (mo)	Weight (kg)	sex	Diagnosis on admission	Type of repair	Type of surgery	Postoperative echocardiographic findings (EF) and cardiac function	Outcome
1	168	41	Female	Ebstein's anomaly, TV regurgitation	Biventricular	Tricuspid valvotomy-valvuloplasty	Satisfactory repair, no residual lesion, good cardiac function (EF: 55%)	Survived
2	72	17.1	Female	ASD, MV arcade	Biventricular	Mitral valvotomy-valvuloplasty	Depressed cardiac function (EF: 30%), no residual lesions, satisfactory repair	Survived
3	132	23.5	Male	DORV, AVSD, PS	Univentricular	Fontan procedure	Satisfactory repair with good cardiac function (EF: 55%), no residual defects	Survived
4	17	8.4	Male	Single ventricle physiology	Univentricular	Pulmonary artery band	Satisfactory repair with good cardiac function (EF: 55%), no residual defects	Survived
5	3	3.49	Female	DORV, PDA, VSD & TR	Univentricular	Atrial septectomy	Sufficient repair, good cardiac function (EF: 55%), no residual defects	Survived
6	2	2.88	Female	Large perimembranous VSD, ASD, PDA, Vascular ring.	Biventricular	PDA closure	Moderate left AV regurgitation, good function	Out-of-hospital late death
7	6	6.5	Male	AVSD, Left AV regurgitation (Down syndrome)	Biventricular	ASD and VSD repair	Mild AV valve regurgitation, good cardiac function	Survived
8	5	4	Male	COA, VSD	Biventricular	Coarctation repair	Satisfactory repair, good cardiac function (EF: 55%), no residual defects	Survived
9	3	4	Female	Truncus arteriosus, VSD, ASD	Univentricular	Pulmonary artery band	Satisfactory repair, good cardiac function (EF: 55%), no residual defects	Survived
10	7	4.8	Female	PDA (Down Syndrome)	Biventricular	PDA closure	Moderately depressed cardiac function (EF:30%), improved with time	Survived
11	24	14.8	Female	TOF, right aortic arch, iatrogenic occluded PA	Biventricular	TOF	Satisfactory repair (EF: 55%)	Survived
12	6	4.79	Male	DILV, LTGA, IAA, PDA	Univentricular	Stage 1 repair of hypoplastic left heart syndrome (Norwood operation)	Residual transverse arch stenosis with gradient of 25, EF: 40%, moderate tricuspid regurgitation with evidence of pulmonary hypertension	Out-of-hospital late death
13	0.6	3.4	Male	CoA, VSD, PDA, PHTN	Biventricular	Coarctation repair	Depressed myocardiatic function (EF:20%), no residual lesions	In-hospital death
14	10	8.9	Male	DTGA, IVS, PHTN	Biventricular	Arterial switch operation	Progressive pulmonary hypertension with tricuspid regurgitation (EF: 40%), pulmonary hypertension did not regress with antihypertensive treatment	In-hospital death
15	1	2.66	Female	Truncus arteriosus Type 1	Biventricular	Repair of truncus arteriosus	Moderate right AV regurgitation, good function (EF: 50%)	In-hospital death

AP = aortopulmonary; ASD = atrial septal defect; AV = atrioventricular; AVSD = atrioventricular septal defect; CoA = coarctation of aorta; DILV = double inlet left ventricle; DORV = double outlet right ventricle; DTGA = dextro transposition of great arteries; IAA = interrupted aortic arch; IVS = intact ventricular septum; LTGA = levo transposition of great arteries; MV = mitral valve; PA = pulmonary atresia; PDA = patent ductus arteriosus; PHTN = pulmonary hypertension; PS = pulmonary stenosis; TGA = transposition of great arteries; TOF = tetralogy of Fallot; TV = tricuspid valve; VSD = ventricular septal defect; EF = ejection fraction.

Table 1 shows details about our CPR patients, their diagnosis, echocardiographic findings, surgical procedures and cardiac function post-operatively. The CPR group (15 patients) was compared with a matching group (1:1). The demographic profiles of all 15 patients who had CPA as well as their matching group who had no CPA are shown in **Table 2**. The compared variables and *p* values are provided in **Table 2**.

During midterm follow-up at 5 years, two of 12 (17%) patients died, and 10 of 12 patients (83%) sur-

vived. Patients were evaluated using PCPC and POPC scales. Including all patients who arrested, five deceased patients (33%) scored 6, one (7%) scored 4, while five (33%) scored 2, and four (27%) scored 1 on both POPC and PCPC. The majority of the matching group (11 patients, 73%) scored 1, three (20%) scored 2, and one (7%) scored 3 on both PCPC and POPC. The median PCPC and POPC scores were 2 (interquartile range: 1–6) for CPR group and 1 (interquartile range: 1–3) for matching group (*p* = 0.018). **Fig. 2** shows the statistical

Table 2. Demographics of CPR group and matching group.

Variables	CPR group	Matching group	<i>p</i>
Number of patients	15	15	
Age (mo)	37.1 ± 56.7	49.7 ± 70.5	0.62
Weight (kg)	11.3 ± 11.4	13.6 ± 14.8	0.66
Female sex (%)	58	46	0.83
RACHS	2.8 ± 1.3	2.5 ± 0.7	0.47
Bypass time (min)	60 ± 57.01	45.4 ± 59.1	0.53
Cross clamp time (min)	32.1 ± 36.2	38.2 ± 49.1	0.72
PCICU stay (days)	23.4 ± 27.9	10.8 ± 15.1	0.16
Hospital stay (days)	52.7 ± 64.9	27.2 ± 30.2	0.21
Cardiopulmonary arrest	19	0	<0.05
CPR duration (min)	13.8 ± 4.6	0	<0.05

CPR = cardiopulmonary resuscitation; PCICU = pediatric cardiac intensive care unit; RACHS = Risk Adjustment for Congenital Heart Surgery.

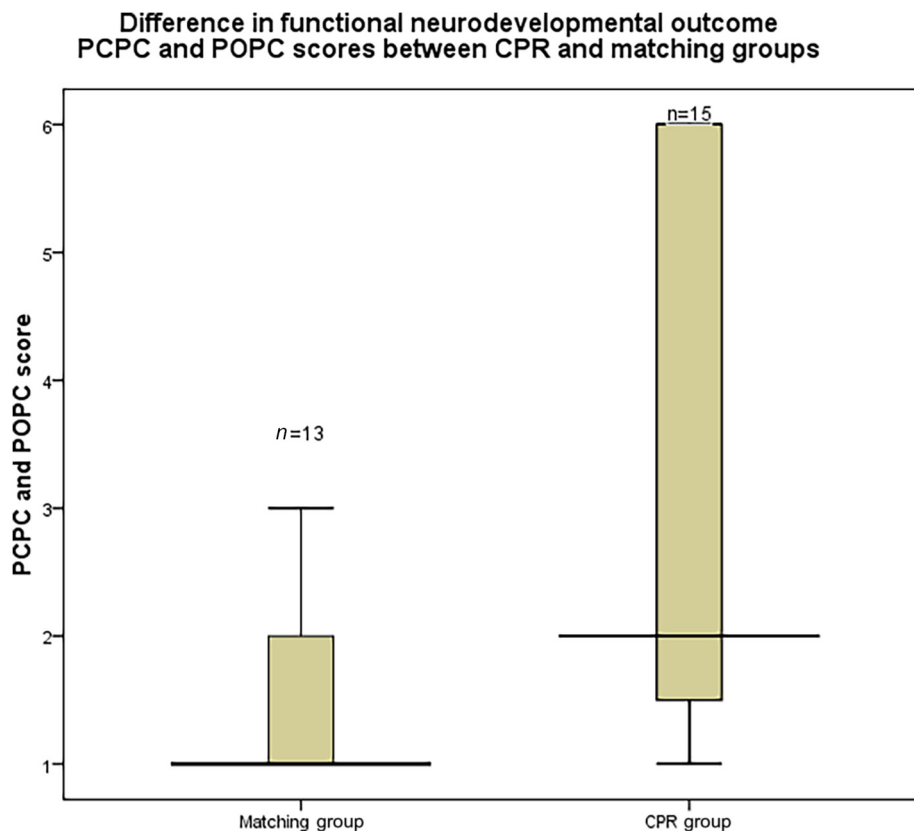


Figure 2. Difference between POPC and PCPC scores of CPR and matching groups. CPR = cardiopulmonary resuscitation; PCPC = Pediatric Cerebral Performance Category; POPC = Pediatric Overall Performance Category.

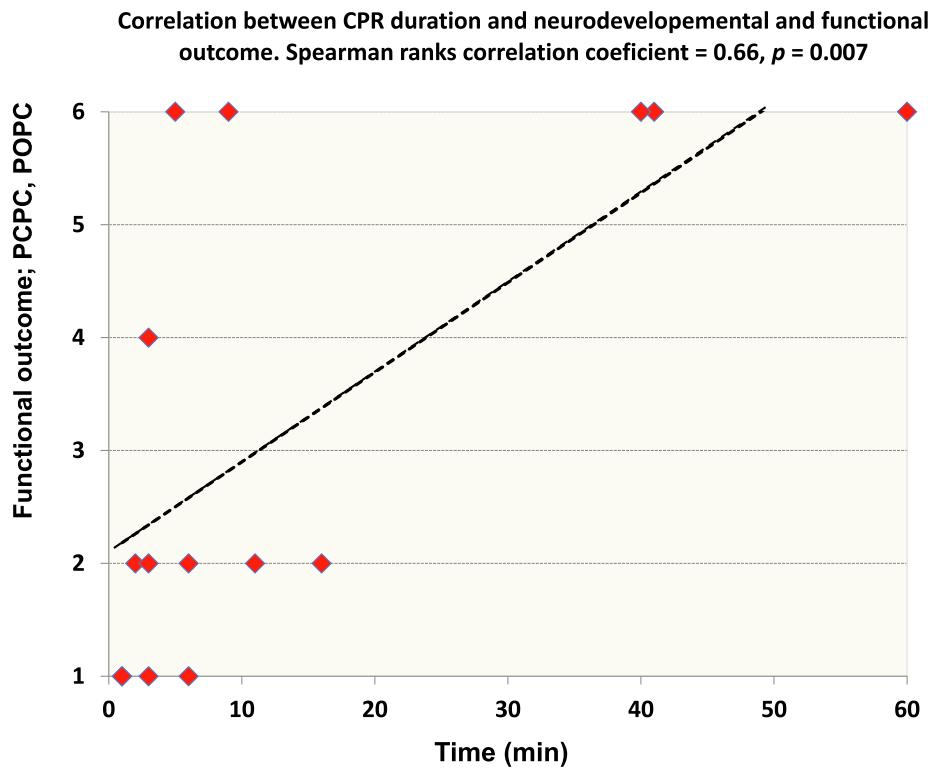


Figure 3. Correlation between CPR duration and functional neurodevelopmental outcome scale. (1 = best, 6 = worst). Red dots represent patients. CPR = cardiopulmonary resuscitation; PCPC = Pediatric Cerebral Performance Category; POPC = Pediatric Overall Performance Category.

difference between POPC and PCPC scores of CPR group and their matching group.

The correlation of the CPR group’s neurodevelopmental scores with CPR duration is seen in Fig. 3. We noted that the longer the duration for CPR, the poorer the POPC and PCPC outcome are. The linear correlation estimated that for each additional 7 minutes of CPR, the POPC/PCPC score would get worse by 1 ranking. Similarly, for each additional minute of CPR, the risk of having poorer outcome (death/severe neurological deficit) will increase by approximately 2%.

Furthermore, multivariate regression analysis comparing subgroup of patients who had poor outcome (deceased or POPC/PCPC ≥ 5) with (acceptable outcome PCPC/POPC < 5) after CPR demonstrated that longer duration of CPR, more CPR events, and late-occurring CPA were associated with poorer outcome Table 3. The survival probability over 5 years of CPR group were demonstrated by Kaplan–Meier survival curve in Fig. 4.

4. Discussion

The incidence of cardiac arrests in children who underwent cardiac surgery in PCICUs is reported

in previous studies at 6–11%, with a survival rate of 37–50% [4–6]. In a larger study by Gupta et al. [15] that included 70,270 patients from 97 centers in both pediatric and cardiac critical care units, the incidence of postoperative cardiac arrest was 2.6%. There were higher rates of cardiac arrests (3%) in children undergoing cardiac surgeries, with a mortality rate of 50%.

In our PCICU, the incidence of CPA was 2% (15 patients) and the immediate survival rate was 80% (12 patients). In contrast to general pediatric arrests, the causes of arrest in our patients were mainly cardiac in 66% and respiratory in 33%. This is probably due to the presence of primary cardiac diseases and need for cardiac surgery in all our cases.

With the increase in survival seen in this population, long-term sequelae such as neurological deficits are observed more frequently [11]. Despite that, few studies investigated neurological and functional outcomes of children suffering CPA after heart surgery. According to a systemic review of motor and cognitive outcomes after early cardiac surgery, infants aged < 6 months undergoing surgery had less than expected cognitive and motor development compared with normal infants [16]. Furthermore, in another study, the authors assessed the neurological status of

Table 3. Characteristics and comparison between poor outcome and acceptable outcome groups after CPR in 15 patients who had CPA after pediatric cardiac surgery.

	Acceptable outcome (alive with PCPC/POPC score <5) n = 10	Poor outcome (deceased or PCPC/POPC ≥5) n = 5	p
Average age at surgery (months)	43.7 ± 60	6.16 ± 4.9	0.29
Average weight (kg)	12.76 ± 12	4.49 ± 2.6	0.3
Female sex (%)	6/10 (60)	2/5 (40)	0.46
Heart diseases	55	32	0.85
• Cyanotic			
• Noncyanotic			
RACHs score (median)	2 (1–3)	3 (1–6)	0.44
Cardiac surgery	6 (60%)4	2 (40%)3	0.46
• Palliative			
• Corrective			
Time between surgery and CPA (days)	3.5 ± 6	22 ± 13	0.032
Bypass time (min)	77.14 ± 28	101.67 ± 71	0.31
Cross clamp time (min)	51.6 ± 23	59.5 ± 34	0.88
Maximal inotropic score	13 ± 6	17 ± 7	0.31
Presence of pulmonary hypertension	2/10 (20%)	2/5 (40%)	0.16
Highest lactic acid prior to CPA (mmol)	3.6 ± 3.1	5.94 ± 5.7	0.2
Total duration of CPR (min)	5.2 ± 4.8	31 ± 23	0.03
Number of CPR (median)	1	2 (range: 1–3)	0.035

CPA = cardiopulmonary arrest; CPR = cardiopulmonary resuscitation; PCPC = Pediatric Cerebral Performance Category; POPC = Pediatric Overall Performance Category; RACHS = Risk Adjustment for Congenital Heart Surgery.

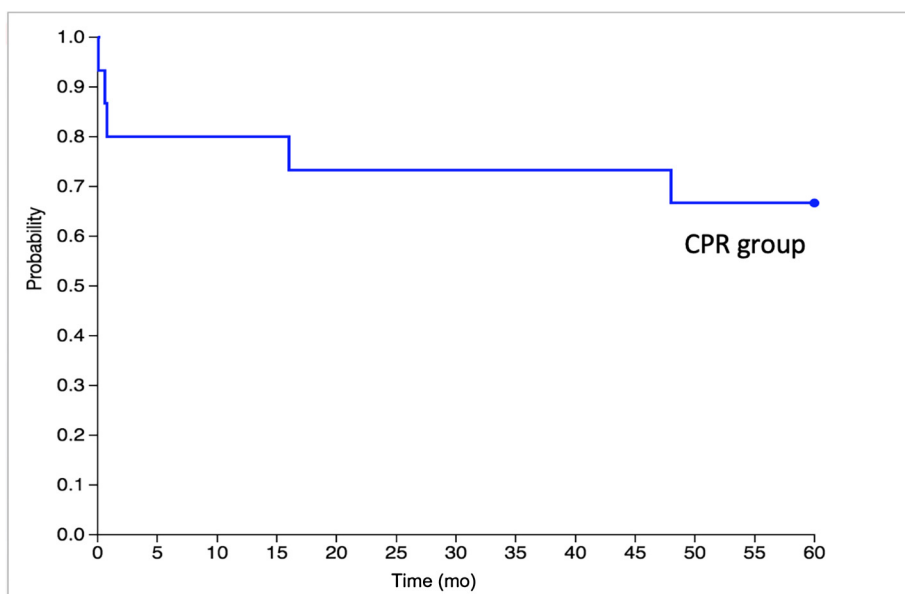


Figure 4. Kaplan–Meier survival probability curve in postoperative cardiac children who had cardiopulmonary arrest and resuscitated. The follow-up time is 60 months. CPR = cardiopulmonary resuscitation.

patients who underwent CPR in PCICU and reported that they can have a good neurological outcome. However, patients were informally assessed and needed further neurological and developmental evaluation [17].

During the 5-year follow-up in our study, out of 12 patients who suffered cardiac arrest after cardiac surgery, five patients are attending regular school, three are syndromic and require special

education, two have Down syndrome, one is independent, and one patient needs substantial caregiver assistance. The third syndromic patient has Kabuki syndrome and has motor developmental delay. Moreover, four patients had to delay school attendance due to staged surgeries or because of caregivers' general concern regarding attending regular public school or independence issues, such as toilet training. Two patients died after

16 months and 4.5 years of discharge, respectively, which decreased midterm overall survival rate to 66%. By contrast, the majority of matching group patients who did not suffer cardiac arrest had normal neurodevelopment, with mild to moderate deficits observed in only three patients. The observed differences between the groups' neurodevelopmental scores were statistically significant indicating worse neurodevelopmental and functional outcome most likely related to CPA in CPR group. None of our three patients who required multiple CPR survived till 5 years; two of them died prior to hospital discharge and one died 4.5 years after discharge. The death causes were related to primary cardiac lesion.

We correlated the CPR group's neurodevelopmental scores with CPR duration as seen in Fig. 3. We observed that with the increase in the duration of CPR, there was worse functional and neurodevelopmental outcome. The linear correlation determined that for each additional 7 minutes of CPR, the functional and neurodevelopmental outcome worsened by 1 ranking.

Furthermore, when we compared children who had poor outcome with children who had acceptable outcome after CPR, multivariate regression analysis identified duration of CPR, number of CPA events, and late CPA as risk factors for poor outcome after CPA post cardiac surgery. A previous study by Matos et al. [3] evaluated neurological outcome after cardiac arrest in regards to duration of CPR. The study found that the probability of a favorable neurological outcome decreased with increasing CPR duration. Moreover, 38.9% of surgical cardiac patients had favorable neurological outcome at 15 minutes, with a decrease to 26.2% at 35 minutes of CPR.

4.1. Limitations

Our study was an observational study reflecting single-center experience. The small sample size must be generalized to a larger population. It is possible that there are additional factors not analyzed in our study that may also affect neurodevelopmental and survival outcomes of children after cardiac surgery.

We attempted to match our CPR cases with comparable cases that were not identical but similar in demographic characteristics, medical condition, cardiac diseases, and surgical risk categories. Selection of matching cases was not blind and personal bias could not be ruled out. Finally, all our cases had arrest in ICU setup that may favor better outcome and, as such, our results cannot be generalized to all in- and out-of-hospital arrests.

5. Conclusion

Our immediate survival rate for in-hospital cardiac arrest after pediatric cardiac surgery was 80% on discharge and decreased to 66% after 5 years of follow-up. Duration of CPR, late-occurring CPA, and number of CPA events were the risk factors for poor outcome. The surviving children after CPA post cardiac surgery had worse neurodevelopmental and functional outcome and may require ample support and extensive rehabilitation due to their neurodevelopmental deficits and functional disabilities.

Conflicts of interest

The authors declare no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jsha.2019.05.035>.

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